Glaucoma Update

Dr. James Thimons, Founding Partner, Medical Director
Ophthalmic Consultants of Connecticut
Chairman, National Glaucoma Society

Financial Disclosures

- Speaker
  - Alcon
  - Allergan
  - PRN
  - Tear Lab
  - Shire
  - Zeiss
  - B&L
  - Diopsys
  - Reichart
  - Glaukos
  - InFocus
  - Aerie
  - Optos
  - Regeneron
  - Novartis
  - Radius
  - Virtual Visual Health
  - Olleyes
  - Thea
  - Falck
  - MOA
  - DHR pro

Welcome to Connecticut

New Concepts in Glaucoma Diagnosis and Treatment

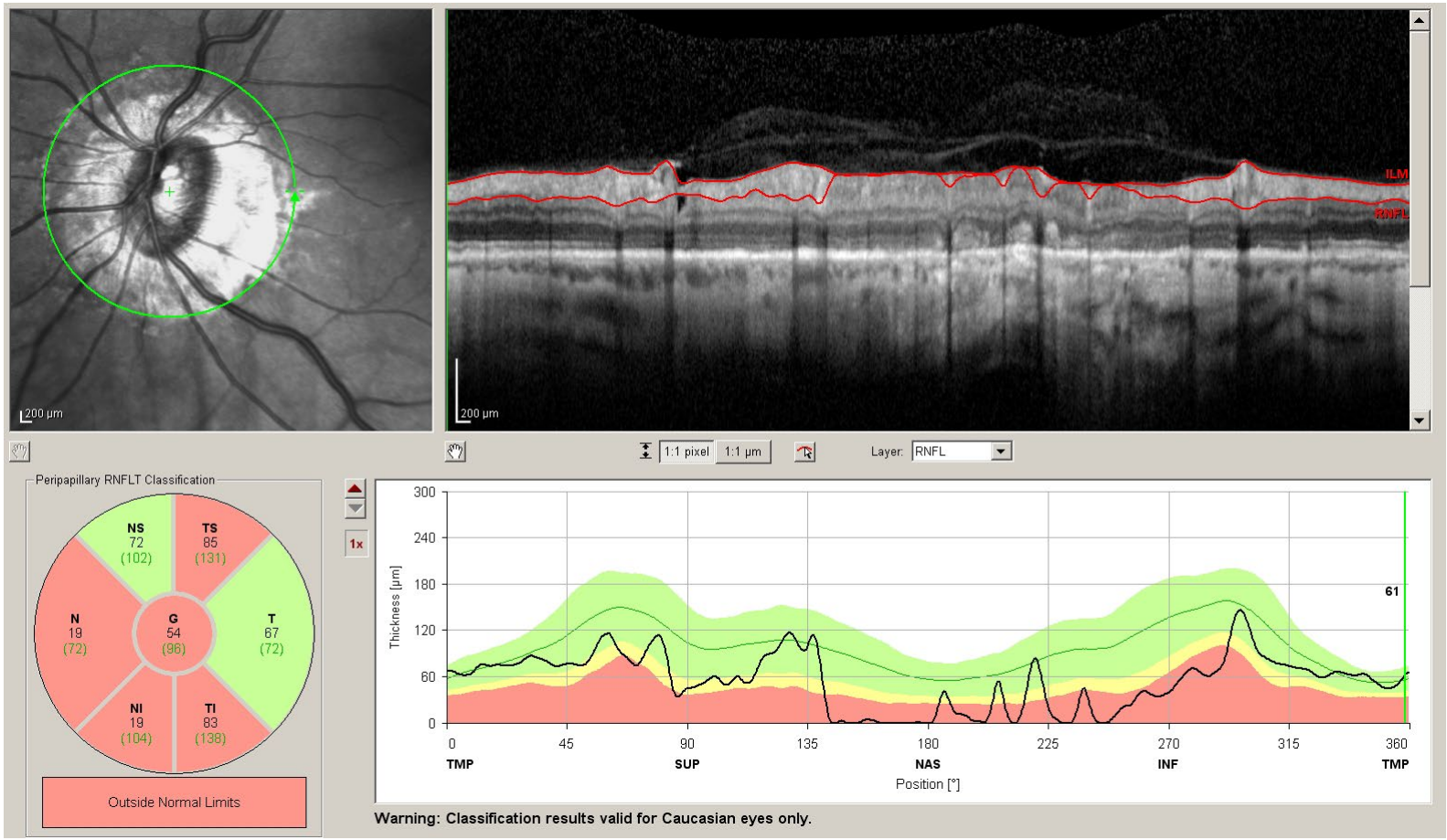
- OCT vs VF
- CH in Glaucoma Suspects
- SLT as Primary Therapy
- Repeat SLT
- OCTA in Glaucoma

The Rock Stars of Eye Care

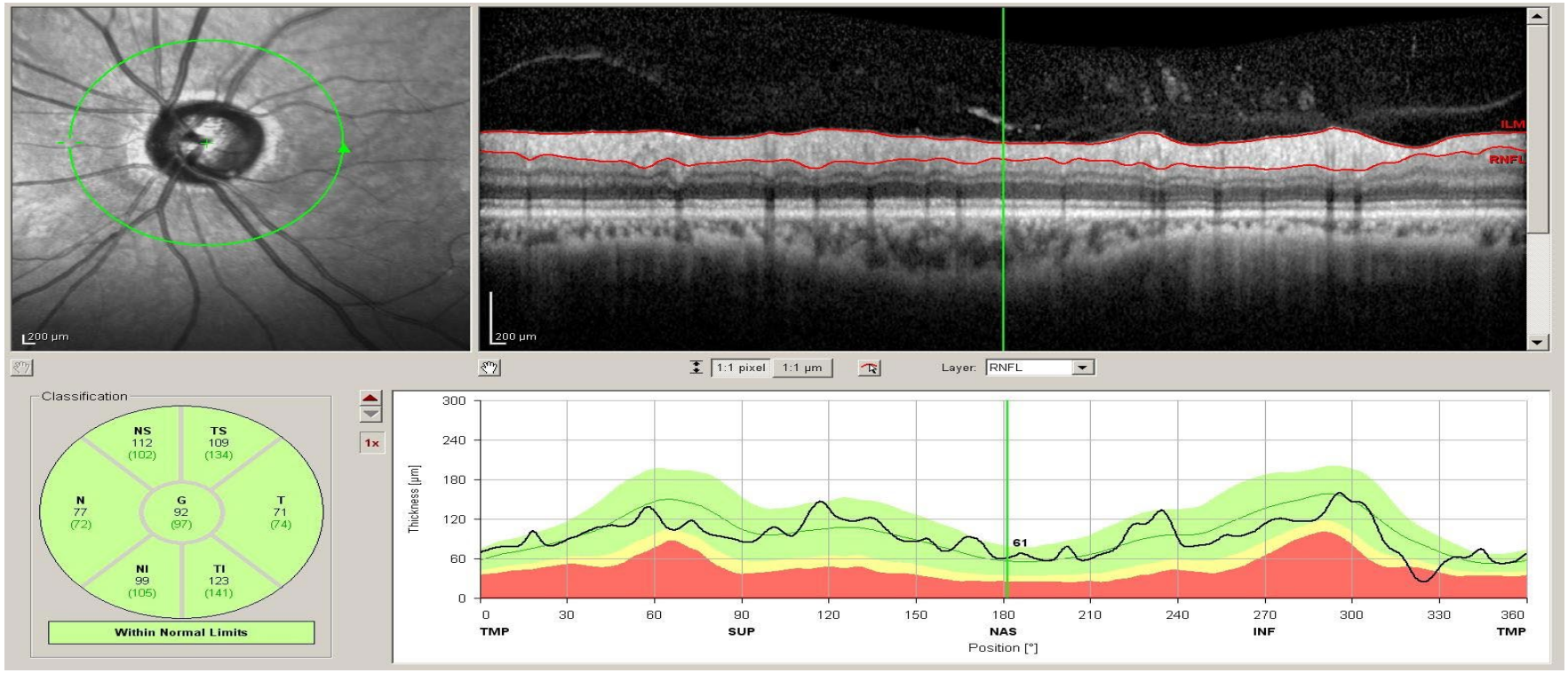
(L-R): Dr Eric Swanson, Dr David Huang, President Joe Biden, Dr James Fujimoto. (Image: Ryan K. Morris and the National Science and Technology Medals Foundation).

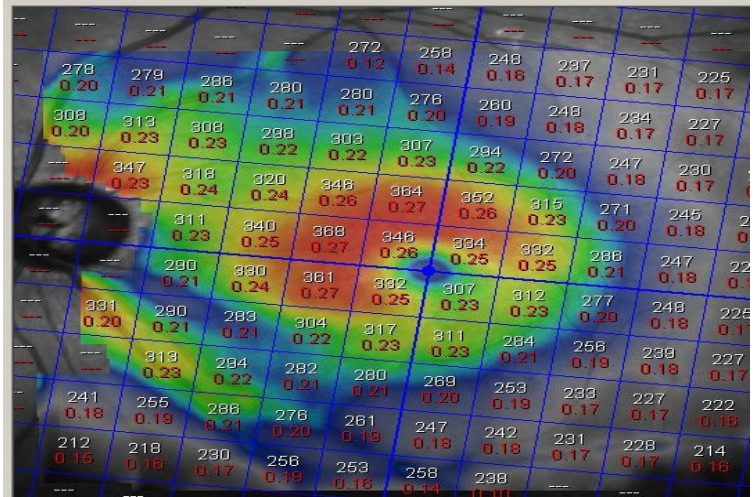

CAUTION
THIS MACHINE
HAS NO BRAIN
USE YOUR OWN

Myopia = “Red Disease”



“Green Disease”





Ganglion Cell Anatomy

- Analysis of VF in RGC loss in Glaucoma
  - 24-2 protocol has 6 degrees separation allowing for thinning the RGC to be missed to due point placement
    - Drazdo t al: Vision Research 2007
  - 10-2 testing substantially improves correlation with RGC analysis
    - Hood and Raza; Vis Science 2011
  - Stamper(1984) identified the relationship between NTG and macular damage with typically near fixation visual field loss.
  - Heijl & Lundqvist 1984
    - 45 patients followed from normal to abnormal VF's using test points at 5,10,15 & 20 degrees from fixation
    - Largest number at 15 degrees but a surprising number at 5 degrees confirming Hood's work showing that early damage occurs in the macula as well as more traditional arcuate zones

Macular Vulnerability Zone

Prog Retin Eye Res. 2013 January ; 32C: 1–21. doi:10.1016/j.preteyeres.2012.08.003.

Glaucomatous damage of the macula

Donald C. Hood[a,b,*,1], **Ali S. Raza**[a,c,1], **Carlos Gustavo V. de Moraes**[d,e,1], **Jeffrey M. Liebmann**[d,e,1], and **Robert Ritch**[d,f,1]

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[b]Department of Ophthalmology, Columbia University, New York, NY 10027-7004, USA

[c]Department of Neurobiology and Behavior, Columbia University, New York, NY, USA

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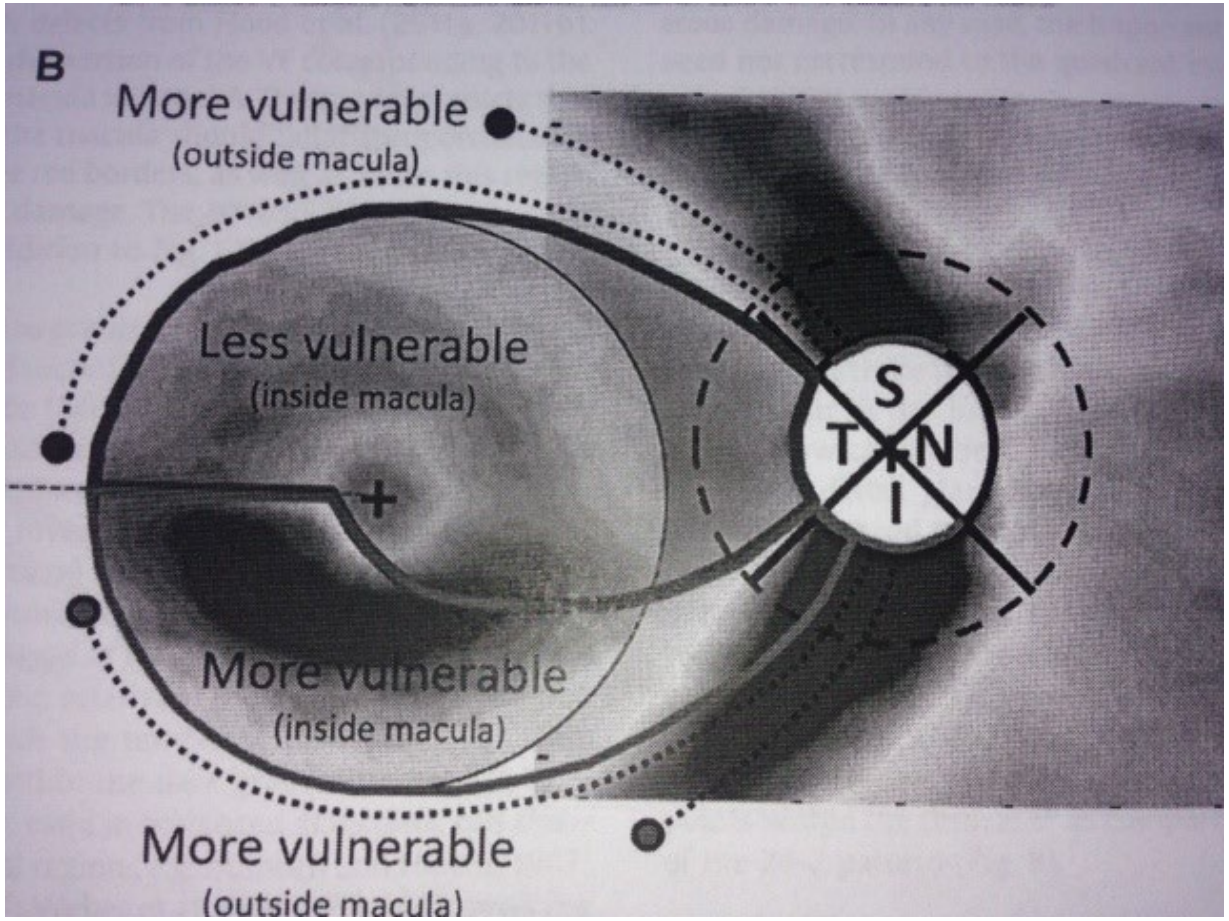
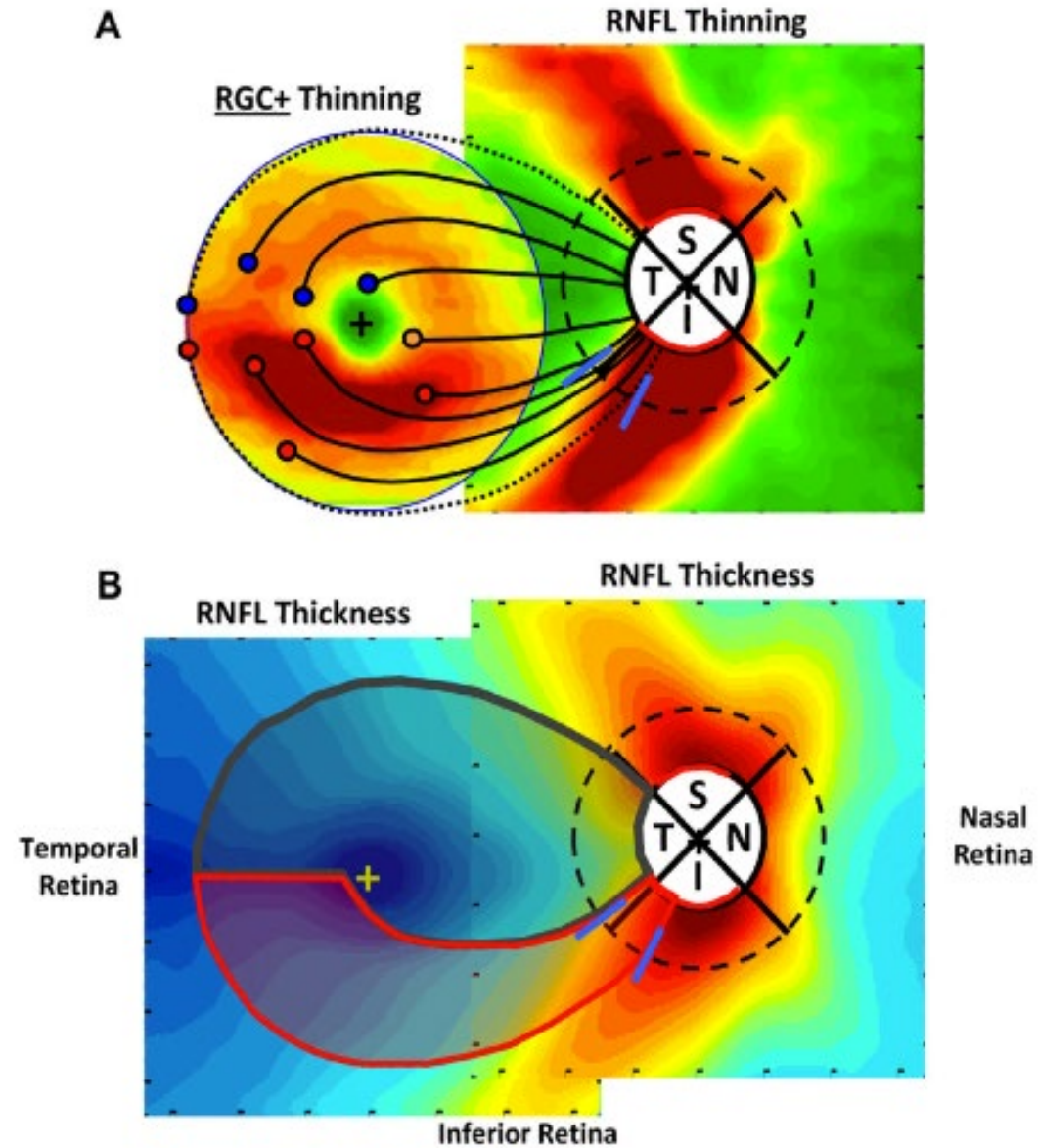
[e]Department of Ophthalmology, New York University, New York, NY, USA

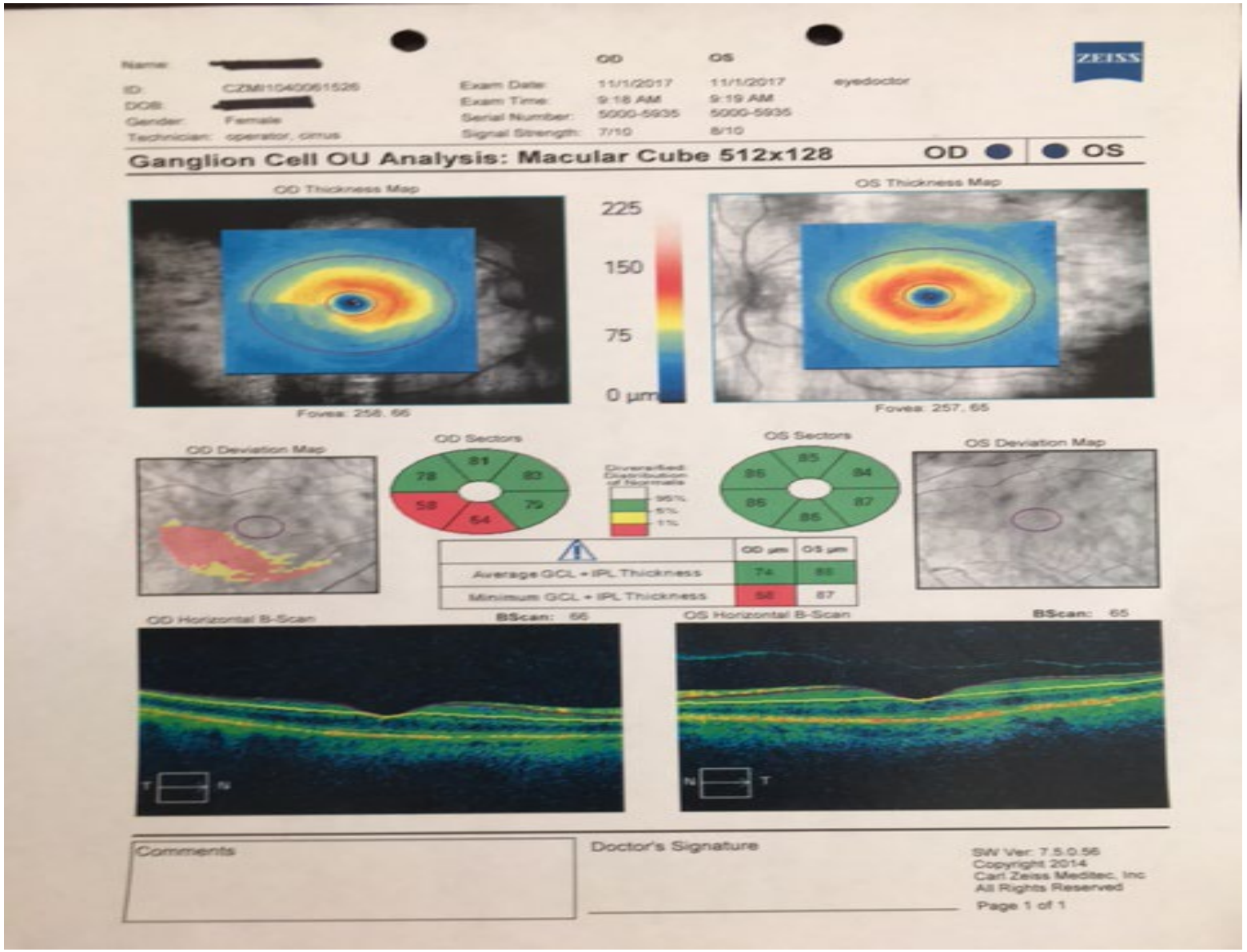
[f]Department of Ophthalmology and Visual Science, New York Medical College, Valhalla, NY, USA

Ganglion Cell Anatomy




A
RNFL Thinning
RGC+ Thinning
S
T
N
I
+
B
RNFL Thickness
RNFL Thickness
Temporal
Retina
Nasal
Retina
Inferior Retina

“Wiper” Defect



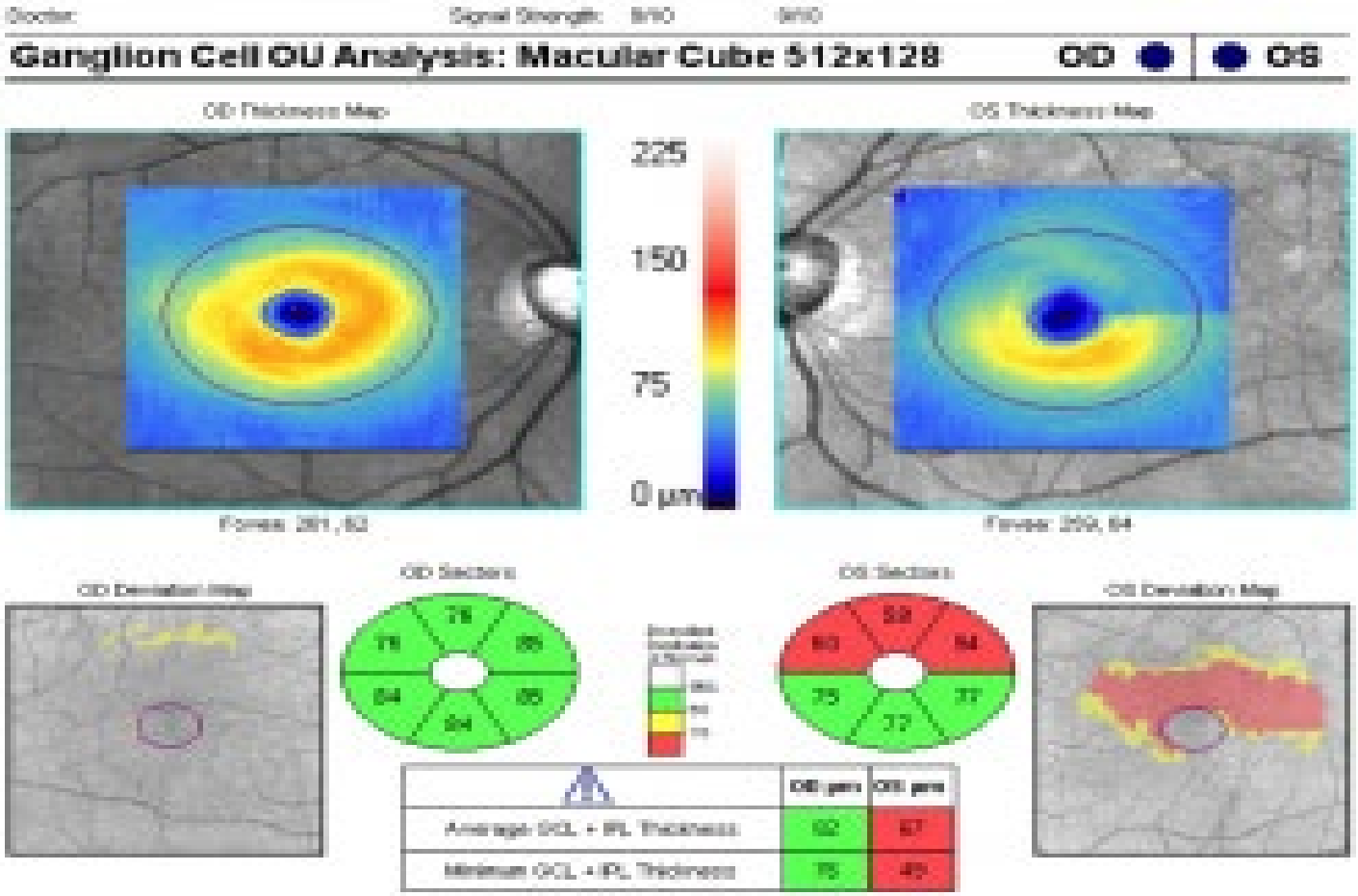
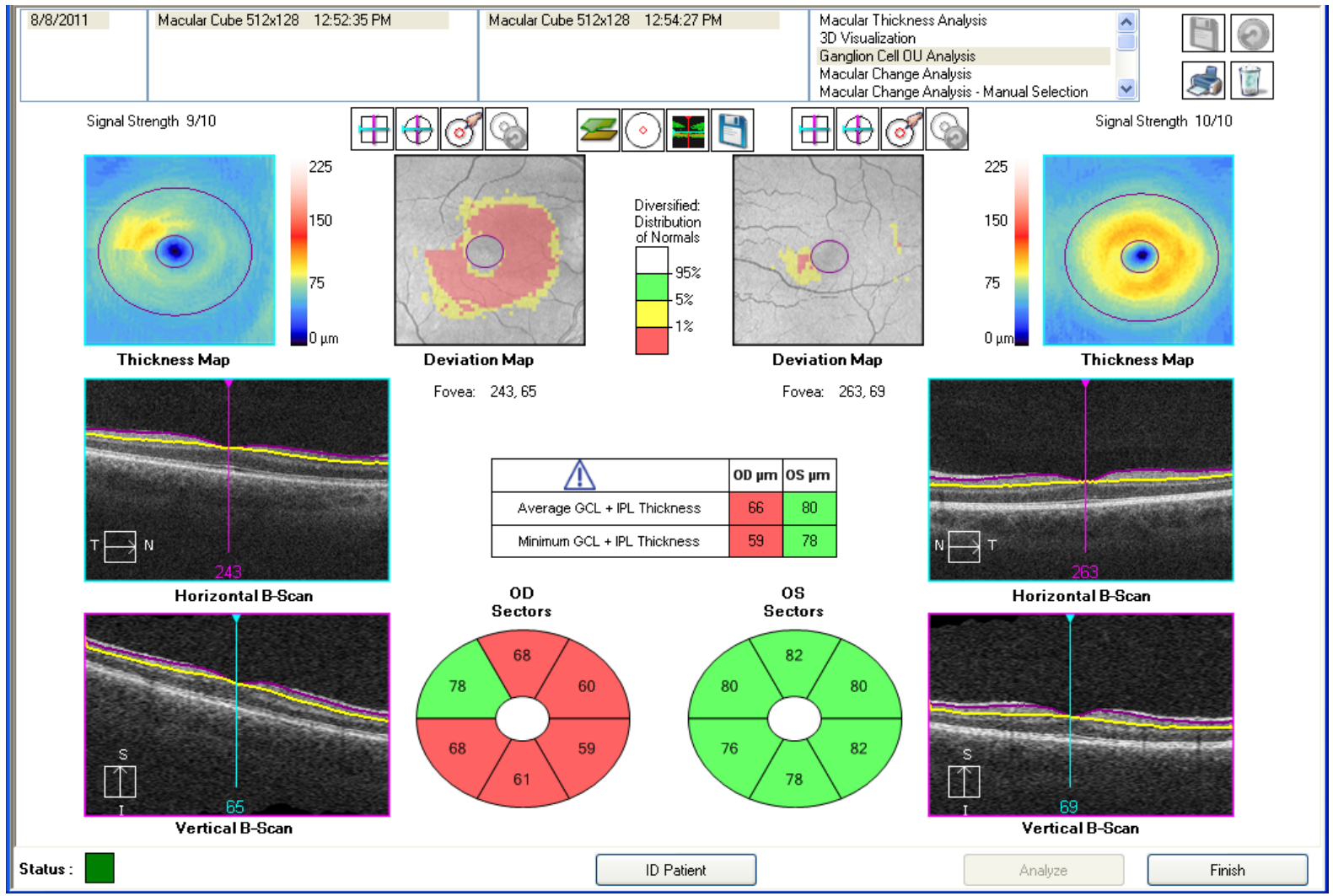


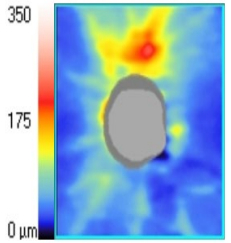
Figure 3: Ganglion cell complex analysis

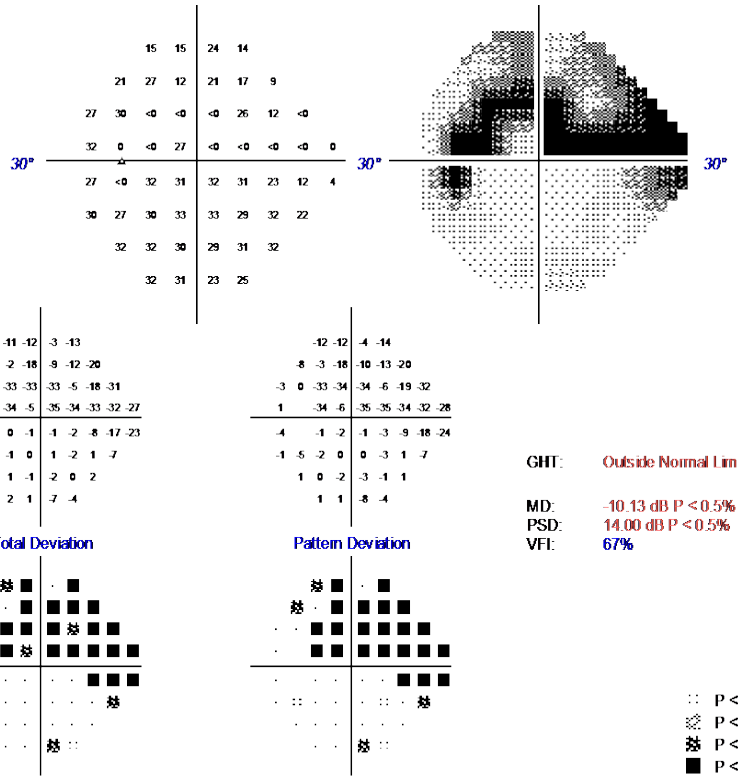
Ganglion Cell Analysis



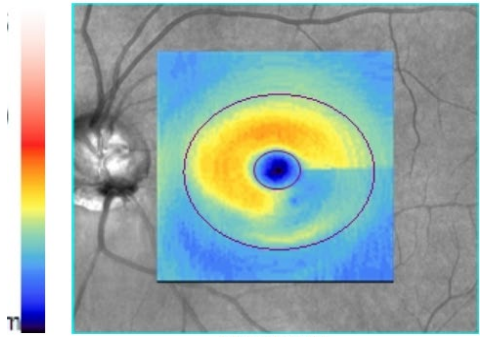
	OD	OS
Average RNFL Thickness	105 µm	89 µm
RNFL Symmetry	53%	
Rim Area	1.47 mm²	1.26 mm²
Disc Area	2.36 mm²	4.35 mm²
Average C/D Ratio	0.61	0.84
Vertical C/D Ratio	0.59	0.77
Cup Volume	0.196 mm³	1.097 mm³

RNFL Thickness Map



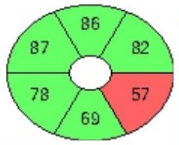


OS Thickness Map



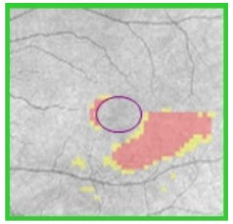
Fovea: 262, 66

OS Sectors

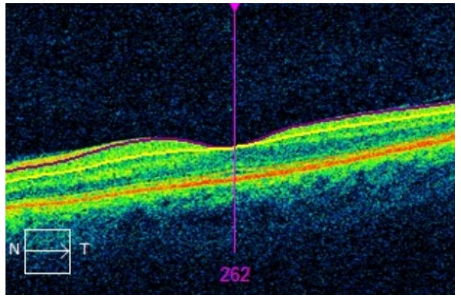


	OD µm	OS µm
ckness	87	76
ckness	84	53

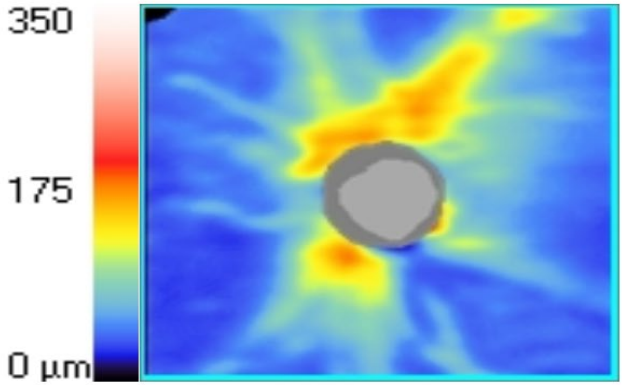
OS Deviation Map

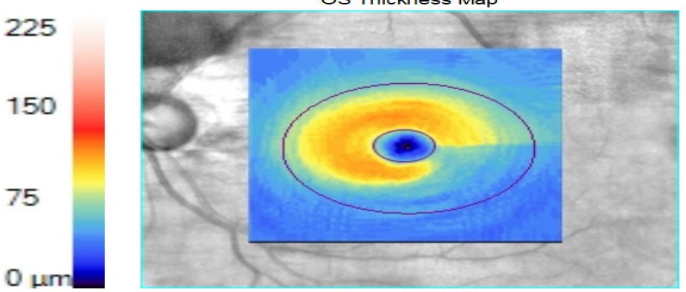


OS Horizontal B-Scan



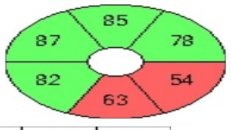
RNFL Thickness Map



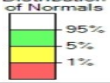


Fovea: 257, 65

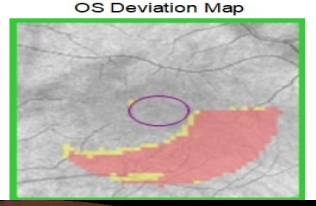
OS Sectors



Diversified Distribution of Normals

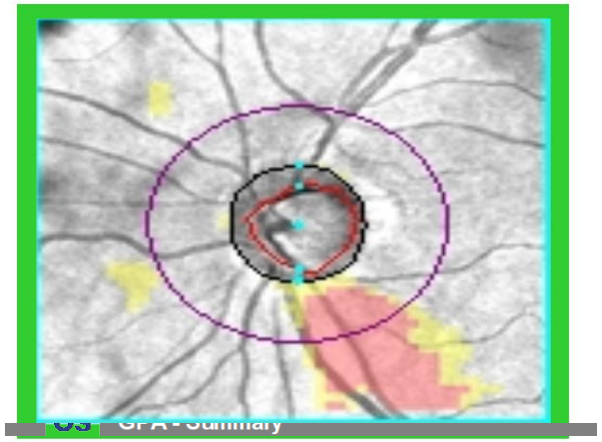


OS Deviation Map



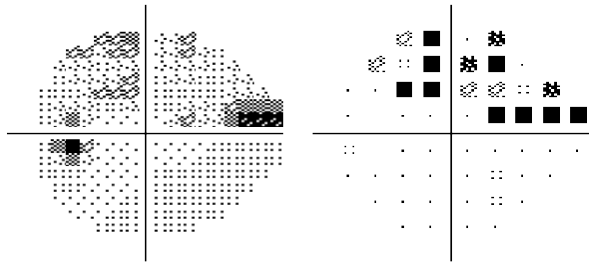
	OD µm	OS µm
+ IPL Thickness	84	75

RNFL Deviation Map



Graytone Pattern Deviation

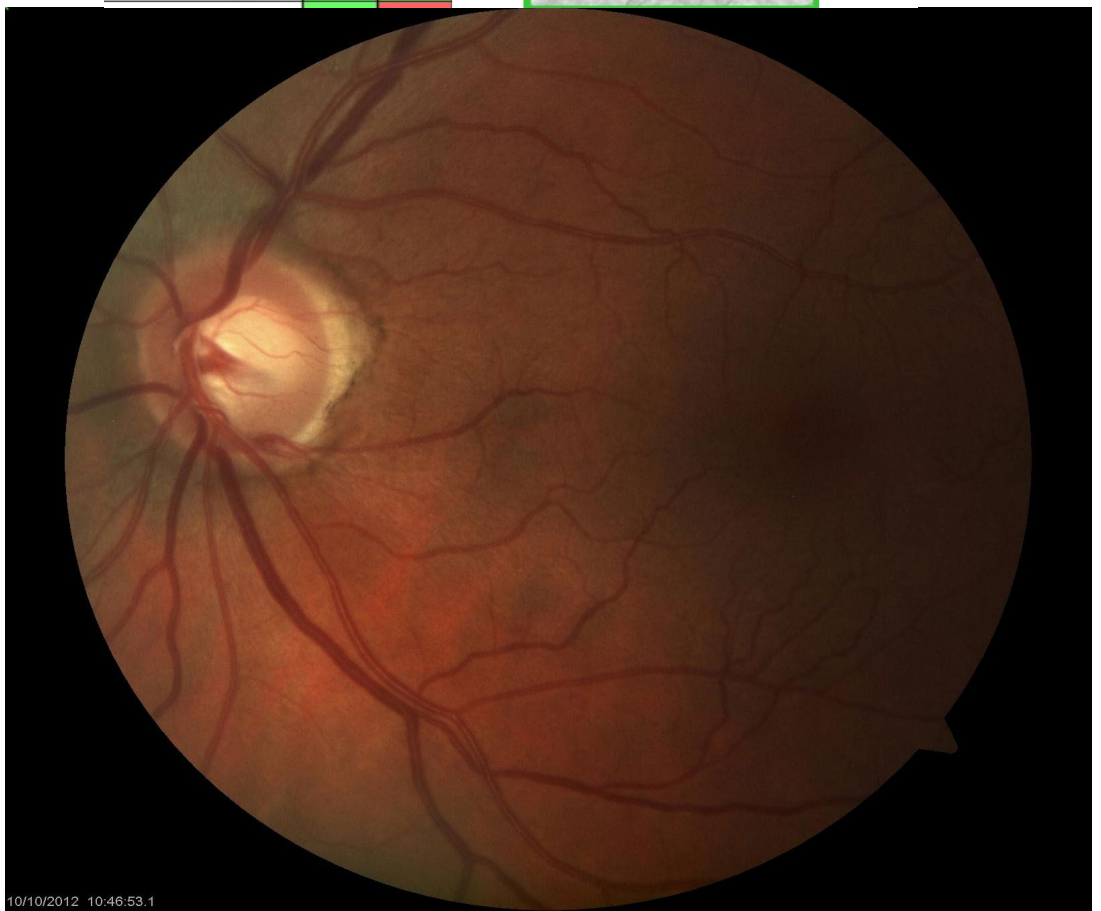
Sep 18, 2012 GHT: Outside Normal Limits
SITA-Standard



FL: 0/15
Fovea: Off
VFI: 91%

FN: 0%

FP: 0%
MD: -3.93 dB P < 1%
PSD: 5.51 dB P < 0.5%

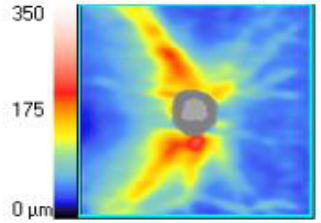


Progression in Glaucoma

- Very complicated to look at progression of glaucoma as a topic itself
- Must confirm if glaucoma is truly progressing
- Many factors have contributed to higher rates of progression
  - CH at baseline
  - CCT at basline
  - Family History
  - Magnitude of IOP lowering
  - Treatment vs. no treatment
  - Macular ganglion cell layer thickness at baseline
  - IOP at baseline
  - Extent of presenting disease burden

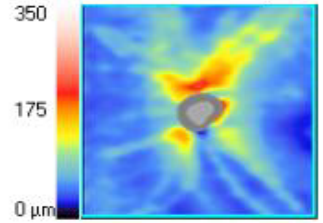
ONH and RNFL OU Analysis:Optic Disc Cube 200x200 OD ● | ● OS

RNFL Thickness Map

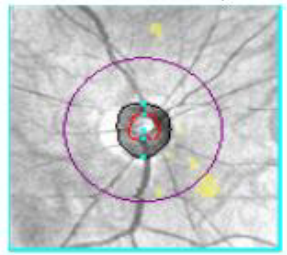


	OD	OS
Average RNFL Thickness	86 µm	72 µm
RNFL Symmetry	57%	
Rim Area	0.88 mm²	0.64 mm²
Disc Area	1.23 mm²	0.97 mm²
Average C/D Ratio	0.54	0.59
Vertical C/D Ratio	0.45	0.61
Cup Volume	0.115 mm³	0.127 mm³

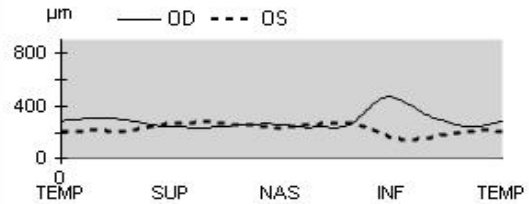
RNFL Thickness Map



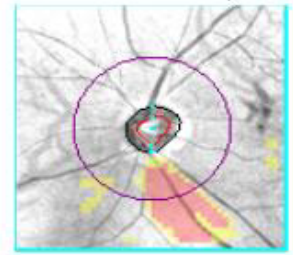
RNFL Deviation Map



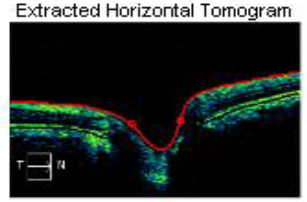
Neuro-retinal Rim Thickness



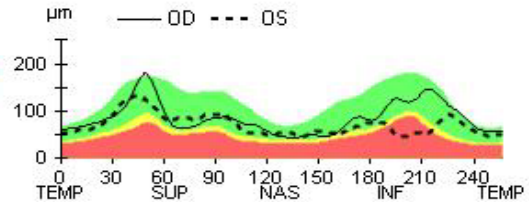
RNFL Deviation Map



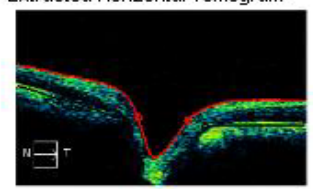
Disc Center(-0.06,-0.03)mm
Extracted Horizontal Tomogram



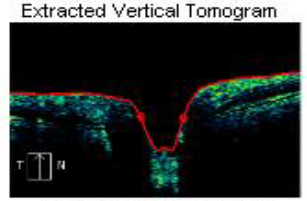
RNFL Thickness

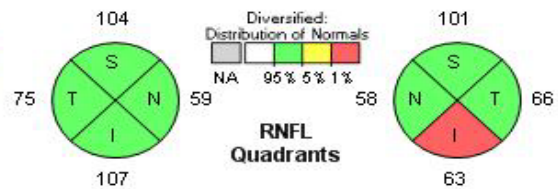


Disc Center(0.00,0.00)mm
Extracted Horizontal Tomogram

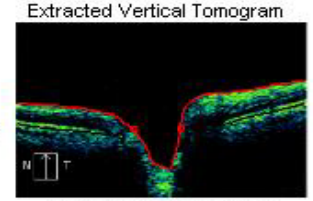


Extracted Vertical Tomogram

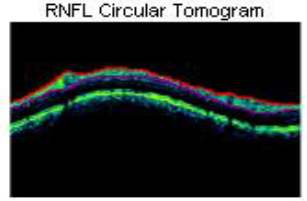




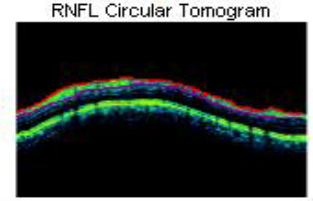
Extracted Vertical Tomogram



RNFL Circular Tomogram



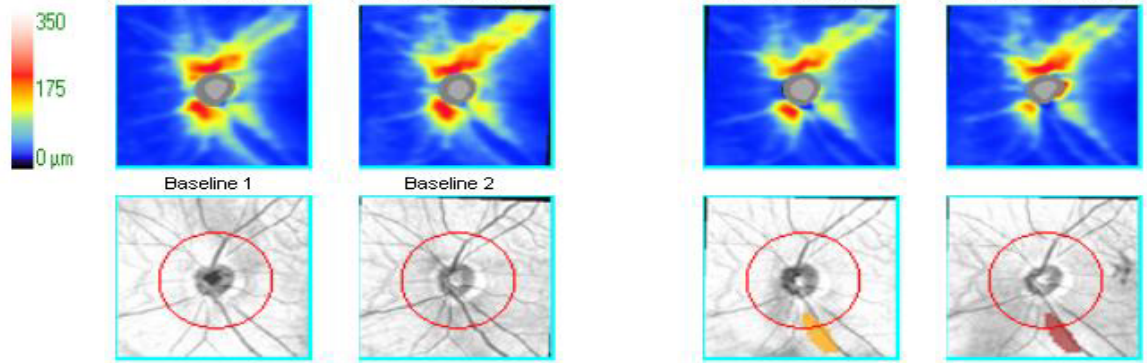
RNFL Circular Tomogram

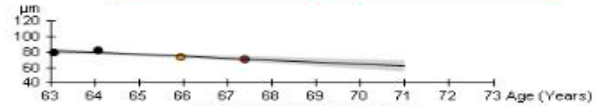


Guided Progression Analysis: (GPA™)

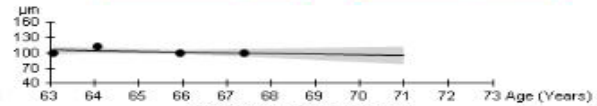
OD ○ | ● OS

Baseline 1	Baseline 2	Exam 3	Exam 4
2/9/2009 8:03:30 AM	2/11/2010 9:57:02 AM	12/19/2011 11:38:25 AM	5/29/2013 11:21:51 AM
4000-3621	4000-3621	4000-3621	4000-3621
SS: 7/10	R2 SS: 9/10	R2 SS: 9/10	R2 SS: 8/10
Average Thickness: 80	Average Thickness: 83	Average Thickness: 74	Average Thickness: 72

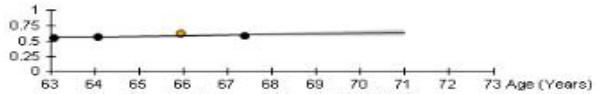




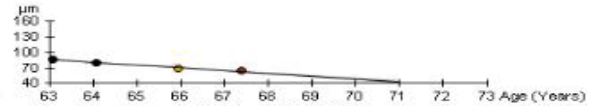
Average RNFL Thickness
Rate of change: -2.42 +/- 3.99 µm/Year



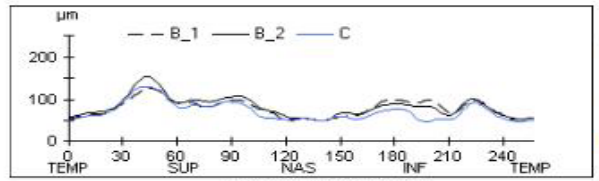
Superior RNFL Thickness
Rate of change: -1.29 +/- 9.05 µm/Year



Average Cup-to-Disc Ratio
Rate of change: 0.01 +/- 0.03 /Year



Inferior RNFL Thickness
Rate of change: -5.59 +/- 2.96 µm/Year



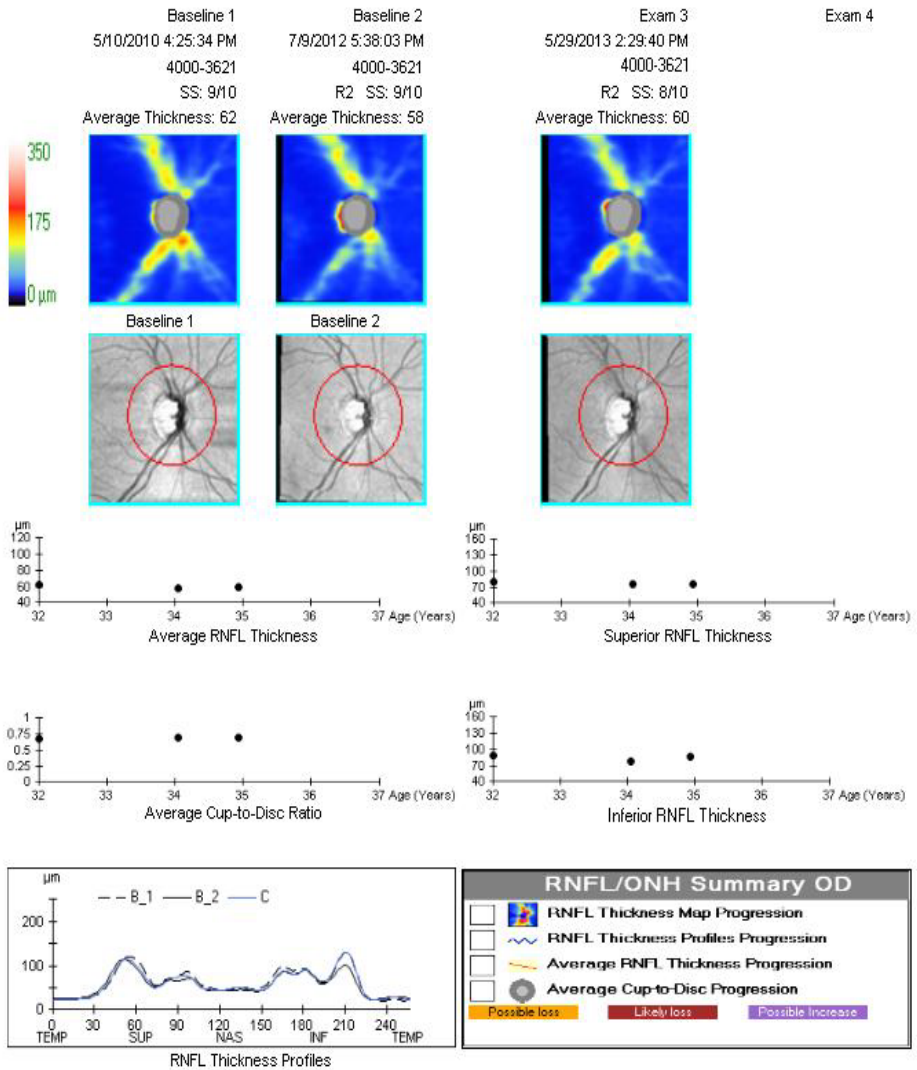
RNFL Thickness Profiles

Comments

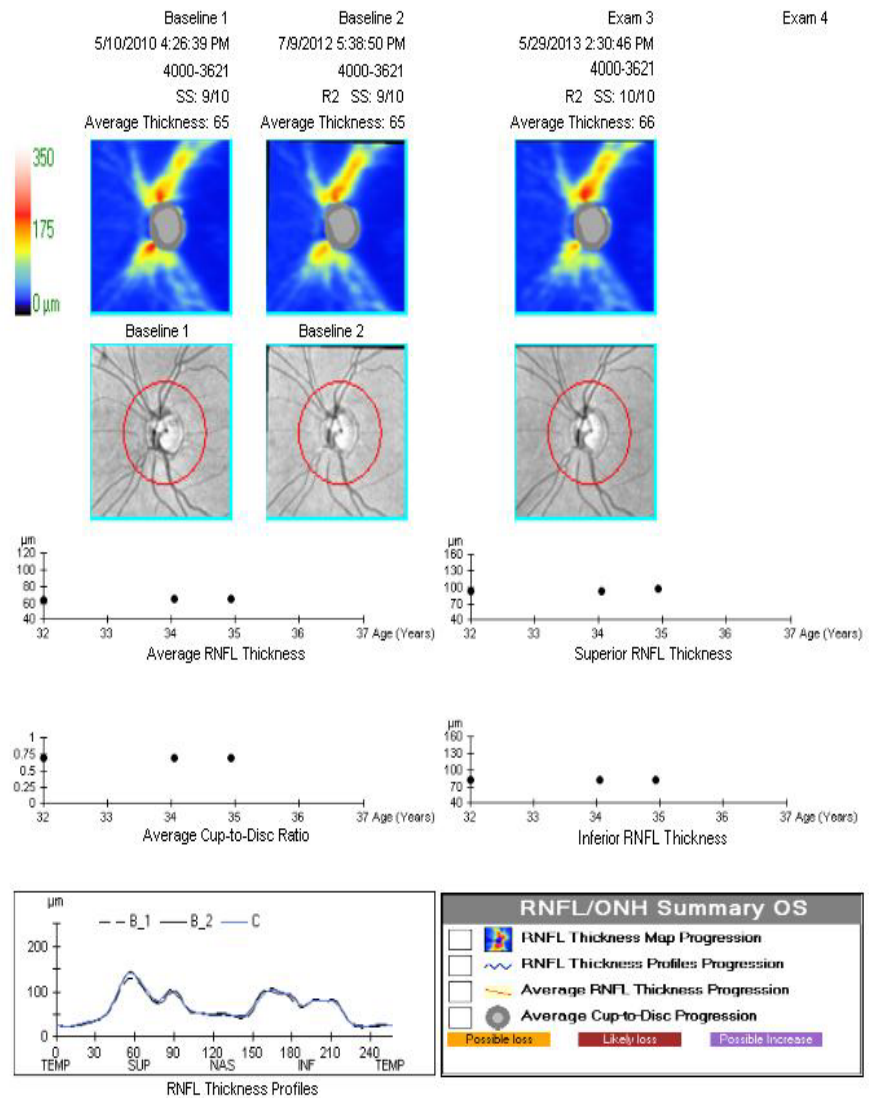
Analysis Edited: 5/29/2013 11:24 AM

Doctor's Signature

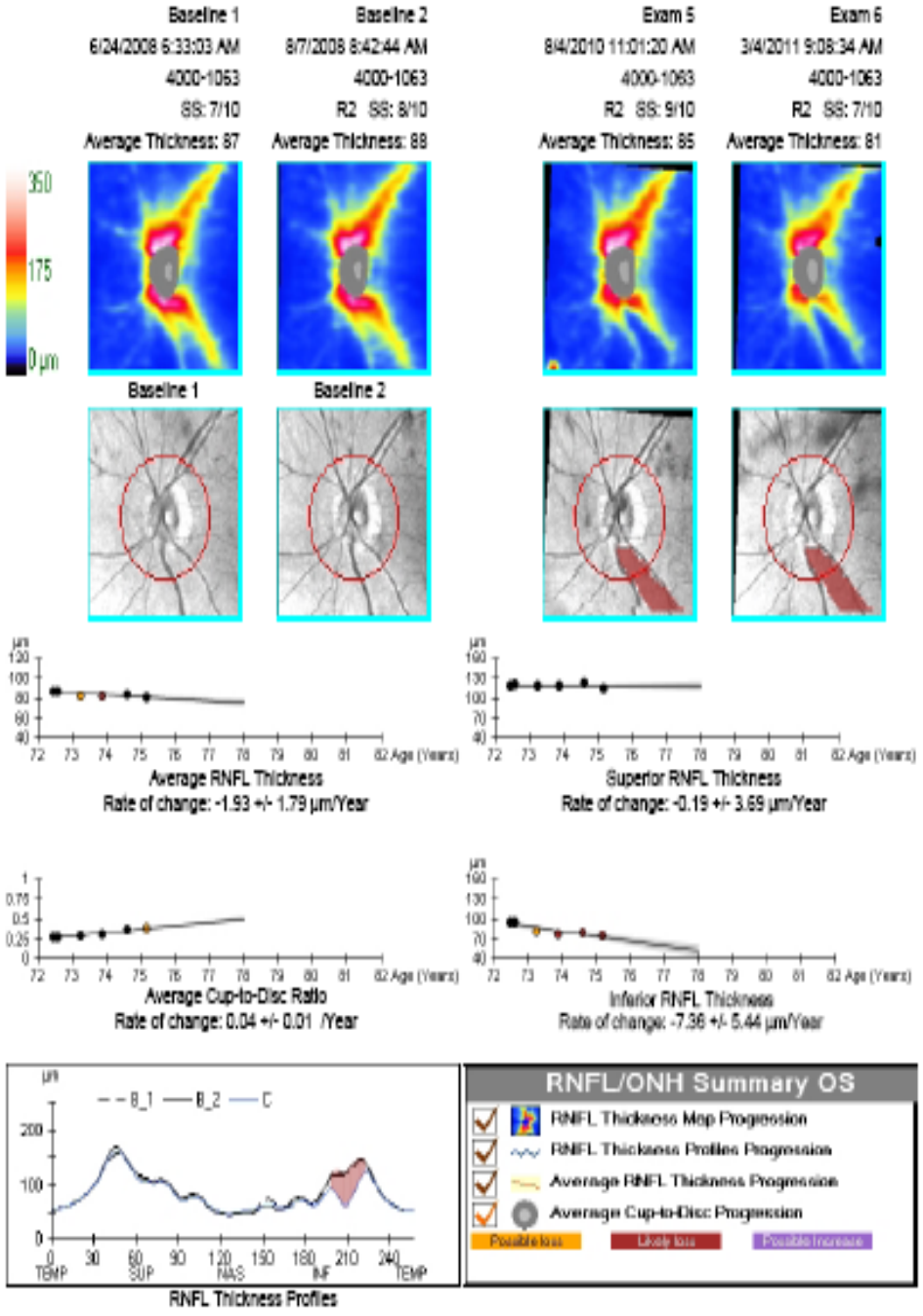
Guided Progression Analysis: (GPA™) OD ● ○ OS



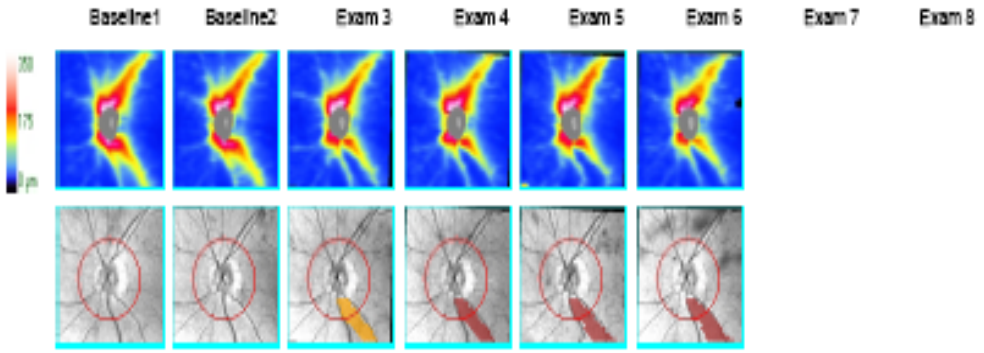
Guided Progression Analysis: (GPA™) OD ○ ● OS



Guided Progression Analysis: (GPA™) OD ○ ● OS



Guided Progression Analysis: (GPA™) OD ○ ● OS



RNFL and ONH Summary Parameters

		Exam Date/Time	Serial Number	Registration Method	SS	Avg RNFL Thickness (µm)	Inf Quadrant RNFL (µm)	Sup Quadrant RNFL (µm)	Rim Area (mm²)	Average Cup-to-Disc Ratio	Vertical Cup-to-Disc Ratio	Cup Volume (mm³)
Baseline1:	1	6/24/2008 6:33:53 AM	4000-1063		6/10	87	97	123	1.32	0.30	0.33	0.028
Baseline2:	2	8/7/2008 8:42:44 AM	4000-1063	R2	8/10	87	97	120	1.28	0.28	0.29	0.025
	3	4/2/2009 3:44:24 PM	4000-1063	R2	7/10	83	82	118	1.25	0.34	0.39	0.040
	4	11/18/2009 2:27:57 PM	4000-1063	R2	7/10	83	79	119	1.23	0.31	0.33	0.030
	5	8/4/2010 11:01:20 AM	4000-1063	R2	9/10	84	81	125	1.24	0.37	0.42	0.036
Current:	6	3/4/2011 9:08:34 AM	4000-1063	R2	7/10	81	76	116	1.20	0.39	0.44	0.053

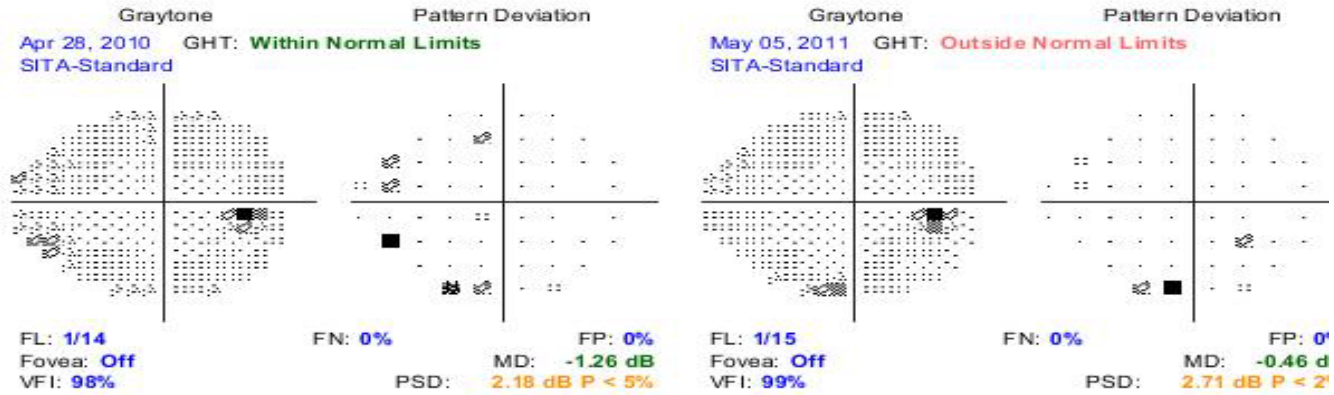
Registration Methods
R2 - Registration based on translation and rotation of OCT fundus
R1 - Registration based only on translation of disc center

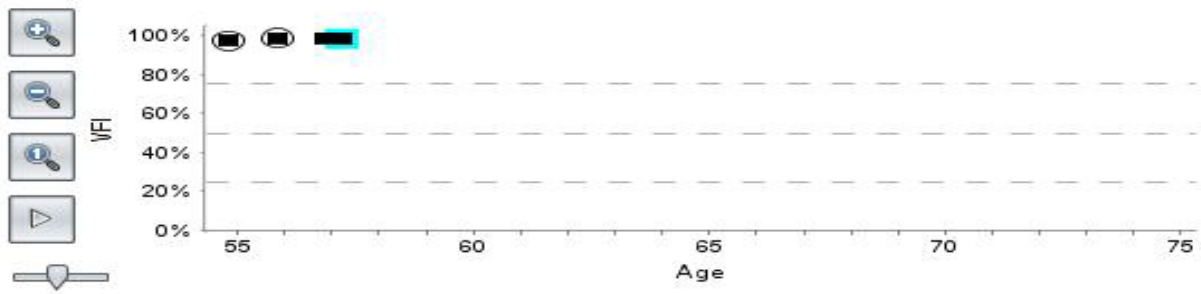
Likely Loss
Possible Loss

Compared to baseline, statistically significant loss of tissue detected. For Average RNFL, Superior RNFL, Inferior RNFL, Rim Area the values have decreased. For Cup-to-Disc Ratios and Cup Volume values have increased.

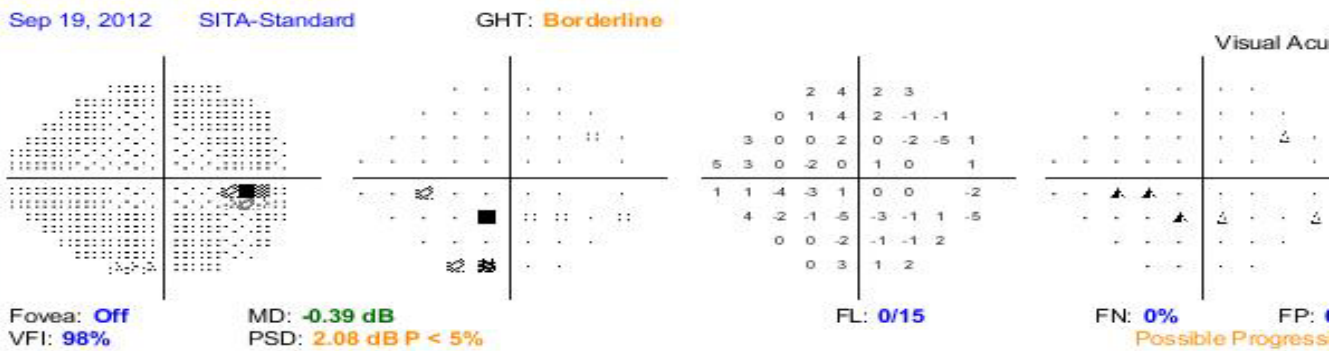
Possible Increase

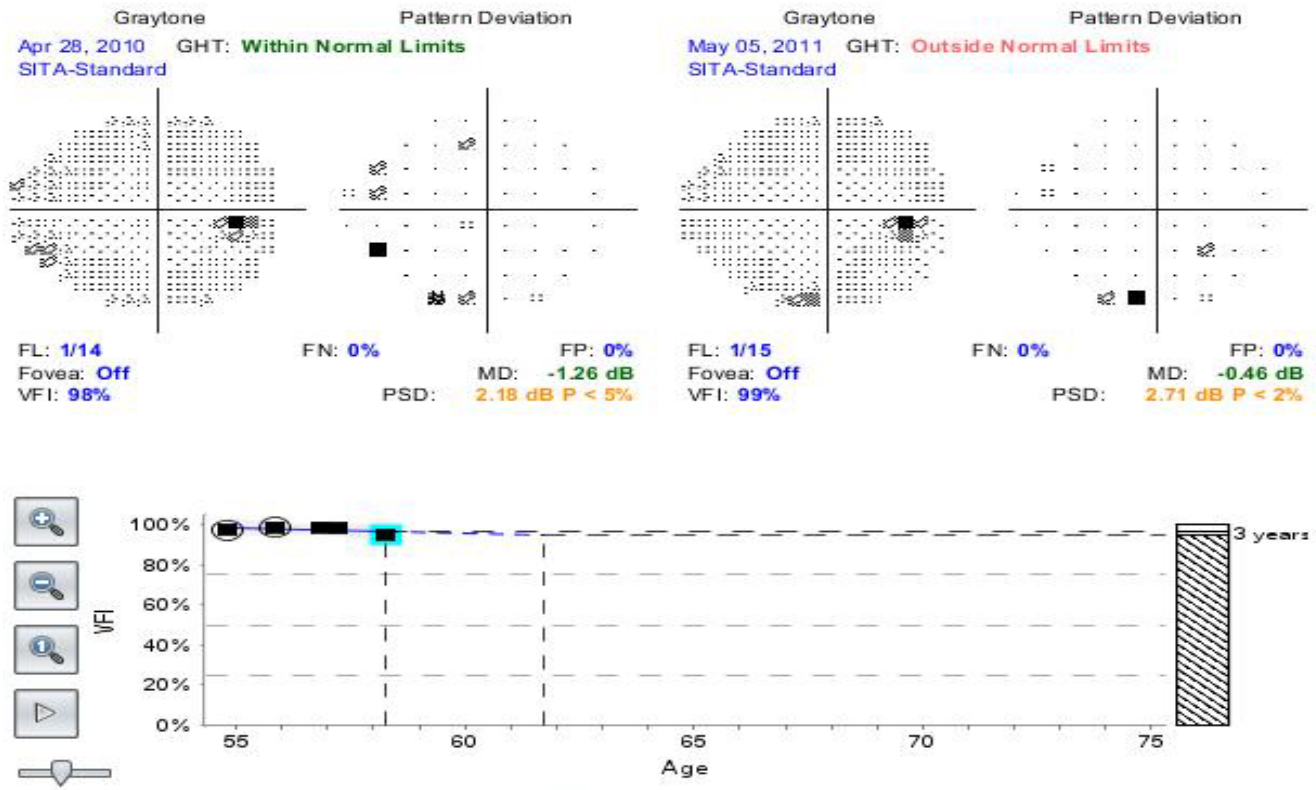
Compared to baseline, statistically significant increase detected. For Average RNFL, Superior RNFL, Inferior RNFL, Rim Area values have increased. For Cup-to-Disc Ratios and Cup Volume values have decreased.

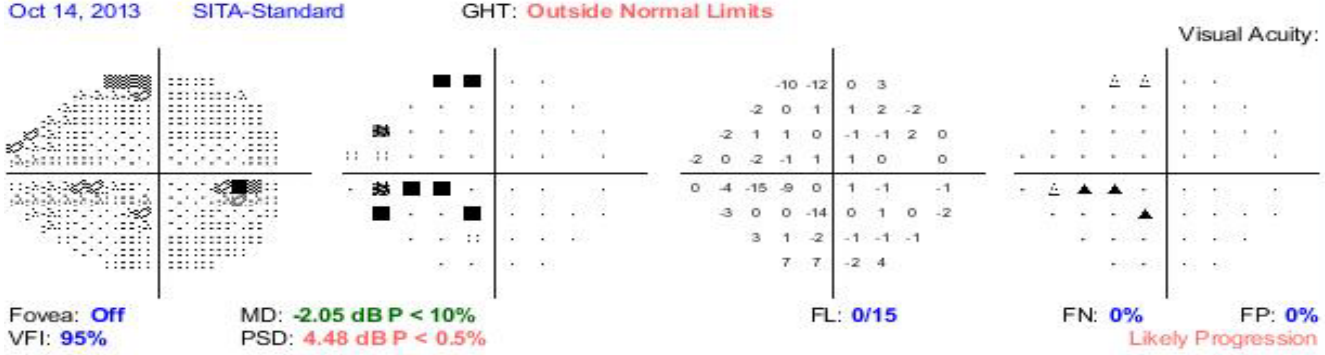




Rate of Progression: Not calculated, not enough exams selected.




Graytone
Pattern Deviation
Apr 28, 2010 GHT: Within Normal Limits
SITA-Standard
FL: 1/14
Fovea: Off
VFI: 98%
FN: 0%
FP: 0%
MD: -1.26 dB
PSD: 2.18 dB P < 5%
Graytone
Pattern Deviation
May 05, 2011 GHT: Outside Normal Limits
SITA-Standard
FL: 1/15
Fovea: Off
VFI: 99%
FN: 0%
FP: 0%
MD: -0.46 dB
PSD: 2.71 dB P < 2%
VFI
100%
80%
60%
40%
20%
0%
55
60
65
70
75
Age
3 years
Rate of Progression: -0.6 ± 1.8% / year (95% confidence)

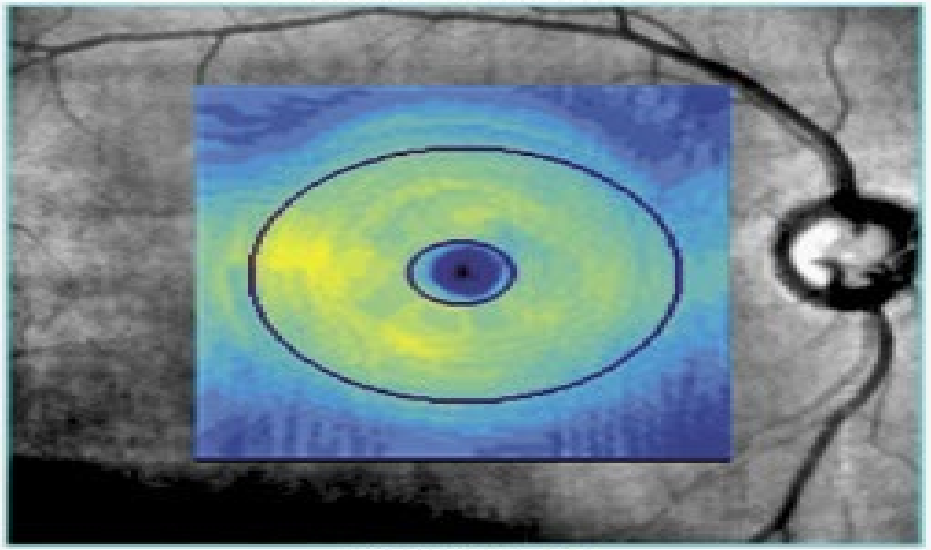

Oct 14, 2013 SITA-Standard GHT: Outside Normal Limits
Visual Acuity:
Fovea: Off
VFI: 95%
MD: -2.05 dB P < 10%
PSD: 4.48 dB P < 0.5%
FL: 0/15
FN: 0%
FP: 0%
Likely Progression

Optical Coherence Tomography as a Biomarker for Diagnosis, Progression, and Prognosis of Neurodegenerative Diseases
Satue, etal AJO 2016

- Recent research using the latest SD OCT imaging technology has demonstrated that an early damage of the anterior visual pathway occurs in MS, PD, and AD and that the ganglion cell layer is the ultimate biomarker for disease diagnosis, severity, and progression.
- Thus, OCT technology should be used as a common and very useful clinical complement in the diagnosis and control of neurodegenerative disorders.
- 85 Citations

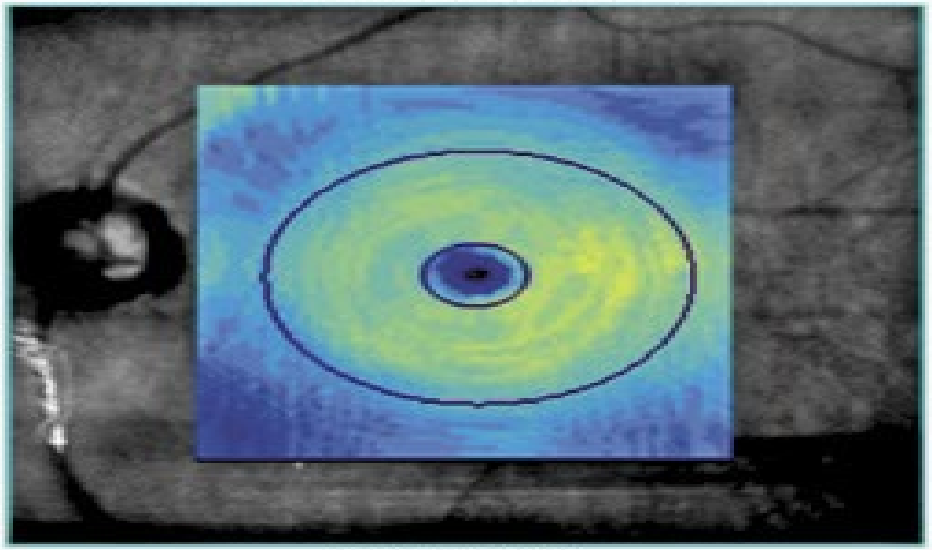
Ganglion Cell OU Analysis: Macular Cube 512x128 — OD ● | ● OS

OD Thickness Map



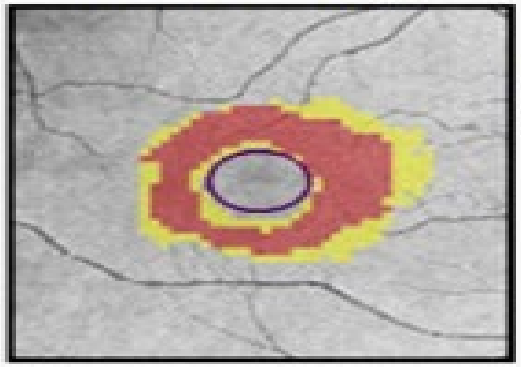
Fovea: 256, 64

OS Thickness Map

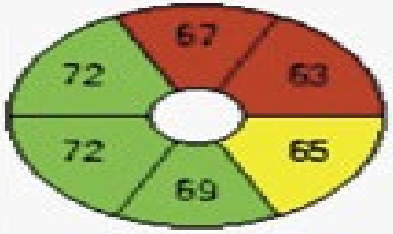


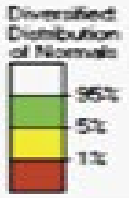
Fovea: 268, 65

OD Deviation Map

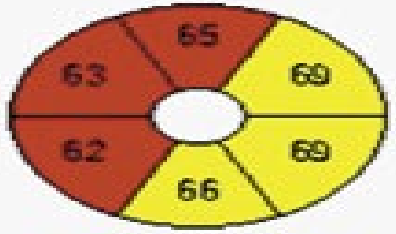


OD Sectors

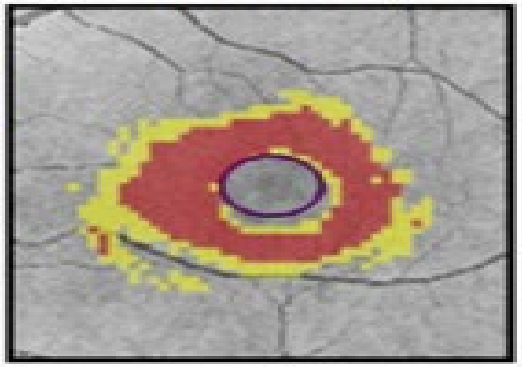




OS Sectors



OS Deviation Map



	OD µm	OS µm
Average GCL + IPL Thickness	68	66
Minimum GCL + IPL Thickness	62	61

American Journal of Ophthalmology
December 2017

Baseline Fourier-Domain Optical Coherence Tomography Structural Risk Factors for Visual Field Progression in the Advanced Imaging for Glaucoma Study

David Huang, MD etal

AIG/ 2017

- A total of 277 eyes of 188 participants were followed up for 3.7 ± 2.1 years.
- VF progression was observed in 83 eyes (30%).
- Several baseline NFL and GCC parameters, but not disc parameters, were found to be significant predictors of progression on univariate Cox regression analysis.
- The most accurate single predictors were the GCC focal loss volume (FLV), followed closely by NFL-FLV. An abnormal GCC-FLV at baseline increased risk of progression by a hazard ratio of 3.1

New Perspectives on Disease Management

- SD-OCT is superior in identifying progression in glaucoma suspects, pre-perimetric glaucoma, mild glaucoma and early moderate disease compared with SAP are superior in identifying progression, after an initial VF to set baseline.
- Average time to identification of statistically significant progression is 2-3 years with SD-OCT and up 6 years with SAP
- Intra-test variability is up to 10x less with OCT(3%) than VF(20%)

New Perspectives on Disease Management

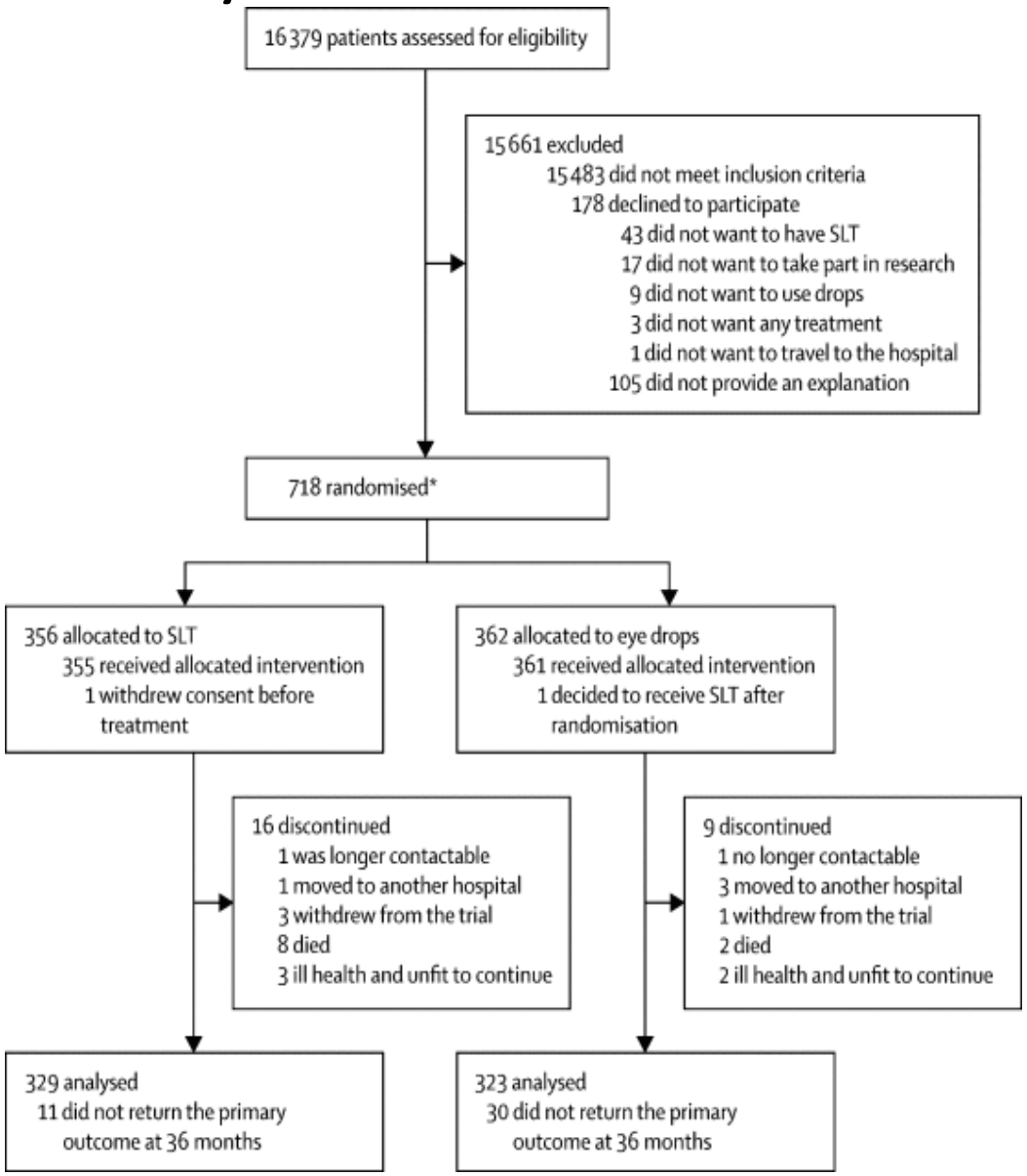
- RNFL “Floor” limits usefulness in late moderate to advanced glaucoma (50-60 microns)
- GCC progression analysis can continue to be useful in late moderate to advanced glaucoma due to density of fibers in the macula and the later involvement of central vision in the disease

THE LANCET
THE “LIGHT” STUDY

VOLUME 393, ISSUE 10180, P1505-1516, APRIL 13, 2019

- **Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial**
- Gus Gazzard, FRCOphth
- Evgenia Konstantakopoulou, PhD
- Prof David Garway-Heath, MD
- Anurag Garg, FRCOphth
- Victoria Vickerstaff, MSc
- Rachael Hunter, MSc
- et al.

The LIGHT Study



LIGHT Study

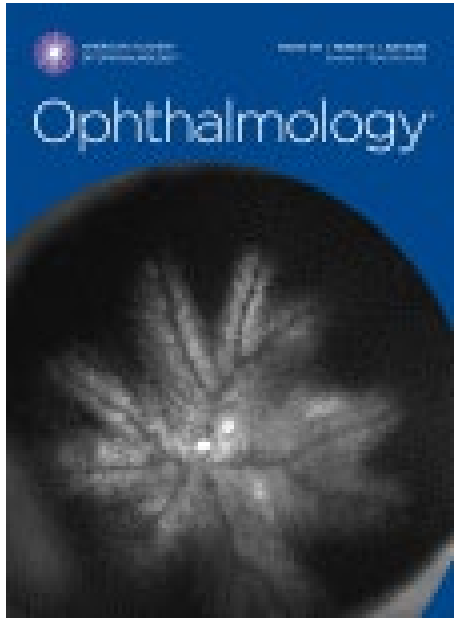
- Standardization of laser delivery was achieved by protocol-defined settings and clinical endpoints.[14]
- Selective laser trabeculoplasty was delivered to 360° of the trabecular meshwork. 100 non-overlapping shots (25 per quadrant) were used, with the laser energy varied from 0·3 to 1·4 mJ by the clinician, using an appropriate laser gonioscopy lens.
- One re-treatment with selective laser trabeculoplasty was allowed, provided there had been a reduction in intraocular pressure after the initial treatment; the next escalation was medical therapy.
- Significant complications of selective laser trabeculoplasty (eg, a spike in intraocular pressure) precluded repetition of selective laser trabeculoplasty.

LIGHT Study

- Drug classes for first, second, or third line treatment were defined by NICE[15] and European Glaucoma Society[19] guidance
- First line was prostaglandin analogues, second line was β blockers, third or fourth line was topical carbonic anhydrase inhibitors or α agonists. Fixed combination drops were allowed.
- Systemic carbonic anhydrase inhibitors were only permitted while awaiting surgery. Maximum tolerated medical therapy was defined by the treating clinician as the most intensive combination of drops an individual could reasonably, reliably, and safely use and thus varied between patients.
- A need for treatment escalation beyond maximum tolerated medical therapy triggered an offer of surgery.

The Light study

- **Findings**
- **Of 718 patients enrolled, 356 were randomised to the selective laser trabeculoplasty and 362 to the eye drops group. 652 (91%) returned the primary outcome questionnaire at 36 months.**
- **Average EQ-5D score was 0·89 (SD 0·18) in the selective laser trabeculoplasty group versus 0·90 (SD 0·16) in the eye drops group, with no significant difference (difference 0·01, 95% CI –0·01 to 0·03; p=0·23).**
- **At 36 months, 74·2% (95% CI 69·3–78·6) of patients in the selective laser trabeculoplasty group required no drops to maintain intraocular pressure at target.**
- **Eyes of patients in the selective laser trabeculoplasty group were within target intracoluar pressure at more visits (93·0%) than in the eye drops group (91·3%), with glaucoma surgery to lower intraocular pressure required in none versus 11 patients.**
- **Over 36 months, from an ophthalmology cost perspective, there was a 97% probability of selective laser trabeculoplasty as first treatment being more cost-effective than eye drops first at a willingness to pay of £20 000 per quality-adjusted life-year gained.**



Efficacy of Repeat Selective Laser Trabeculoplasty in Medication-Naive Open-Angle Glaucoma and Ocular Hypertension during the LiGHT Trial

AnuragGargFRCOphth;[1] VictoriaVickerstaffMSc[2,3] NeilNathwaniBSc[1] DavidGarway-HeathMD[1] EvgeniaKonstantakopoulouPhD[1] GarethAmblerPhD[4] CateyBunceDSc[1,5,6] RichardWormaldFRCOphth[1,6] KeithBartonFRCS[1] GusGazzardMD[1] Laser

Repeat SLT

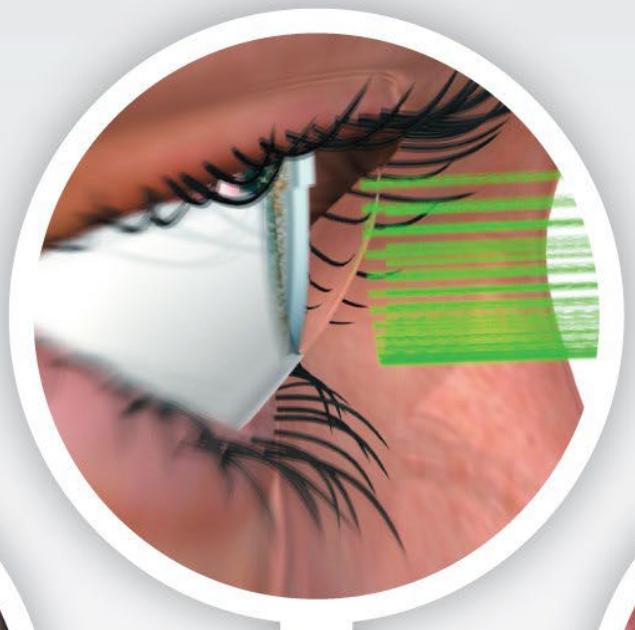
- Results
- A total of 115 eyes of 90 patients received repeat SLT during the first 18 months of the trial. Pretreatment IOP before initial SLT was significantly higher than before retreatment IOP of repeat SLT (mean difference, 3.4 mmHg; 95% confidence interval [CI], 2.6–4.3 mmHg; $P < 0.001$).
- Absolute IOP reduction at 2 months was greater after initial SLT compared with repeat SLT (mean difference, 1.0 mmHg; 95% CI, 0.2–1.8 mmHg; $P = 0.02$).
- Adjusted absolute IOP reduction at 2 months (adjusting for IOP before initial or repeat laser) was greater after repeat SLT (adjusted mean difference, −1.1 mmHg, 95% CI, −1.7 to −0.5 mmHg; $P = 0.001$).
- A total of 34 eyes were early failures (retreatment 2 months after initial SLT) versus 81 later failures (retreatment >2 months after initial SLT). No significant difference in early absolute IOP reduction at 2 months after repeat SLT was noted between early and later failures (mean difference, 0.3 mmHg; 95% CI, −1.1 to 1.8 mmHg; $P = 0.655$).
- Repeat SLT maintained drop-free IOP control in 67% of 115 eyes at 18 months, with no clinically relevant adverse events.

1

Camera-guided system enables precise **non-contact procedure**

Advanced image-processing algorithm **locates exact treatment area**

2

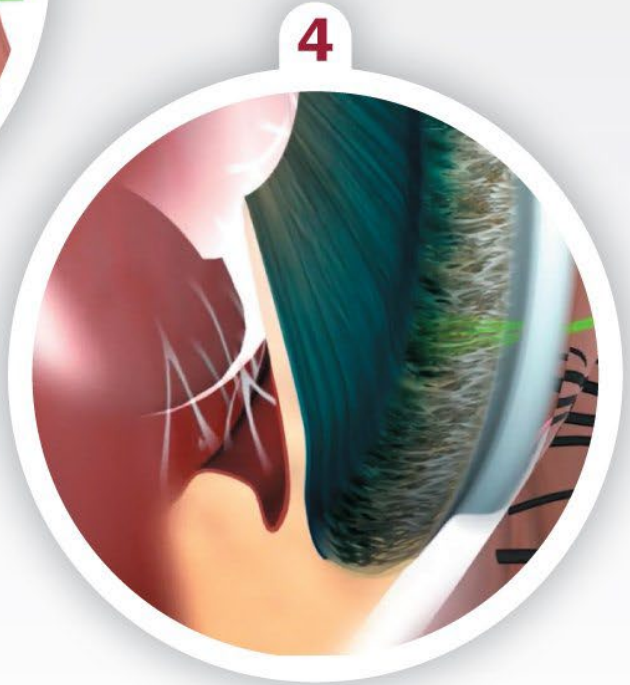


3

100 laser beams are directed to the trabecular meshwork

Delivery in **1.2 seconds**

4



IN VIEW: The investigational non-invasive, non-contact procedure is performed with automated laser technology that delivers 100 spots to the trabecular meshwork through the limbus in just 1.2 seconds. *(Images courtesy of BELKIN Laser Ltd.)*

WATCH THE PROCEDURE Go to OphthalmologyTimes.com/1Second

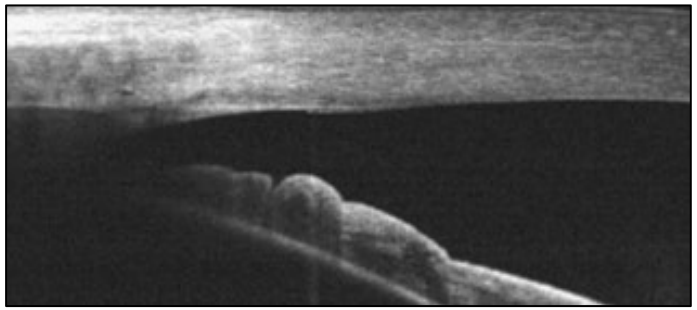
Belkin DSLT

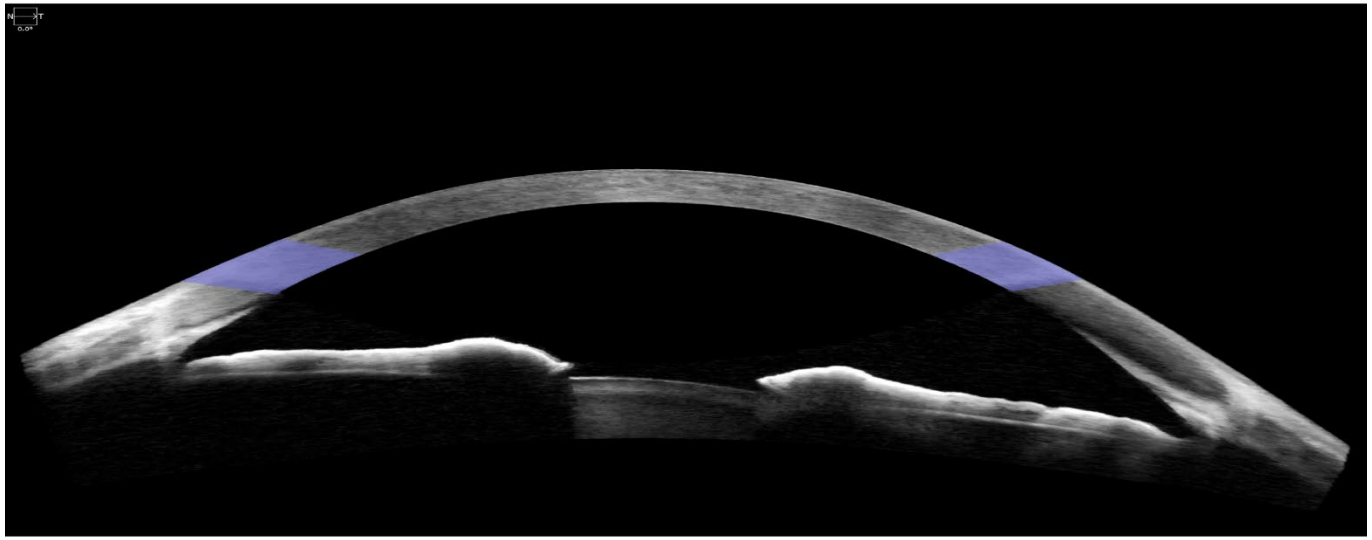
- An investigational IOP-lowering modality, direct selective laser trabeculoplasty (DSLT) (BELKIN Laser), is being developed for its potential as a first-line treatment for ocular hypertension (OHT) open-angle glaucoma (OAG) and possibly for angle-closure glaucoma (ACG) that overcomes the limitations of current initial therapeutic options.
- The non-invasive, non-contact procedure is performed with automated laser technology that delivers 100 spots to the trabecular meshwork through the limbus in just 1.2 seconds.
- A proof-of-concept study provided evidence for the efficacy and safety of the transscleral approach to laser beam delivery using a conventional SLT instrument, and studies are under way outside of the United States using the external automatic glaucoma laser device itself

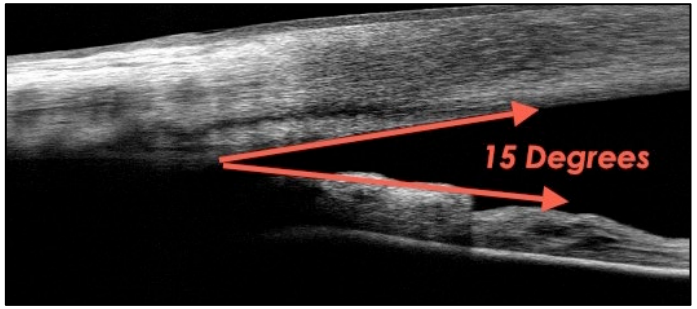
Belkin DSLT

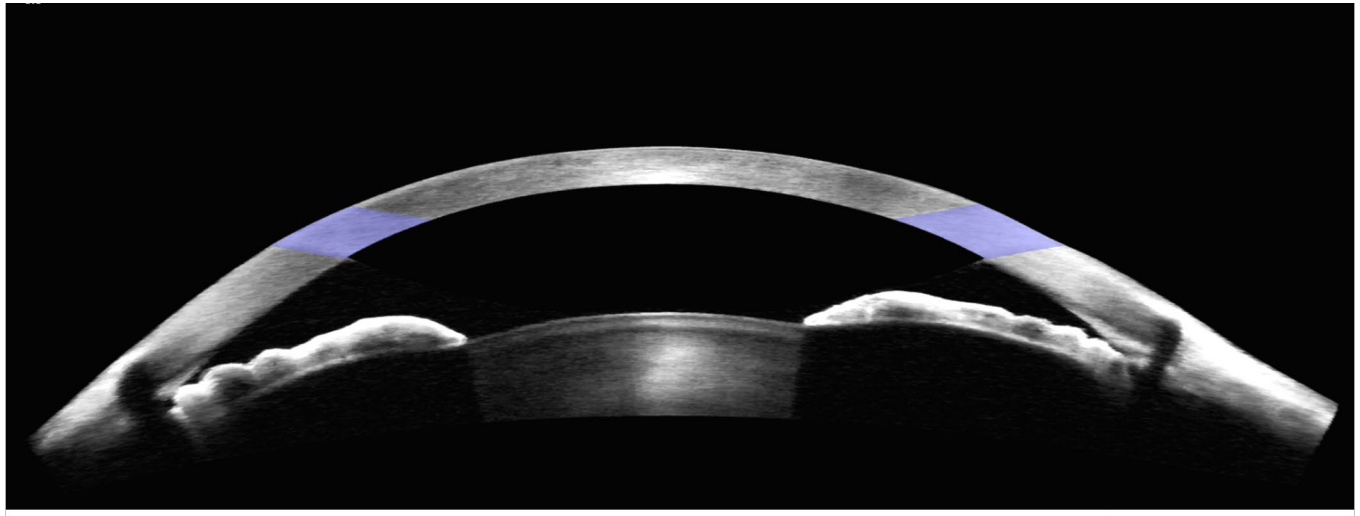
- **Results**: In the trial group (N=16), IOP decrease from an average of 20.21 mmHg before treatment to 15.50 at 6 months.
- The corresponding numbers for the control group (n=16), were 21.14 mmHg and 15.00. There was no statistical difference between the two groups in IOP reduction.
- Complications rate was significantly higher in the control group ($p<0.0001$, OR 6.881, 95% CI 1.676/28.248).
- Anterior chamber inflammation and superficial punctate keratitis rates were significantly higher in the control group and compared to the study group ($p=0.006$).

Normal/Shallow Chamber

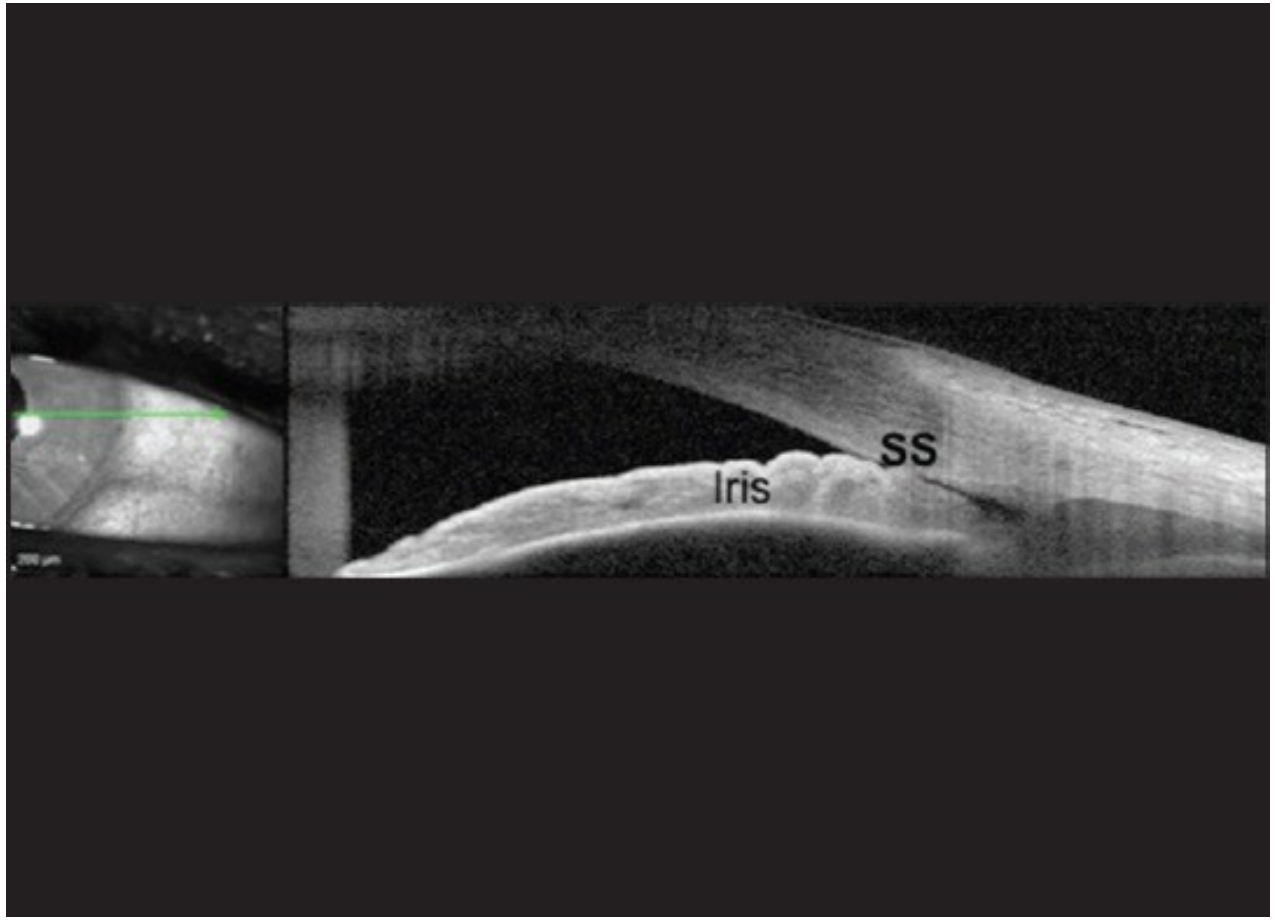




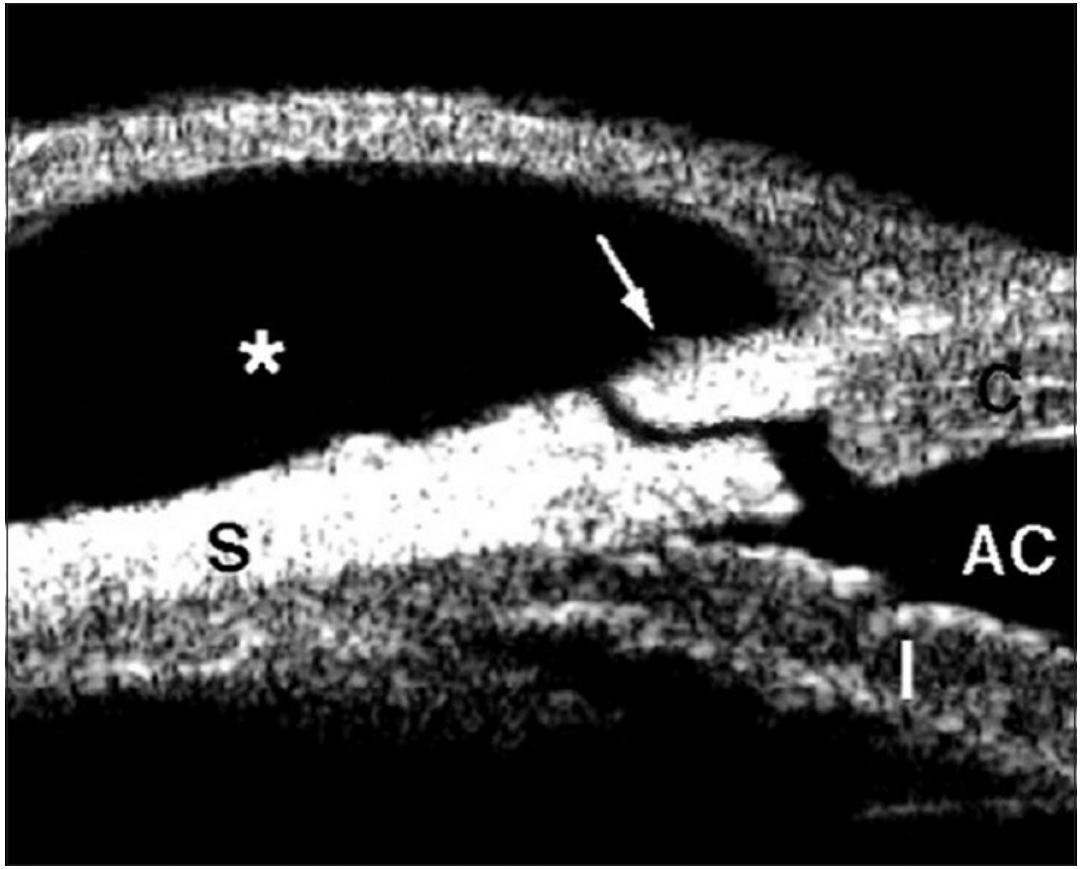


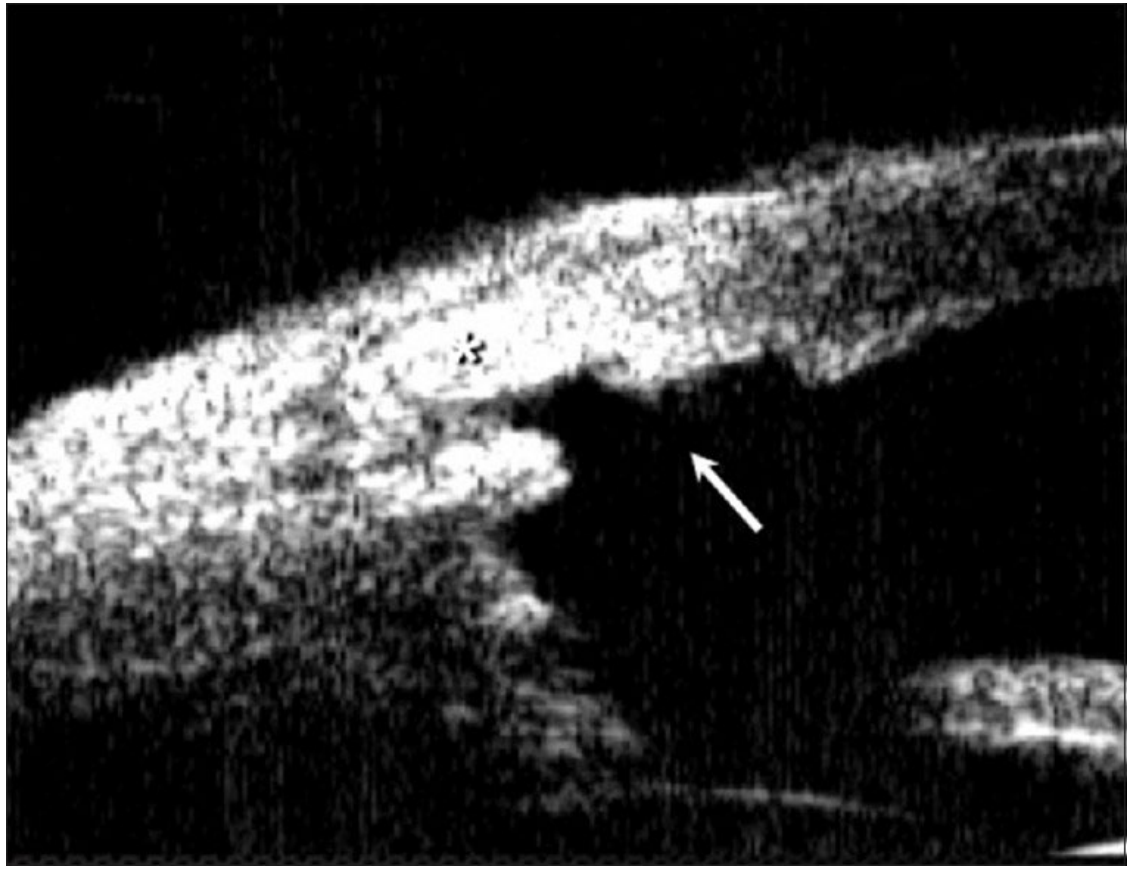


Primary Angle Closure

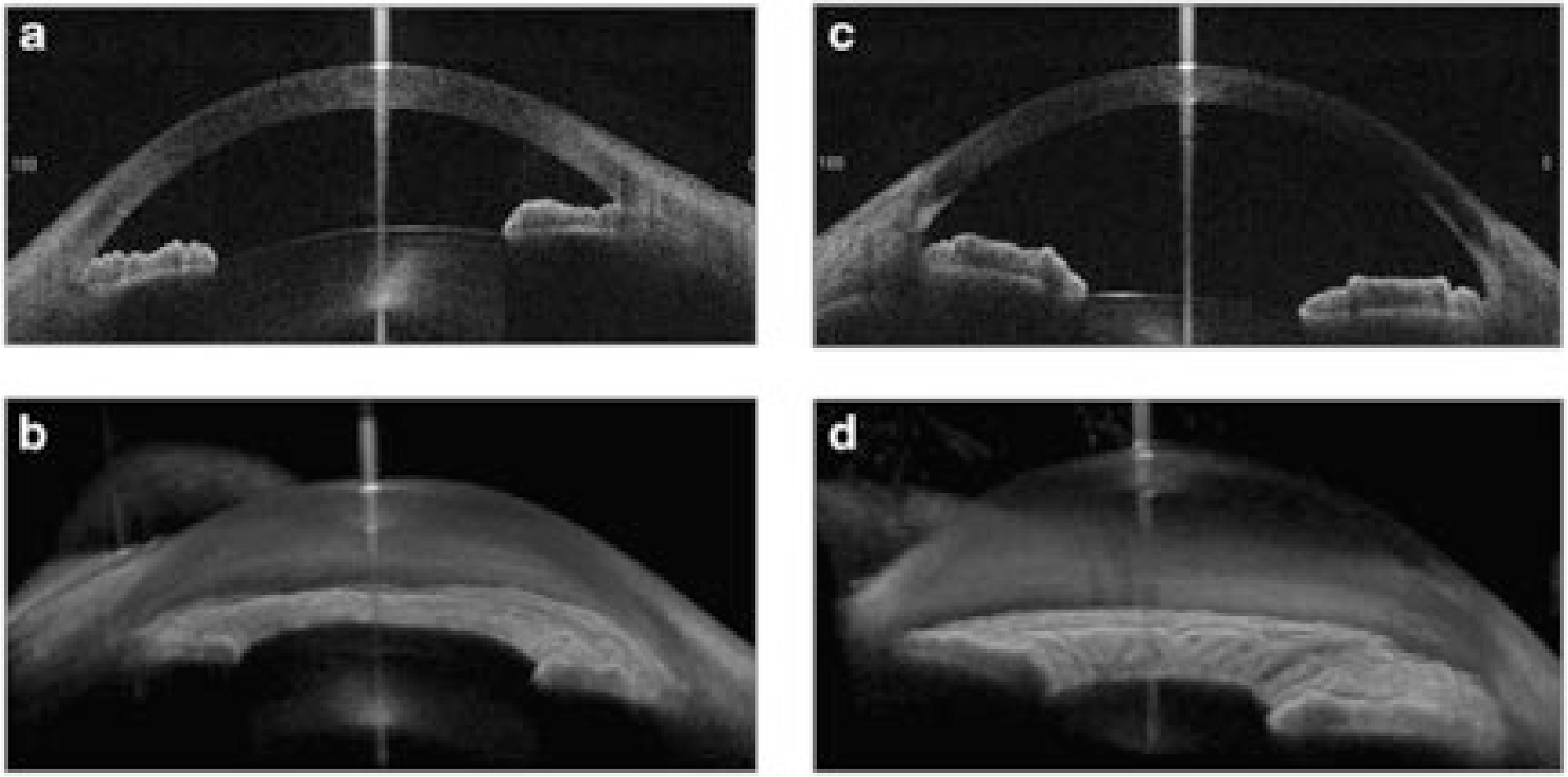


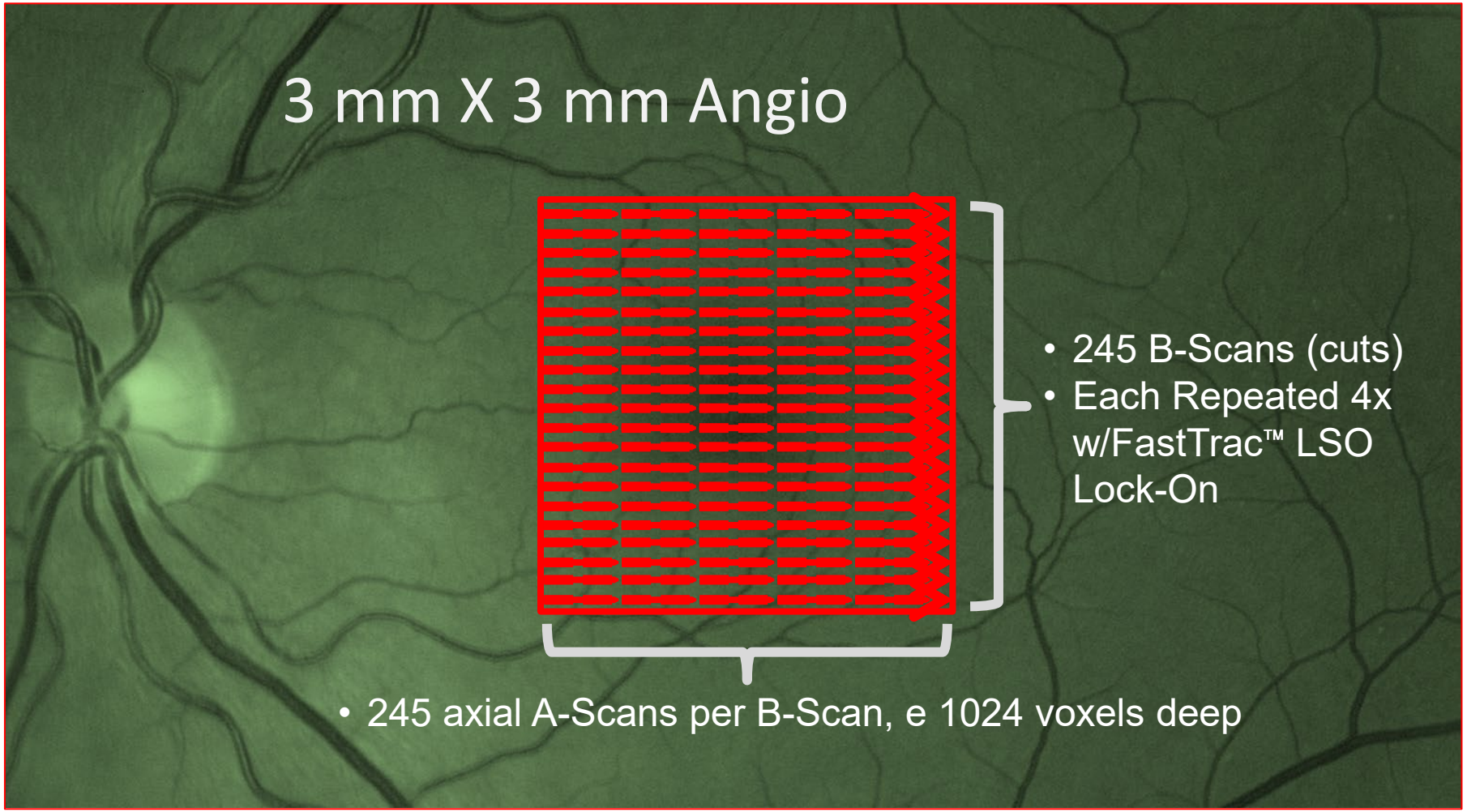
Bleb Morphology





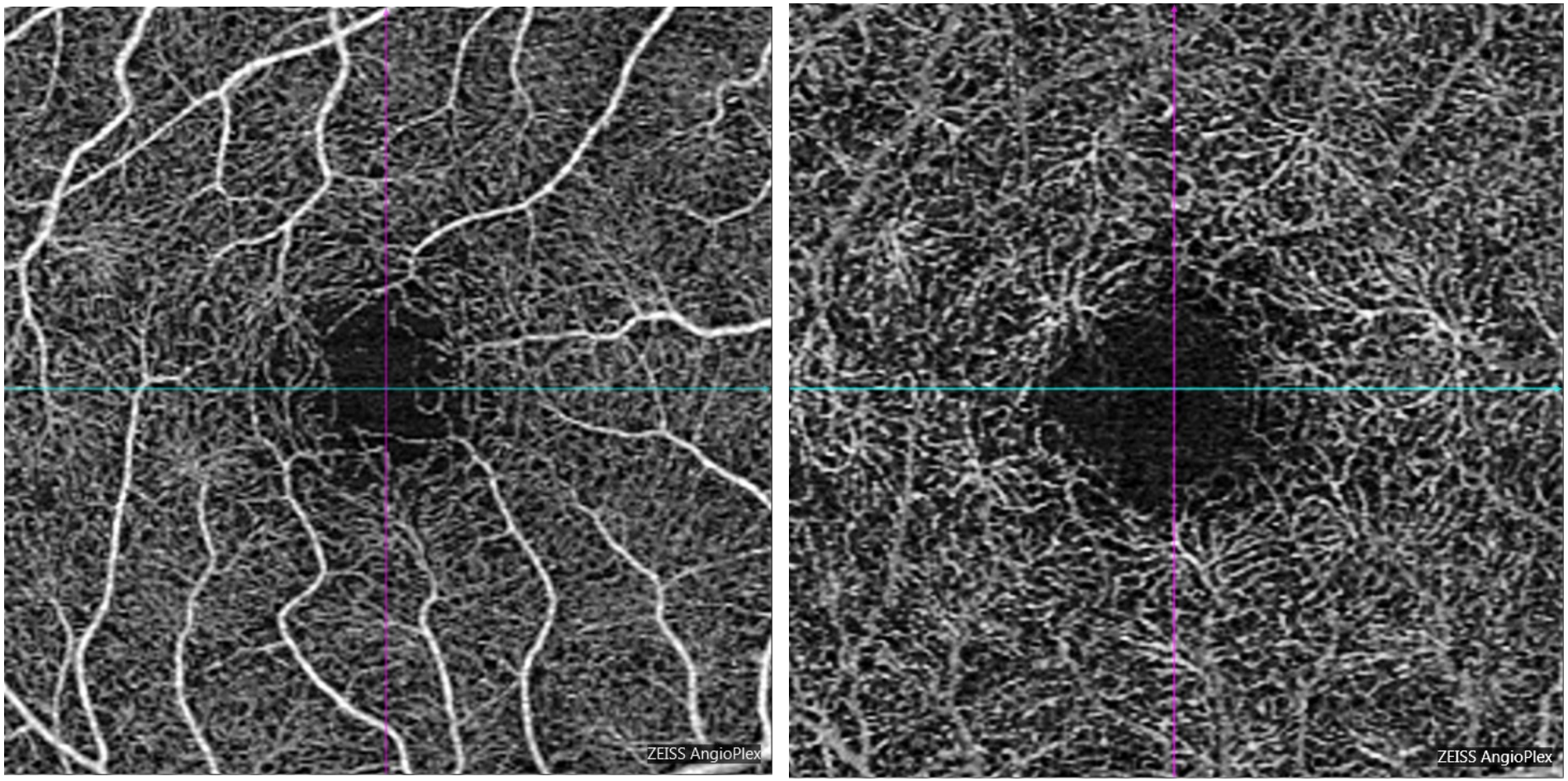
Casia Swept Source AS-OCT (Tomey)



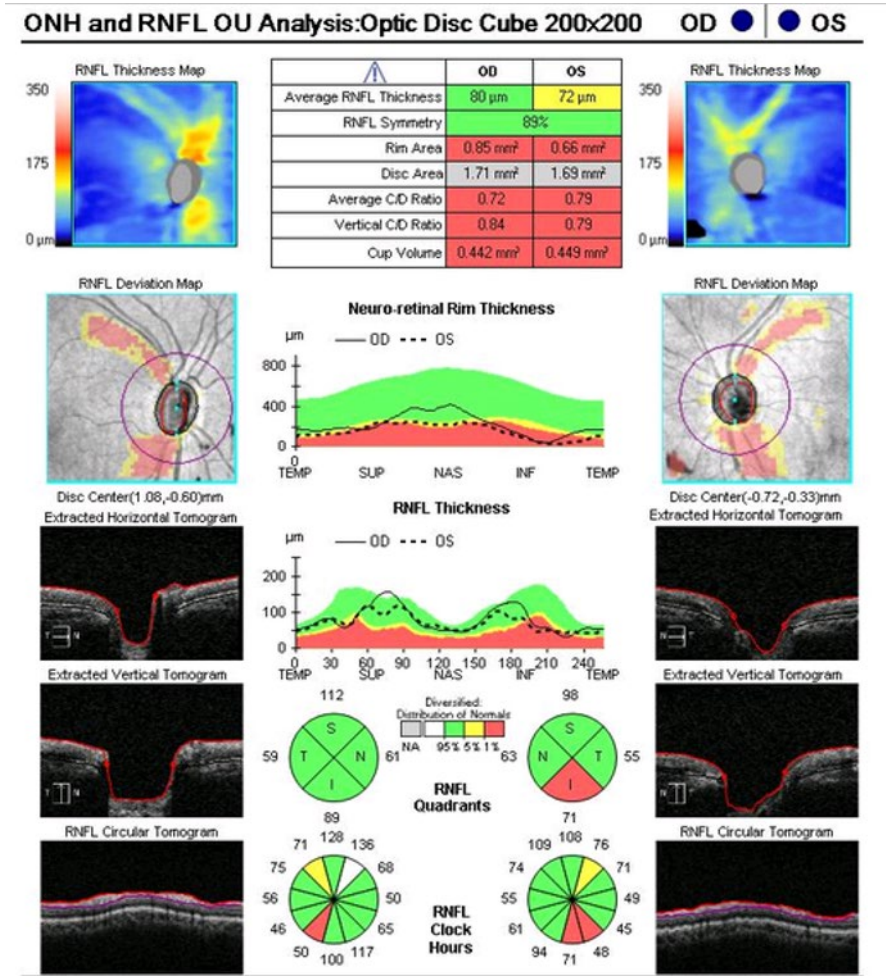


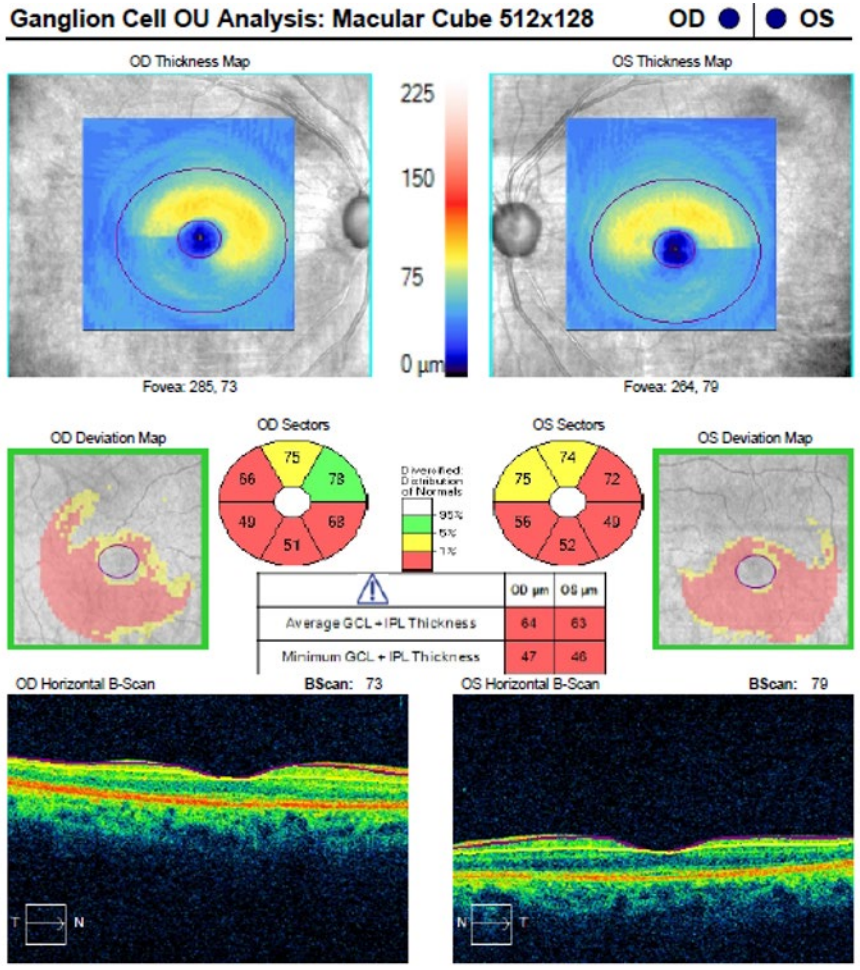
Total = **240,000 A-scans,** ~ 5.0 secs

Normal 3x3 Angio Cube OD - Full Retina (L) and Deep Plexus (R)

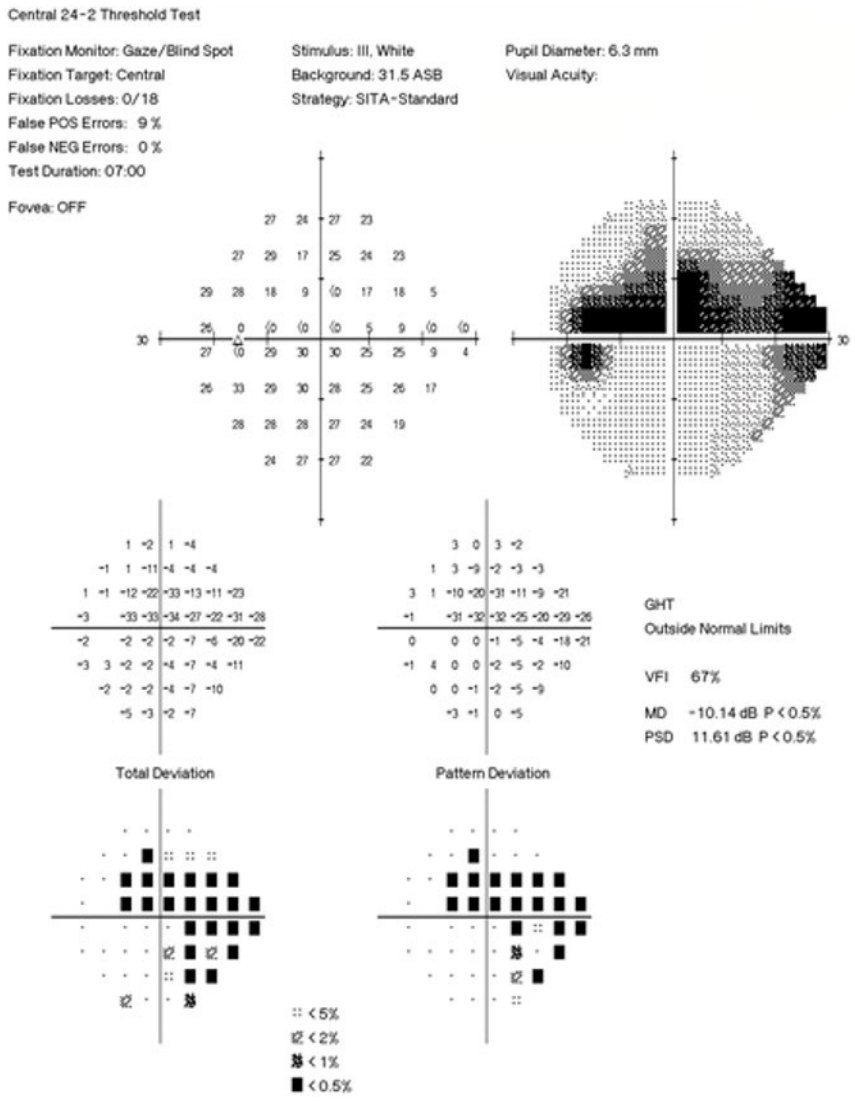


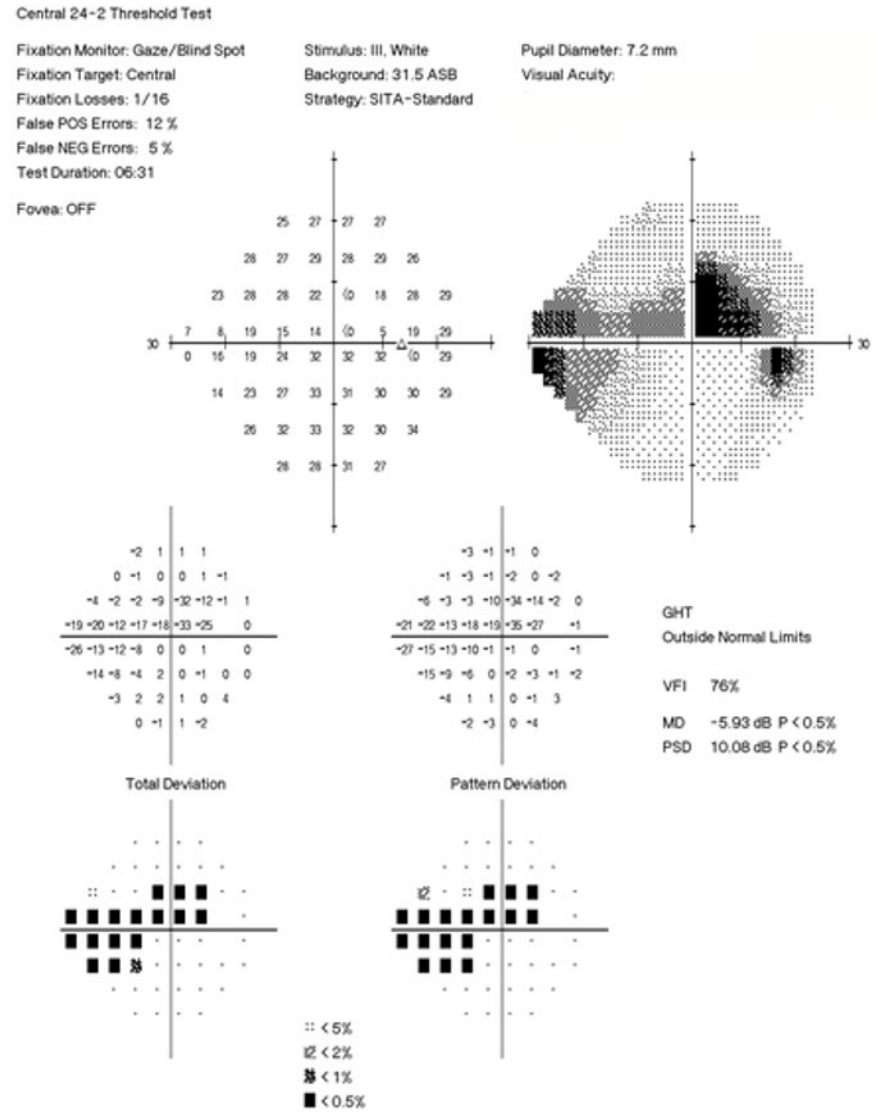
Glaucoma


ONH and RNFL OU Analysis:Optic Disc Cube 200x200
OD
OS
RNFL Thickness Map
350
175
0 µm
Average RNFL Thickness 80 µm 72 µm
RNFL Symmetry 89%
Rim Area 0.85 mm² 0.66 mm²
Disc Area 1.71 mm² 1.69 mm²
Average C/D Ratio 0.72 0.79
Vertical C/D Ratio 0.84 0.79
Cup Volume 0.442 mm³ 0.449 mm³
RNFL Deviation Map
Neuro-retinal Rim Thickness
µm
OD
OS
800
400
0
TEMP
SUP
NAS
INF
TEMP
Disc Center(1.08,-0.60)mm
Disc Center(-0.72,-0.33)mm
Extracted Horizontal Tomogram
RNFL Thickness
200
100
0 30 60 90 120 150 180 210 240
Extracted Vertical Tomogram
Diversified Distribution of Normals
NA 95% 5% 1%
RNFL Quadrants
S
T
N
I
112
59
61
89
98
55
63
71
RNFL Circular Tomogram
RNFL Clock Hours
71 128 136
75 68
56 50
46 65
50 100 117
109 108 76
74 71
55 49
61 45
94 71 48


Ganglion Cell OU Analysis: Macular Cube 512x128
OD
OS
OD Thickness Map
OS Thickness Map
225
150
75
0 µm
Fovea: 285, 73
Fovea: 264, 79
OD Deviation Map
OD Sectors
OS Sectors
OS Deviation Map
75
66
78
49
68
51
74
75
72
56
49
52
Diversified Distribution of Normals
95%
5%
1%
OD µm
OS µm
Average GCL + IPL Thickness 64 63
Minimum GCL + IPL Thickness 47 46
OD Horizontal B-Scan
BScan: 73
OS Horizontal B-Scan
BScan: 79
T
N

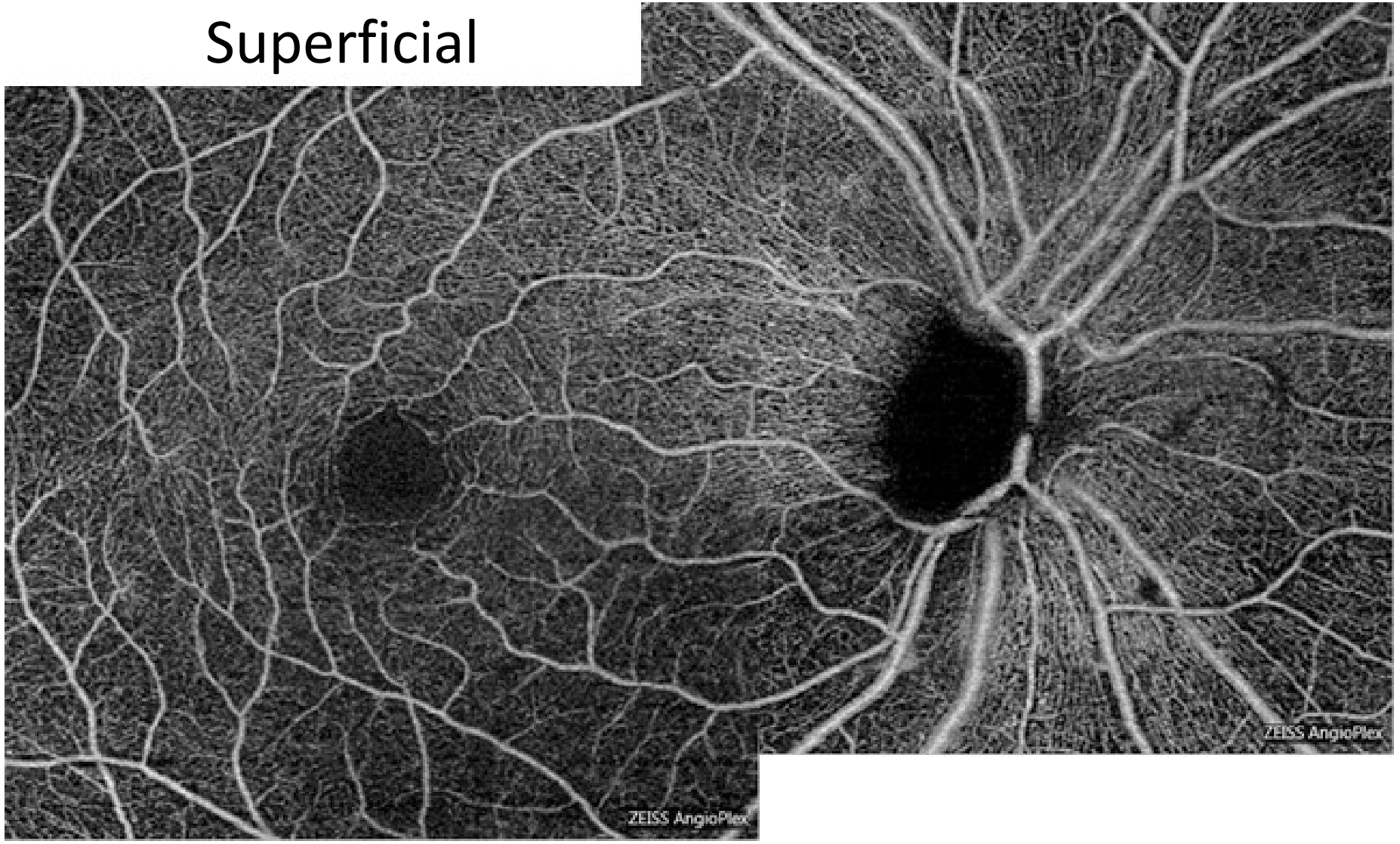
Glaucoma


Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/18
False POS Errors: 9 %
False NEG Errors: 0 %
Test Duration: 07:00
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 6.3 mm
Visual Acuity:
GHT
Outside Normal Limits
VFI 67%
MD -10.14 dB P < 0.5%
PSD 11.61 dB P < 0.5%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
< 1%
< 0.5%


Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 1/16
False POS Errors: 12 %
False NEG Errors: 5 %
Test Duration: 06:31
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 7.2 mm
Visual Acuity:
GHT
Outside Normal Limits
VFI 76%
MD -5.93 dB P < 0.5%
PSD 10.08 dB P < 0.5%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
< 1%
< 0.5%

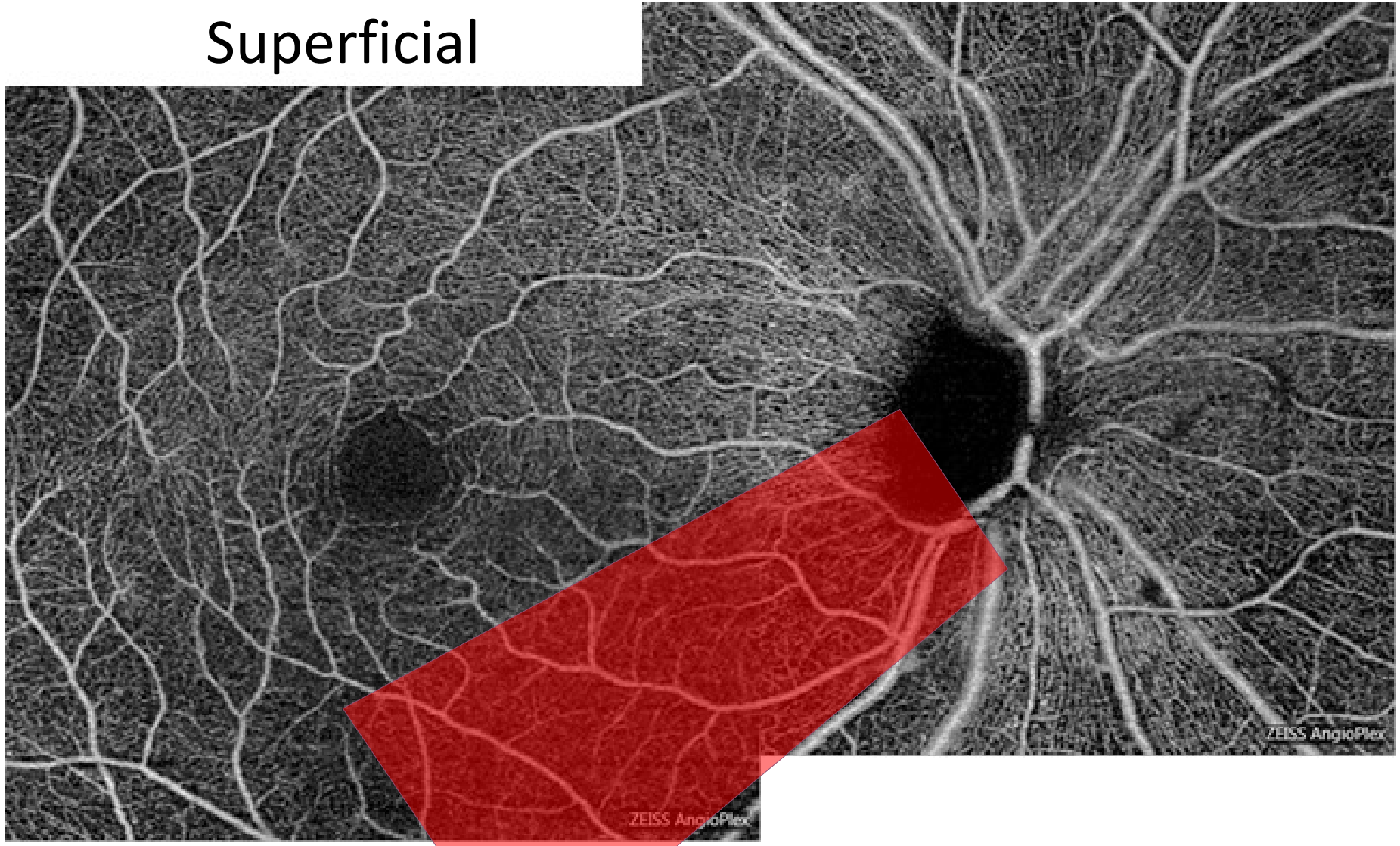
Glaucoma

Superficial

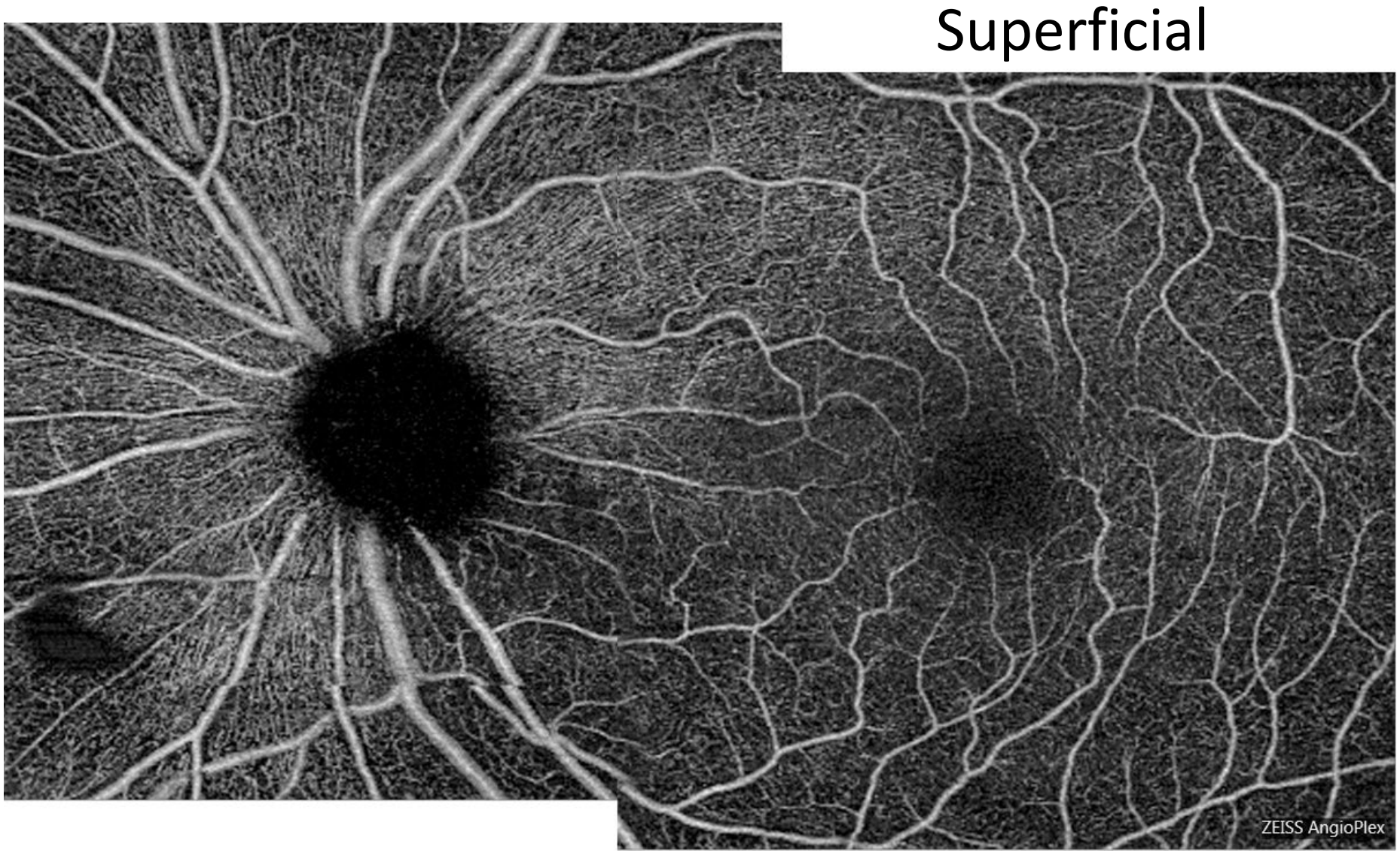


Glaucoma

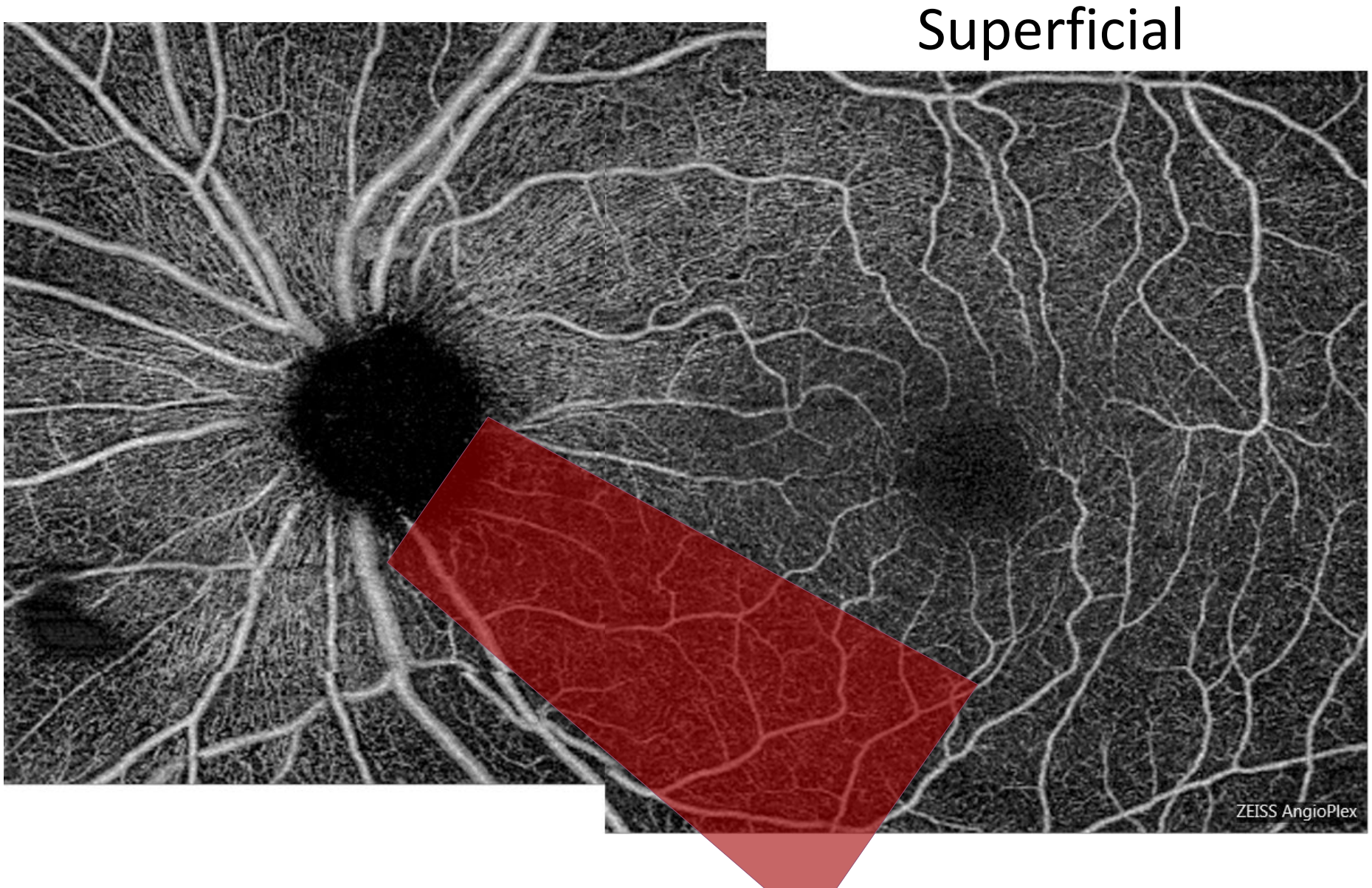
Superficial



Glaucoma

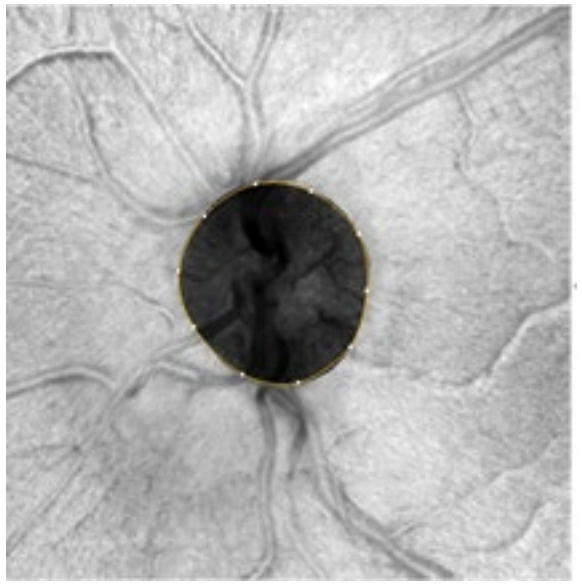


Glaucoma

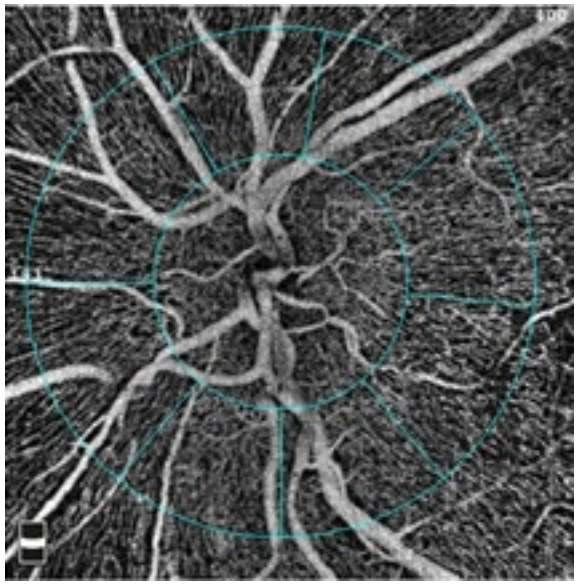


OCTA the New View (Normal Eye)

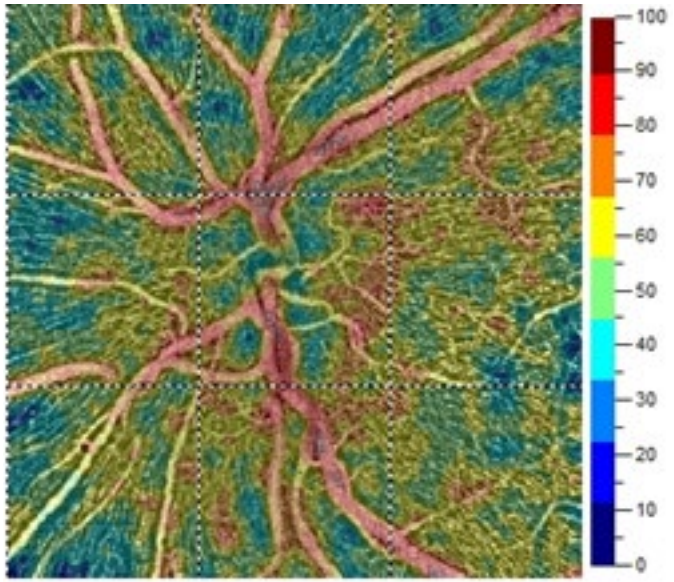
OCT En Face



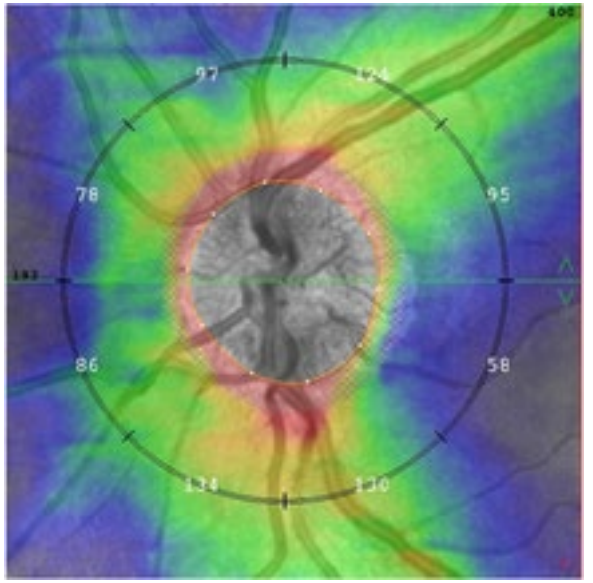
RPC



RPC Vessel density



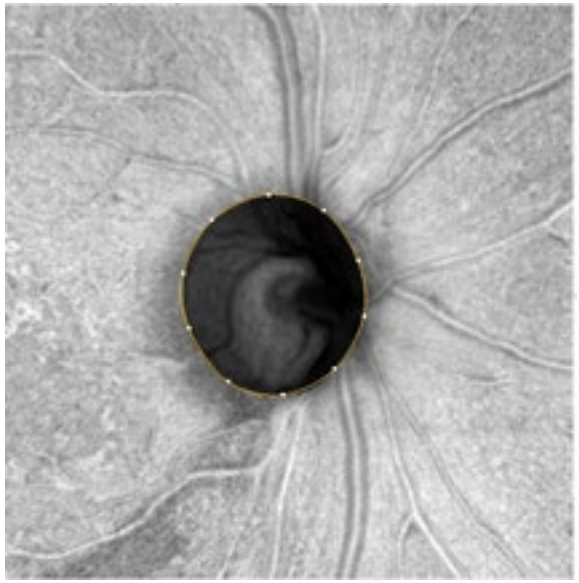
RNFL Thickness



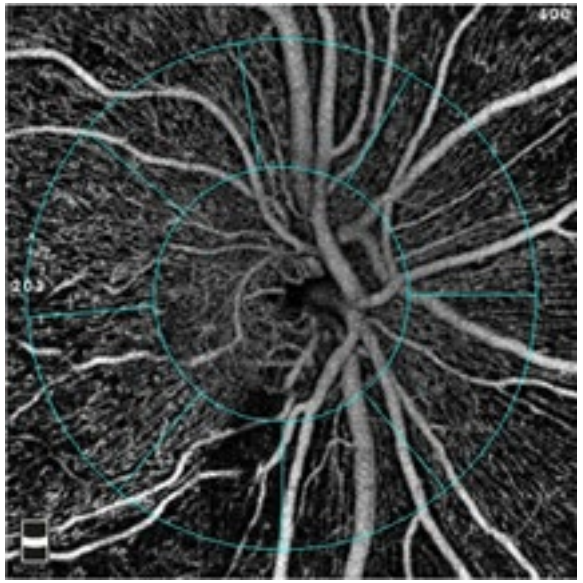
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

OCTA Moderate Glaucoma

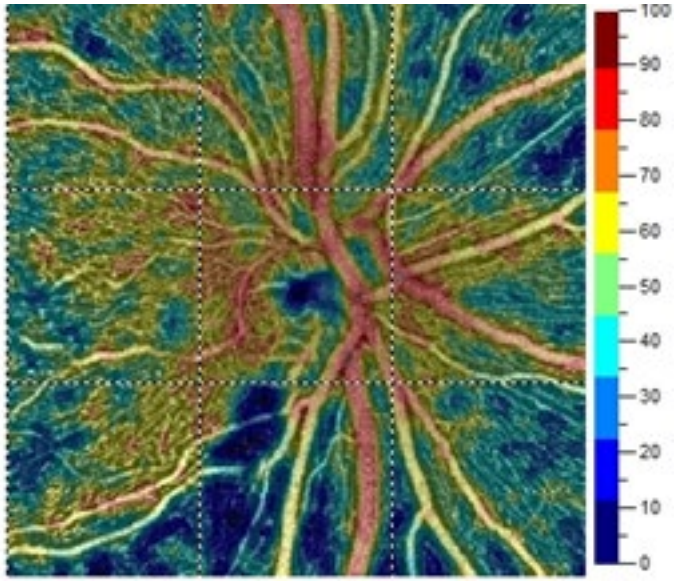
OCT En Face



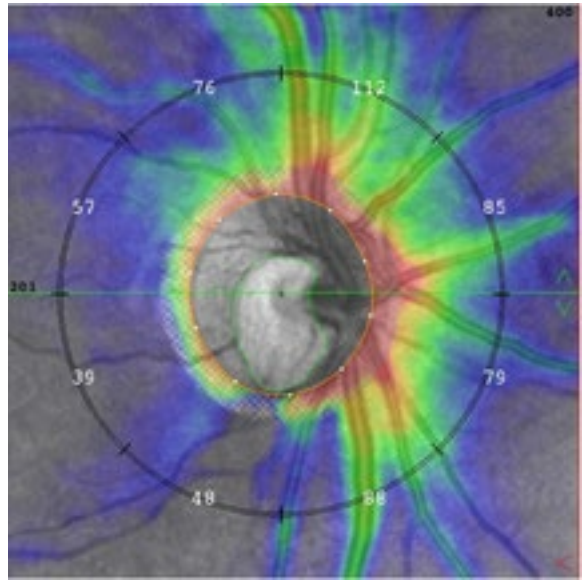
RPC



RPC Vessel density



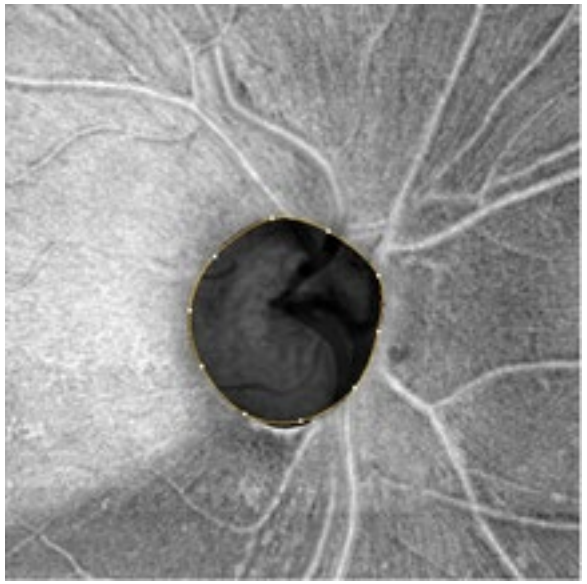
RNFL Thickness



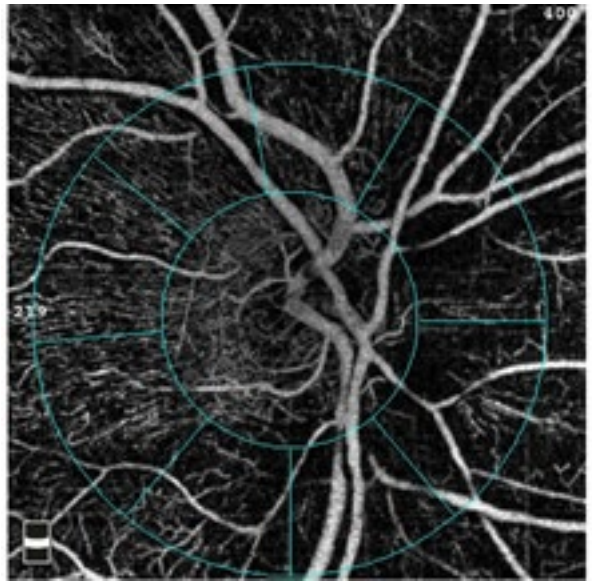
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Advanced Glaucoma

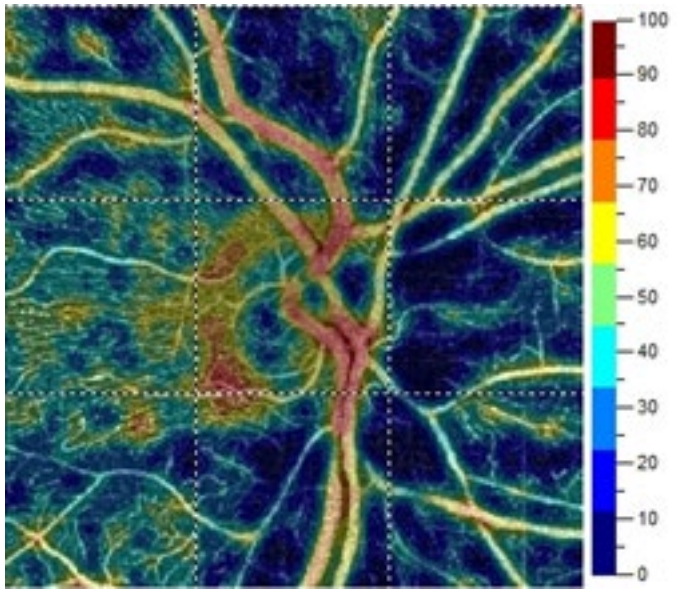
OCT En Face



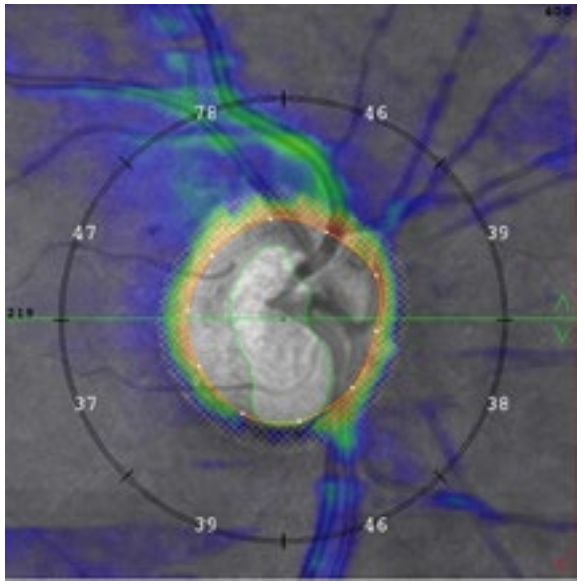
RPC



RPC Vessel density



RNFL Thickness



Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

OPHTHALMOLOGY VOLUME 127, ISSUE 4

Measuring Glaucomatous Focal Perfusion Loss in the Peripapillary Retina Using OCT Angiography

David Huang, MD et al

.

Participants

A total of 47 patients with primary open-angle glaucoma (POAG) and 36 normal participants were analyzed.

Methods

One eye of each subject was scanned using an AngioVue (Optovue, Fremont, CA) 4.5-mm OCTA scan centered on the disc.

En face nerve fiber layer (NFL) plexus angiogram was generated. With the use of custom software, a capillary density map was obtained by computing the fraction of area occupied by flow pixels after low-pass filtering by local averaging 21×21 pixels.

The low-perfusion map is defined by local capillary density below 0.5 percentile over a contiguous area above 98.5 percentile of the normal reference population. The LPA parameter is the cumulative area, and the FPL is the percent capillary density loss (relative to normal mean) integrated over the LPA.

Measuring Glaucomatous Focal Perfusion Loss in the Peripapillary Retina Using OCT Angiography

David Huang, MD et al

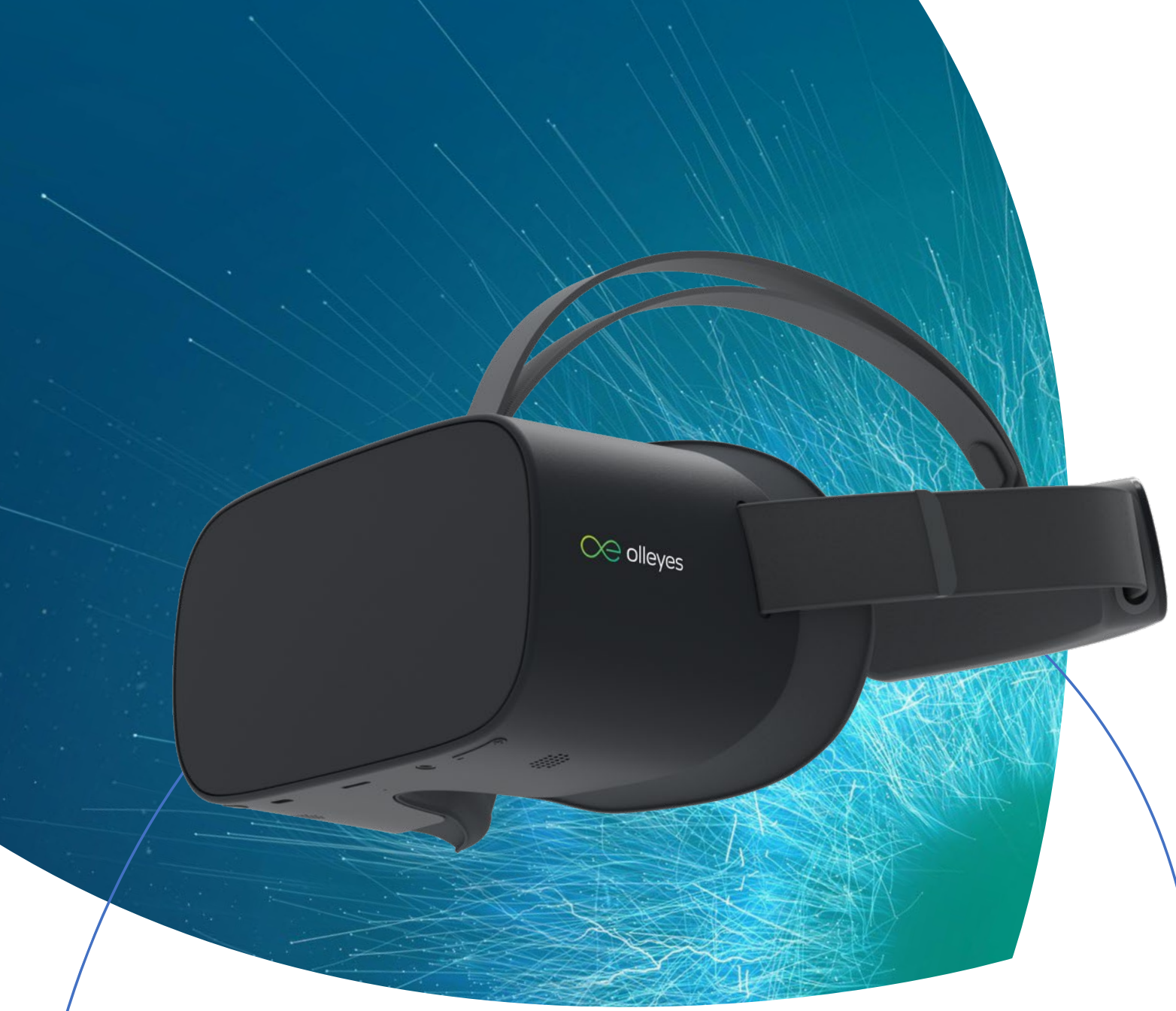
- Main Outcome Measures
- Peripapillary retinal LPA and FPL.
- Results
- Among patients with POAG, 3 had preperimetric glaucoma and 44 had perimetric glaucoma, with visual field (VF) mean deviation (MD) of −5.14±4.25 decibels (dB). The LPA was 3.40±2.29 mm^2 in those with POAG and 0.11±0.18 mm^2 in normal subjects ($P < 0.001$). The FPL was 21.8%±17.0% in those with POAG and 0.3%±0.7% in normal subjects ($P < 0.001$).
- The diagnostic accuracy as measured by the area under the receiver operating curve was 0.965 for both LPA and FPL, with a sensitivity of 93.7% at 95% specificity. The repeatability as measured by intraclass correlation coefficient was 0.977 for LPA and 0.958 for FPL.
- The FPL had excellent correlation with VF MD (Spearman's rho = −0.843), which was significantly ($P = 0.008$) better than the correlation between NFL thickness and VF MD (rho = 0.760). The hemispheric difference correlation between FPL and VF (Spearman's rho = 0.770) was significantly ($P < 0.001$) higher than the hemispheric difference correlation between LPA and VF (rho = 0.595).

Measuring Glaucomatous Focal Perfusion Loss in the Peripapillary Retina Using OCT Angiography
David Huang, MD et al

- Conclusions
- The low-perfusion map and LPA and FPL parameters are able to assess the location and severity of focal glaucoma damage with good agreement with VF.

Virtual Reality:
The Next Generation of Visual Field Testing

- **Melbourne Rapid Field**
- **Heru**
- **Virtual Visual Health**
- **OllEyes**



olleyes

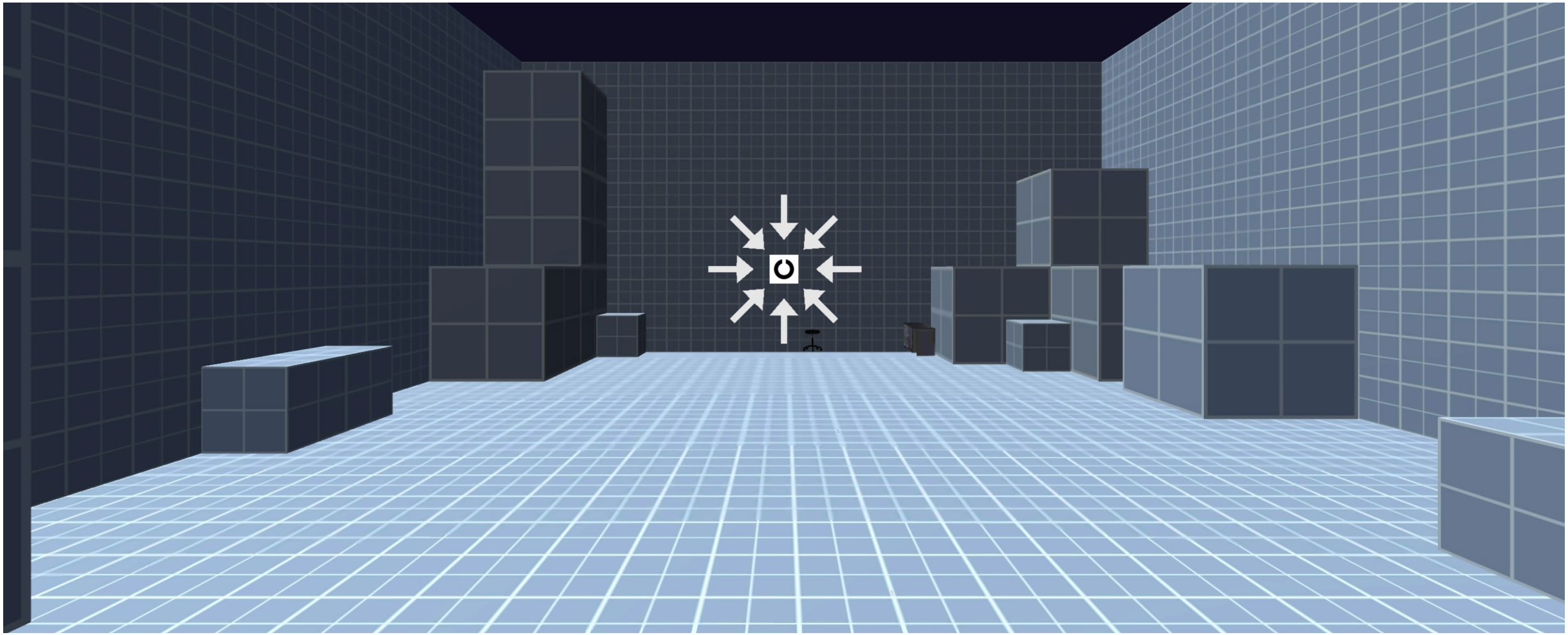
VisuALL VRP
Product Information

Our VisuALL field software

Visual Field

- Normal T - 10-2/24-2/30-2 (4min/eye)
- Pediatric Normal T - 10-2/24-2 (5-6min/eye)
- AVA Fast (+PEDs) - 24-2/30-2 (1.5min/Eye)
- AVA Standard (+PEDs) - 24-2/30-2 (2 min/eye)
- 150° Esterman Test 150°
- Ptosis Test

Olleyes Visual Acuity



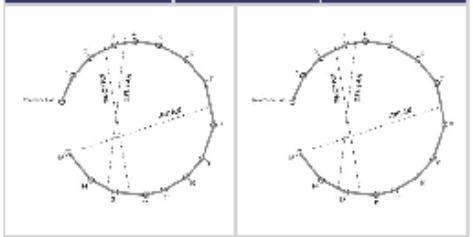
Color Vision

Visu**ALL VRP**

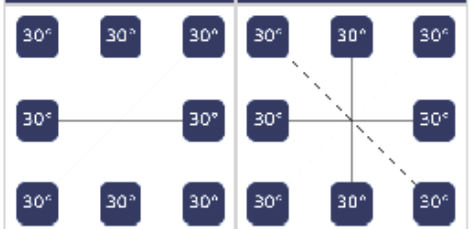
visuAll

name			examDate	duration
			03-12-2022	6:50
testId	dateOfBirth	gender	time	strategy
			2:04 PM	C-Suite

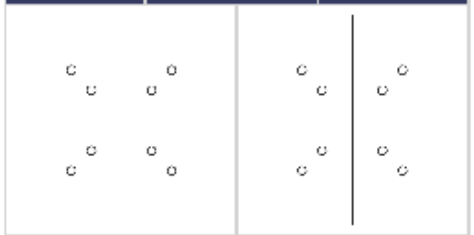
Color (1:16)		
Method	FMH Panel D15	
	Right	Left
Defect	False	False



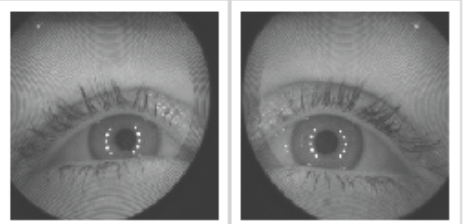
Extraocular Movement (2:24)	
Full ✓	
Right	Left
Full ✓	Full ✓



Visual Fields (0:24)		
Method	Suprathreshold (G-V)	
Full	Right ✓	Left ✓



Pupils (2:03)		
PERRL		
	Right	Left
Light	2.65	2.77
Dark	5.34	5.66
Shape		
React	4.00	4.48
APD		



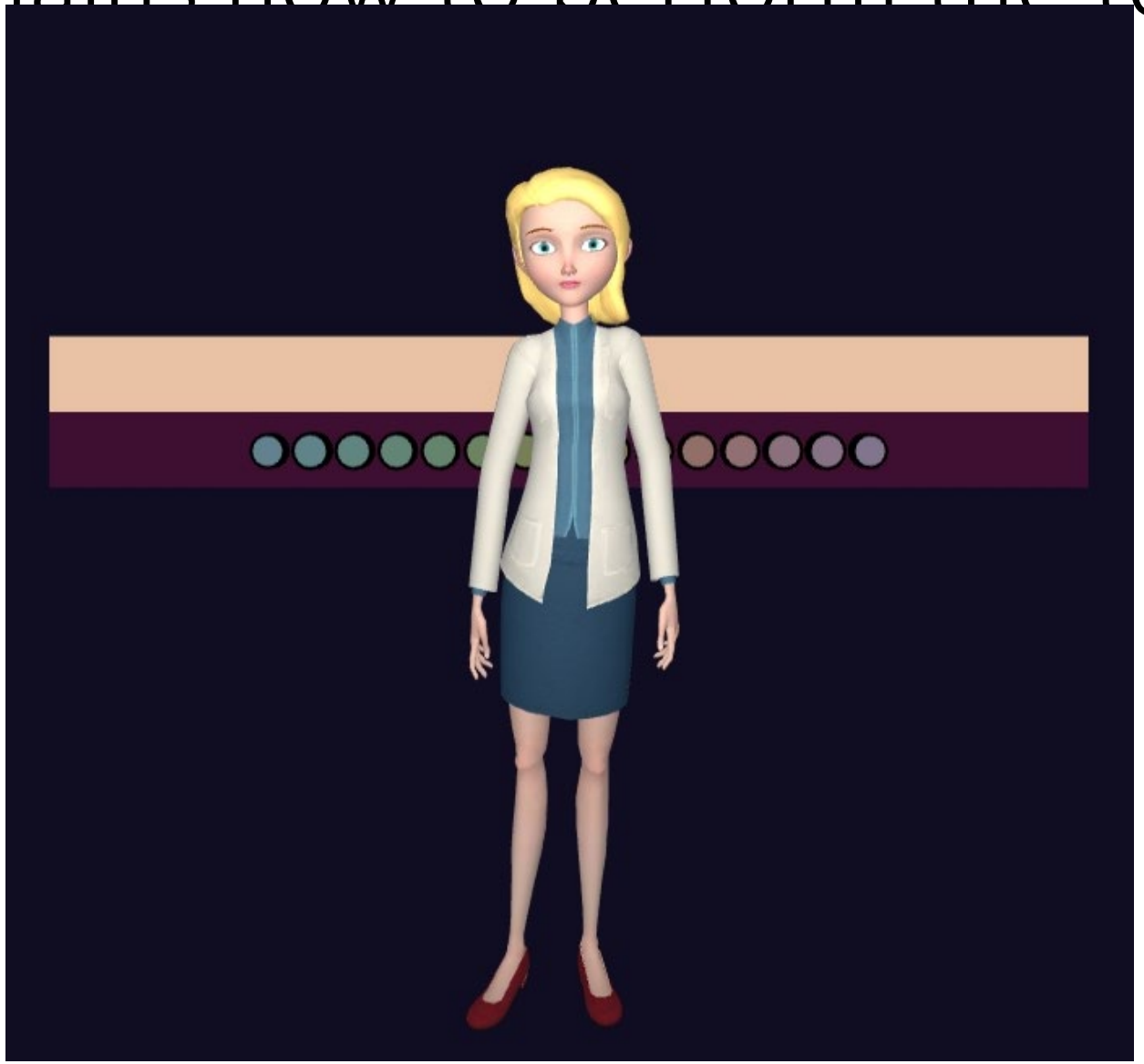
Visual Acuity (0:42)		
Method	LandoltC	
Correction		
Distance	Right	Left
cs	20/20	20/20
cc		
ph		
Near		
cs		
cc		

doctor's signature

office	operator	doctor
PRACTICE NAME PRACTICE ADDRESS STATE. 4444	One, Operator	McDoctor, Doctor

Comprehensive Test Suite Report

Annie explains how to perform the test



Glaukos Enters into a Collaboration and Marketing Agreement with Radius XR, Inc.

Advancing Next-Generation Wearable Patient Engagement and Diagnostic Technology Designed to Enable More Efficient Detection of Eye Diseases

Aliso Viejo, CA – July 17, 2023 – Glaukos Corporation (NYSE: GKOS), an ophthalmic medical technology and pharmaceutical company focused on novel therapies for the treatment of glaucoma, corneal disorders and retinal diseases, announced today that it has entered into a collaboration and marketing agreement with Radius XR, Inc., whereby Glaukos will become the exclusive sales agent to market, promote and solicit orders for the Radius XR™ wearable patient engagement and diagnostic system within the United States. Radius will continue to lead development and commercialization efforts for Radius XR.


Disinfectable
Soft Face Cushion
Portable
Balanced Design
alleyes
VisuALL ETS


1
VIRTUAL FIELD


OCTOPUS


Test NG
Status: Stopped
Questions: 121
Stm Size: 3
Stg Color: 36db
Speed: 0.7Sec
Threshold
Interactive Fast Threshold
Superior_50
Ptosis 9 pt
30-2
20 pt screen
N30-1
24-2
User Presets
M.M.D
MICRO MEDICAL DEVICES


iPTS 2000

Radius XR Strategic Imperatives

Elevate engagement to breakthrough competitive and cluttered landscape

- Deployment strategy leveraging GKOS relationships, products, and IG Initiatives
- Utilize tip of the sphere influencers to move market

Prove efficacy

- Utilize study data to establish equivalency with HFA
- Leverage clinical data to drive differentiation with “other headsets”

Capitalize on practice efficiency

- Elevate value proposition of patient engagement that can deliver greater efficiencies to a practice
- Identify and share case studies of practices that have incorporated Radius XR into their standard of care

- Radius is a portable vision diagnostic and patient engagement system that combines
  - Medical-grade diagnostics
  - Business management
  - Patient education tools
- In a single wearable AR/VR device
- The total hardware and software system helps medical professionals:
  - Diagnose patients accurately
  - Grow their eyecare practices
  - Enhance patient engagement
  - Reduce staff workload by enabling patients to perform self-guided vision exams with minimal supervision

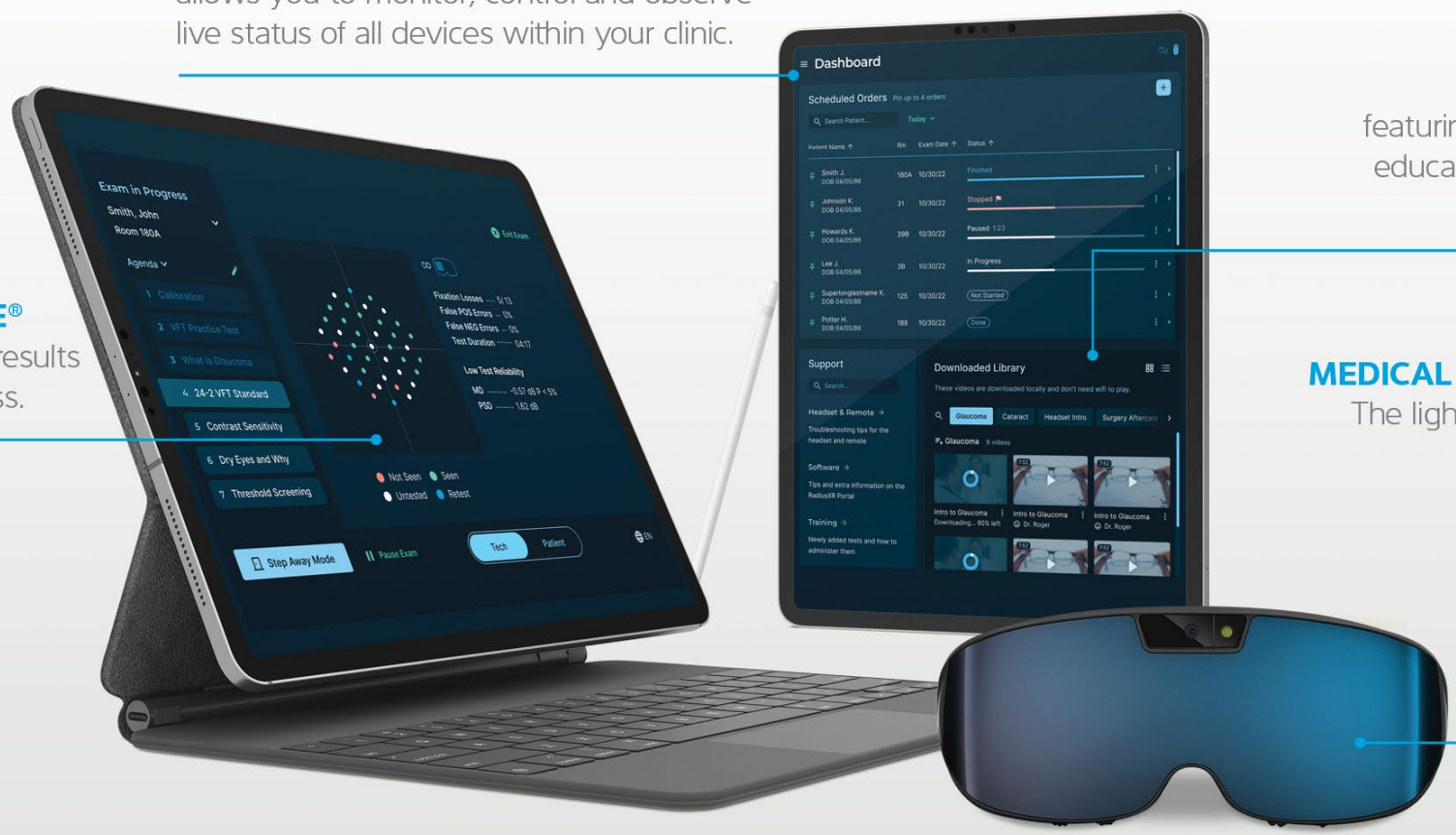
GLAUKOS & radius XR

RADIUS IN-CLINIC DASHBOARD

allows you to monitor, control and observe live status of all devices within your clinic.

RADIUS IN-LIVE®

reliability indices, results and exam progress.



EYEVIA®

featuring immersive patient education, personalized for your practice.

MEDICAL GRADE HEADSET

The lightest ever. Only 6 oz.

Visual Field Tests:

- 24-2 RATA Standard
- 24-2 RATA Fast
- 10-2 RATA Standard
- Radius RAPID

Multimodal Diagnostic + Business Platform

Vision Tests

+ Visual Field
  - 24-2 RATA Standard
  - 24-2 RATA Fast
  - 10-2 Standard
  - Radius RAPID (2-Zone Threshold Screener)

Practice Management

- Patient Education
- Media Mgmt
- Workflow Tools
- Patient Intake
- EHR Integration
- Remote Patient Monitoring

figma.com

Patients / Smith, Johnson

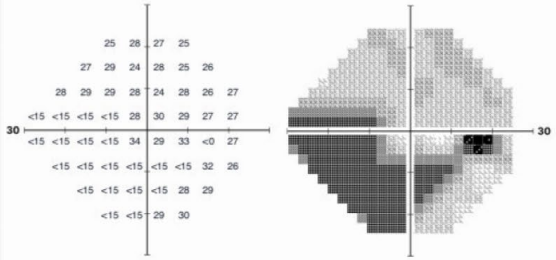
Name: N/A
Patient ID:
DOB: N/A

24-2 Threshold Test

Fixation Monitor: Blind Spot
Fixation Target: Central
Fixation Losses: 2 / 16
False POS Errors: 1 %
False NEG Errors: 19 %
Test Duration:

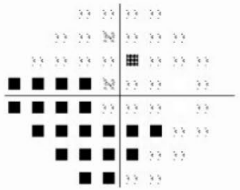
Stimulus: III, White
Background: 31.5 ASB
Strategy: Radius Adaptive

Date: 09/22/2022
Time: 04:35 AM
Age: 74

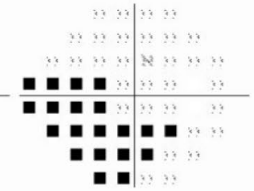


VFI N/A
MD -8.01 dB P < 0.5%
PSD 6.93 dB P < 0.5%

Total Deviation



Pattern Deviation



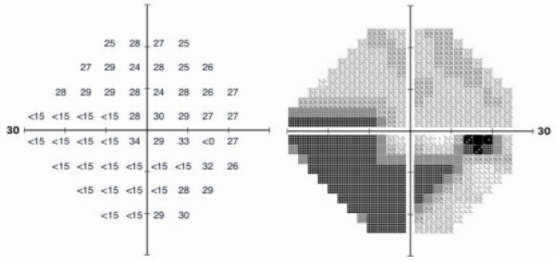
Name: N/A
Patient ID: OD1
DOB: N/A

24-2 Threshold Test

Fixation Monitor: Blind Spot
Fixation Target: Central
Fixation Losses: 2 / 16
False POS Errors: 1 %
False NEG Errors: 19 %
Test Duration:

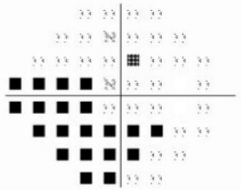
Stimulus: III, White
Background: 31.5 ASB
Strategy: Radius Adaptive

Date: 09/22/2022
Time: 04:35 AM
Age: 74

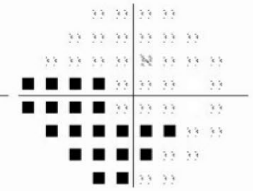


VFI N/A
MD -8.01 dB P < 0.5%
PSD 6.93 dB P < 0.5%

Total Deviation



Pattern Deviation



Name: N/A
Patient ID: OD1

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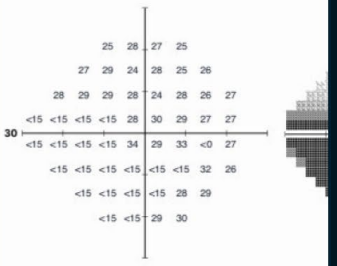
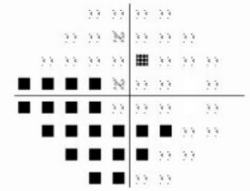
Fixation Monitor: Blind Spot
Fixation Target: Central
Fixation Losses: 2 / 16
False POS Errors: 1 %
False NEG Errors: 19 %
Test Duration:



Total Deviation



24-2 OD

Standard

Fast

Exam

Change Analysis

3 Selected

Merge Baseline

Merge Post Baseline

11/23/2022 Stnd	11/23/2022 Fast	11/23/2022 Stnd	11/23/2022 Fast	11/23/2022 Stnd	11/23/2022 Fast	11/23/2022 Stnd	11/23/2022 Fast
FL 5/13	FL 5/13	FL 5/13	FL 5/13	FL 5/13	FL 5/13	FL 5/13	FL 5/13
FP 14%	FP 14%	FP 14%	FP 14%	FP 14%	FP 14%	FP 14%	FP 14%
FN 16%	FN 16%	FN 16%	FN 16%	FN 16%	FN 16%	FN 16%	FN 16%

CORNEAL HYSTERESIS:
The Newest Disruptive Technology
In Glaucoma

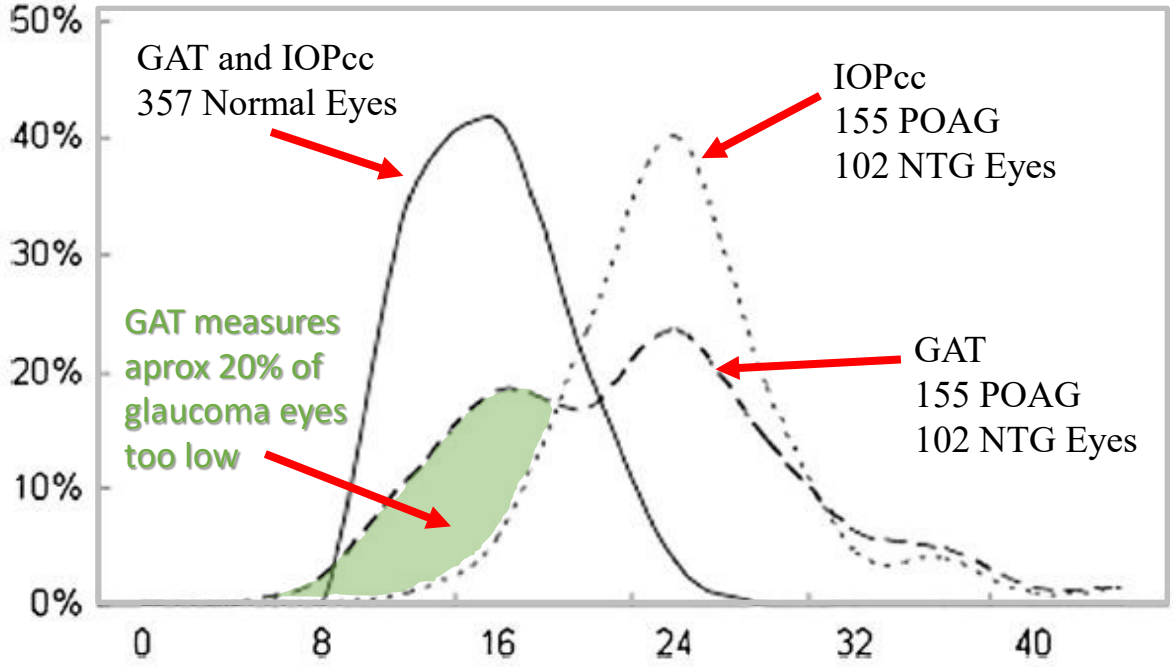
- **2002: Clinical research with ORA commences**
- **2005: The 1st generation ORA was made commercially available**
- **2012: Generation II ORA was launched**
- **3rd Generation "ORA G3" introduced September 2015**

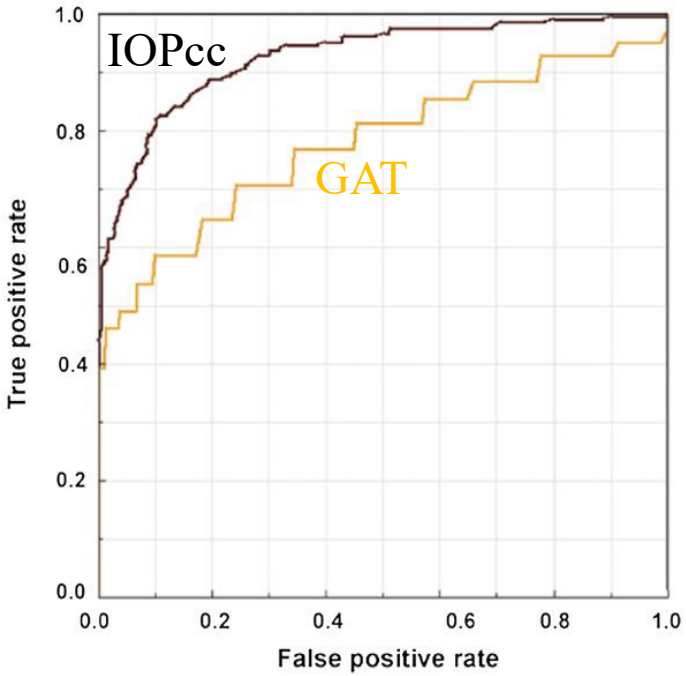
  Measures:
  - Corneal Hysteresis (CH)
  - Goldmann-correlated IOP (IOP_g)
  - Corneal compensated IOP (IOP_{CC})

IOPcc Key Benefit #2
IOPcc is superior for glaucoma risk assessment

IOPcc is clinically superior to GAT, other NCTs, and iCare because it is more associated with Glaucoma risk, status of glaucoma, and glaucoma progression

"the results of this study suggest that IOPcc may represent a superior test for the evaluation of glaucoma"





AUC .93 for IOPcc vs .78 for GAT

Not shown here from this study:

- **39%** of NTG eyes would be re-classified as POAG with IOPcc
- Average IOPcc was **5 mmHg higher** than GAT in NTG eyes

Goldmann applanation tonometry compared with corneal-compensated intraocular pressure in the evaluation of primary open-angle Glaucoma
Joshua R Ehrlich, Nathan M Radcliffe, and Mitsugu Shimmyo

Corneal Compensated IOP

- Superior to Goldmann in all forms of post Refractive Surgery IOP measurements

Central Corneal Thickness and Corneal Hysteresis Associated With Glaucoma Damage

NATHAN G. CONGDON, MD, MPH, AIMEE T. BROMAN, MA, KAREN BANDEEN-ROCHE, PHD, DAVINDER GROVER, MPH, AND HARRY A. QUIGLEY, MD

- 230 POAG or suspected POAG patients were included in the study
- 3 years or more FU
- Minimum 5 VF exams

	OR	LCL	UCL	*P*-value
Age per year <65	1.12	1.01	1.24	.03
Age per year >65	1.08	1.01	1.15	.02
GAT IOP per mmHg	1.22	0.95	1.58	.12
Treatment	1847.6	3.16	10^6	.02
IOP by treatment interaction	0.79	0.61	1.03	.08
CCT per 100 microns	1.65	0.66	0.98	.30
Years with glaucoma	1.00	0.96	1.04	.98
Baseline IOP	0.99	0.93	1.06	.79
CH per mmHg	0.81	0.66	0.98	**.03**

GAT Goldmann Applanation Tonometry; IOP intraocular pressure; OR odds ratio; LCL lower confidence limit; UCL upper confidence limit. CCT Central Corneal Thickness; CH Corneal Hysteresis

Conclusions: Corneal Hysteresis was the parameter most associated with progressive field worsening

Congdon NG et al. *Am J Ophthalmol.* 2006;141:868-875.

BJO

Significance of corneal biomechanical properties in patients with progressive normal-tension glaucoma

Jong Hyuk Park, Roo Min Jun and Kyu-Ryong Choi

Br J Ophthalmol published online January 2, 2015

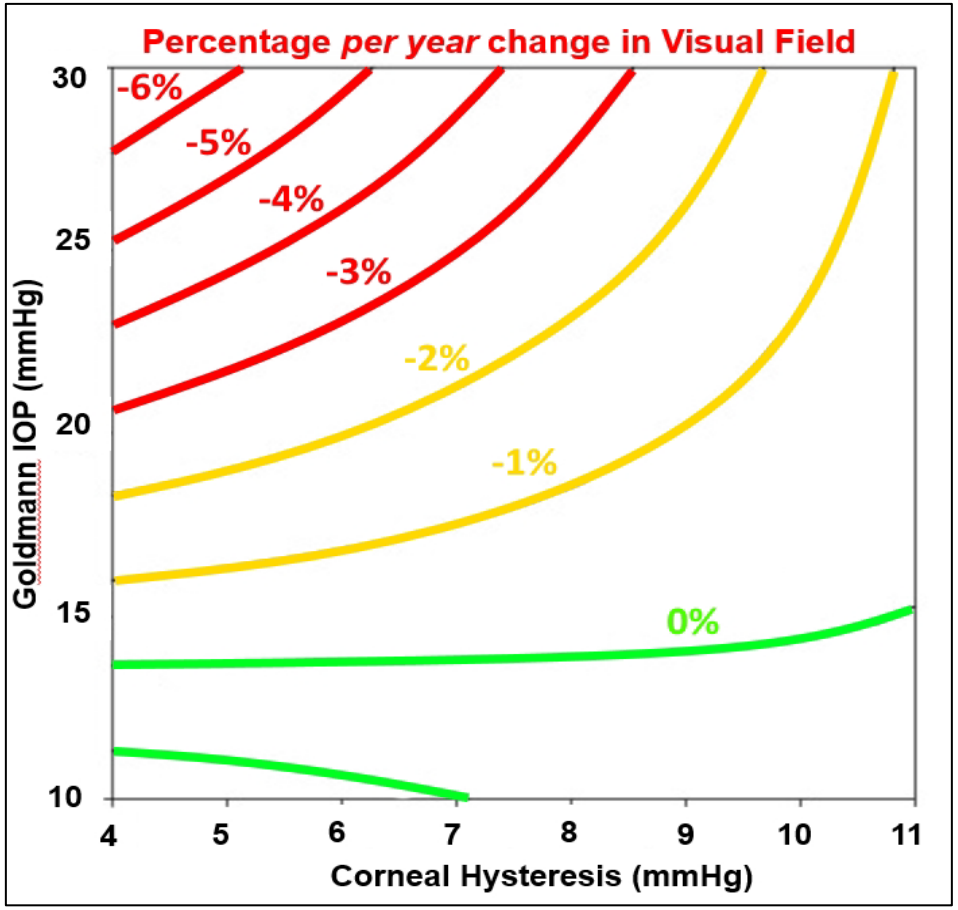
	β (95% CI)	*P-Value*
Baseline VF MD (dB)	1.18 (0.96 to –1.44)	0.12
CCT (µm)	0.99 (0.97 to 1.01)	0.35
Subfoveal choroidal thickness	0.99 (0.98 to 1.00)	0.08
RNFL thickness (average)	0.96 (0.92 to 0.99)	0.04
RNFL thickness (temporal)	0.97 (0.94 to 1.01)	0.09
RNFL thickness (inferior)	0.98 (0.96 to 1.01)	0.13
Corneal Hysteresis (mmHg)	0.32 (0.17 to 0.62)	<0.01

- 82 progressing eyes of NTG patients under treatment
- Eyes were split into two groups: higher & lower than average CH
- Of the **39 eyes with low CH, 26 (66.7%) showed progression**
- Of the **43 eyes with high CH, 15 (34.9%) showed progression**

These findings suggest that CH can be used as one of the prognostic factors for progression, independent of corneal thickness or IOP

Park Et. Al Br J Ophthalmol. 2015 Jan 2. pii: bjophthalmol-2014-305962. doi: 10.1136/bjophthalmol-2014-305962.

Corneal Hysteresis as a Risk Factor for Glaucoma Progression: A Prospective Longitudinal Study



The relationship between CH and IOP is complex (*and important*):

For eyes with lower CH, the impact of IOP was significantly larger than in eyes with higher CH levels.

"The Effect of IOP on rates of progression was *dependent upon Corneal Hysteresis*"

Medeiros FA et al. *Ophthalmology*. 2013;120:1533-1540.

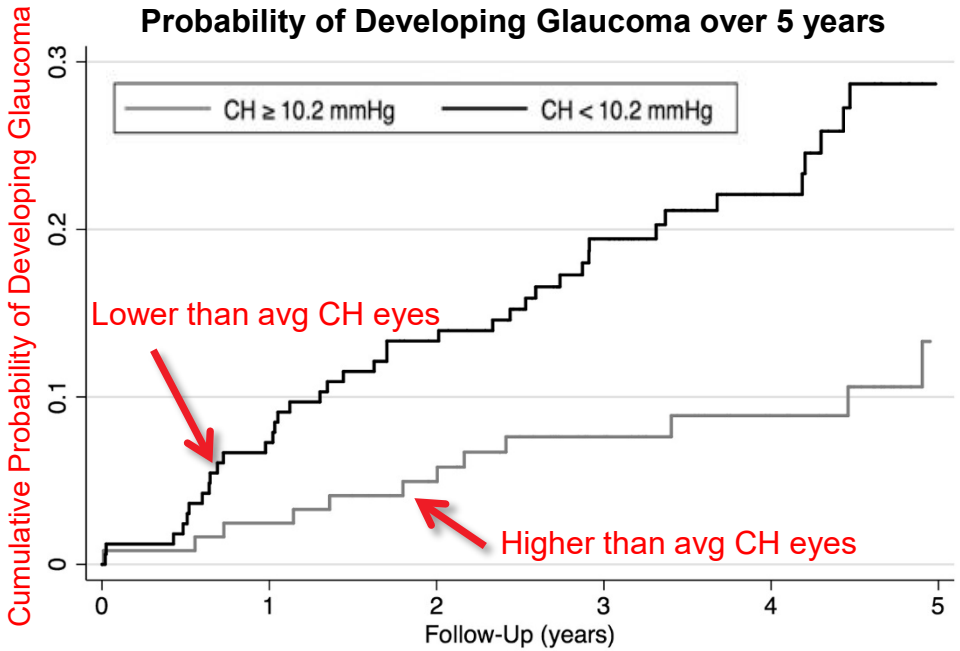
A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor for Predicting Development of Glaucoma

CAROLINA N. SUSANNA, ALBERTO DINIZ-FILHO, FÁBIO B. DAGA, BIANCA N. SUSANNA, FEILIN ZHU, NARA G. OGATA, AND FELIPE A. MEDEIROS

Purpose: To investigate the role of CH as a risk factor for **development** of glaucoma in a prospective longitudinal study.

Results: Fifty four (19%) of the 287 eyes developed repeatable visual field defects during a 4 year follow-up.

CH was *independently* predictive of conversion to glaucoma even when adjusted for age, IOP, and CCT.

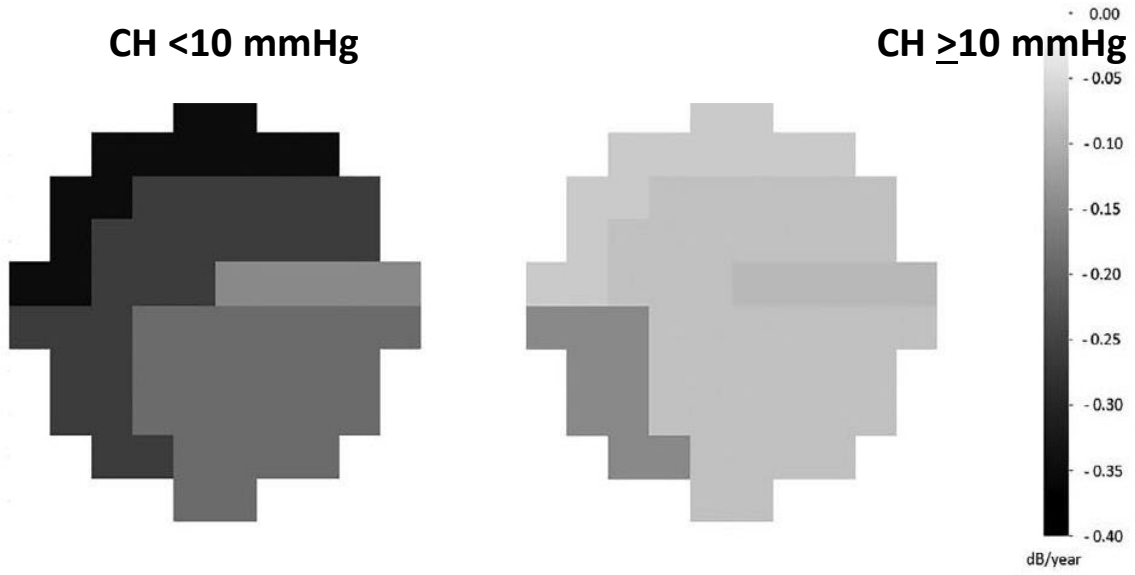


Each 1mmHg lower CH was associated with an increase of 21% in the risk of developing glaucoma during follow up

A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor for Predicting Development of Glaucoma
Am J Ophthalmol. 2018 Mar; 187: 148–152. Feilin Zhu , Alberto DinizFilho, Linda M. Zangwill , Felipe A. Medeiros

CH as a Risk Factor for Central Visual Field Progression in Glaucoma

Zonal rates of change (dB/y) in the 10-2 test



"These results show that CH is a significant predictor of glaucomatous central and peripheral VF progression. Given the substantial influence of central VF impairment on the performance and quality of life, our findings suggest that CH should be considered in the risk assessment of disease progression in clinical practice."

Kamalipour A, Moghimi S, Eslani M, Nishida T, Mohammadzadeh V, Micheletti E, Girkin CA, Fazio MA, Liebmann JM, Zangwill LM, Weinreb RN. A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor of Central Visual Field Progression in Glaucoma. Am J Ophthalmol. 2022 Mar 10;240:159-169. doi: 10.1016/j.ajo.2022.02.025. Epub ahead of print. PMID: 35278360.

INTRODUCING

Tono-Vera® Tonometer

and ReichertSync® Software

Canada Product Launch Presentation

Introducing…

Tono-Vera® Tonometer

Truly Objective Tonometry

Your guided view to precise IOP measurements

- Tono-Vera is Reichert's newest handheld tonometer used during routine eye exams by eyecare professionals: Opticians, Optometrists, Ophthalmologists and eyecare technicians
- The device measures intraocular pressure (IOP) of the human eye
- Utilizes rebound technology, which takes an IOP measurement quickly, eliminating the need for topical anesthesia
- ActiView™ Positioning System: ***quickly*** guides user to the apex of the cornea, providing ***confidence*** in IOP readings
- Automatically measures when aligned, providing a more objective and repeatable result in as few as **three measurements**
- Measurements are made using Ocu-Dot tonometer probes which are sanitized and single use. One probe per patient set of eyes
- The Tono-Vera System includes a charging* base that **conveniently stores and efficiently dispenses Ocu-Dot® Tonometer Probes**
- Features built-in Bluetooth® wireless data transmission via ReichertSync®
- Available in two models; Rechargeable or AA Battery

**rechargeable model only*

Camera view of the eye **with interactive alignment system** guides the user to the ideal distance and centration

When properly positioned, **takes IOP measurements automatically**

Reliable IOP results in **as few as 3 measurements.** Ring color indicates the **reliability of the measurement**

Innovative **FlexiSoft™ Forehead Rest** designed for more control and comfort

Differentiating Features	Reichert® Tono-Vera®	icare® ic100	CUSTOMER *Value*
Positioning Guide	ActiView™ Positioning System	None	Proper positioning is the key to reliable IOP measurements
Minimum Number of Measurements Required	3	6	Intelligent averaging permits accurate and reliable results in fewer measurements
Measurement Mode	Auto and Manual Modes	Manual Mode	True automatic measurement ensures faster and more reliable IOP results
Base & Storage Solutions	Included multi-purpose base	Suboptimal accessory	Perfect for docking and charging* your device while also storing and dispensing Ocu-Dot Probes
Battery	Rechargeable ***or*** Four- AA batteries option	Four AA Batteries	Battery options to meet your needs. Interchangeable battery solution for ultimate flexibility
Screen	Back of device	Lefthand side of device	Comfortable viewing for left or right-handed users
Bluetooth	Yes	No	Convenient Data Transfer, Eliminates transcription errors

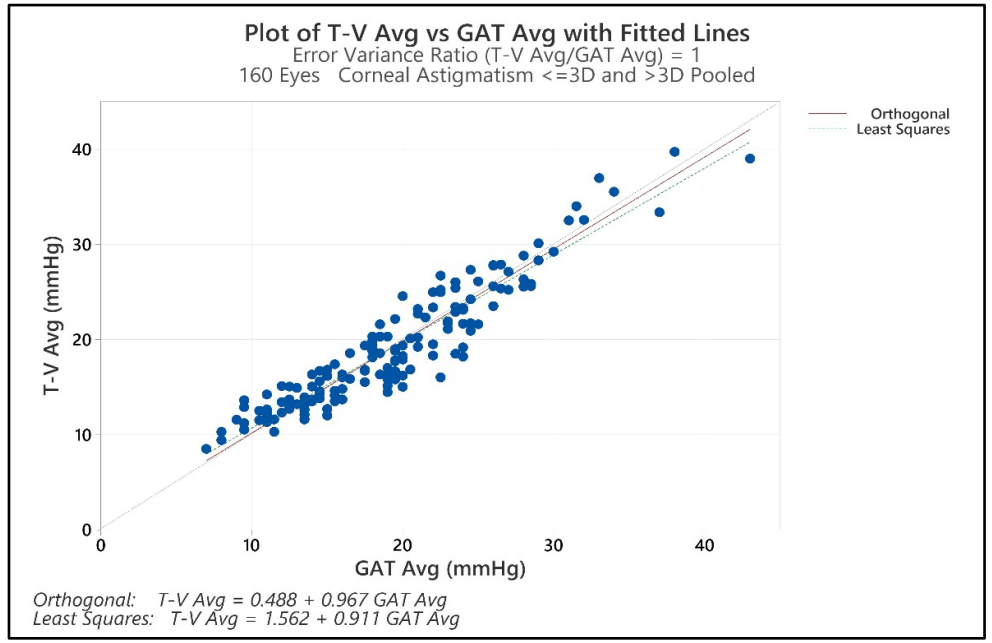
Tono-Vera® Tonometer – **Clinical Performance**

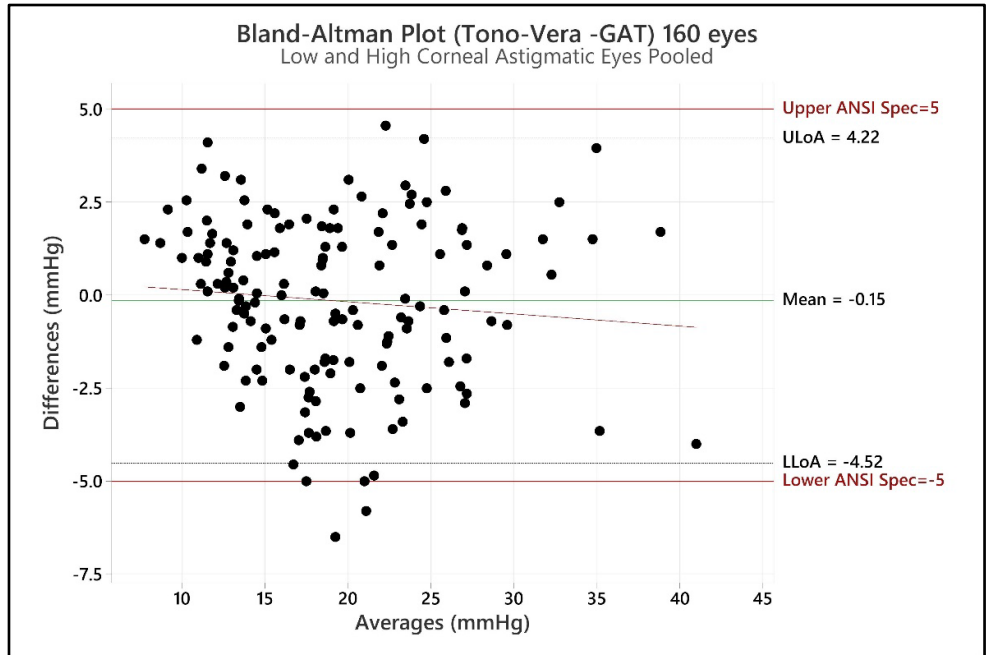
Results from FDA ANSI Z80.10 & ISO 8612-2009 trial

IOP Range (mmHg) Defined By GAT		Astigmatism	N Eyes	Average GAT IOP (mmHg)	Average TV IOP (mmHg)	Measurement Pair Difference > ±5 mmHg	Percentage of Measurement Pair Differences > ± 5 mmHg
Low IOP	7 to 16	≤3D	49	12.7	13.3	0	0.00%
Medium IOP	>16 to < 23	≤3D	43	19.6	19.1	1	2.27%
High IOP	≥ 23	≤3D	45	27.4	26.7	1	2.17%
Low IOP	7 to 16	>3D	11	13.1	12.9	0	0.00%
Medium IOP	>16 to < 23	>3D	10	19.4	18.2	0	0.00%
High IOP	≥ 23	>3D	2	27.0	26.3	0	0.00%
Total			160	19.17	19.03	2	1.25%

Average IOP values from Goldmann Applanation and Tono-Vera were not significantly different (19.17 and 19.03 respectively, p=0.40, paired t-test). The total least squares regression analysis indicated strong agreement between the two tonometers (slope +0.97, offset +0.49 mmHg, standard deviation 2.11 mmHg). Only 2 IOP measurement pairs that exceeded the + 5 mmHg limits of agreement required in ANSI Z80.10-2014 and ISO 8612-2009, which is within the range of acceptability specified in the standards.

Tono-Vera meets the requirements of ANSI Z80.10-2014 and ISO 8612-2009, demonstrating accuracy comparable to Goldmann tonometry.





Tonography: The New Horizon in Glaucoma Managment

Setting a Target Outflow Facility Value

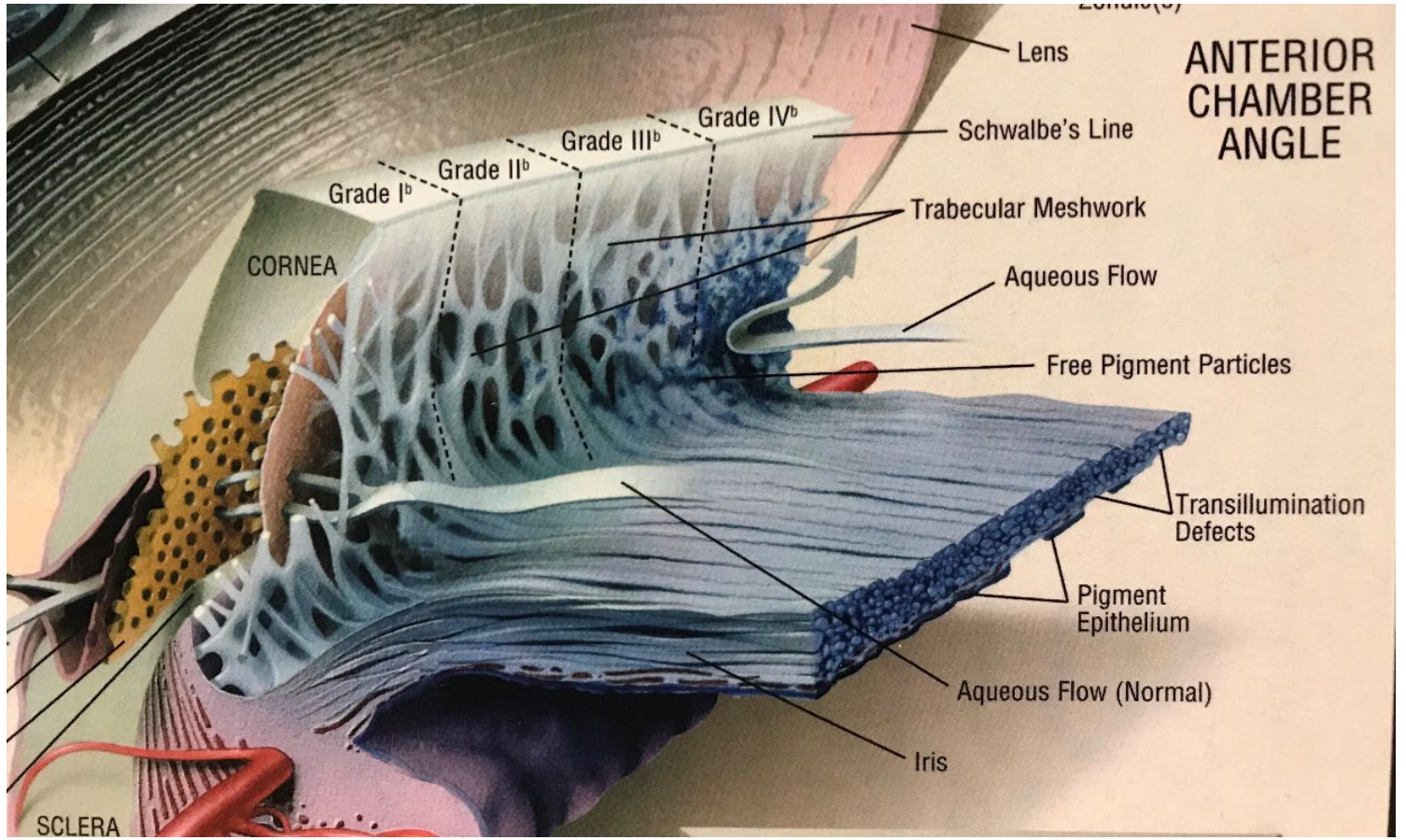
Is Measuring IOP Alone Enough?

- Does Not Validate Therapeutic Response
- Does Not Predict Risk
- Only Valid if You Obtain Multiple Measurements Over 24 Hours
- Patients with Untreated Glaucoma Can Have Normal IOP

Baltimore Eye Survey, Johns Hopkins University Study

Aqueous Humor Dynamics

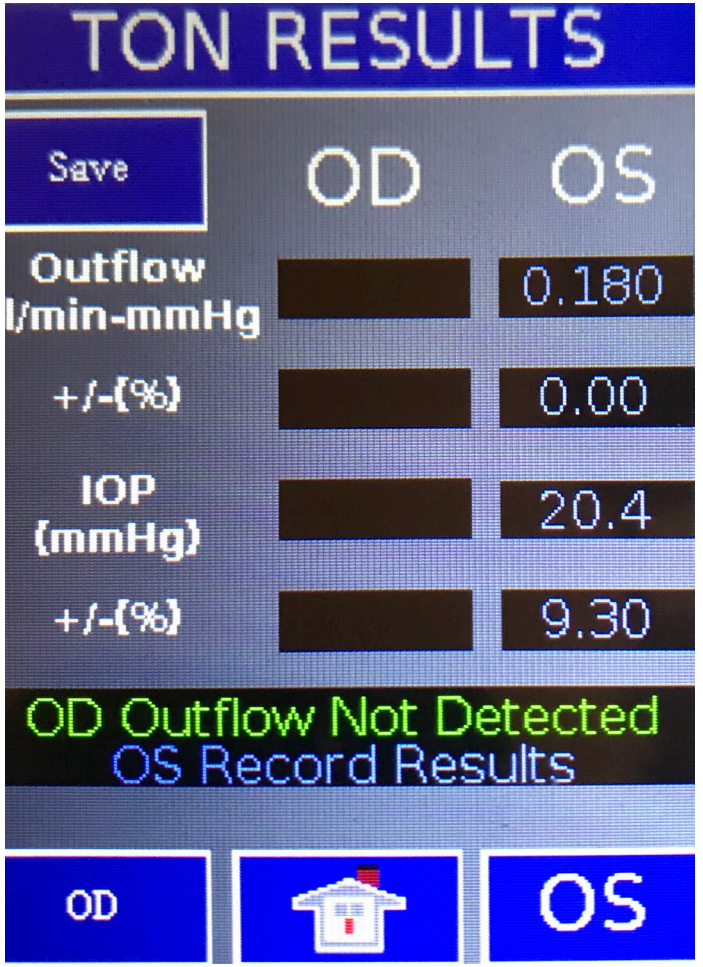
Aqueous Humor Outflow Pathway



Falck Medical Multisystem

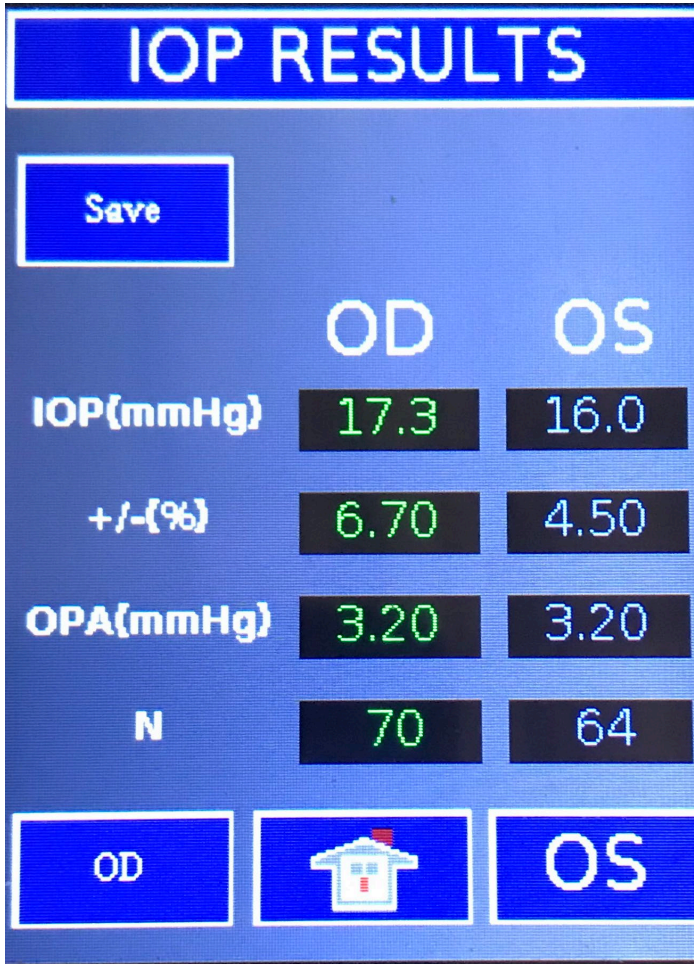
TONOGRAPHY

- ✓ Optical Aqueous Humor Outflow Measurement.
- ✓ Aqueous Outflow Decreased in Glaucoma.
- ✓ Decreased Outflow = Increased TM Resistance.
- ✓ Decreased Outflow = Increased IOP Fluctuation.
- ✓ Document Therapeutic Efficacy of Outflow Interventions.
- ✓ Document Need for Additional Intervention.
- ✓ Glaucoma risk assessment.



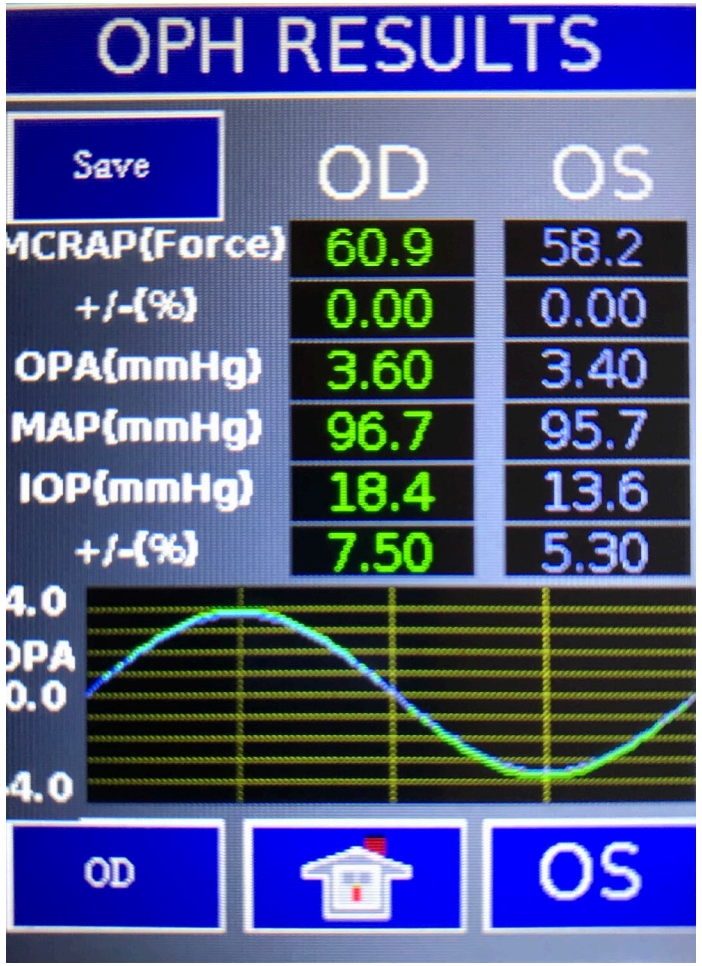
Intraocular Pressure

- ✓ Optical Applanation Measurement
- ✓ Compensates for Corneal Biomechanics
- ✓ Multiple Serial IOP Measurements – N Value
- ✓ Systolic and Diastolic IOP
- ✓ Average IOP Displayed
- ✓ IOP Variation with Cardiac Cycle - OPA
- ✓ Precision Displayed



OPHTHALMODYNAMOMETRY

- ✓ Mean Central Artery Pressure (MCRAP) measurement.
- ✓ Data Captured During Multiple Cardiac Cycles.
- ✓ Mean Arterial BP Displayed.
- ✓ MCRAP – IOP = True Ocular Perfusion Pressure (OPP).
- ✓ Reduced OPP is a risk factor for glaucoma progression.
- ✓ Abnormal OPH - Increased Risk of Stroke



Aqueous Humor Dynamics

- IOP is directly related to aqueous humor production and inversely related to aqueous humor outflow.
- The rate of aqueous humor production is not constant.
- The rate of aqueous humor outflow is constant.
- IOP varies throughout the day.
- The variability of aqueous humor production is the source of IOP variation.
- Using IOP alone can lead to the incorrect conclusion.
- Eyes with untreated glaucoma may have normal IOP when evaluated.
-

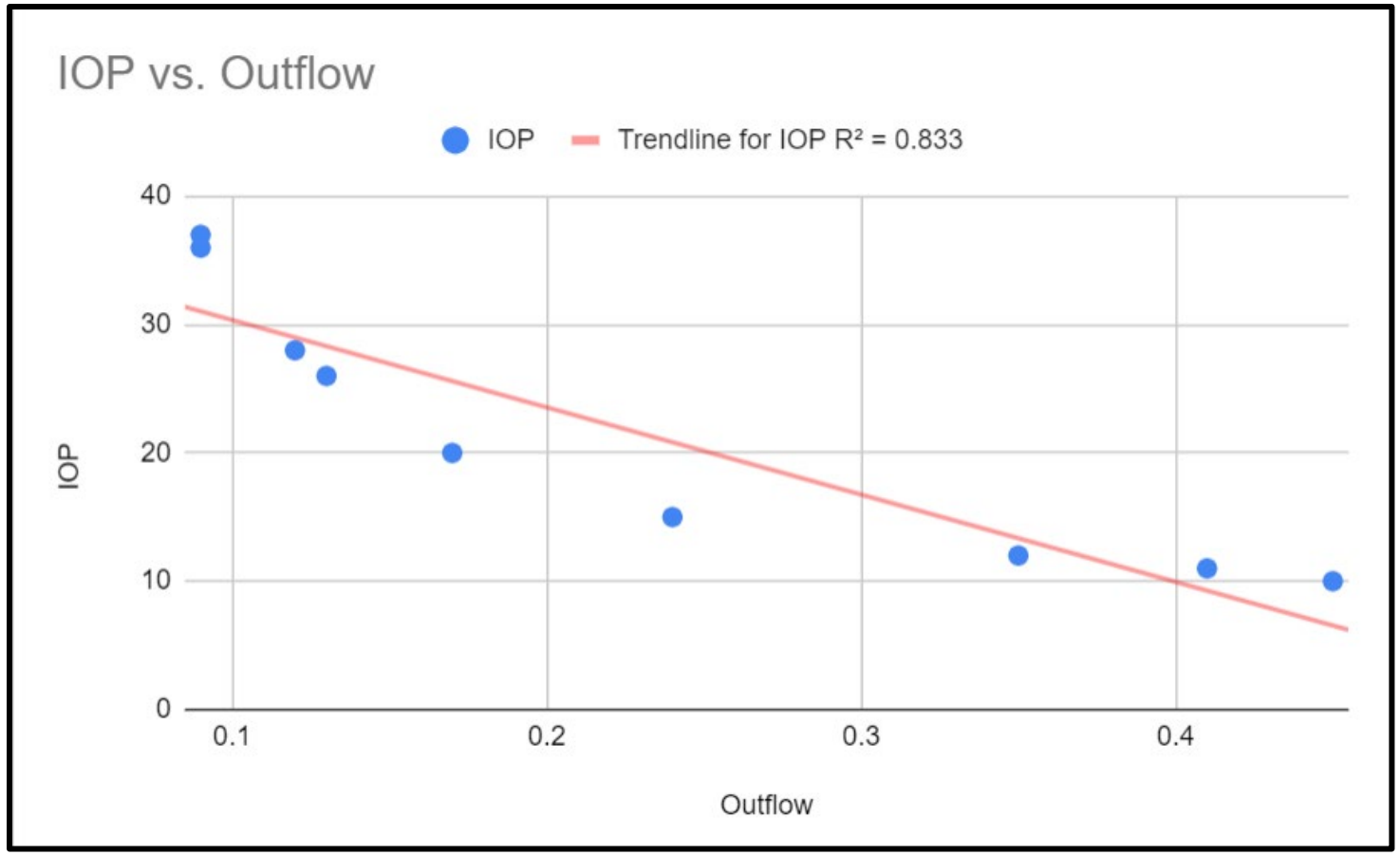
Why Measure Outflow Facility?

- Impaired Outflow Facility is the Primary Cause of Glaucoma
- Outflow Facility Measurements Predict IOP In and Out of the Office
- New Technology Available to Measure Outflow Facility - FMAT1 Tonography
- Outflow Facility Measurements Predict Risk

Reference: Chandler and Grant’s Glaucoma

Outflow Facility Measurements Predict IOP

- FMAT1 FDA Clinical Study Confirms
- IOP = (- 68)(Outflow) + 37, r^2= - 0.83



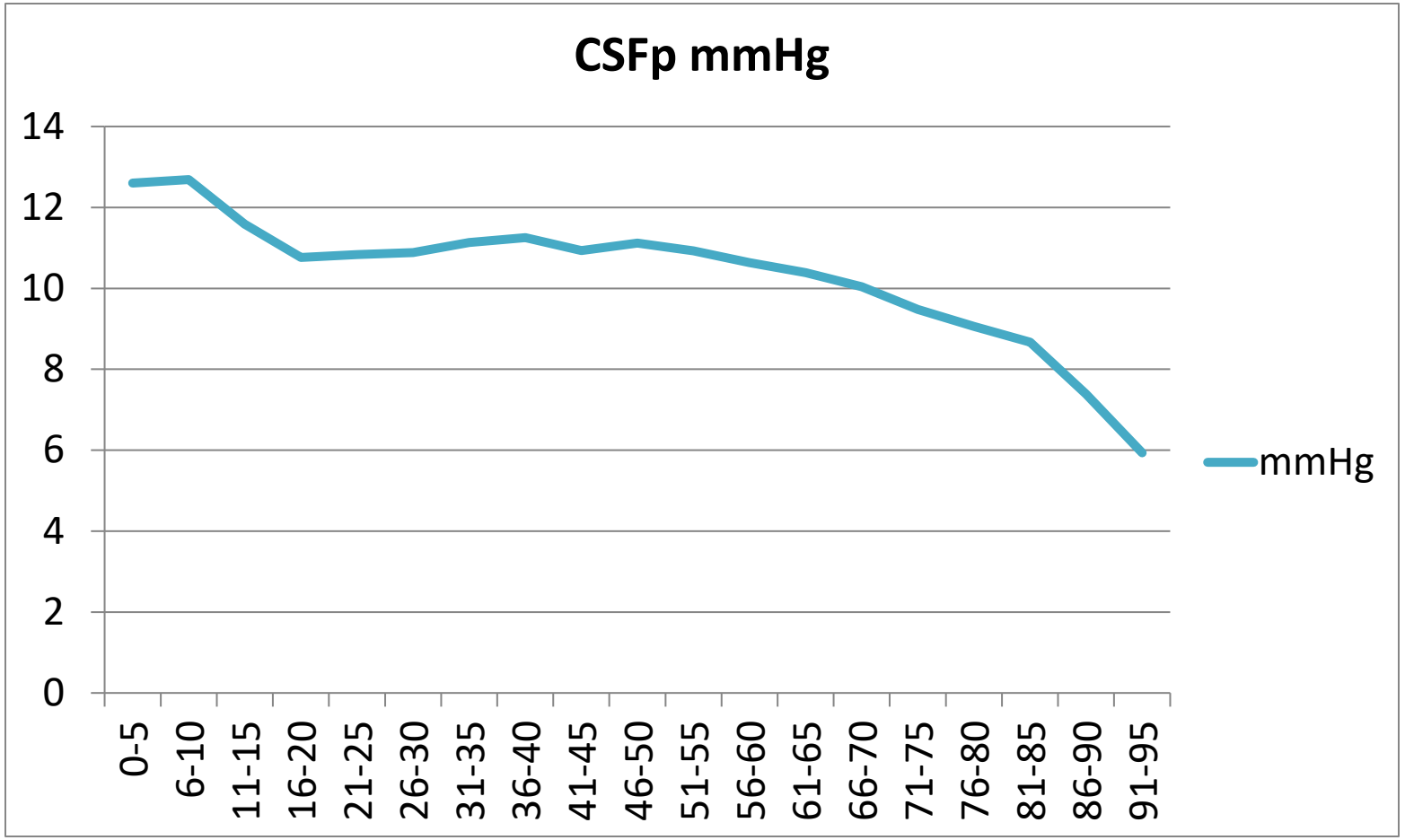
- **Eqiunox the Future of Glaucoma Therapy**

Visual Impairment and Intracranial Pressure - VIIP

Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-duration Space Flight

Thomas H. Mader, MD,[1] C. Robert Gibson, OD,[2] Anastas F. Pass, OD, JD,[3] Larry A. Kramer, MD,[4] Andrew G. Lee, MD,[5] Jennifer Fogarty, PhD,[6] William J. Tarver, MD,[6] Joseph P. Dervay, MD,[6] Douglas R. Hamilton, MD, PhD,[7] Ashot Sargsyan, MD,[7] John L. Phillips, PhD,[8] Duc Tran, DO,[2] William Lipsky, MD,[2] Jung Choi, OD,[2] Claudia Stern, MD, PhD,[9] Raffi Kuyumjian, MD,[10] James D. Polk, DO[6]

ICP changes with Age



Fleischman, D. et al presented at ARVO 2011

Clin Ophthalmol. 2019; 13: 1947–1953.
Published online 2019 Oct 2. doi: 10.2147/OPTH.S217736
PMCID: PMC6778771
PMID: 31631962

8 hrs Safety Evaluation Of A Multi-Pressure Dial In Eyes With Glaucoma: Prospective, Open-Label, Randomized Study

Thomas W Samuelson,[1] Tanner J Ferguson,[2] Nathan M Radcliffe,[3] Richard Lewis,[4] Justin Schweitzer,[5] Russell Swan,[5] and John P Berdahl[5]

Equinox

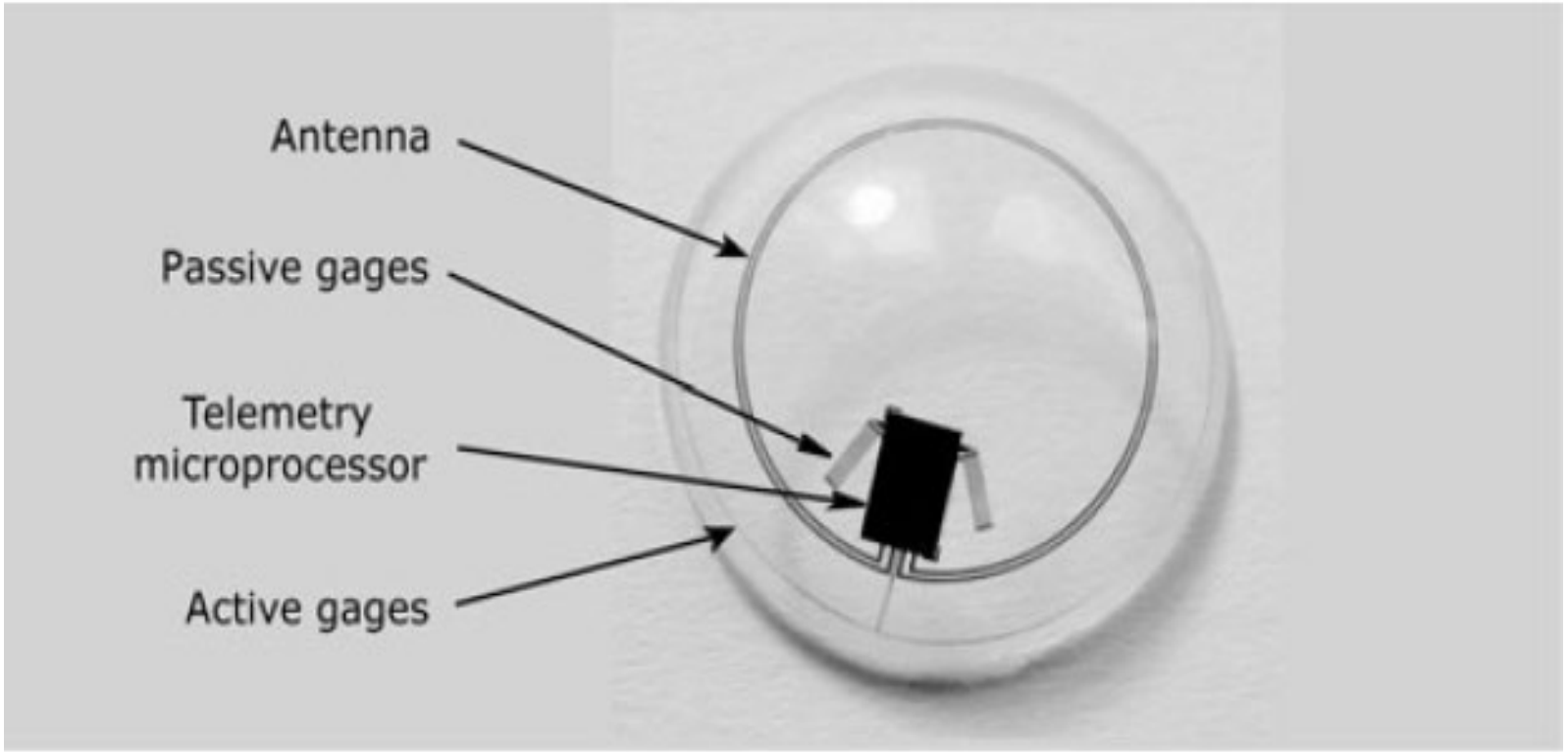
- Dr. Berdahl and colleagues studied 51 patients whose IOPs were 16 mm Hg.
- The investigators programmed a 25% pressure decrease into the goggles and the IOPs decreased to about 13 mmHg
- When a 50% pressure reduction was programmed into the goggles the IOPs decreased to about 11 mmHg, and with a 75% pressure reduction the IOPs decreased to about 10 mm Hg, he reported.


equinox
equinox
v1.00:1234

Triggerfish Contact Lens Monitor

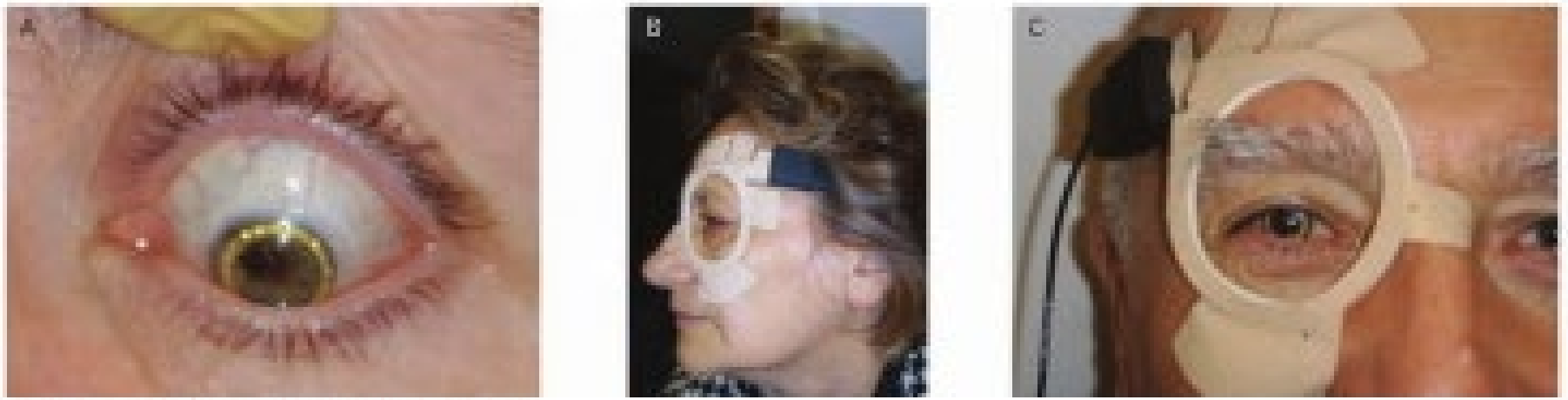
- Provides 24 hour IOP monitoring, including the sleep period
- Takes measurement every five minutes
  - 288 times per day
- At the five minute measurement, obtains 300 data points
  - 10 Hz for 30 seconds
- Main concern is that instrument does not provide IOP measurement
  - Provides change in corneal curvature, based upon peripheral corneal measurement that correlates with change in IOP
  - Detect fluctuations in IOP

Triggerfish Contact Lens 24-Hour IOP Monitoring Device

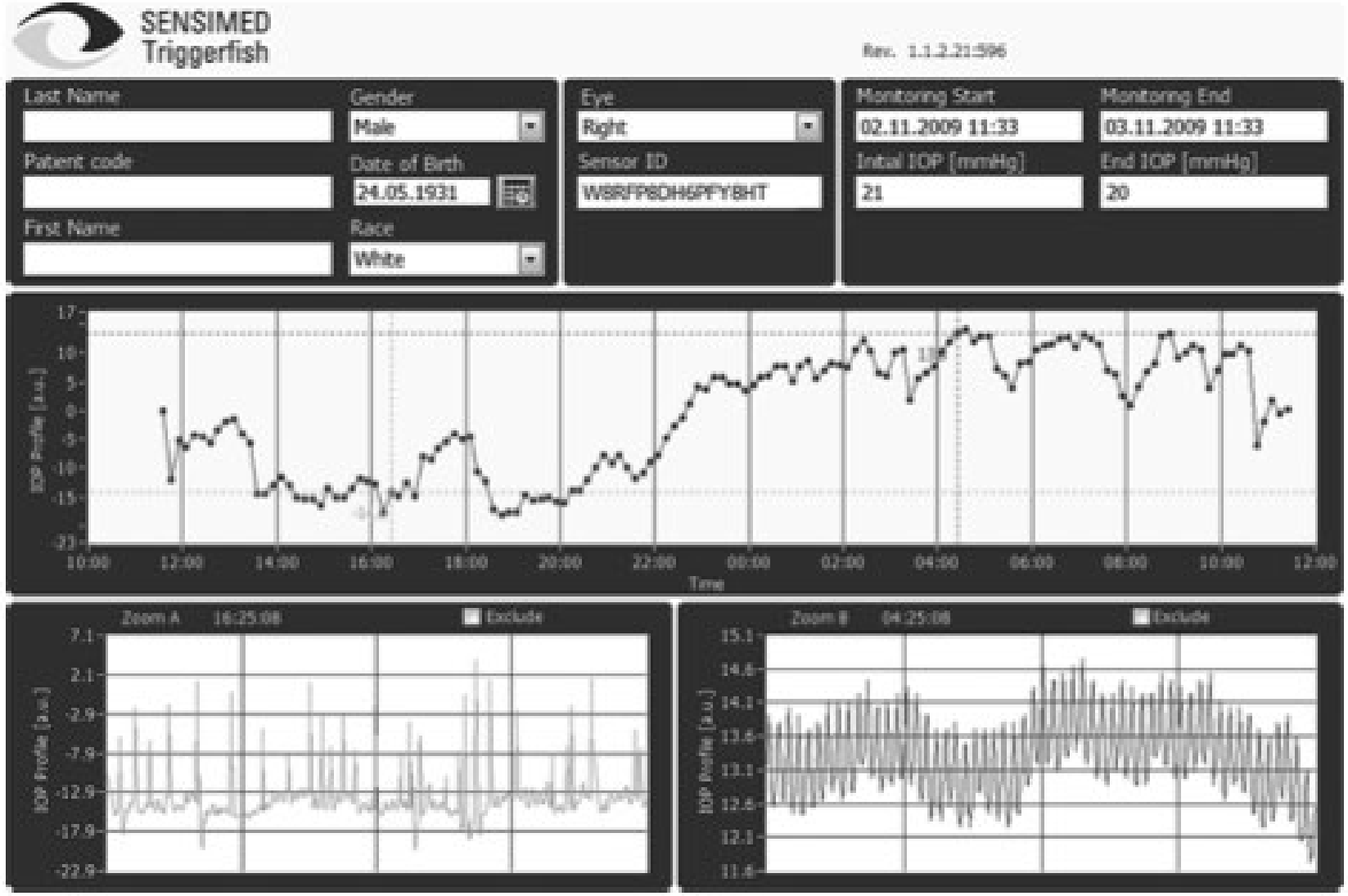


Leonardi M, et al. Wireless contact lens sensor for intraocular pressure monitoring: assessment on enucleated pig eyes. Acta Ophthalmol. 2009: 87: 433–437

Figure 1: Placement of the Sensimed Triggerfish® and Antenna



A: Well-positioned contact lens; B: Lateral view; C: Frontal view.


SENSIMED
Triggerfish
Rev. 1.1.2.21:596
Last Name
Patient code
First Name
Gender
Male
Date of Birth
24.05.1931
Race
White
Eye
Right
Sensor ID
W8RFP8DH6PPYBHT
Monitoring Start
02.11.2009 11:33
Intial IOP [mmHg]
21
Monitoring End
03.11.2009 11:33
End IOP [mmHg]
20
IOP Profile [a.u.]
Time
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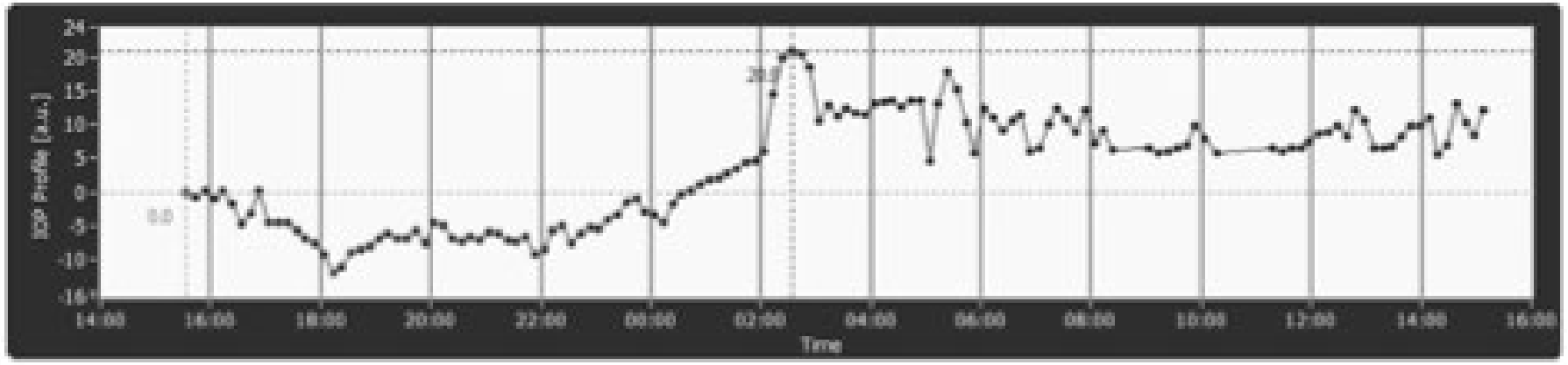
Exclude
Zoom B 04:25:08
Exclude


ICP Profile [a.u.]
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08:00
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12:00
14:00
16:00
Time

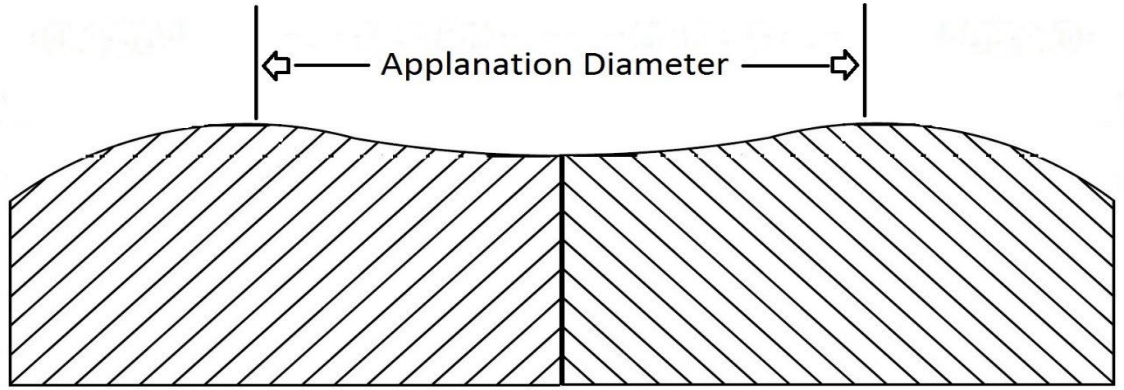
CATS: Correcting Applanation Tonometry Surface

Inventor Sean McCafferty MD

Sean McCafferty is an Ophthalmologist with a degree in Mechanical Engineering and a Master of Science in optical engineering. This unique combination of skills equipped him to envision the CATS™ Tonometer Prism design in 2011.

After years of work, the device became FDA cleared in October 2018.

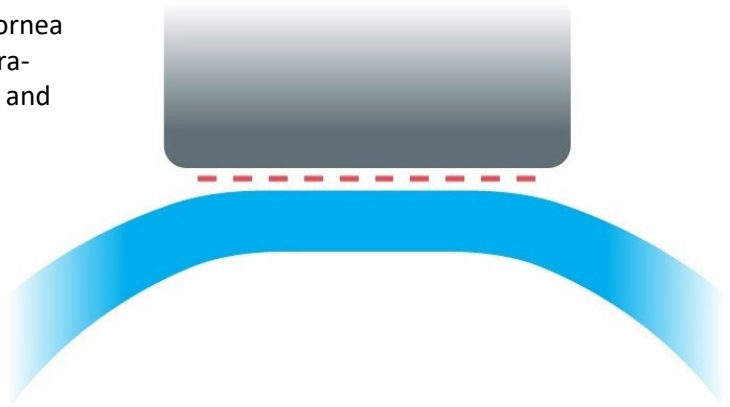
CATS is simply a replacement prism for any Goldmann applanation or Perkins tonometer. The CATS Tonometer Prism™ utilizes a concave contact surface to minimize mechanical bending resistance of the cornea. The device also features a tapered edge, which helps to reduce the influence of tear-film adhesion.



CATS: Correcting Applanation Tonometry Surface

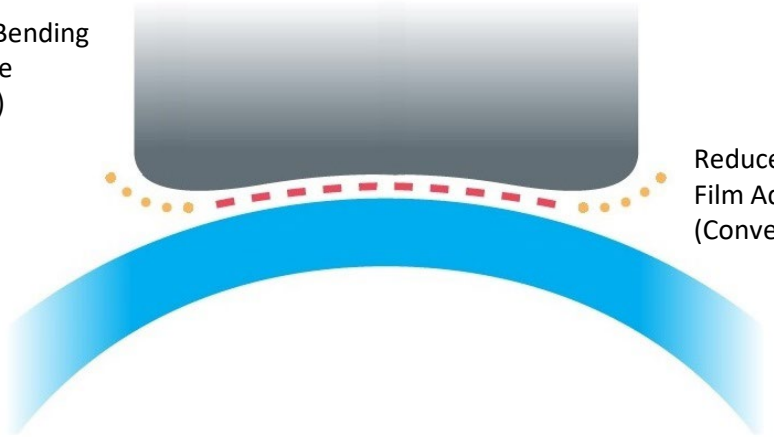
Traditional GAT Prism – No change in 65 Years

Flattens the Cornea Amplifying Intra-Corneal Stress and IOP errors



CATS™ Tonometer Prism – the New Shape of IOP

Reduces Bending Resistance (Concave)



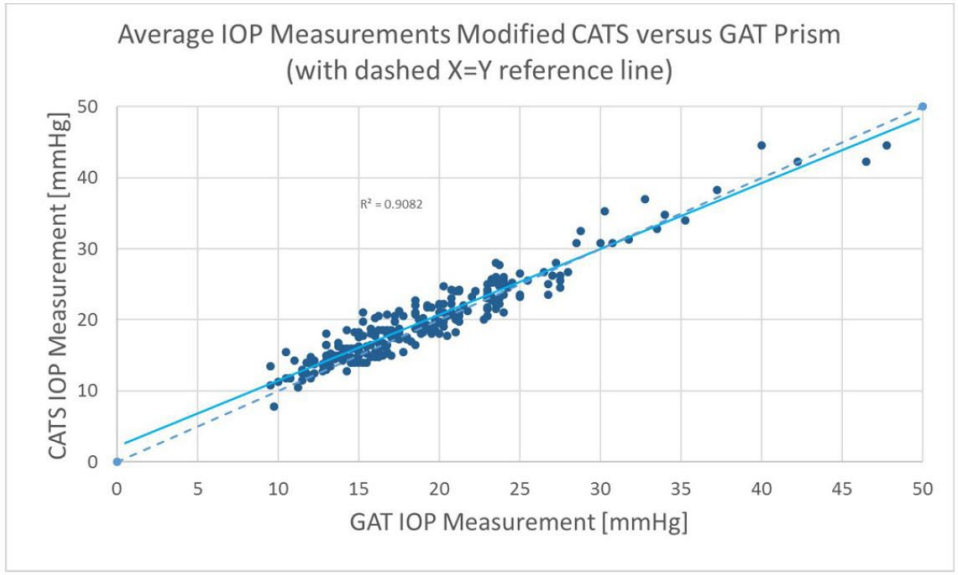
Reduces Tear Film Adhesion (Convex)

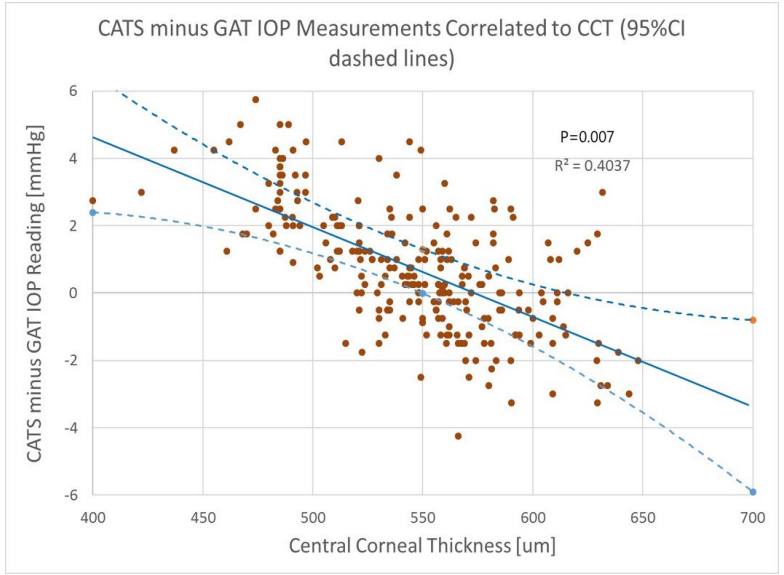
CATS: Compare CATS to GAT in Normal Eyes

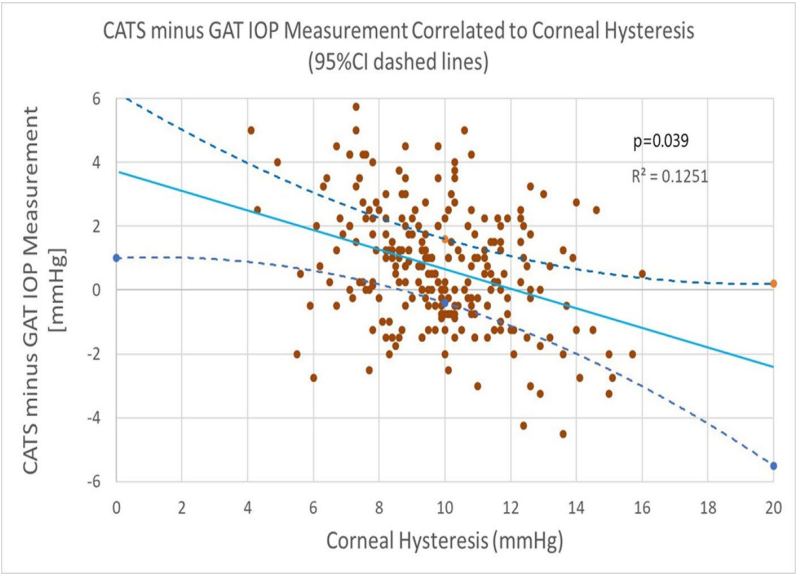
Purpose:

1. Compare CATS to GAT in 243 Normal Eyes with Central Corneal Thickness between 400 – 650 Microns

2. Evaluate the impact of corneal properties on GAT and CATS





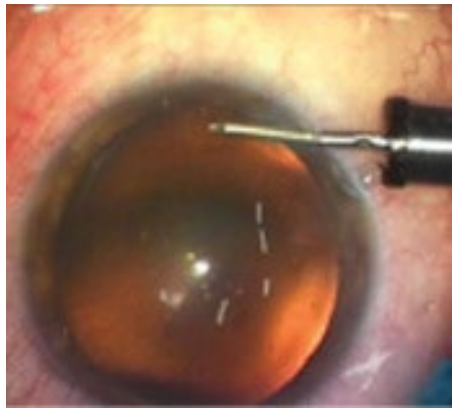


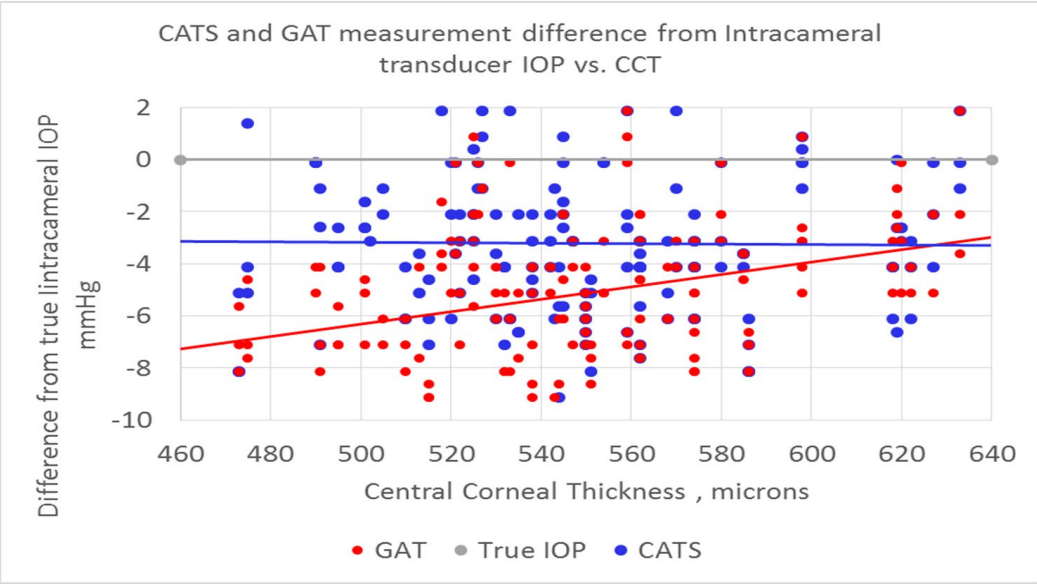
A significant reduction in CATS prism's sensitivity to CCT and CH was demonstrated compared with the traditional GAT prism

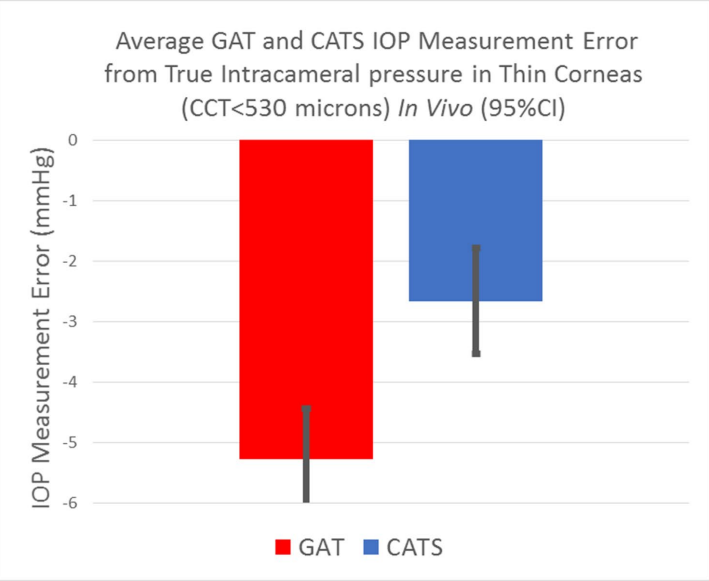
CATS Intercameral Pressure Validation

Methods:

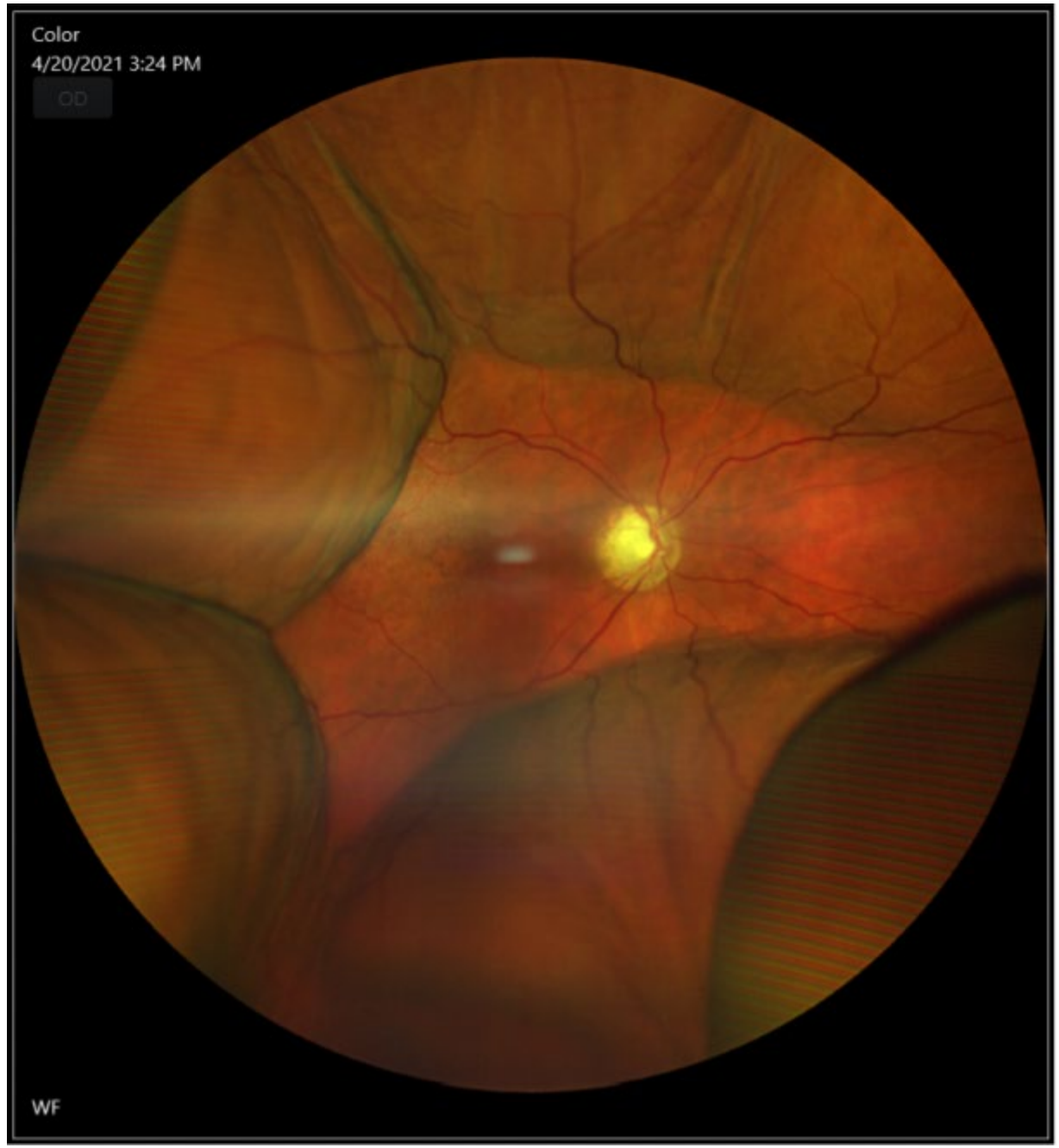
- Intracameral IOP measured on 58 eyes undergoing cataract surgery
- IOP manometrically modulated to 10, 20, and 40 mmHg
- Difference between the CATS and GAT IOP measurements from true intracameral pressure correlated to the error parameters







The CATS prism is significantly more accurate compared to the GAT prism compared to true intracameral pressure, and is unaffected by CCT.

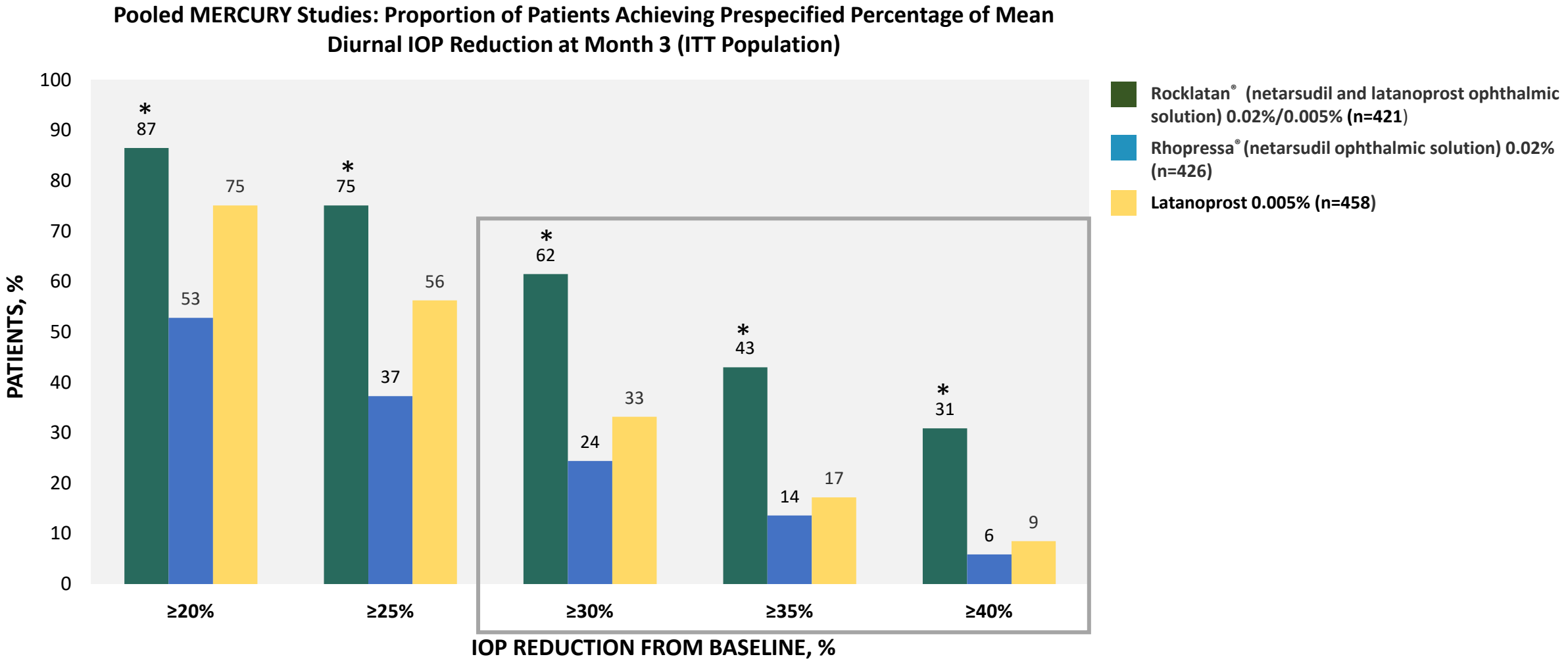

Color
4/20/2021 3:24 PM
OD
WF

A Great Year for Glaucoma Therapy

New Age PGA's

- Rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% is a new combination drug product and has a white cap
- Rocklatan® is available in a 1-month supply (2.5 mL)
- Protect from light.
- Must remain refrigerated

Over 60% of Rocklatan® Patients Achieved ≥30% Mean IOP Reduction at 3 Months[1]



*P<0.0001 vs Rhopressa® and latanoprost. ITT, intent-to-treat

1.Data on file, Aerie Pharmaceuticals, Inc.

VYZULTA®
(latanoprostene bunod ophthalmic solution), 0.024%

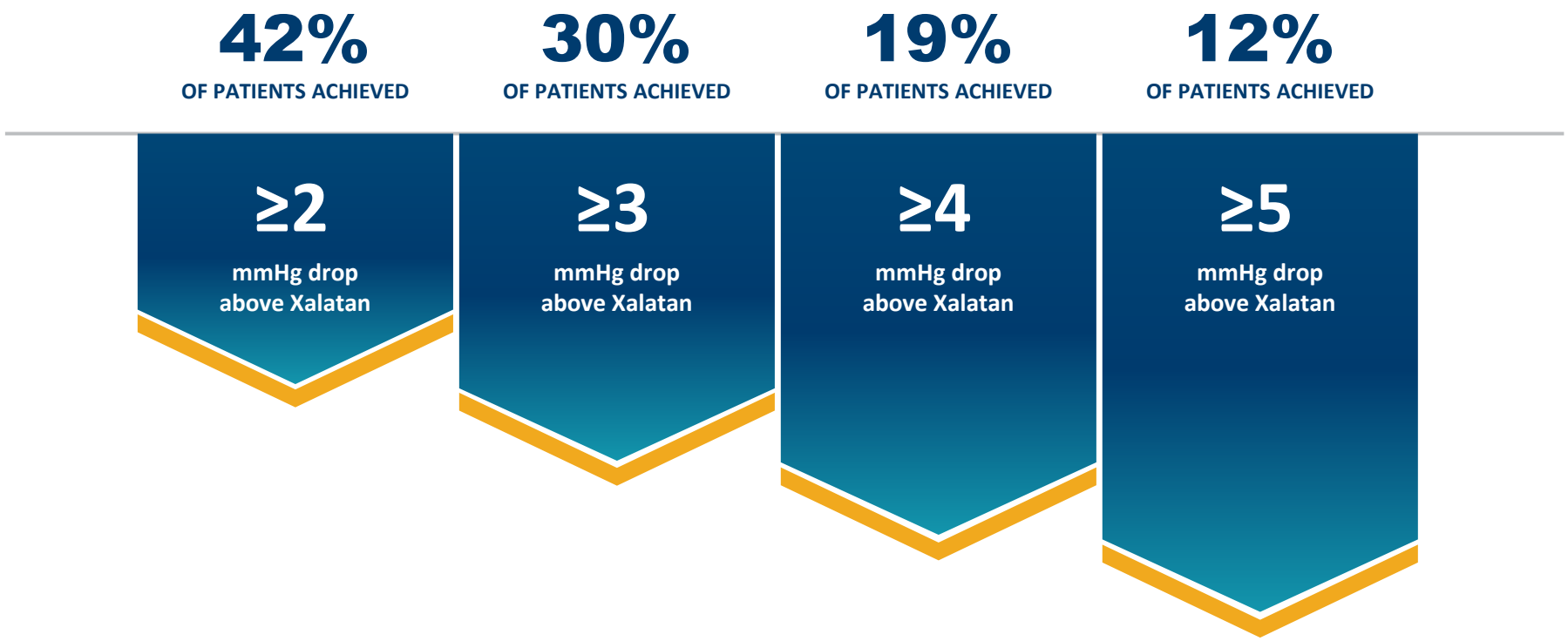
VYZULTA® is the **only nitric oxide-releasing agent** that targets both the trabecular meshwork and the uveoscleral pathway to reduce IOP in patients with open-angle glaucoma and ocular hypertension

IOP, intraocular pressure.

VYZULTA Prescribing Information. Bausch & Lomb Incorporated. 2019.

VYZULTA® Delivered Greater IOP Reductions Than Xalatan[1,2]

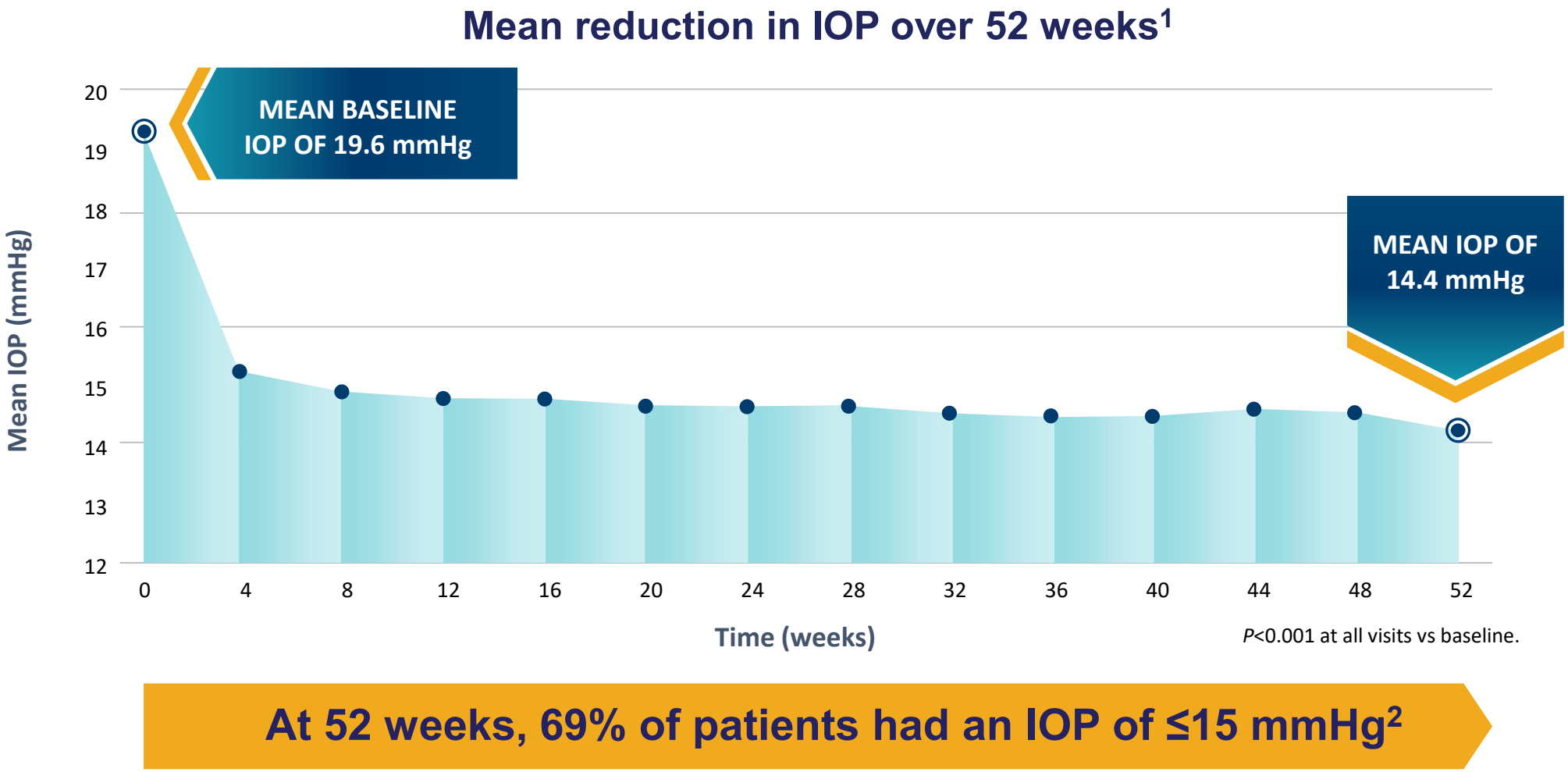
Percent of patients treated with VYZULTA who achieved greater IOP reductions than Xalatan*



*Post hoc analysis; Xalatan 0.005%, mean diurnal IOP reduction of 7.8 mmHg at Day 28.

1. Weinreb RN, et al. *Br J Ophthalmol*. 2015;99(6):738-745.

VYZULTA® Resulted in Significant Long-Term Reductions in IOP



At 52 weeks, 69% of patients had an IOP of ≤15 mmHg[2]

1. Kawase K et al. *Adv Ther*. 2016;33(9):1612-1627. doi:10.1007/s12325-016-0385-7

Preservative Free Latanoprost

Preservatives in IOP lowering medications

BRAND NAME	ACTIVE INGREDIENT	PRESERVATIVE
EYE DROPS WITH BENZALKONIUM CHLORIDE (BAK)		
Iopidine	Apraclonidine 0.5%, 1%	BAK 0.01%
Betoptic S	Betaxolol 0.25%	BAK 0.01%
Betoptic	Betaxolol 0.5%	BAK 0.01%
Lumigan	Bimatoprost 0.01%	BAK 0.02%
Lumigan	Bimatoprost 0.03%	BAK 0.005%
Lumify	Brimonidine 0.025%	BAK 0.01%
Alphagan	Brimonidine 0.2%	BAK 0.005%
Combigan	Brimonidine 0.2%/timolol 0.5%	BAK 0.005%
Azopt	Brinzolamide 1%	BAK 0.01%
Simbrinza	Brinzolamide 1%/brimonidine 0.2%	BAK 0.003%
Trusopt	Dorzolamide 2%	BAK 0.0075%
Cosopt	Dorzolamide 2%/timolol 0.5%	BAK 0.0075%
Xalatan	Latanoprost 0.005%	BAK 0.02%
Rocklatan	Latanoprost 0.005%/netarsudil 0.02%	BAK 0.02%
Vyzulta	Latanoprostene 0.024%	BAK 0.02%
Betagan	Levobunolol 0.25%, 0.5%	BAK 0.004%
Rhopressa	Netarsudil 0.02%	BAK 0.015%
Isopto Carpine	Pilocarpine 1%	BAK 0.01%
Timoptic	Timolol 0.25%, 0.5%	BAK 0.01%

EYE DROPS CONTAINING ALTERNATIVE PRESERVATIVES		
Alphagan P	Brimonidine 0.1%, 0.15%	Purite® (stabilized oxychloro complex) 0.005%
Xelpros	Latanoprost 0.005%	Potassium sorbate
Timoptic-XE	Timolol-XE 0.25%, 0.5%	Benzododecinium bromide 0.012%
Travatan Z	Travoprost 0.004%	sofZia®

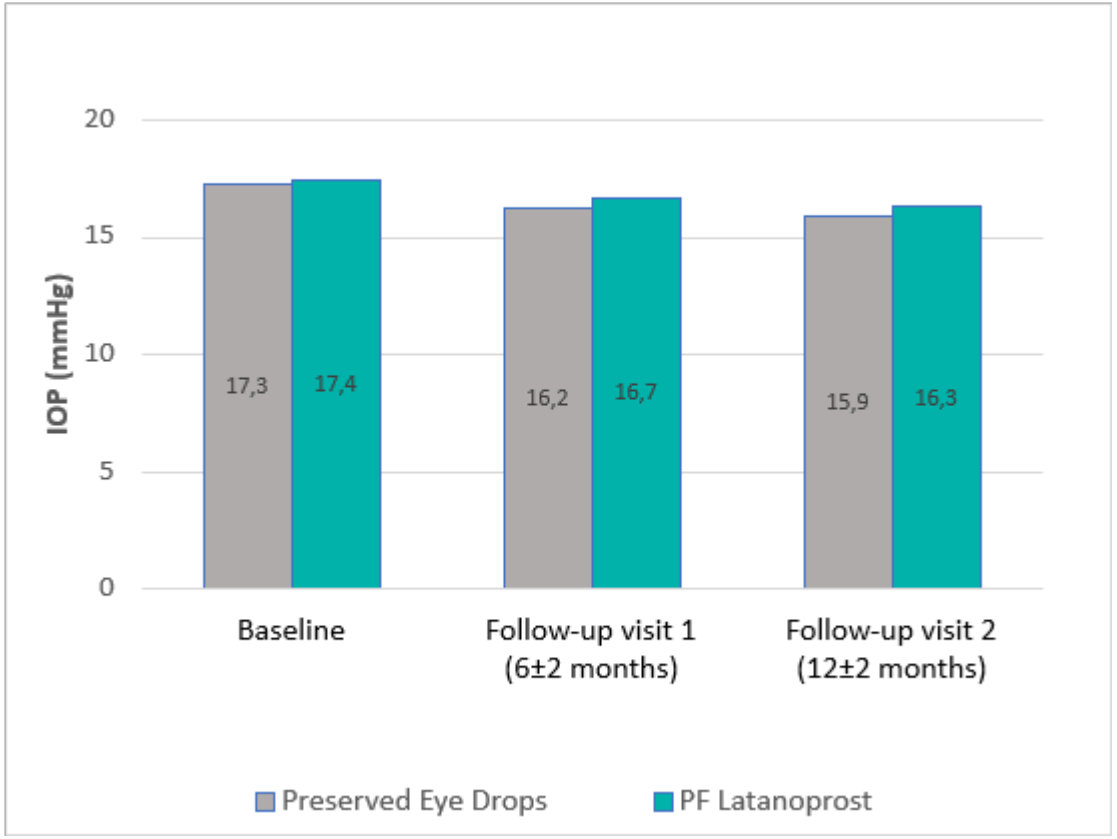
PRESERVATIVE-FREE EYE DROPS		
Cosopt PF	Dorzolamide 2%/timolol 0.5%	Preservative-free
PF Latanoprost	**Latanoprost 0.005%**	**Preservative-free**
Zioptan	Tafluprost 0.0015%	Preservative-free
Timoptic in Ocudose	Timolol 0.25%, 0.5%	Preservative-free

BAK is the most used preservative in topical ophthalmic formulations

PF-Latanoprost has been approved by the FDA for use in the United States.

IOP Lowering: PF-latanoprost vs. Preserved glaucoma medications*[1]

PF-latanoprost vs. preserved glaucoma medication at 6 months and 12 months



The most common preserved glaucoma treatments were:

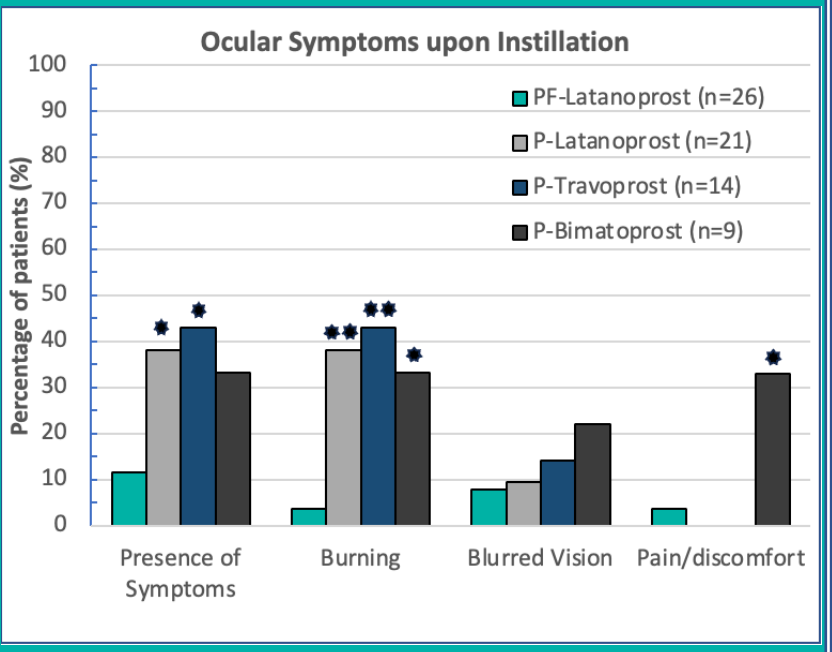
- preserved beta-blockers (21.2%)
- preserved latanoprost (20.7%)
- preserved travoprost (9.8%)
- preserved bimatoprost 0.01% (5.6%).

*Multicenter, international, prospective, noninterventional real-life study conducted in France, the Netherlands, Norway, Poland, and Sweden

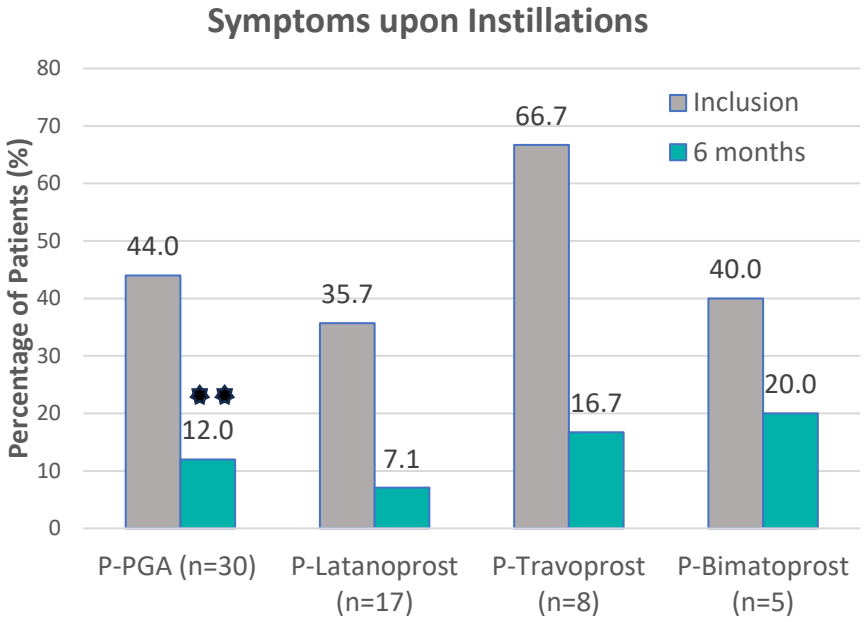
1. Economou et al. Clinical Ophthalmology 2018: 12; 2399-2407.

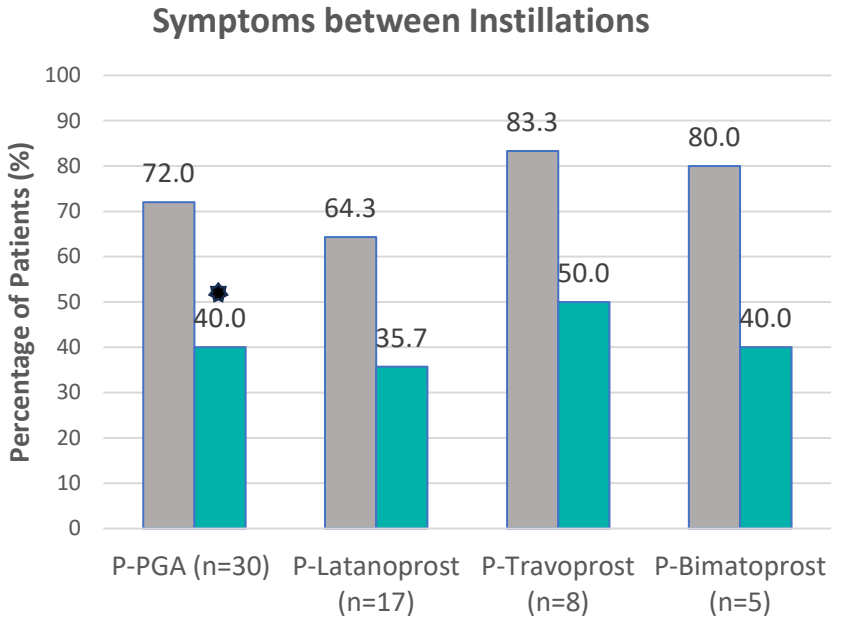
Ocular symptoms after switching to PF-Latanoprost*[1]

Inclusion Visit



Six Months After Switching to PF-Latanoprost

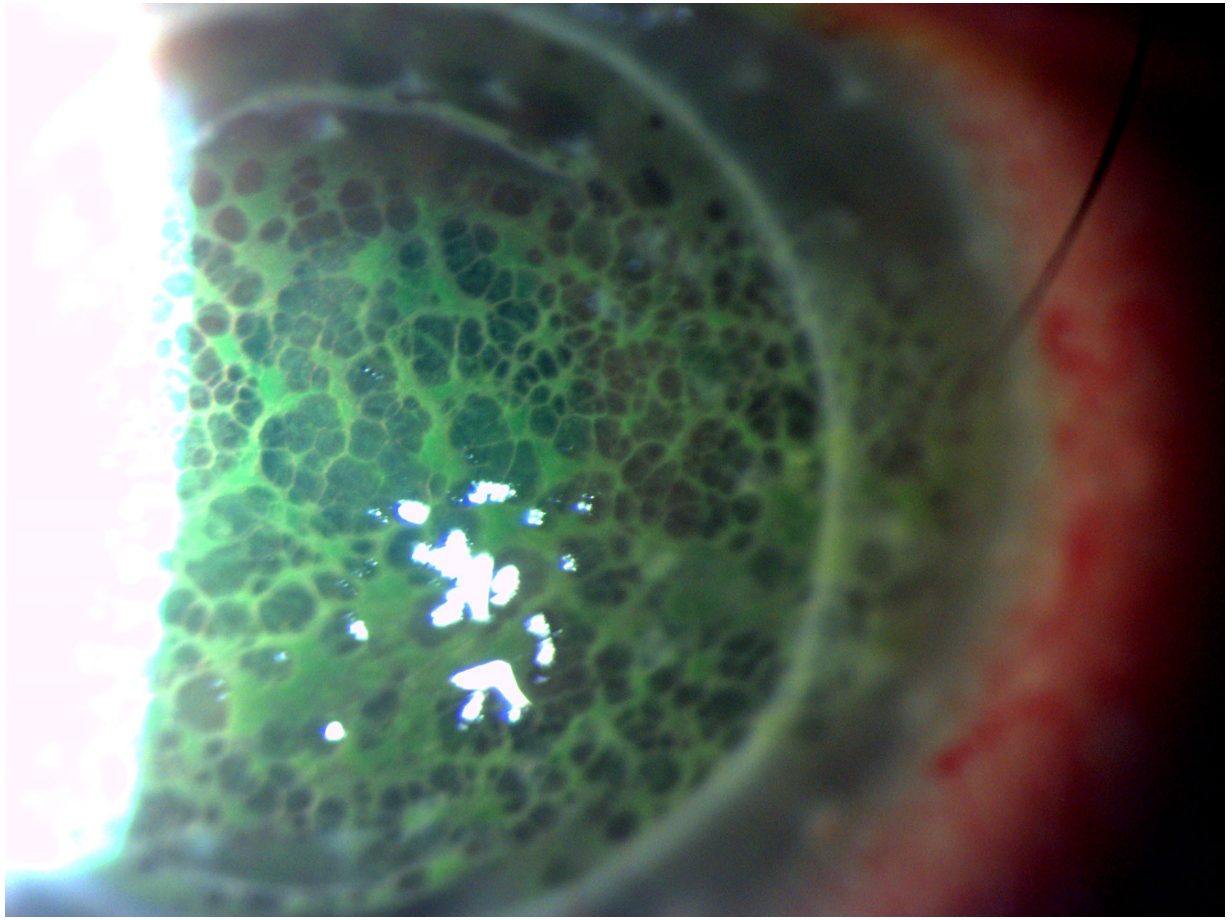


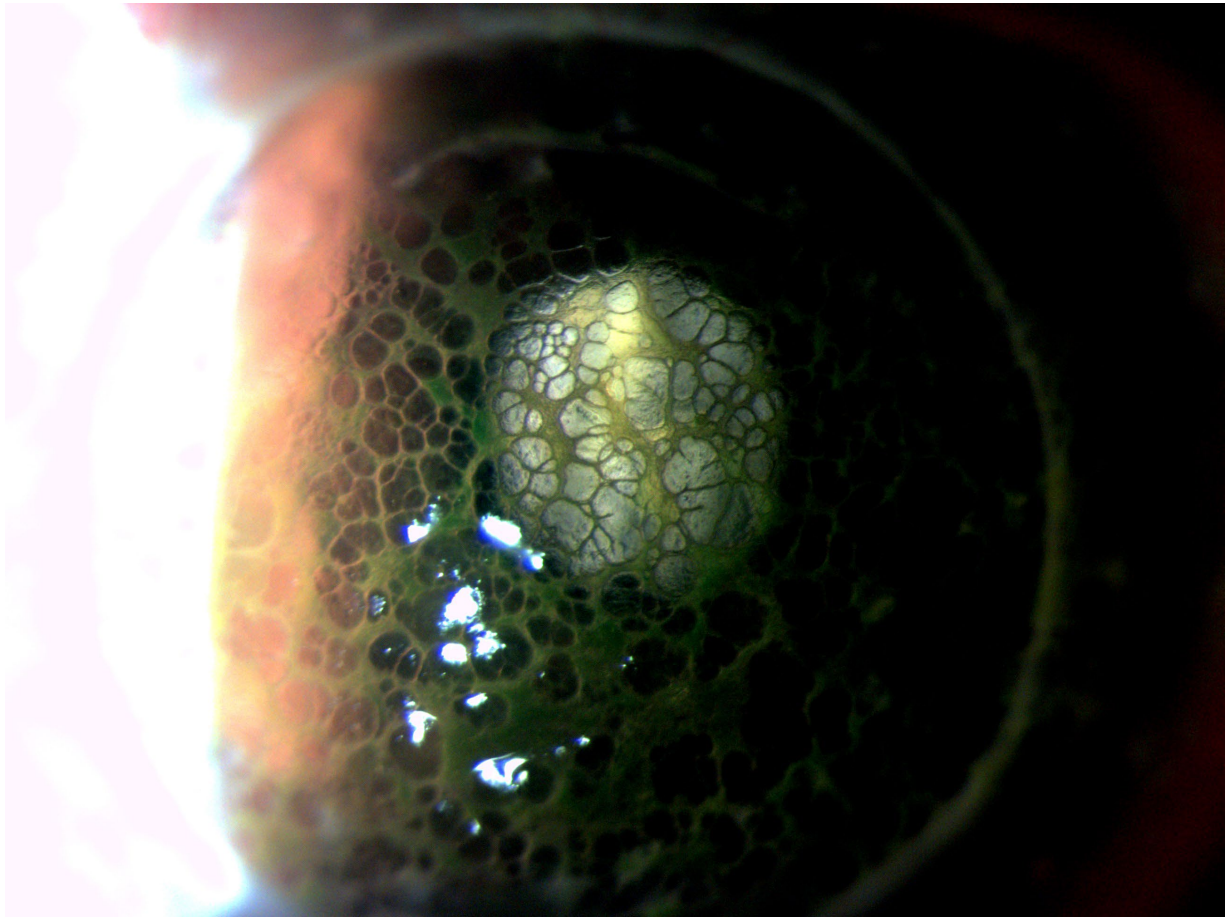


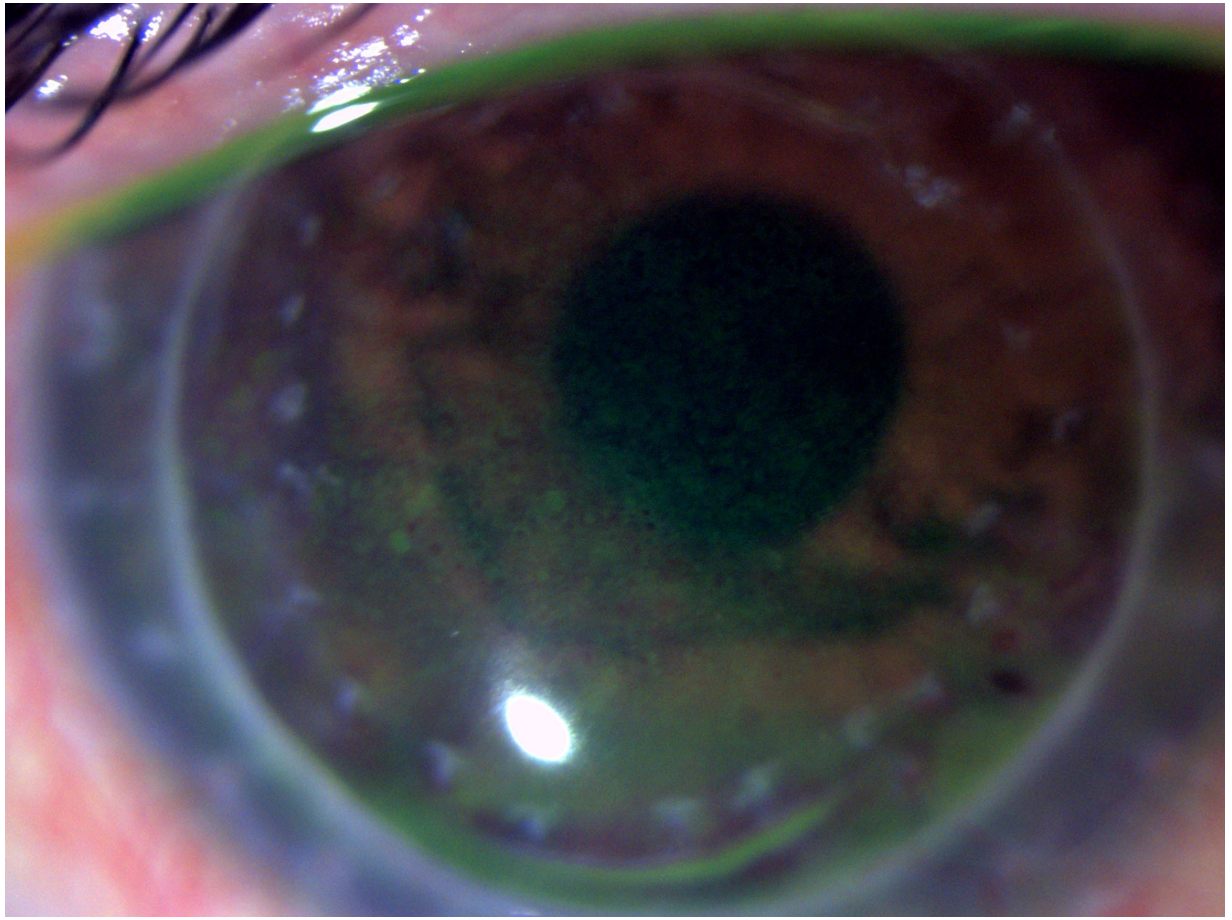
- **Percentage of patients with at least one symptom upon instillation was reduced after 6 months. The reduction was statistically significant when all preserved PGAs were analyzed together (12% vs 44%, p = 0.026).**
- **Percentage of patients with at least one symptom between instillations was reduced for each preserved prostaglandin and overall (40% vs 72%, p = 0.045).**

*Observational cross-sectional study conducted in France

1. El Ameen et al. Eur J Ophthalmol. 2019, 29:645-653







Alternate Day Therapy in Glaucoma

Trans Am Ophthalmol Soc. 2009 Dec; 107: 167–181.
PMCID: PMC2814574
PMID: 20126493

From The Bedside to the Bench and Back Again: Predicting and Improving the Outcomes of SLT Glaucoma Therapy

Jorge A. Alvarado, MD,* Rumiko Iguchi, MS, Richard Juster, PhD, Julie A. Chen, MD, and Amde Selassie Shifera, MD

IOP DIFFERENCE (MM HG) BETWEEN CONDITIONS

IOP, intraocular pressure; N, number; SD, standard deviation; PGA, prostaglandin analogue; SLT, selective laser trabeculoplasty.
*All *P* values are for the paired *t* statistic and are 2-sided.

N EYES = 24	**A. MEAN % DIFFERENCE (SD)**	**B. MEAN % DIFFERENCE (SD)**
IOP_{PGA}-$IOP_{BASELINE}$	−5.58 (2.38); $P < .001$*	−25.37% (8.86); $P < .001$
IOP_{SLT}-$IOP_{BASELINE}$	−6.60 (2.44); $P < .001$	−29.93% (7.05); $P < .001$
IOP_{SLT}-IOP_{PGA}	−1.02 (1.81); $P = .011$	−5.33% (11.39); $P = .031$

Alternate Day Therapy

- Twice daily dosing increases IOP relative to once daily dosing
- Xalatan and Lumigan combined can increase IOP, even to 50s
- anytime IOP is >30 with prostaglandin, it is overdosed
- Once daily can be overdose if there is inflammation/endogenous prostaglandin

Persistence of IOP Response

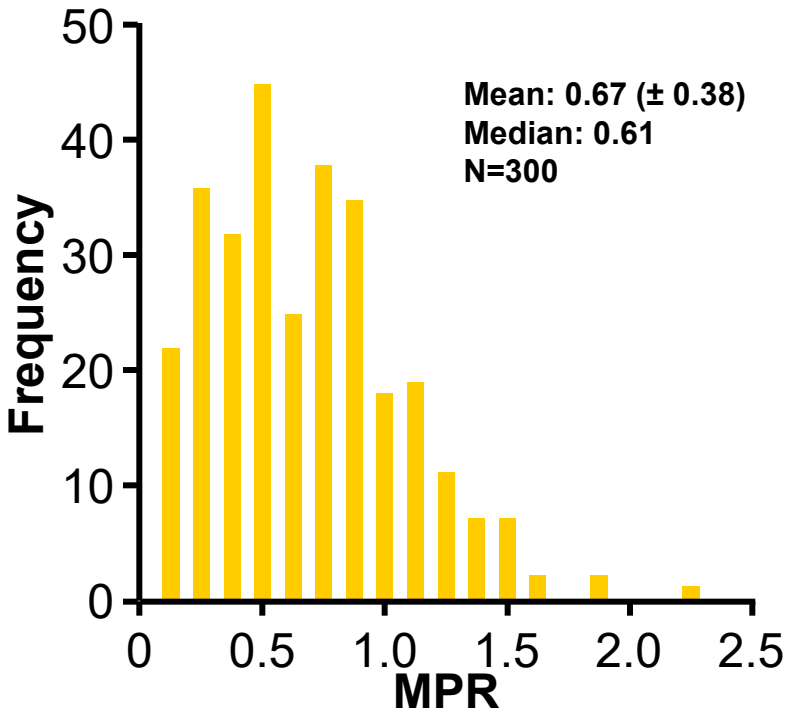
- Labovitz RA et al; Arch Ophth 2001
- Comparison of Lumigan vs: Timolol
- Maintenance of IOP at 48 hours post D/C 5.6mmHg
- 7.2 - 8.2 mmHg at peak effect
- 28 Day control showed less than
- Timolol was 3.4-3.9 mmHg at peak.

Alternate Day Therapy Post SLT

- SLT somewhat less effective in patients already on prostaglandin
  - Suggesting that part of SLT induces prostaglandin like effects
- QD prostaglandin could be an overdose after SLT
  - Especially first year after laser

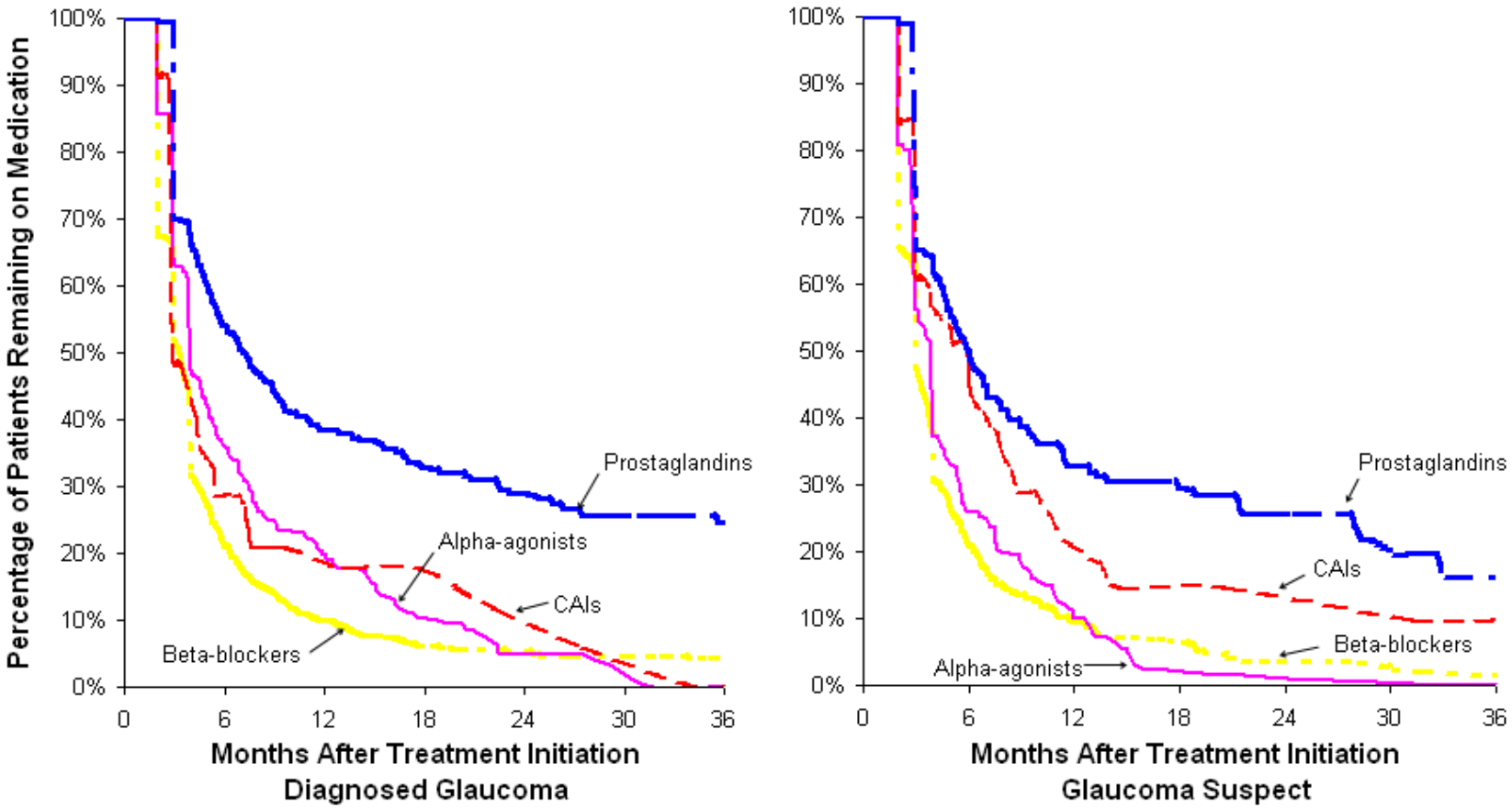
GAPS: MPR for Retrospective Pharmacy Claims Data and Survey Patients

- All pharmacy claims
  - Mean, 0.64 (±0.42)
  - Median, 0.57
  - N=13,956
- Survey patients
  - Mean, 0.67 (±0.38)
  - Median, 0.61
  - N=300
- Patients ≥1 year of continuous claims data
  - Only 10% refilled medication without interruption for 1 year
  - 54% stopped and then restarted initial medication
  - N=10,260



Continuous Use

Nordstrom, Friedman…Quigley, AJO, 2005



Durysta

Durysta

- Bimatoprost is a prostamide that has been shown to reduce IOP when administered topically
- A biodegradable implant has been developed
- The implant is designed to be placed intracamerally in the eye and provide slow release of bimatoprost over time

Gonioscopic photographs of bimatoprost sustained-release implant 10 µg in the anterior chamber of an eye of a representative patient diagnosed with open-angle glaucoma

IOP = intraocular pressure

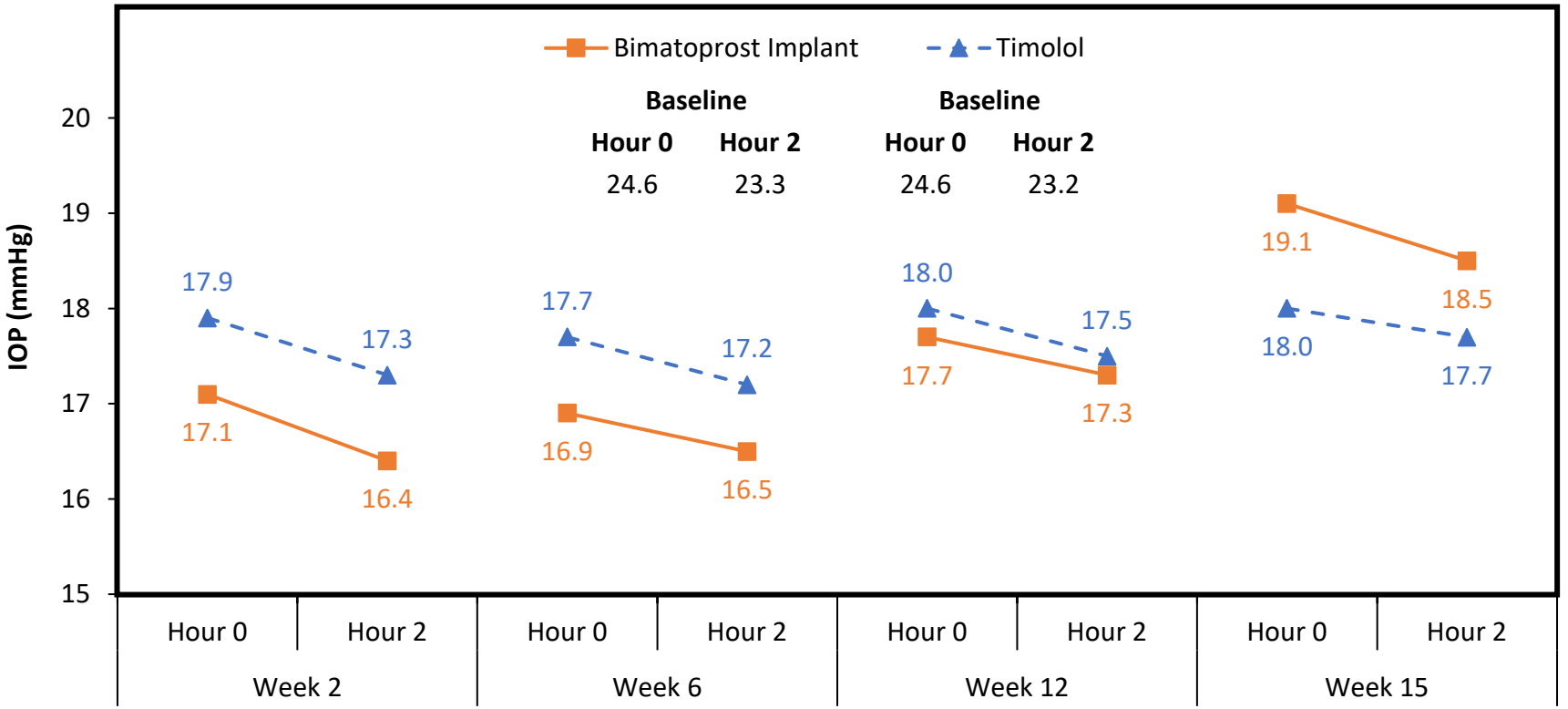
Lewis R, et al. *Am J Ophthalmol* 2017;175:137-147.

Durysta-Brimatoprost Implant

Mean IOP by Treatment Group and Treatment Difference in Mean IOP

ARTEMIS Study 1

Primary Endpoint



Bimatoprost Implant vs. Timolol (95% CI)

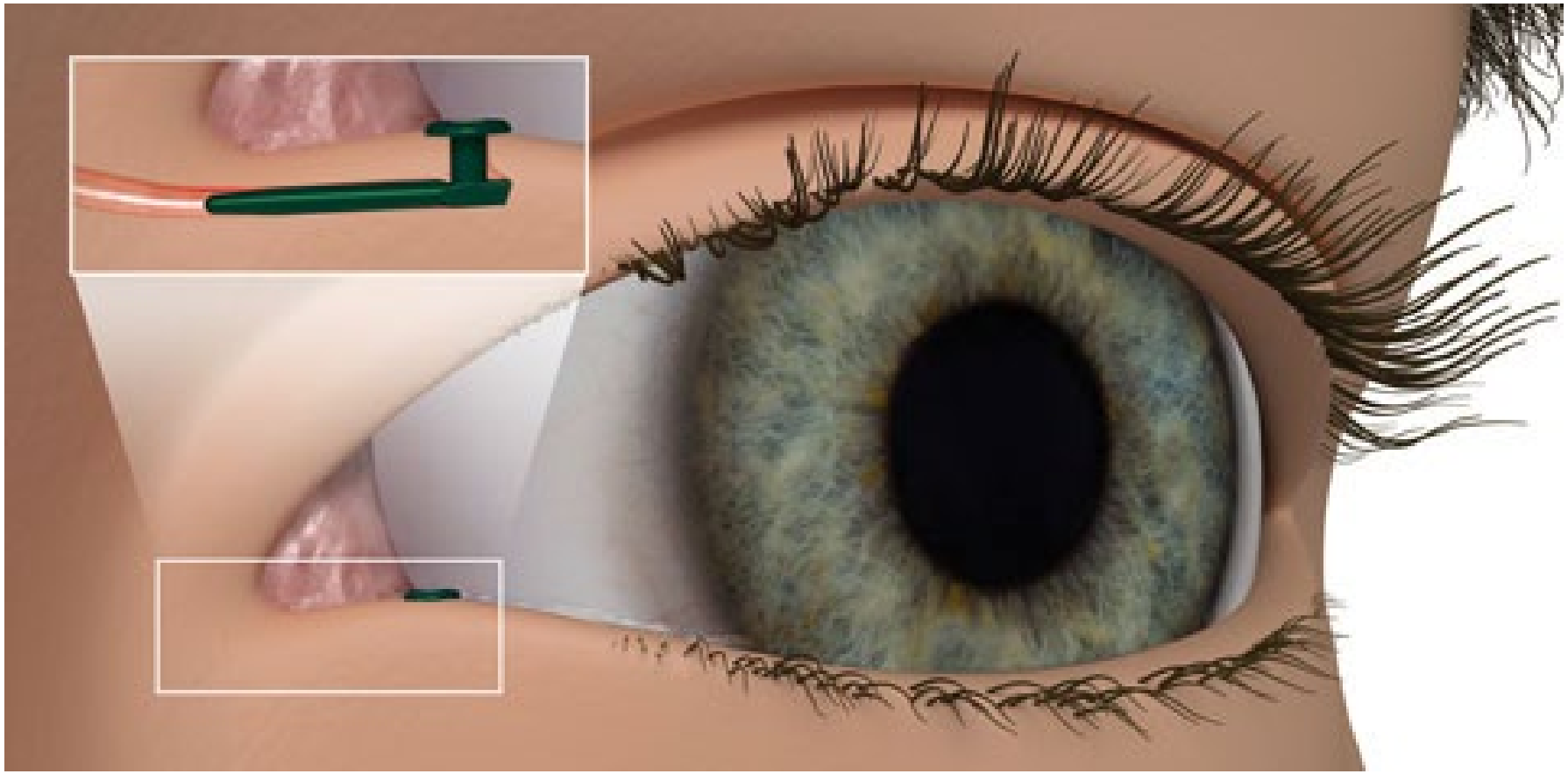
Hour 0	-0.8 (-1.47, -0.14)	-0.8 (-1.47, -0.21)	-0.3 (-1.09, 0.43)	1.1 (0.22, 1.89)
Hour 2	-0.9 (-1.50, -0.31)	-0.7 (-1.27, -0.04)	-0.2 (-0.90, 0.46)	0.9 (0.10, 1.64)

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

Mati Therapeutics

- The Evolute has an L-shaped design and is inserted into the nasolacrimal duct. The device is cosmetically invisible, but can be easily seen with eversion of the lower lid.
- The glaucoma product has a core of latanoprost-polymer matrix that is surrounded by silicone, and it delivers the medication into the tear film at a constant rate.
- In a phase II clinical trial, the latanoprost punctal plug was found to be comfortable. It was associated with a 20% lowering from baseline IOP over a 3-month period, and in two separate clinical trials.
- Retention rate of 92% and 96%, respectively.

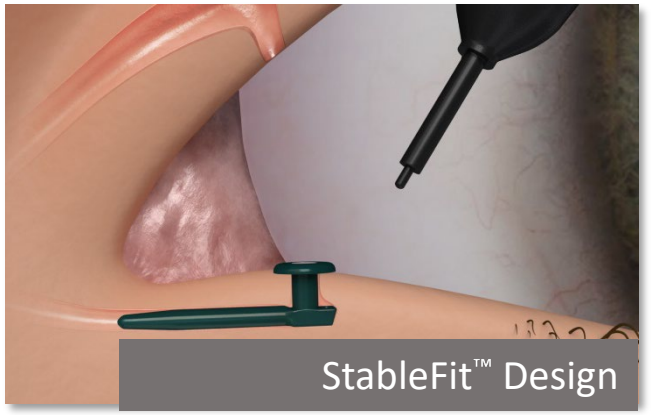
Mati Therapeutics

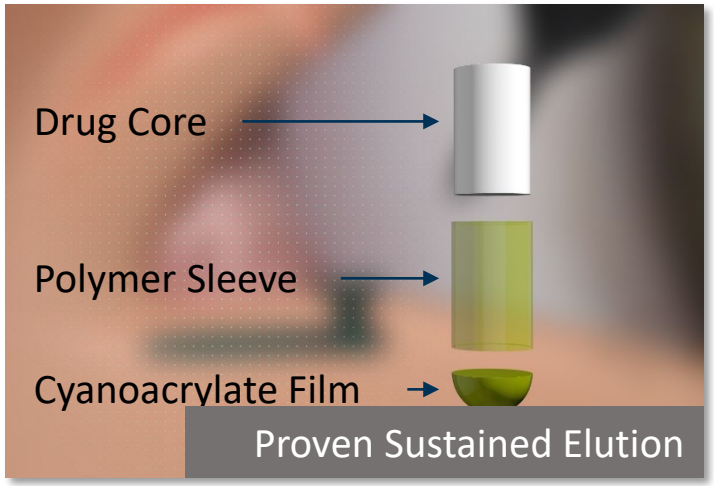


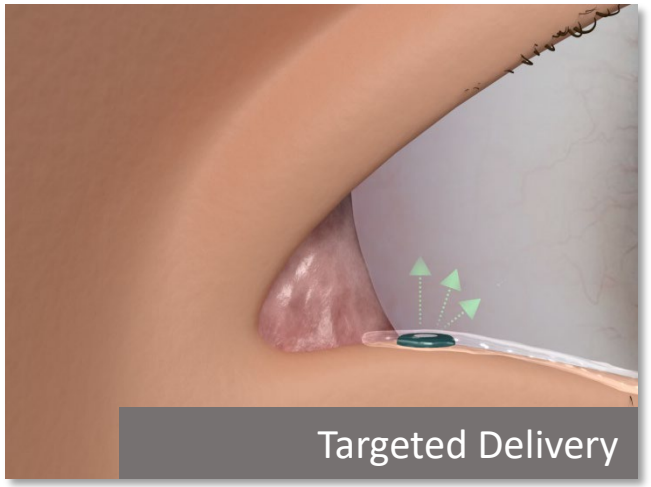
Evolute® Punctal Plug Delivery System

Successful By Design

1. Easy to place and remove
2. Cosmetically invisible – easy to identify
3. Tolerable
4. Consistent, sustained efficacy
5. Use in multiple disease states





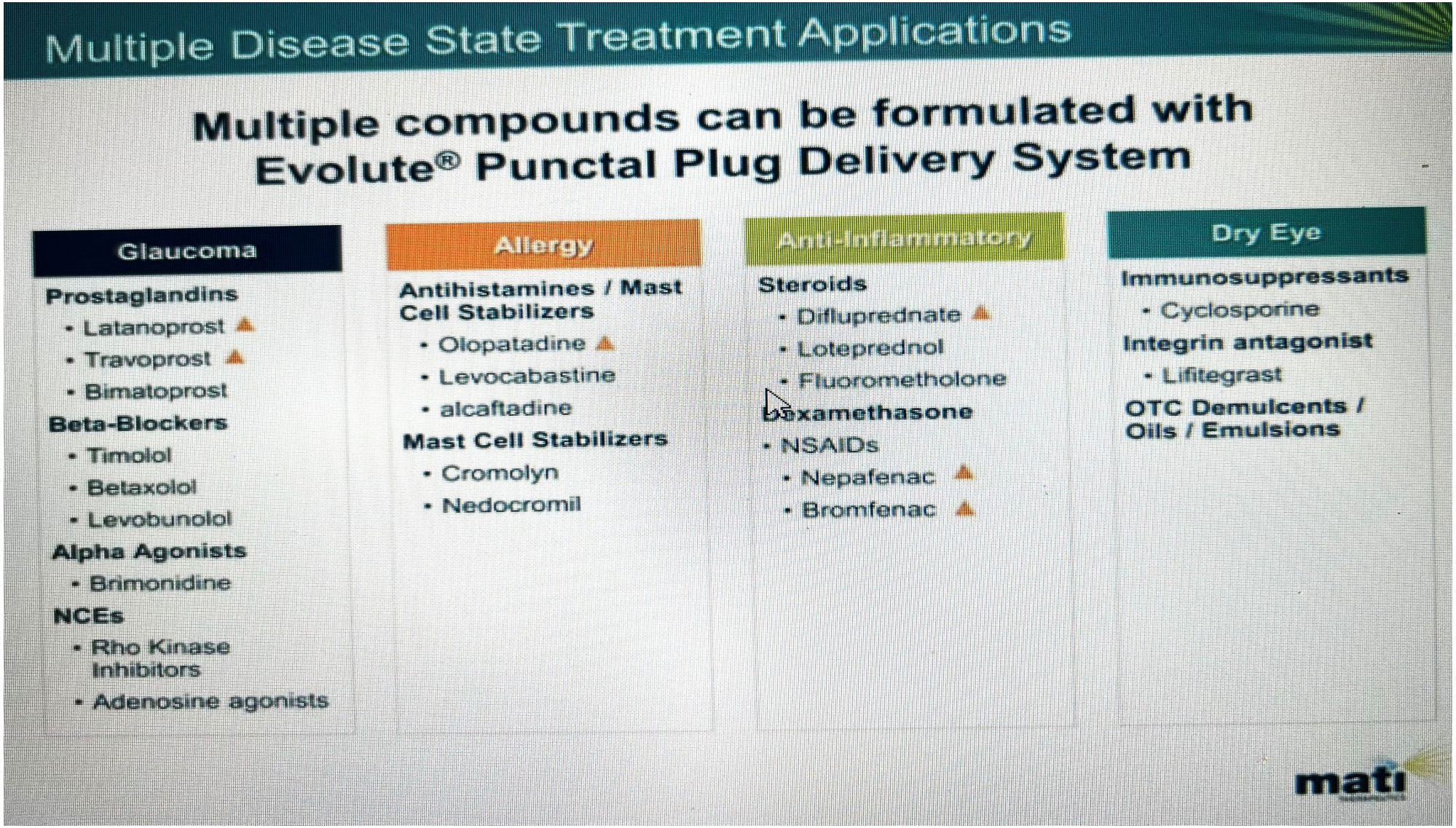


Excellent Plug Retention Rates Over 12 Weeks

U.S. Phase II Multi-center Trials – Lower Puncta

Study	Week 4	Week 8	Week 12
Glau 12 (n = 92)	98%	97%	96%
Glau 13 (n = 87)	98%	96%	92%

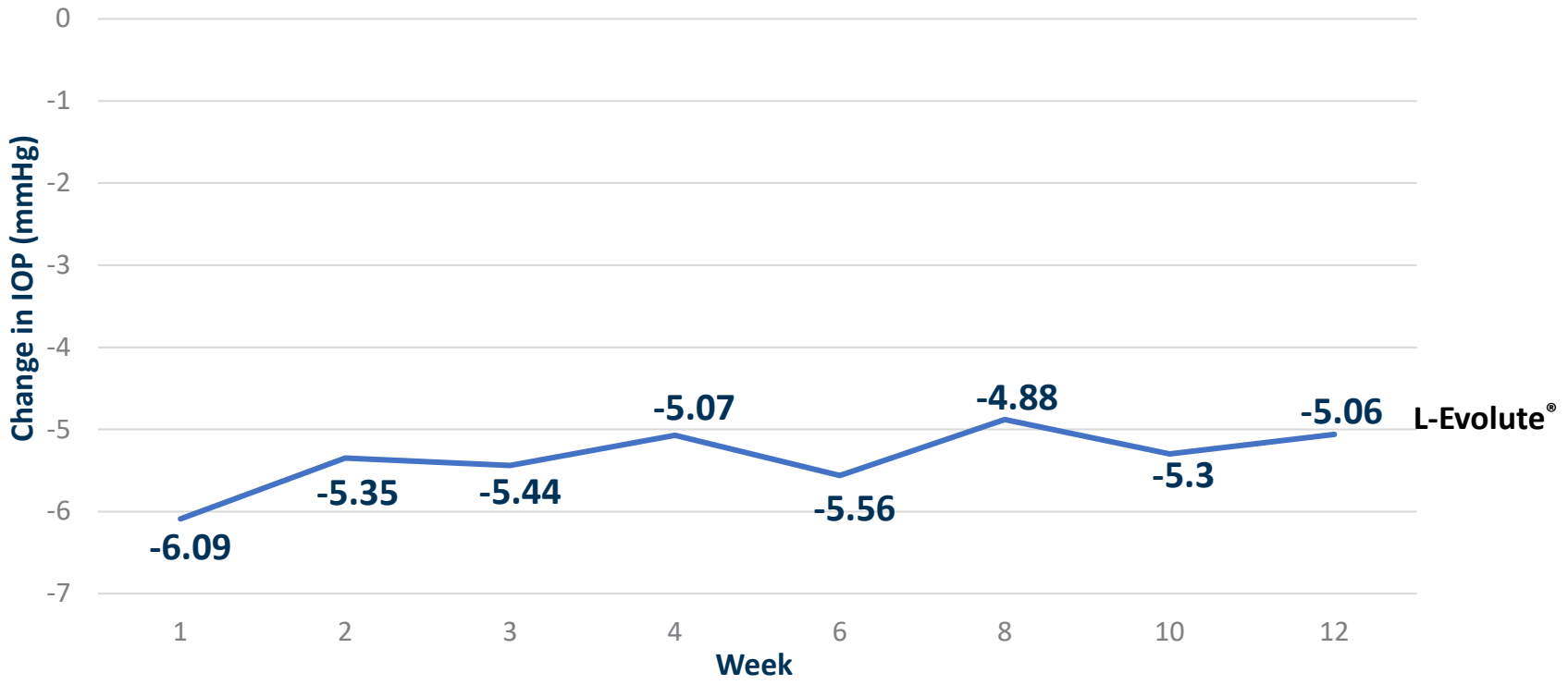
Mati


Multiple Disease State Treatment Applications
Multiple compounds can be formulated with Evolute® Punctal Plug Delivery System
Glaucoma
Prostaglandins
• Latanoprost
• Travoprost
• Bimatoprost
Beta-Blockers
• Timolol
• Betaxolol
• Levobunolol
Alpha Agonists
• Brimonidine
NCEs
• Rho Kinase Inhibitors
• Adenosine agonists
Allergy
Antihistamines / Mast Cell Stabilizers
• Olopatadine
• Levocabastine
• alcaftadine
Mast Cell Stabilizers
• Cromolyn
• Nedocromil
Anti-Inflammatory
Steroids
• Difluprednate
• Loteprednol
• Fluorometholone
Dexamethasone
• NSAIDs
• Nepafenac
• Bromfenac
Dry Eye
Immunosuppressants
• Cyclosporine
Integrin antagonist
• Lifitegrast
OTC Demulcents / Oils / Emulsions
mati

Ph II U.S. Multi-center 12 Week Results:

L-Evolute® with Previously Shown Elution Profile

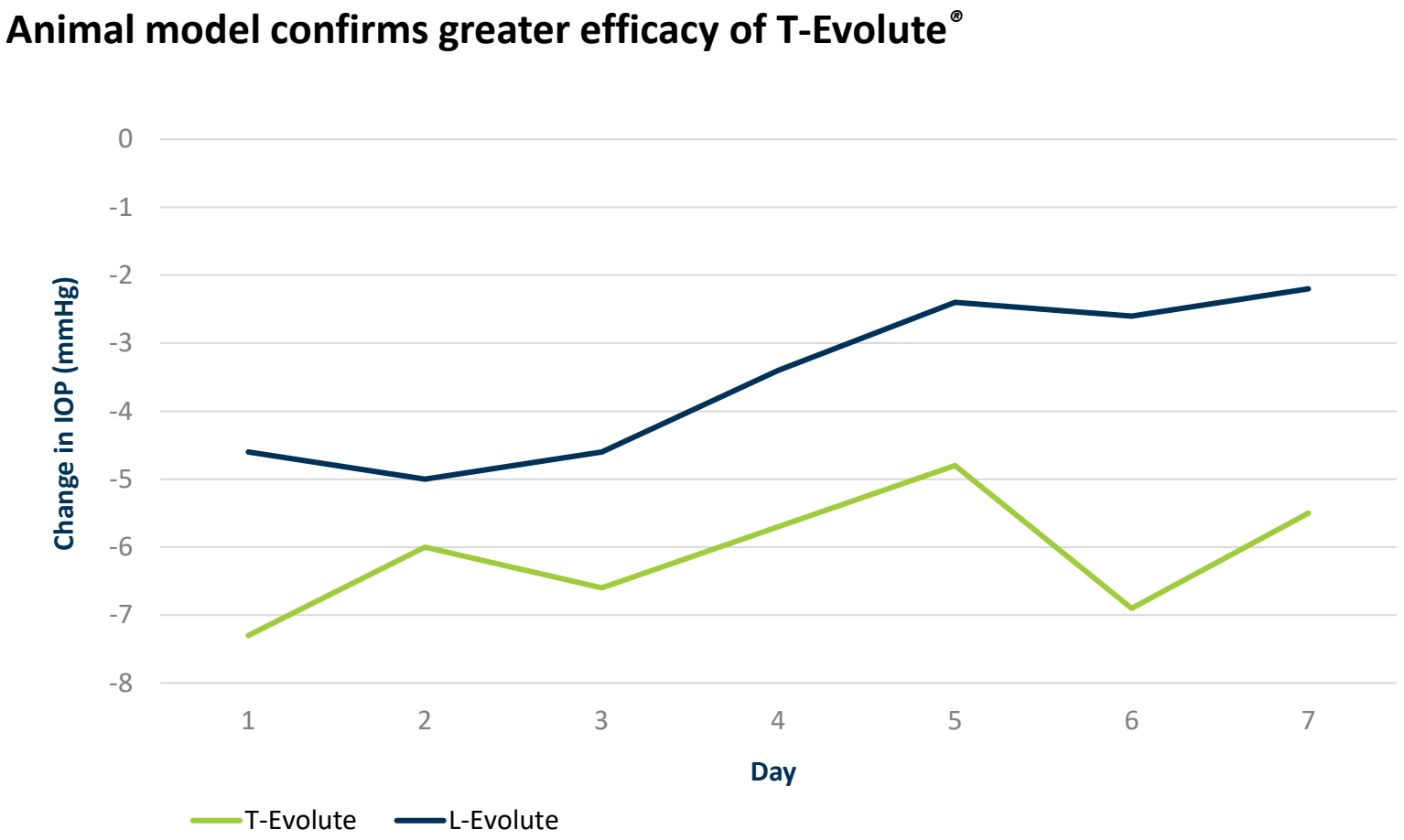
Development data to date shows the T-Evolute® should out perform the L-Evolute® shown above in humans



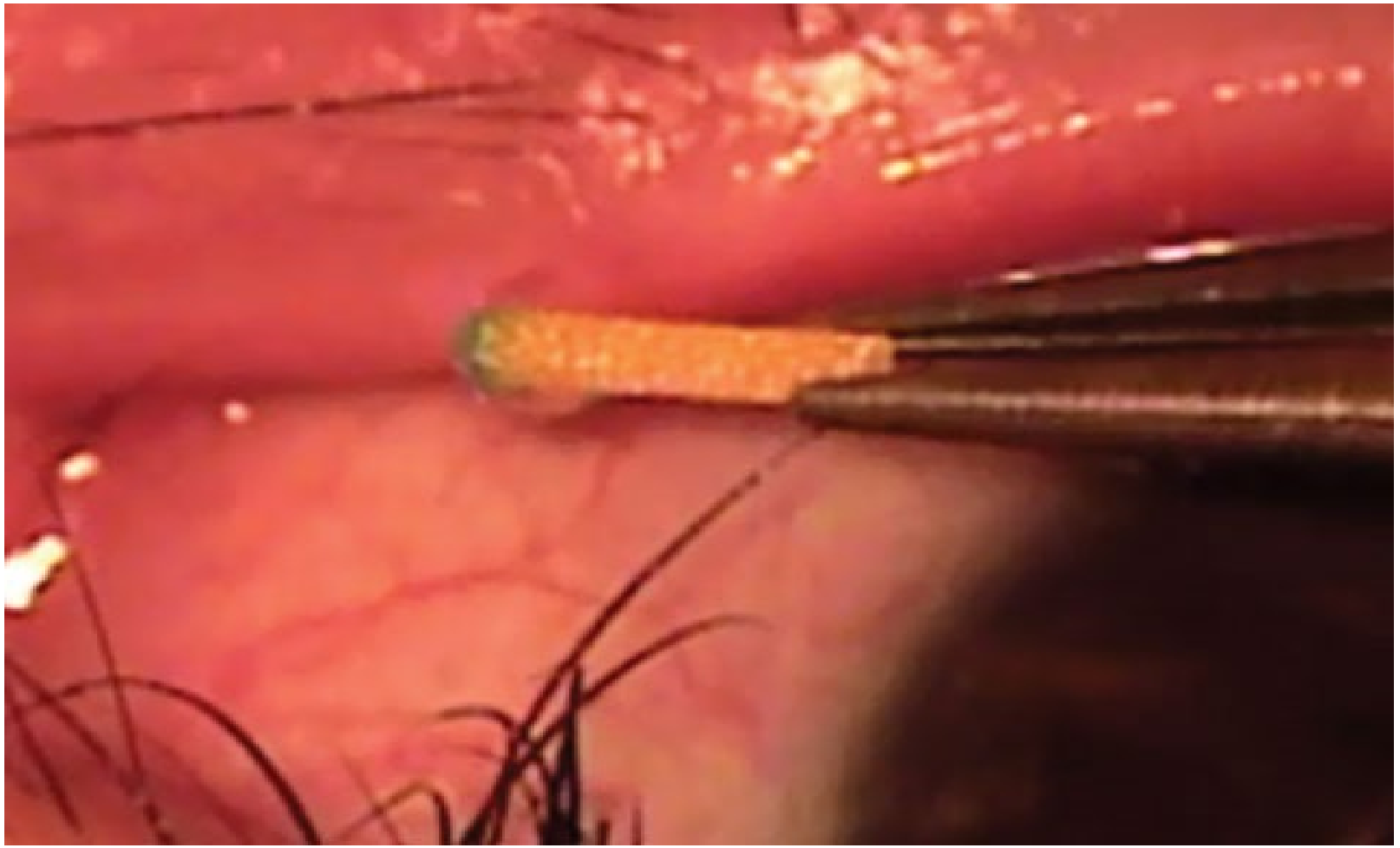
All IOP included, regardless of plug loss/removal

*95% CI excludes 0, indicating a p-value of <.05

Animal IOP Model (Mean Time Points) -Travoprost



Ocular Therapeutix



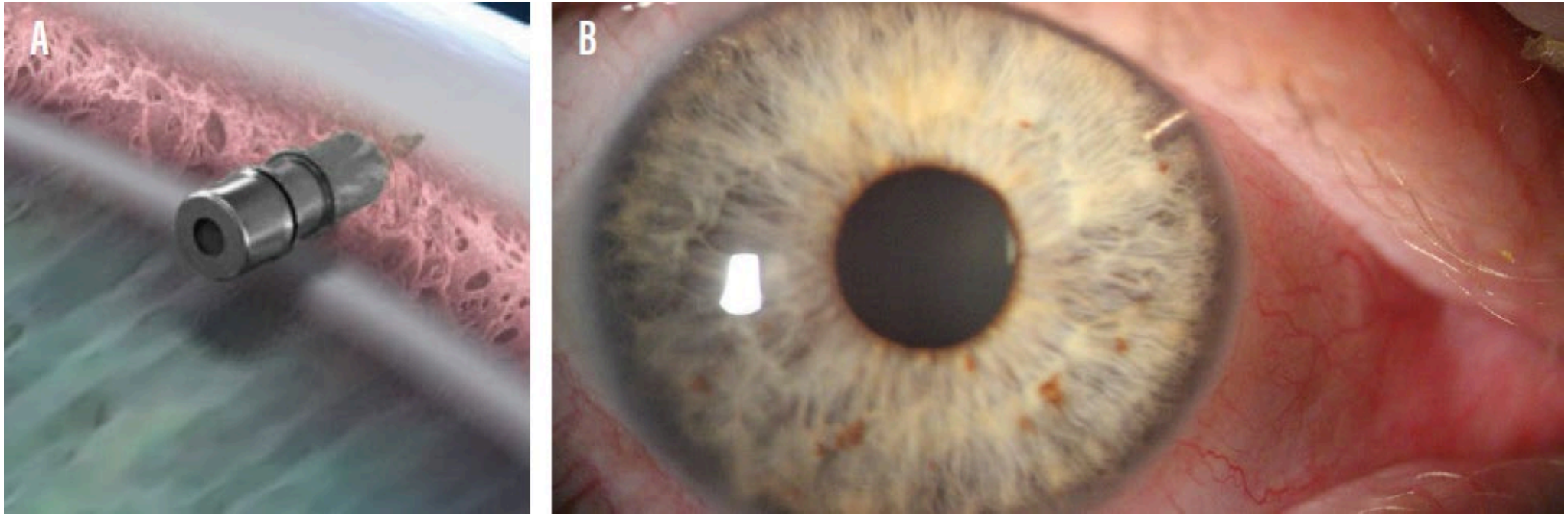
Ocular Therapeutix

- Phase II study randomly assigned 73 patients into two groups to receive either the travoprost plug with twice daily artificial tears or timolol 0.5% twice daily with placement of a drug-free punctal plug.
- At 90 days, there was a 4.5 to 5.7 mm Hg reduction from baseline IOP in patients who had the travoprost punctal plug, which was clinically meaningful.
- However, the control group had an average IOP lowering of 6.4 to 7.6 mm Hg.
- The safety profile was good—no hyperemia was seen. The retention rate at 60, 75, and 90 days was 91%, 88%, and 48%, respectively.

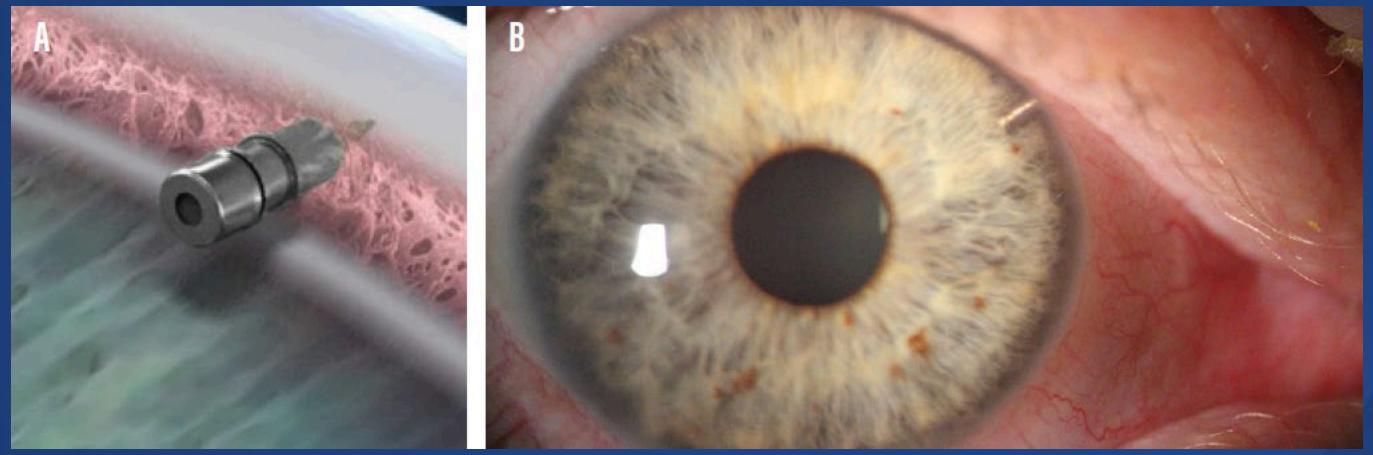
Glaukos iDose

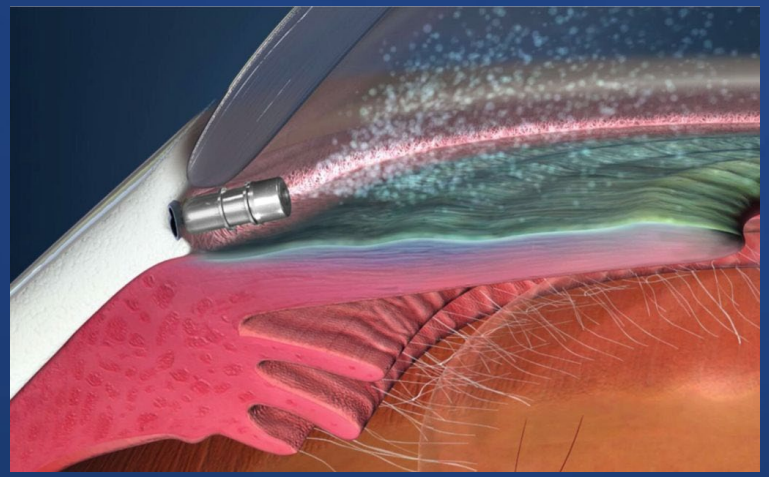
- The iDose is a titanium implant that is comparable in size to Glaukos' proprietary devices for microinvasive glaucoma surgery
- The 150-patient, multicenter, randomized, double-blind phase 2 trial evaluated two models of the iDose delivery system with different travoprost elution rates in comparison to a topical timolol maleate ophthalmic solution, 0.5%.
- The unit is filled with a formulation of travoprost specific to the device and capped with a membrane designed for continuous controlled drug elution into the anterior chamber.

Glaukos IDose TR



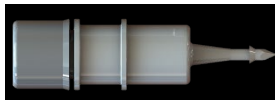
iDose-Travoprost Implant





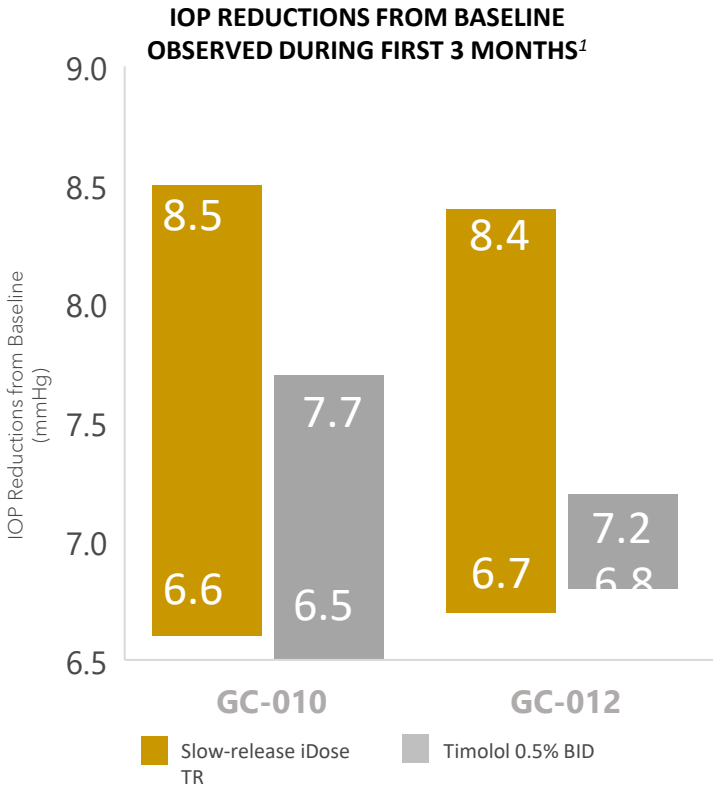
Glaukos Idose TR

- For each of the two Phase 3 *iDose TR* pivotal trials, GC-010 and GC-012, both the fast- and slow-release *iDose TR* arms achieved the pre-specified primary efficacy endpoint of non-inferiority to the active comparator arm (twice-daily topical timolol ophthalmic solution, 0.5%) through 3 months.
- For the GC-010 trial, the intraocular pressure (IOP) reductions from baseline over the first 3 months were 6.6-8.5 mmHg in the slow-release *iDose TR*arm, versus 6.6-7.7 mmHg in the timolol control arm (mm Hg range represents IOP reduction means across the six U.S. Food and Drug Administration (FDA) pre-specified timepoints of 8 a.m. and 10 a.m. at Day 10, Week 6 and Month 3).
- For the GC-012 trial, IOP reductions from baseline over the first 3 months were 6.7-8.4 mm Hg in slow-release *iDose TR* arm, versus 6.8-7.2 mmHg in the timolol control arm.
- 93% of slow-release *iDose TR* subjects remained well-controlled on the same or fewer IOP-lowering topical medications at 12 months compared to screening after a single administration of *iDose TR,* versus 67% of timolol control subjects in both Phase 3 trials.
- Additionally, 81% of slow-release *iDose TR* subjects were completely free of IOP-lowering topical medications at 12 months across both trials.



iDose Phase 3 data achieves primary efficacy endpoints

In 2 pivotal trials, iDose TR fast- and slow-release doses achieved pre-specified primary efficacy endpoints as agreed upon with US FDA (non-inferiority to topical timolol through 3 months)



- 1,150 subjects randomized across both Phase 3 trials
- Mean baseline IOP of ~24 mmHg in each study
- ~81% of slow-release iDose TR subjects had open-angle glaucoma; 19% ocular hypertension
- 67% of slow-release iDose TR subjects were on at least 1 IOP-lowering medication at screening, including 23% of subjects that were on 2 or more

1 mmHg range represents IOP reduction means across the six U.S. FDA pre-specified timepoints of 8AM and 10AM at Day 10, Week 6 and Month 3 ; iDose TR is not approved by the FDA

Phase 3 and Phase 2b duration data for iDose TR

	AT 12 MONTHS	AT 24 MONTHS	AT 36 MONTHS
PH 3	93%		
PH 2B	92%	72%	69%

Percentage of slow-release iDose TR subjects **well-controlled on the same or fewer IOP-lowering topical medications**

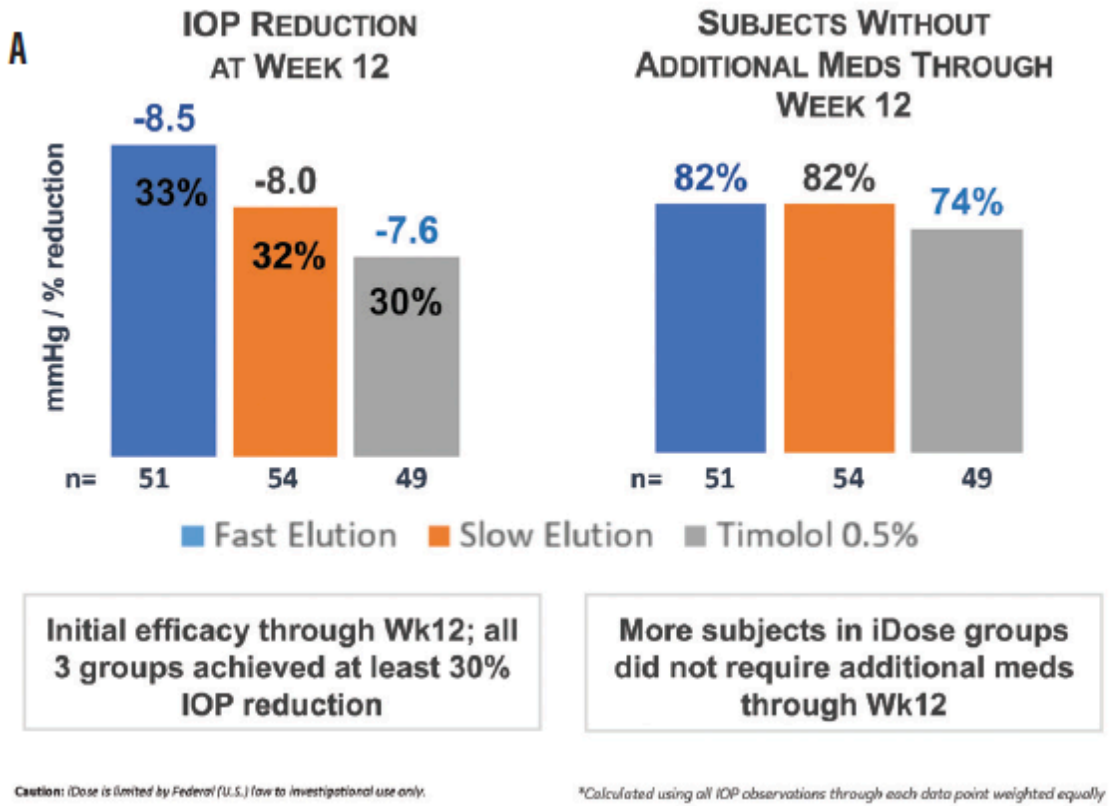
81% of slow-release iDose TR subjects in the Phase 3 trials were completely free of IOP-lowering topical medications at 12 months

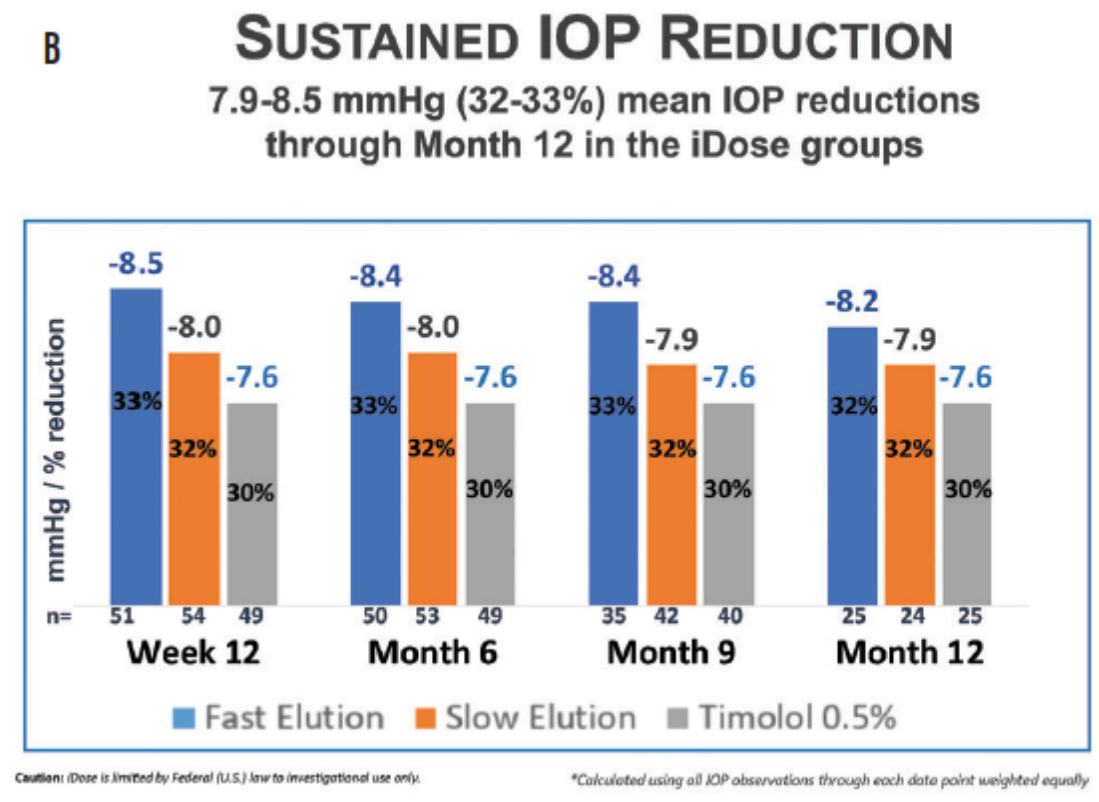
iDose TR is not approved by the FDA

Glaukos IDose TR

- *iDose TR* demonstrated excellent tolerability with 98% of slow-release *iDose TR* subjects continuing in the trial at 12 months, versus 95% of timolol control subjects across both Phase 3 trials.
- *iDose TR* demonstrated a favorable safety profile through 12 months, with no adverse events of corneal endothelial cell loss, no serious corneal adverse events and no adverse events of periorbital fat atrophy.
- Notably, conjunctival hyperemia occurred at a very low rate of 3% for slow-release *iDose TR* subjects. The most frequent adverse event for slow-release *iDose TR* subjects was mild transient iritis at a rate of 6% in both Phase 3 trials.
- In-office administration of *iDose TR* was successfully employed with various subjects across multiple sites with outcomes that were consistent with the Phase 3 trials, thus demonstrating the feasibility of *iDose TR* administration in the office setting.

Glaukos Idose TR





Glaukos IDose TR

- Results from the exchange trial demonstrated a second administration of *iDose TR* and removal of the original *iDose TR* implant was safe and well-tolerated, with the second *iDose TR* demonstrating a favorable safety profile over a 12-month evaluation period.
- Additionally, no subject in the exchange trial exhibited a greater than 30% endothelial cell loss over the extended evaluation period of more than five years on average.
- Glaukos plans to include the exchange trial's positive data set in its upcoming U.S. Food and Drug Administration (FDA) New Drug Application (NDA) submission targeted for the first quarter of 2023.

Cannabinoids

Marijuana & Glaucoma

TABLE 1. MARIJUANA SIDE EFFECTS*[5,14]

OCULAR	SYSTEMIC
• Conjunctival hyperemia	• Tachycardia
• Decreased lacrimation	• Decreased blood pressure
• Photophobia	• Orthostatic hypotension
• Ptosis	• Euphoria or dysphoria
• Blepharospasm	• Impaired coordination
• Nystagmus	• Difficulty with concentration, problem solving, memory
• Impairment of accommodation	• Decreased testosterone
	• Impaired immunity

**Any route of administration*

Marijuana & Glaucoma Therapy

American Glaucoma Society:

“Although marijuana can lower the intraocular pressure, its side effects and short duration of action, coupled with a lack of evidence that its use alters the course of glaucoma, preclude recommending this drug in any form for the treatment of glaucoma at the present time.”

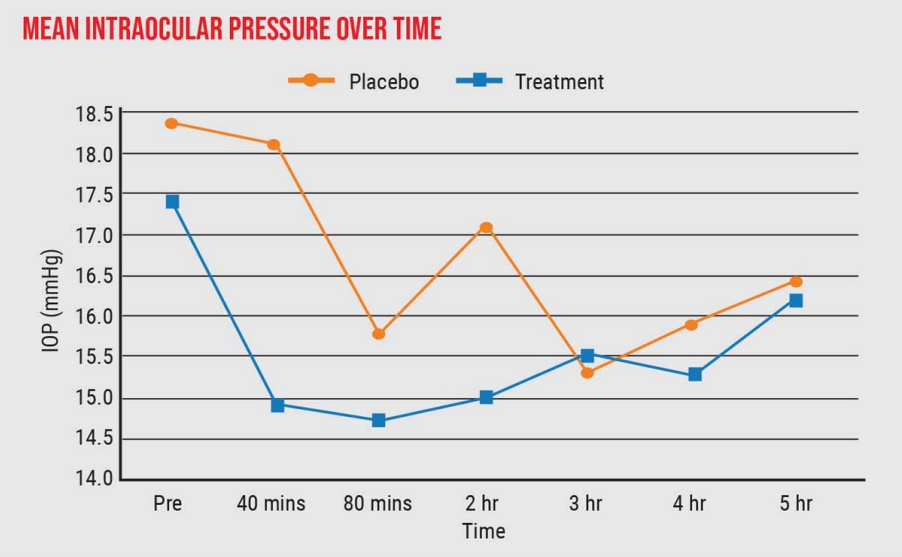
Cannabis, Glaucoma and Intraocular Pressure

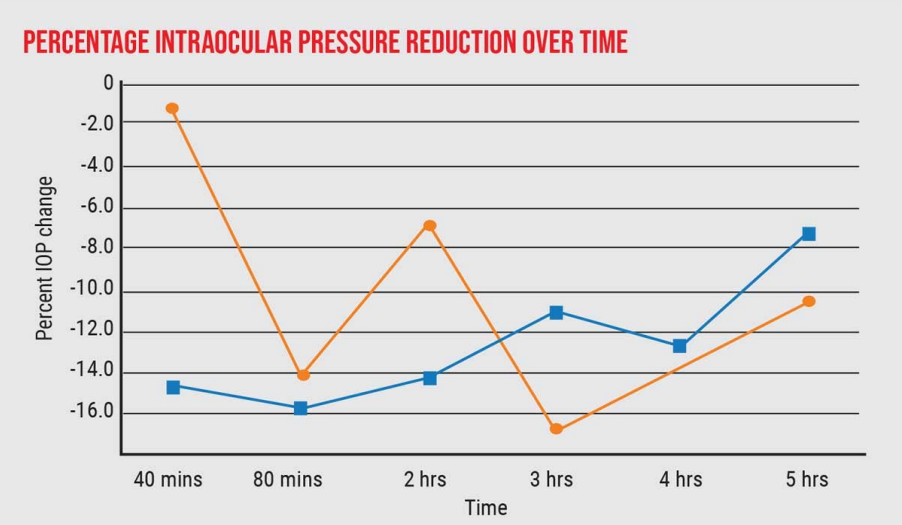
- Because of the Schedule I status and the stigma associated with it, all research on cannabis basically ceased in the 1980s; it was just too difficult to get around the regulations.
- Among other things, limited high-quality data has impacted the current American Academy of Ophthalmology and American Glaucoma Society positions on the use of cannabis to treat glaucoma.
- They don't support it, largely because there's too little information to justify such support.
- Sameh Mosaed, Etal (Review of Ophthalmology 2022)

Cannabis, Glaucoma and Intraocular Pressure

Sameh Mosaed, MD / Review of Ophthalmology

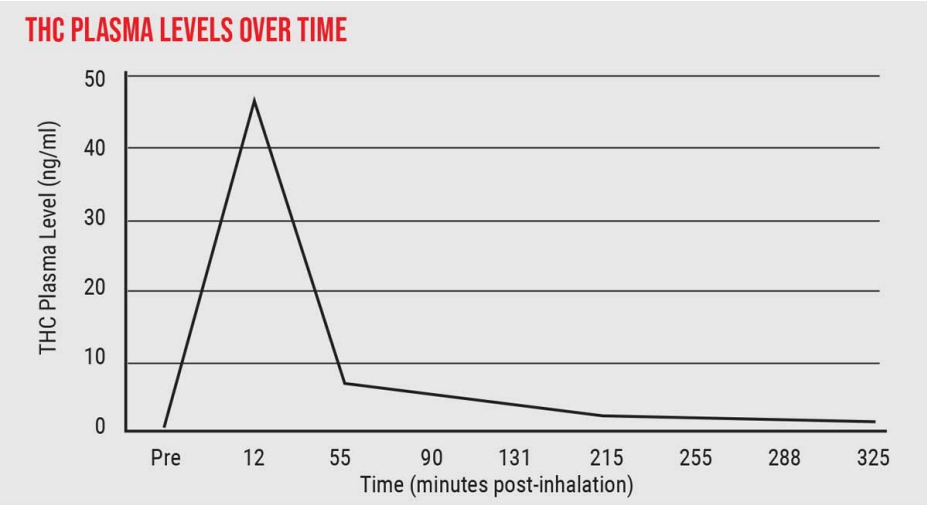
Dr. Mosaed is a professor of ophthalmology and director of the Glaucoma Division of the Gavin Herbert Eye Institute at UC Irvine.
.Dr. Singh is a professor of ophthalmology and chief of the Glaucoma Division at Stanford University School of Medicine.
Dr. Netland is Vernah Scott Moyston Professor and Chair at the University of Virginia in Charlottesville.

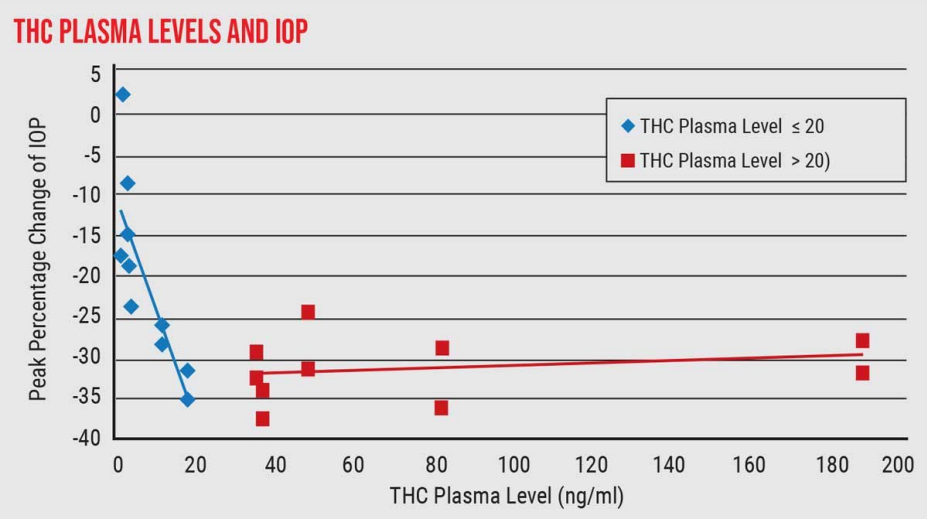




One of the author's studies found a substantial and significant decrease in IOP in subjects smoking cigarettes with THC, compared to placebo. The patients went from a mean IOP of 17.5 mmHg prior to smoking down to lower than 15 mmHg, 15 percent below baseline.

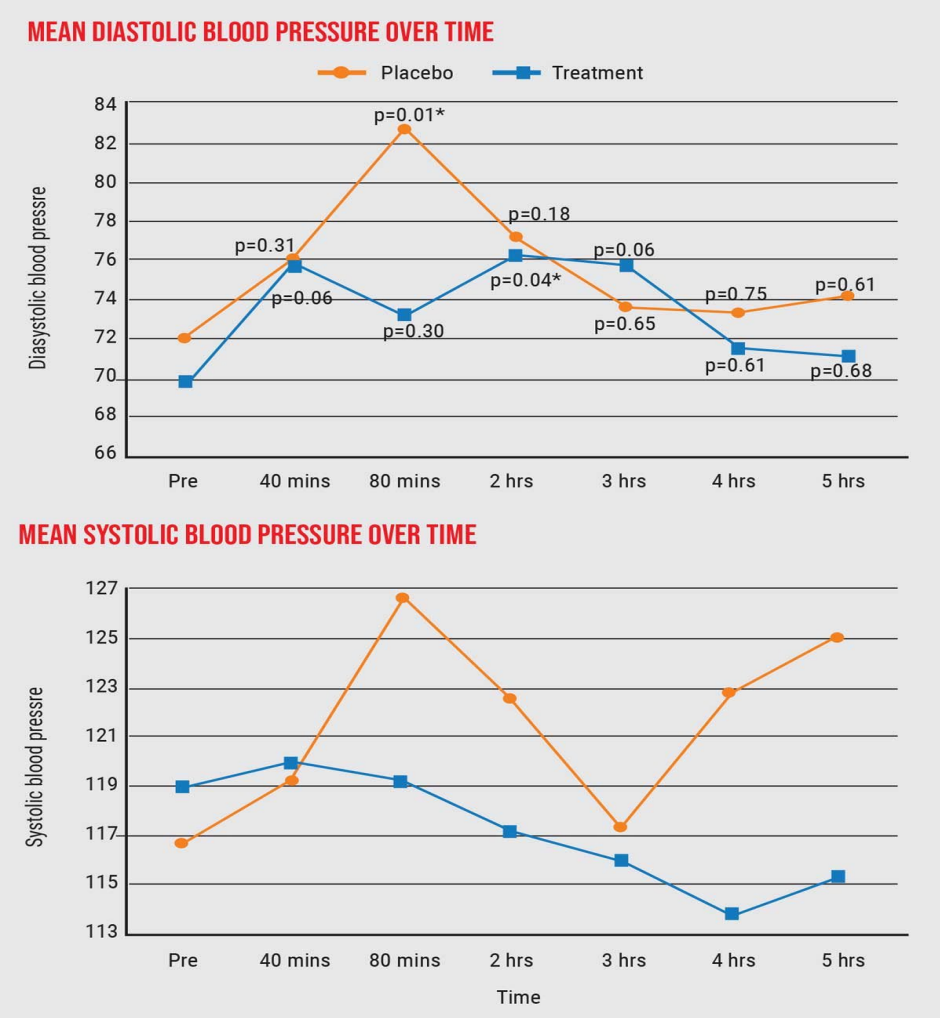
Cannibis, Glaucoma and Intraocular Pressure





THC is metabolized quickly, soon disappearing from the bloodstream. (Top graph) Decline in IOP paralleled rising THC plasma levels up to 20 ng/ml; above that, IOP did not decline. (Bottom graph) This suggests that a limited intake of THC—possibly a small enough amount to avoid psychotropic effects—could accomplish significant IOP lowering

Cannabis, Glaucoma & Intraocular Pressure



The data revealed only one point of statistically significant difference between the placebo group and cannabis group in diastolic or systolic blood pressure (asterisk).

Cannabis, Glaucoma and Intraocular Pressure

- Many people talk about marijuana when they really should be discussing *cannabis*.
- Cannabis is a genus of flowering plants in the *Cannabaceae* family, which consists of three primary species: *Cannabis sativa*; *Cannabis indica*; and *Cannabis ruderalis*.
- The term marijuana has negative connotations; it's used to refer to specific varieties of cannabis that contain more than 0.3 percent THC. CBD, on the other hand, has no psychotropic effects.
- Cannabis contains multiple compounds—more than 480, of which about 65 have been identified as phytocannabinoids (including CBD and THC).
- Cannabis also contains about 120 compounds that give it its characteristic aroma—mainly volatile terpenes and sesquiterpenes. Not surprisingly, most patients don't know much about cannabis; many don't even understand the distinction between THC and CBD.

Cannabis, Glaucoma & Intraocular Pressure

- We found a substantial and significant decrease in IOP in subjects smoking cigarettes with THC compared to placebo. The patients went from an average IOP of 17.5 mmHg prior to smoking, down to lower than 15 mmHg, 15 percent lower than baseline.
- A 15-percent reduction, when you start out with normal pressure, is quite significant—on a par with what you'd see with a single-agent IOP-lowering eye drop.
- The lower pressure was sustained for up to three hours.
- In terms of systolic and diastolic blood pressure, we found no statistically significant differences between the placebo group and cannabis group. There were some differences, as the graphs show *(graph below)*, but the differences were only statistically significant at a single time point (marked with an asterisk).
- We confirmed that THC is metabolized very quickly; it gets absorbed into tissues and disappears from the bloodstream very quickly.
- There was a linear correlation between THC level in the blood plasma and IOP reduction, up to about 20 ng/ml of THC. Additional elevation of plasma THC, however, didn't correlate with further IOP lowering. *(See graph above.)* In other words, achieving 20 ng/ml of blood plasma level of THC was all that was required to achieve the maximum IOP-lowering effect.

Mechanisms of Cannabis in Glaucoma (GT 4/18)

- Marijuana and THC have been shown to lower IOP in 60% to 65% of both normal individuals and patients with glaucoma. Mean IOP reduction in one study was about 25%.[5]
- An ocular hypotensive effect has been reported when the drug is smoked or ingested and when THC is inhaled or administered orally, sublingually, or intravenously.[6]
- The duration of action is short, about 3 to 4 hours.
- There appears to be a dose-response relationship between the amount of marijuana consumed and the degree of IOP reduction, although the length of efficacy does not improve at higher doses.[5]
- Topical administration of THC to the eye does not lower IOP.[7,8]
- THC is a highly lipophilic compound and cannot be administered in a water-based vehicle.
- In one placebo-controlled double-masked study using an oil-based vehicle, no IOP-lowering effect was demonstrated. Both the placebo (vehicle) and the study drug caused significant ocular irritation.[7]

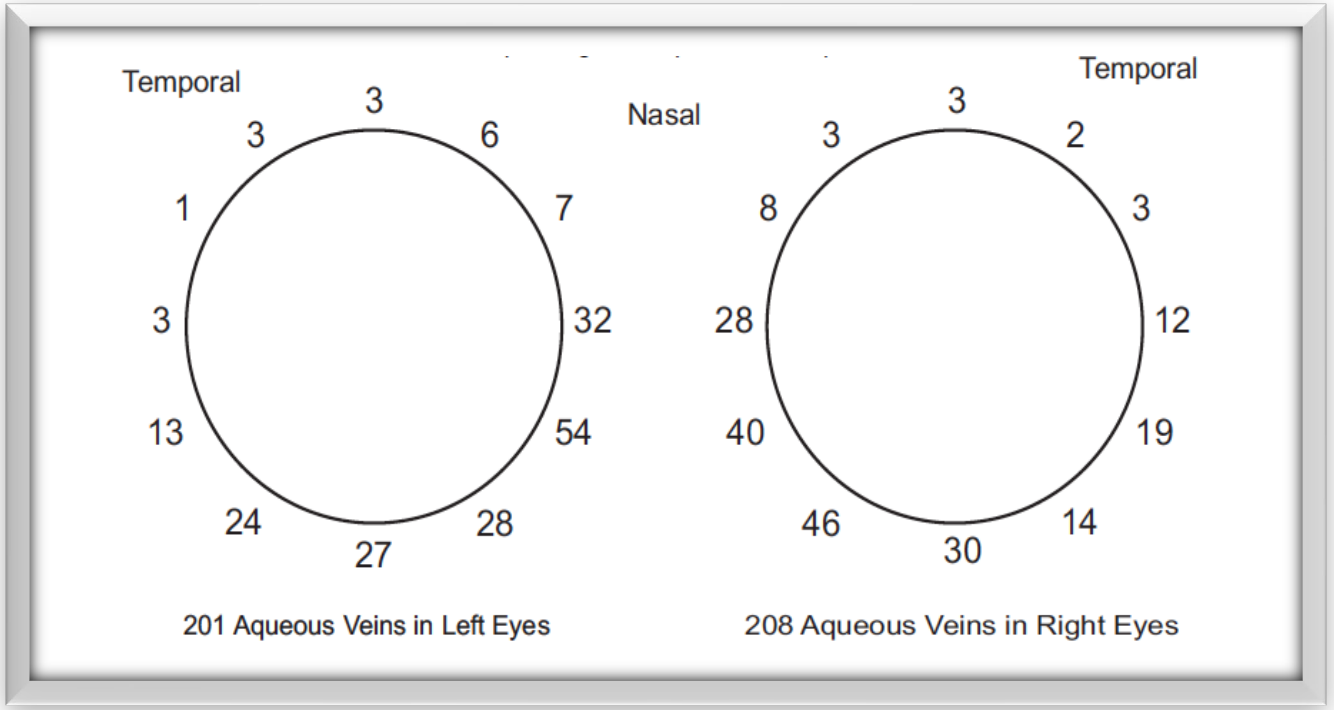
MIGS Glaucoma Video Grand Rounds

MIGS or LIGS?

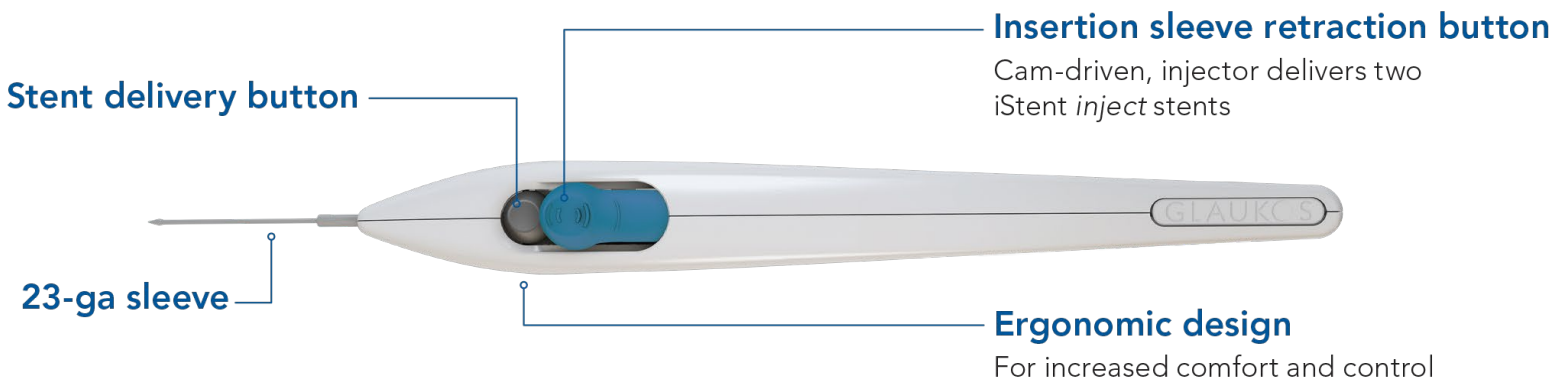
- Trabecular Bypass/Canal Enhancement
  - Istent G1
  - Istent Inject
  - Hydrus
- Goniotomy
  - Trabectome
  - Kahook Dual Blade
  - Omni
  - GATT
- Canal Expansion
  - ABIC
  - Omni
- Suprachoroidal Space
  - None (Cypass)
- Entire Outflow System Bypass
  - Xen
  - Innfocus
- Cycclophotocoagulation
  - ECP
  - TCP

Distribution of Aqueous Veins

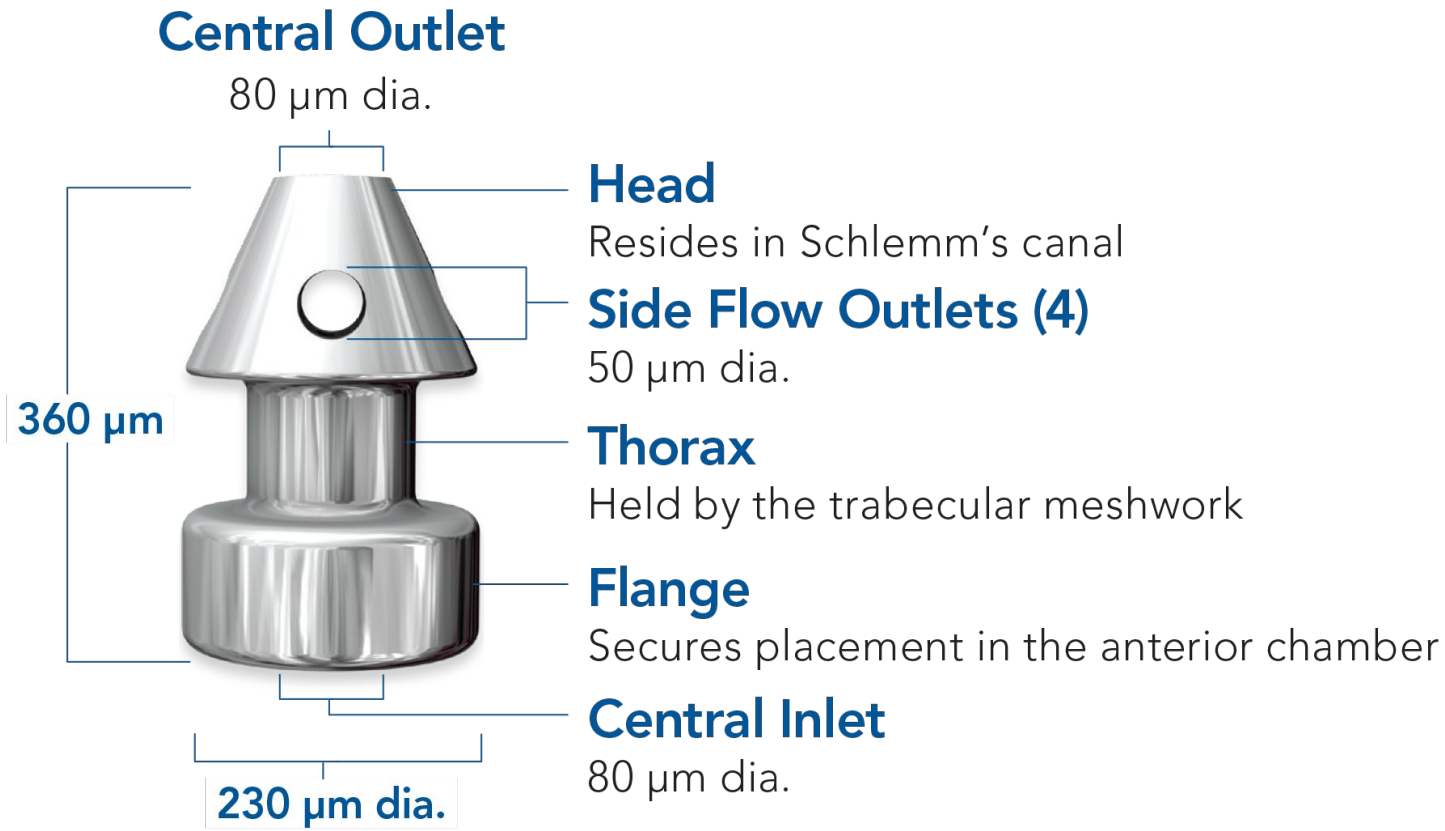
(Among 409 Aqueous Veins)



De Vries 1947


Stent delivery button
Insertion sleeve retraction button
Cam-driven, injector delivers two iStent *inject* stents
23-ga sleeve
Ergonomic design
For increased comfort and control

Microbypass Stent



Head
Resides in Schlemm's canal

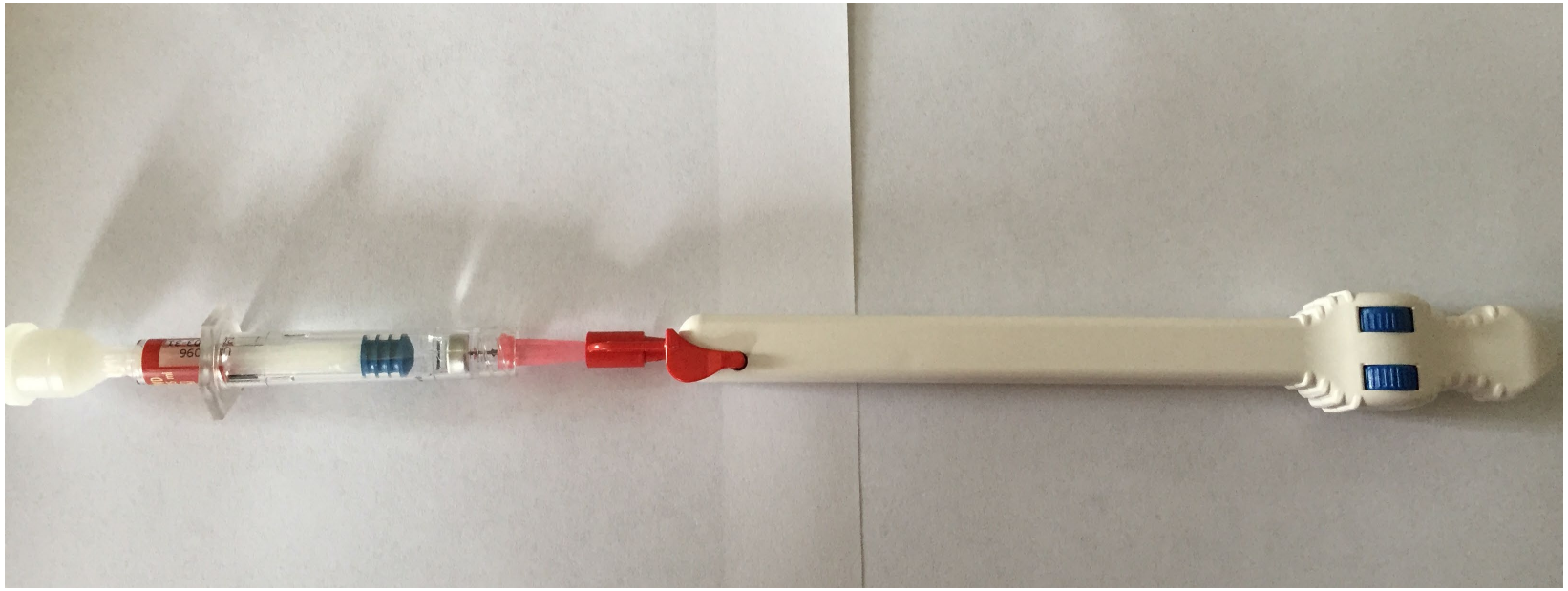
Side Flow Outlets (4)
50 µm dia.

Thorax
Held by the trabecular meshwork

Flange
Secures placement in the anterior chamber

Central Inlet
80 µm dia.

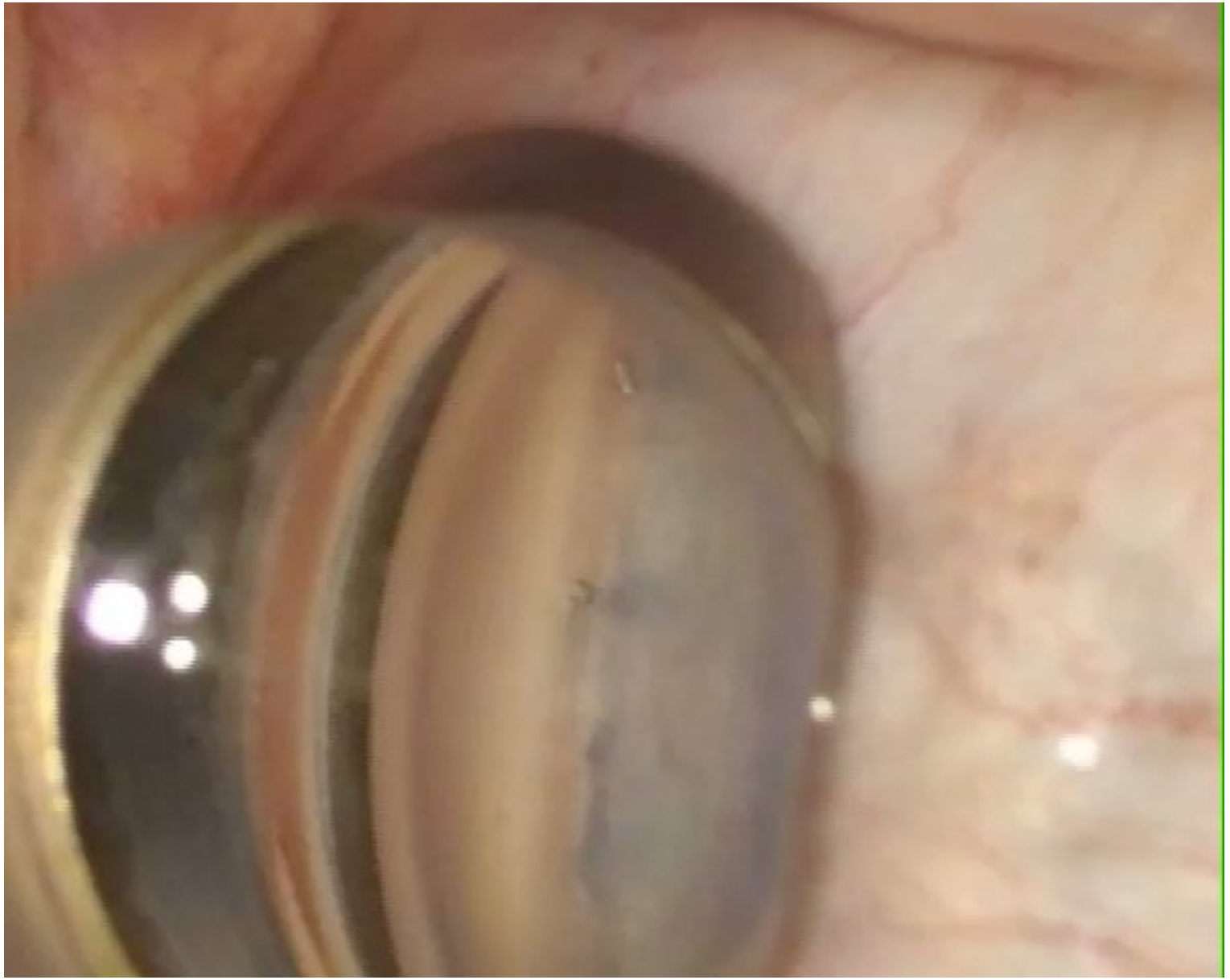
Ab Interno Viscocanalostomy (Visco 360)



Case Report

- 75 year old female with modérate POAG but with some angle narrowing
- Treated with latanoprost and timolol/brimonidine
- IOP 20/21 Peak IOPs 26/27
- Inferior thinning of RNFL on OCT, with VF nasal steps
- Visual acuity 20/50 OU due to modérate NS cataracts
- Treated with combined OMNI/cataract OU
- Several days of post-op microhyphema
- IOP 18/19 on no meds post-op

Ab interno Viscocanalostomy



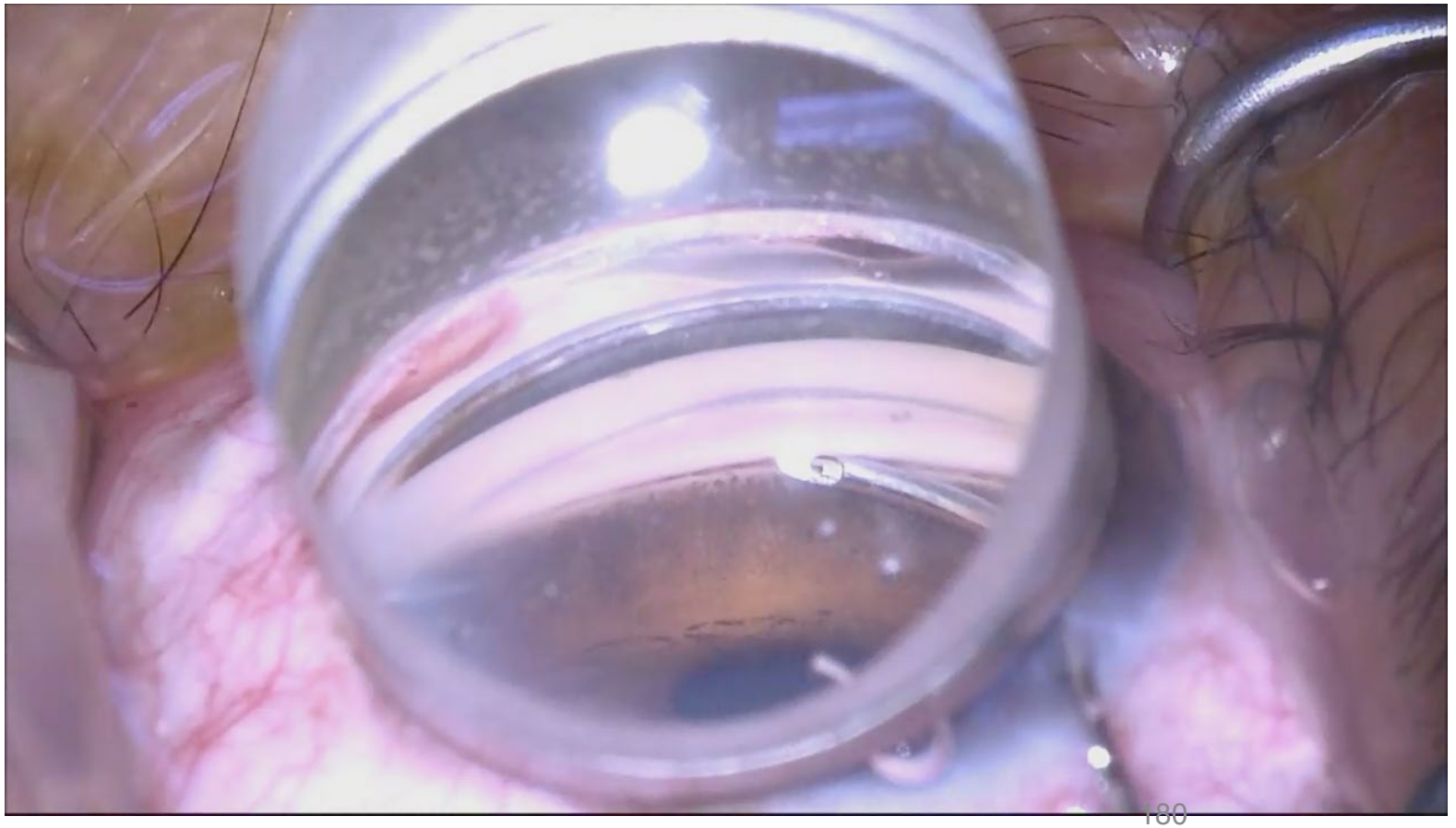
Ivantis /Hydrus Microstent

- The FDA's approval was based on the 24-month results from the HORIZON trial, the largest MIGS study to date.
- The study included 556 mild to moderate glaucoma patients randomly assigned to undergo cataract surgery with or without the microstent.
- More than 77% of patients with the implant exhibited a significant decline in unmedicated IOP, compared with 58% of the control group.
- On average, the device reduced IOP by 7.5 mmHg, approximately 2.3 mmHg more than the cataract surgery-only group.

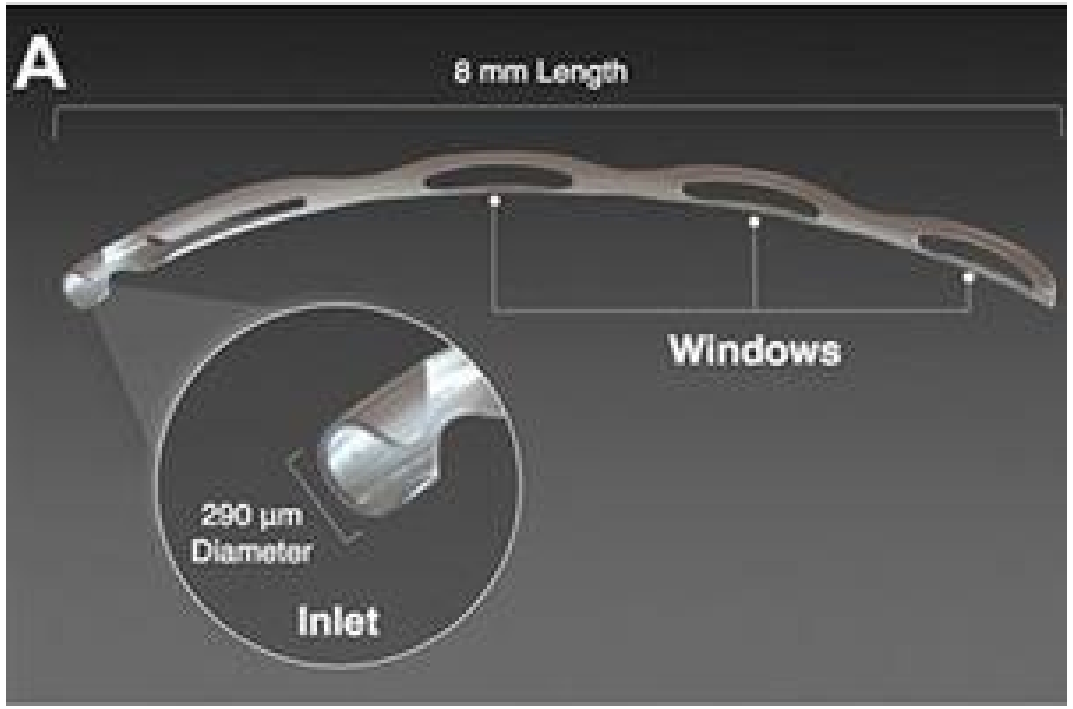
Hydrus™ Aqueous Implant

- **Flexible canal “scaffold”**
- Composed of biocompatible alloy (Nitinol)
- Scalloped and open design allows aqueous flow
- 3 clock-hour length targets multiple collector channels

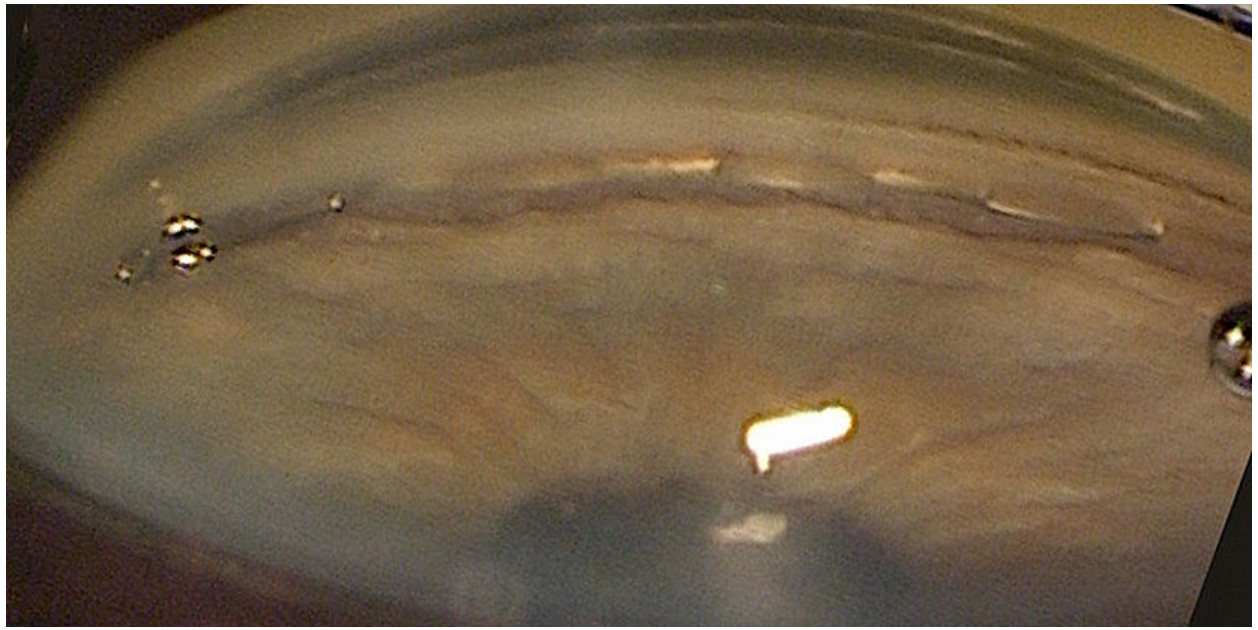
Hydrus



Hydrus Microstent



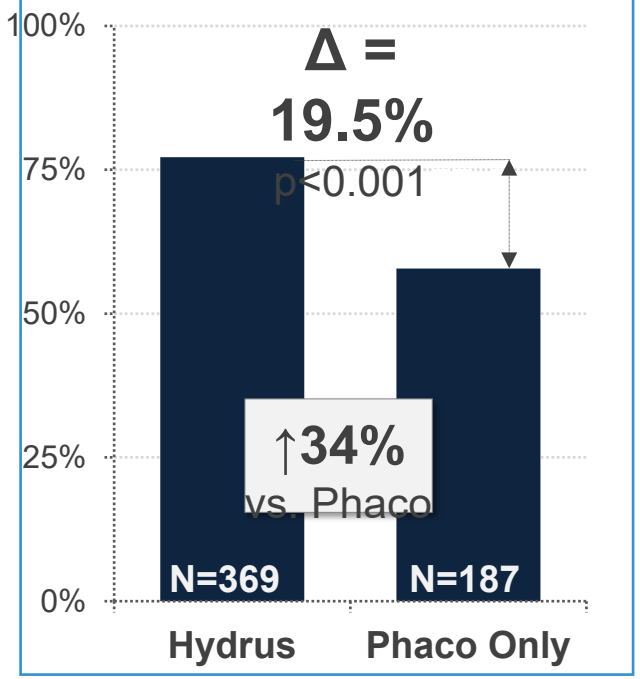
Hydrus Microstent



Primary Endpoint Comparison

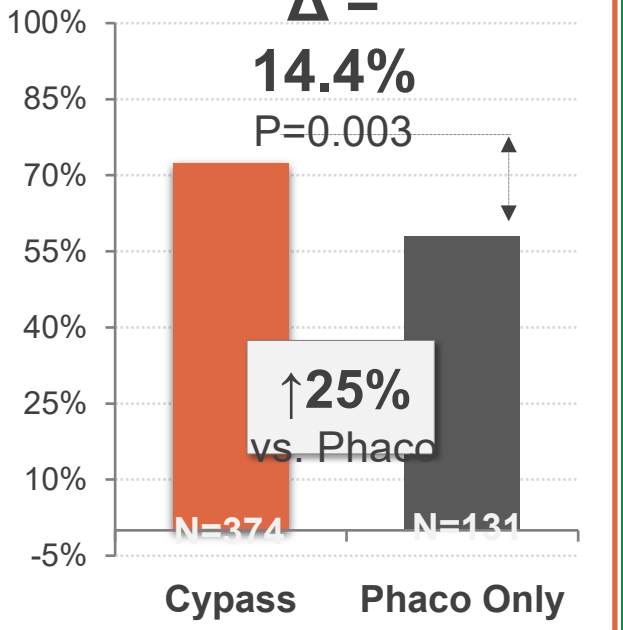
IOP REDUCTION ≥ 20% AFTER MEDICATION WASH OUT

HORIZON: 24 Months[1]



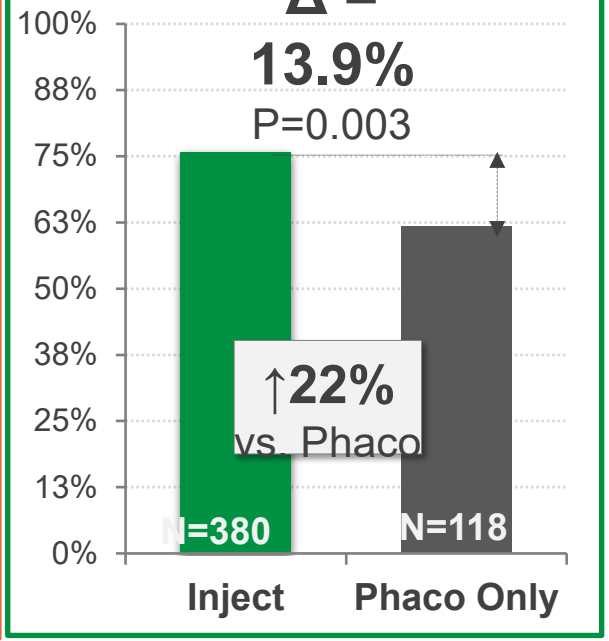
Intention-to-Treat analysis

COMPASS: 24 Months[2]



Intention to Treat Analysis

INJECT IDE: 24 Months[3]



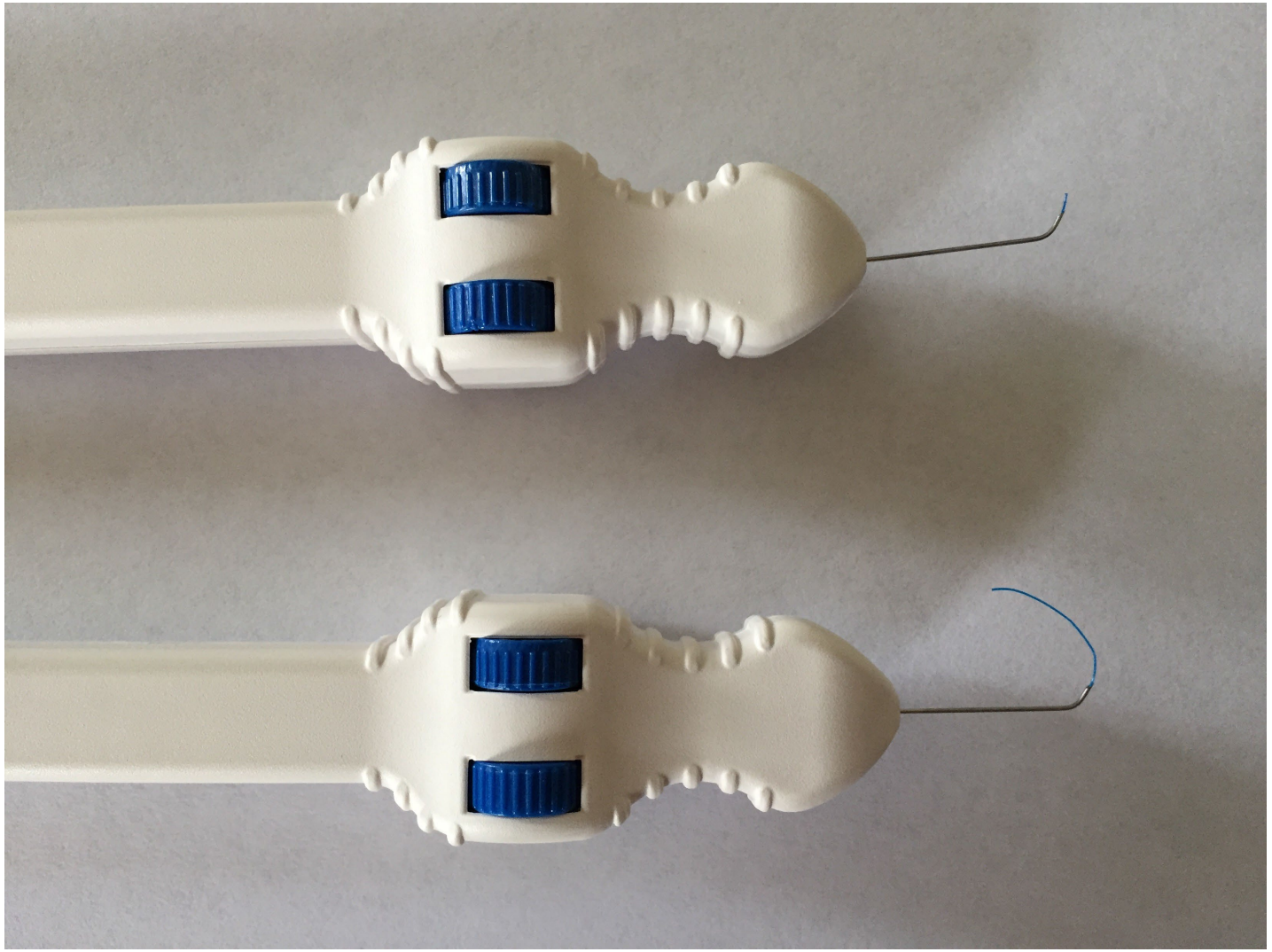
Per Protocol Analysis

1. Samuelson TW, Chang DF, Marquis R, et al. A Schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: The HORIZON Study. *Ophthalmology* 2019;126:29-37.
2. US Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): CyPass® System (Model 241-S) . US Food and Drug Administration website https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150037B.pdf. Published July 29, 2016..
3. US Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): iStent inject Trabecular Micro-Bypass System. US Food and Drug Administration website. https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170043b.pdf. Published June 21, 2018.

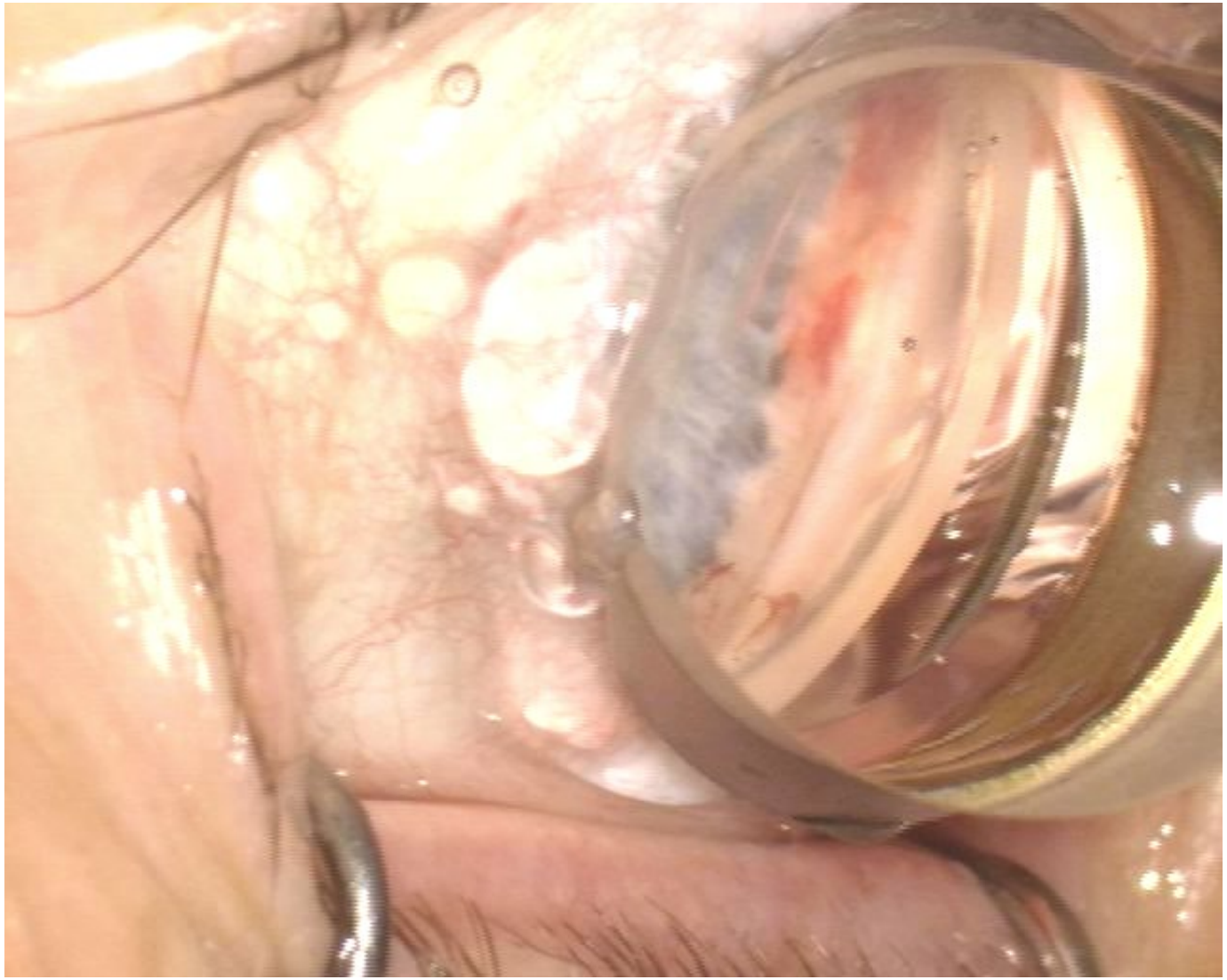
Case Report

- 65 year old female with modérate POAG sp cataract surgery with dry eyes
- Treated with latanoprost and timolol/dorzolamide
- IOP 18 OU Peak IOPs 25 OU
- Inferior thinning of RNFL on OCT, with VF mild nasal steps
- Visual acuity 20/25 OU
- Treated with Trab360 goniotomy OU
- Two days of post-op microhyphema
- IOP 18 OU post op off meds
- Ocular surface improved

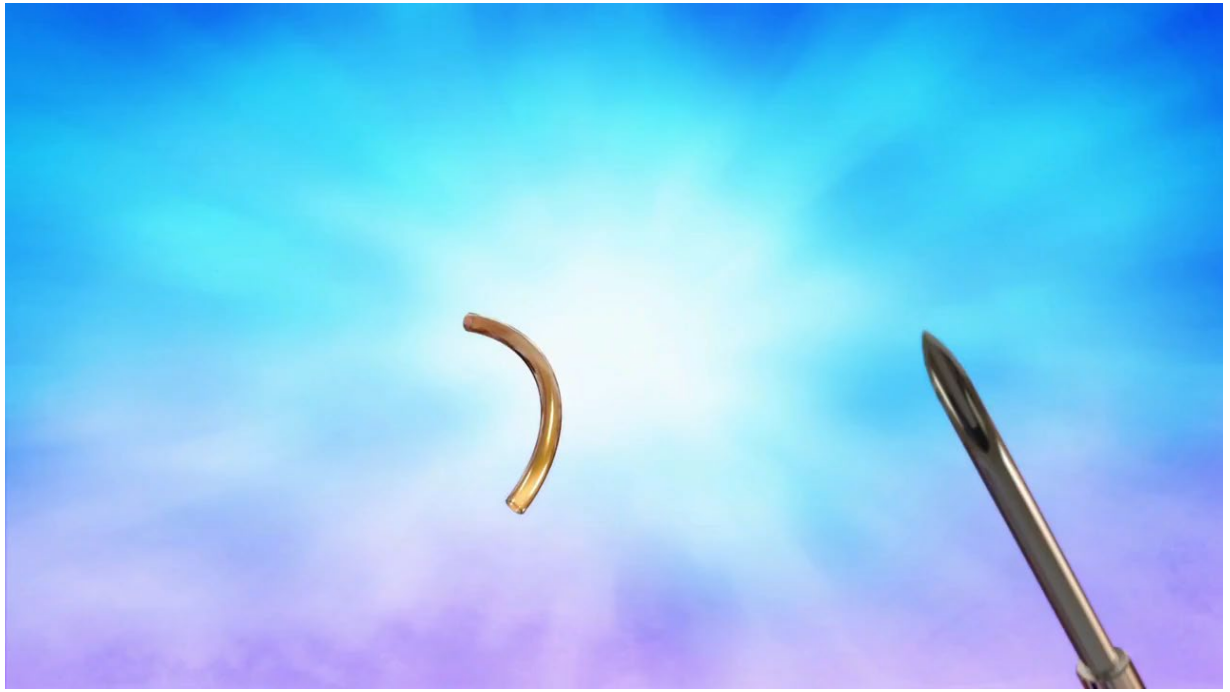
Ab Interno Trabeculotomy (Trab 360)



Trab 360



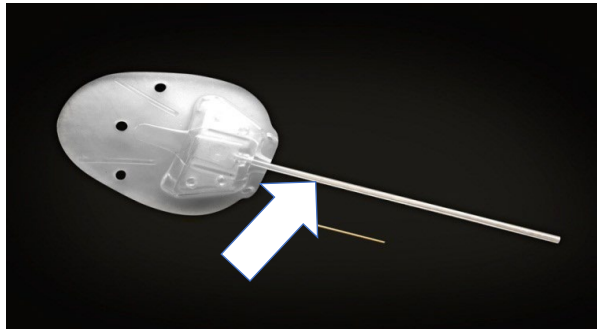
XEN



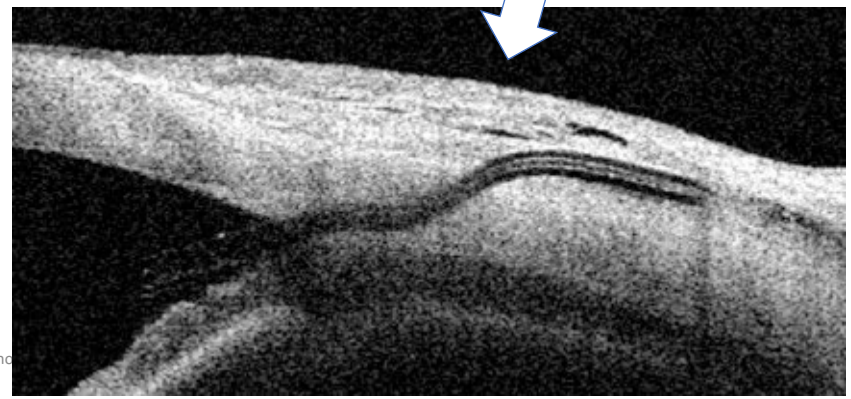
XEN Glaucoma Implant™ Mechanism of Action

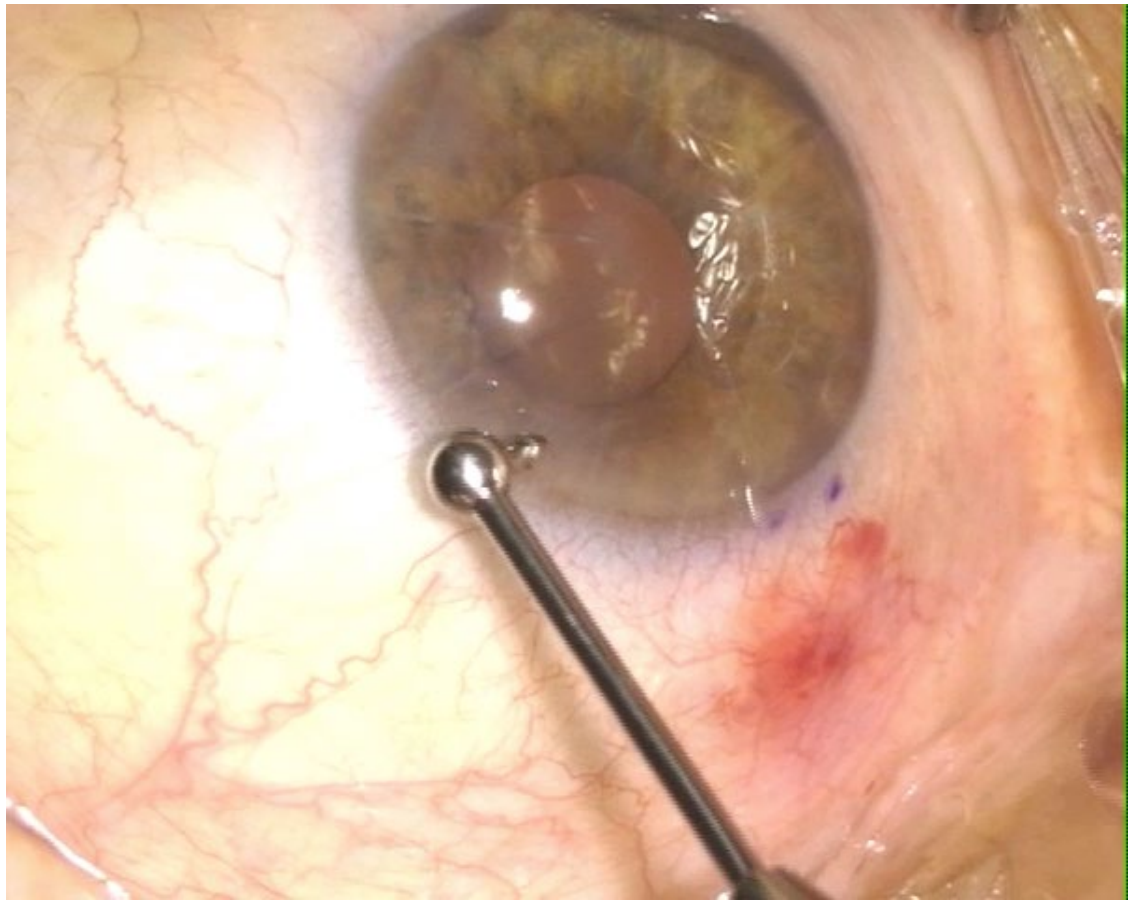
Ab Interno Sub-Conjunctival Drainage

- Surgical "Gold Standard" IOP reduction in minimally invasively procedure
- Clinically proven outflow pathway
- Bypasses all potential outflow obstructions
- Conjunctiva sparing: alternative surgical options remain
- Single implant delivers desired effectiveness



Gelatin Material is Tissue Conforming



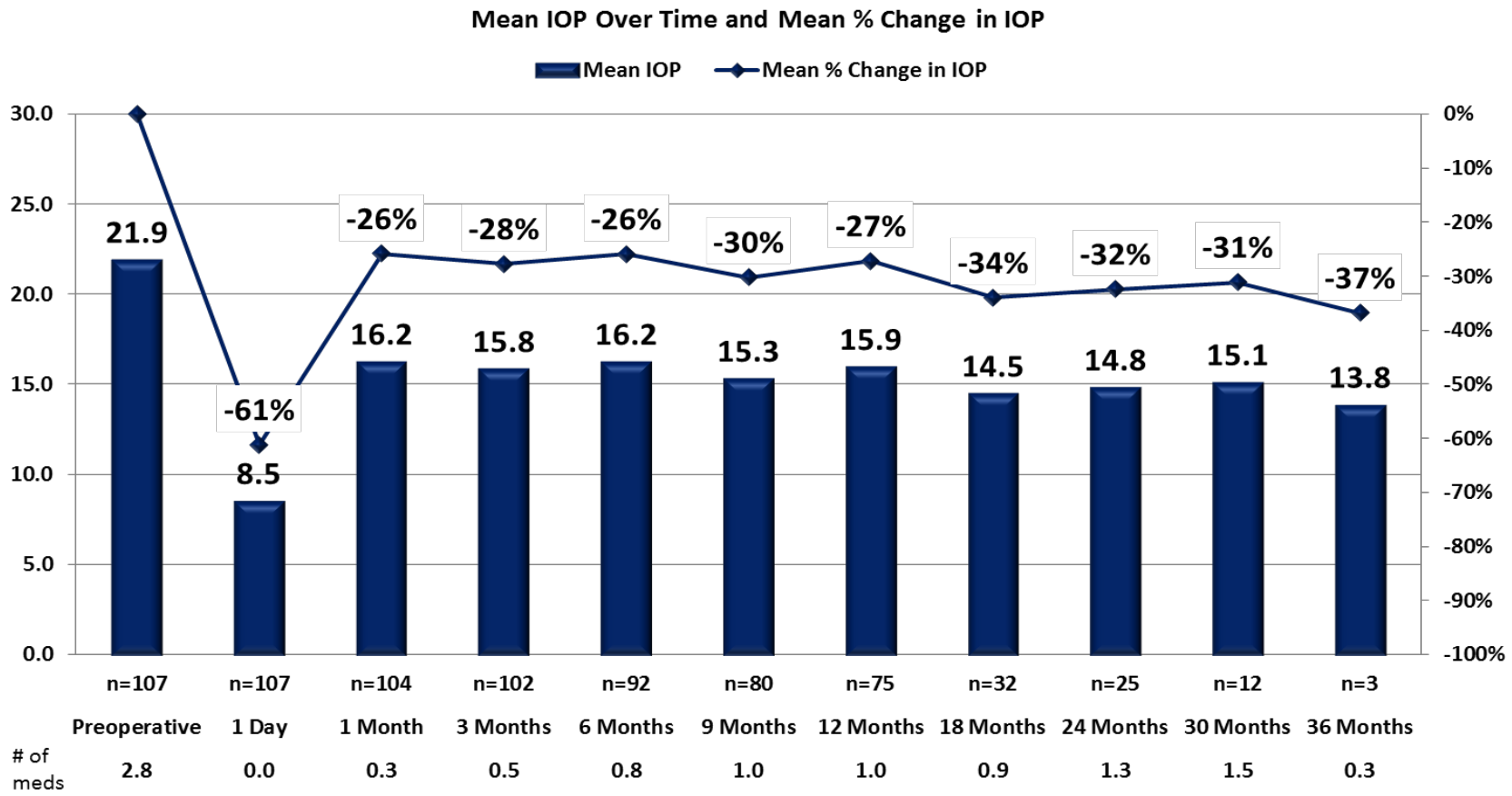


Case Report

- 66 year old female with modérate POAG sp cataract surgery with dry eyes sp SLT
- Treated with bimatoprost and timolol/dorzolamide
- IOP 21 OU Peak IOPs 25 OU
- Inferior and Superior thinning of RNFL on OCT, with VF defects above and below
- Target IOP 15
- Treated with Xen OU
- IOP 8 OU post op Day 1 off meds
- IOP 12/13 after 3 months

POAG Only

Summed patients: primary, combined and refractory

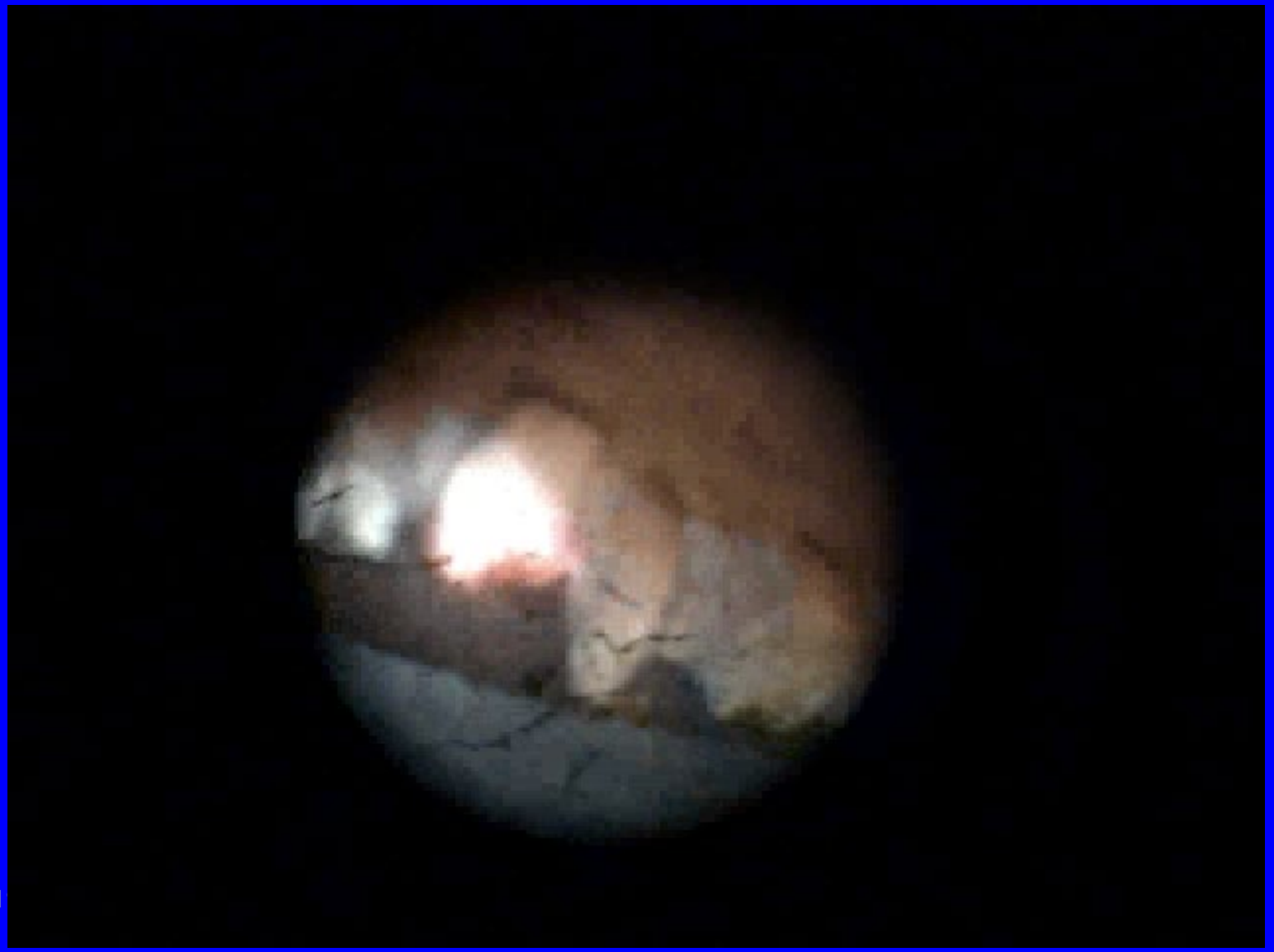


**Mean preoperative IOP is best medicated. Patients were not washed out prior to surgery.*

Case Report

- 85 year old asían female sp angle closure right eye/ narrow angle plateau iris OS
- Sp LPI OU
- Va 20/80 right eye, 20/50 left Eye
- IOP 30 OD 20 OS on maximal meds including diamox
- Treated w/cataract/ECP surgery to shrink ciliary processes
- IOP 15 - tapered off meds over two months

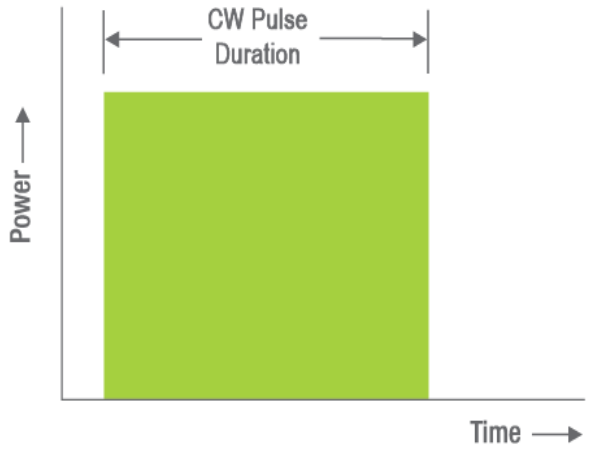
Plateau iris -sp angle closure



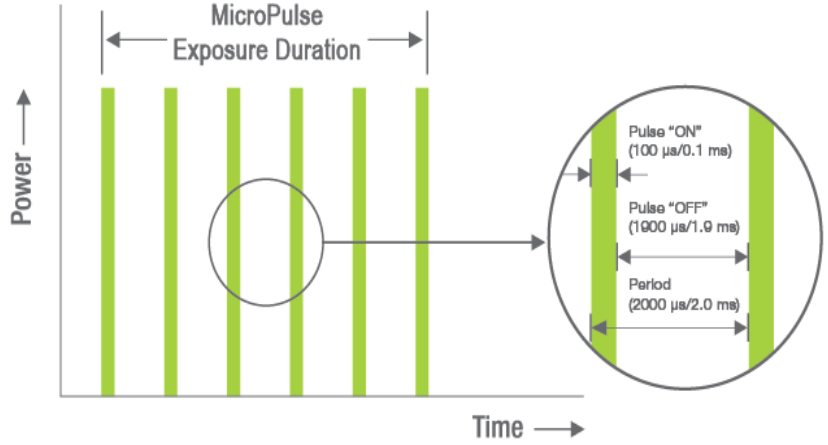
How MicoPulse® Works

MicroPulse technology finely controls thermal elevation by “chopping” a continuous-wave (CW) beam into an envelope of repetitive short pulses.

Continous-Wave (CW) Mode



MicroPulse Mode

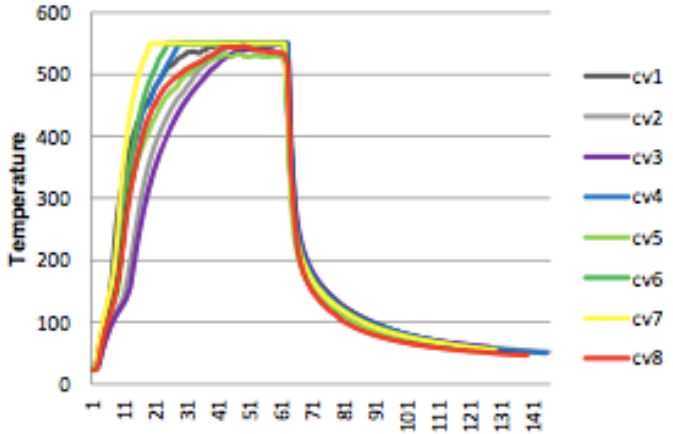


Micropulse Transscleral Cyclophotocoagulation

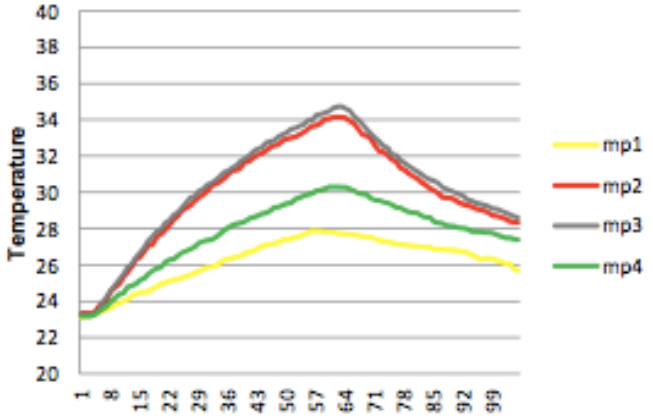
NUHS National University Health System

TEMPERATURE GENERATED

* **Conventional** CPC – T max **> 550 ⁰ C**
* **Micropulse** CPC – T max **35 ⁰ C**



G probe

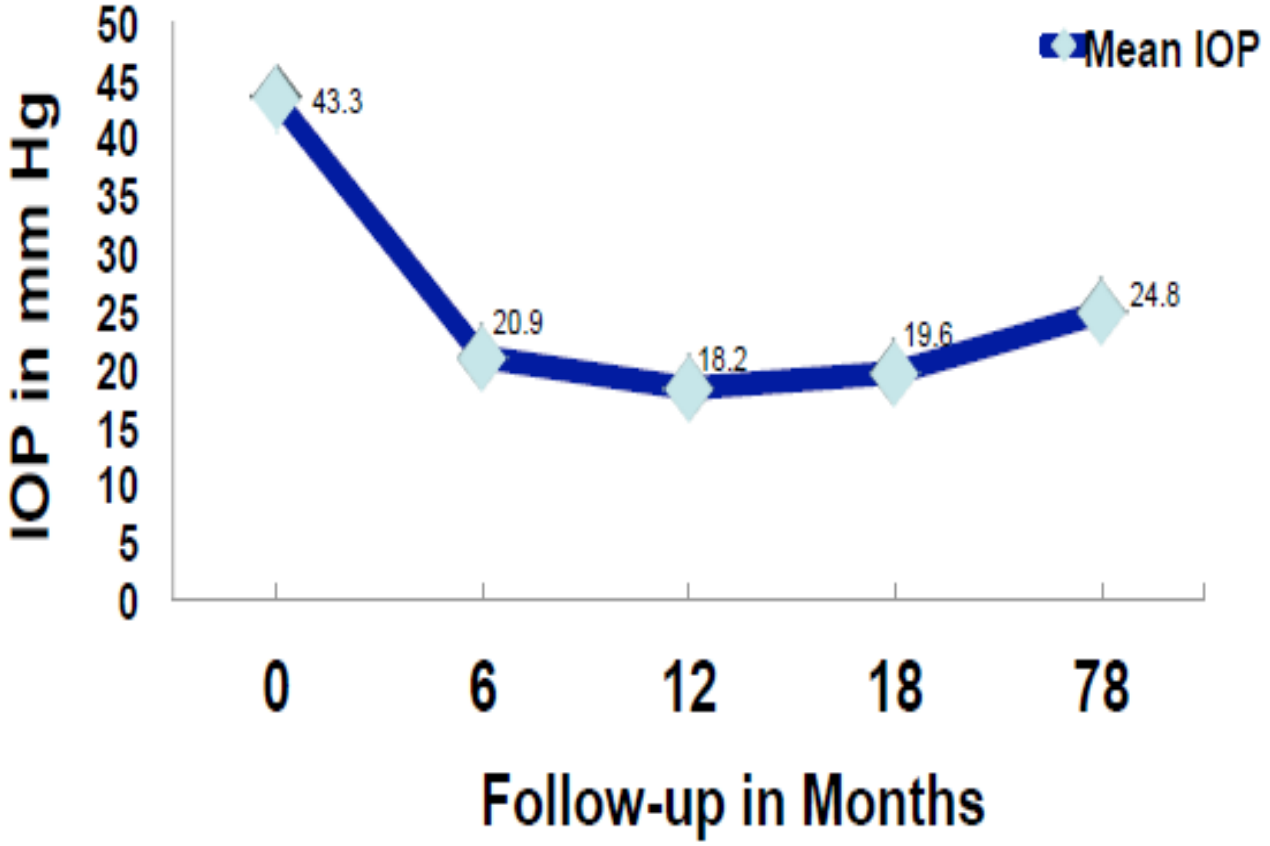


Micropulse CPC probe

NUH National University Hospital

NUS National University of Singapore

6½ Year Results Show Long-Term Efficacy & Durability



- 43% IOP reduction at 78 months (N=14)
- Meds reduced from mean of 1.8 to 1.1

Chew P, Aquino M. Long Term Efficacy of MicroPulse Diode Transscleral Cyclophotocoagulation in the Treatment of Refractory Glaucoma. EGS abstract, Prague, Czech Republic, June 19-22, 2016.

New Technology in Eye Care:
The Rise of the Machines

Dr. James Thimons, Founding Partner, Medical Director
Ophthalmic Consultants of Connecticut
Chairman, National Glaucoma Society

Disclosures

- Speaker
  - Alcon
  - Allergan
  - PRN
  - Tear Lab
  - Shire
  - Zeiss
  - B&L
  - Diopsys
  - Reichart
  - Glaukos
  - InFocus
  - Aerie

Welcome to Connecticut

What's the Latest Glaucoma News

OCT Artifacts Common With Combined Glaucoma, High Myopia

K. Patricia Bouweraerts, MA | December 13, 2023

Optical coherence tomography (OCT) artifacts are common among patients with both high myopia and glaucoma, according to the findings of a study published in the *Journal of Glaucoma*.

Small Optic Discs, Asian Ethnicity Raise Glaucoma Progression Risk

Lisa Kuhns, PhD | January 4, 2024

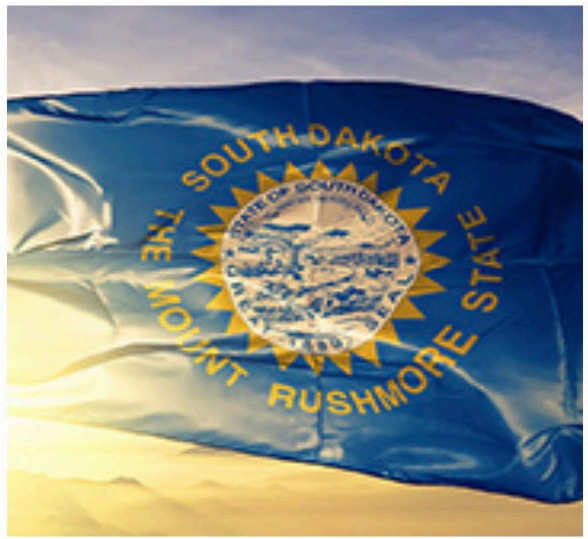
Individuals of Asian ethnicity who have small optic discs have increased odds of glaucomatous progression compared with those with White ethnicities who have equally small discs, according to a study published in *Ophthalmology Glaucoma*. The research also shows that patients with small discs who have an increased range or an increased peak of intraocular pressure (IOP) have a greater incidence of progression, and that IOP peak is also associated with increased risk in patients with large optic discs.

OCT Artifacts Common With Combined Glaucoma, High Myopia

K. Patricia Bouweraerts, MA | December 13, 2023

Optical coherence tomography (OCT) artifacts are common among patients with both high myopia and glaucoma, according to the findings of a study published in the *Journal of Glaucoma*.

AOA News

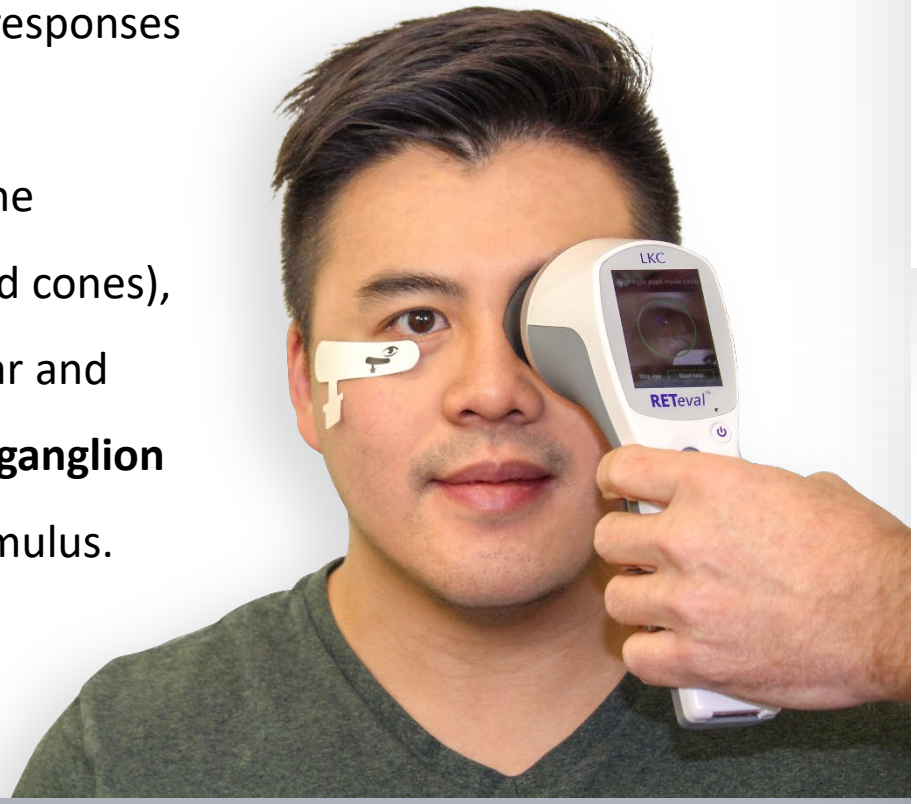


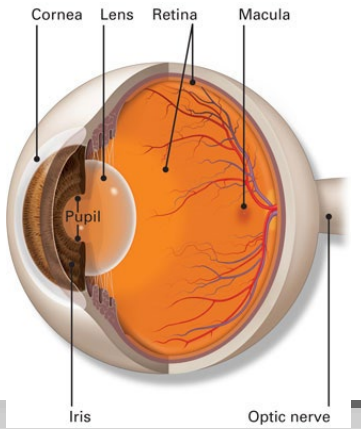
South Dakota secures scope expansion for injections, optometric laser procedures

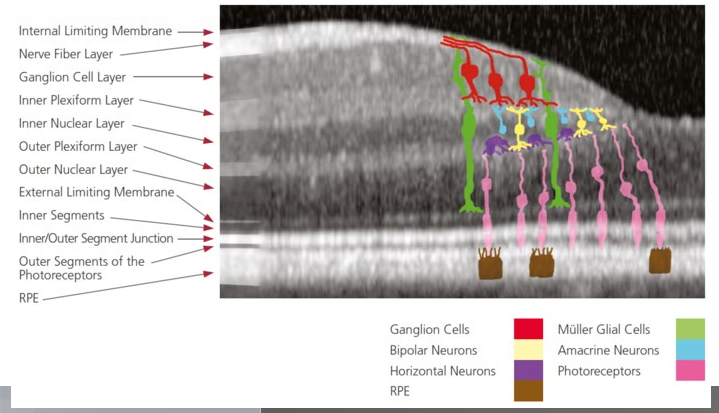
South Dakota's scope victory makes it the twelfth state in the nation to authorize doctors of optometry for ophthalmic lasers, bolstering patients' access to this level of care. Read More

Electroretinography: Finally Physiologic Data

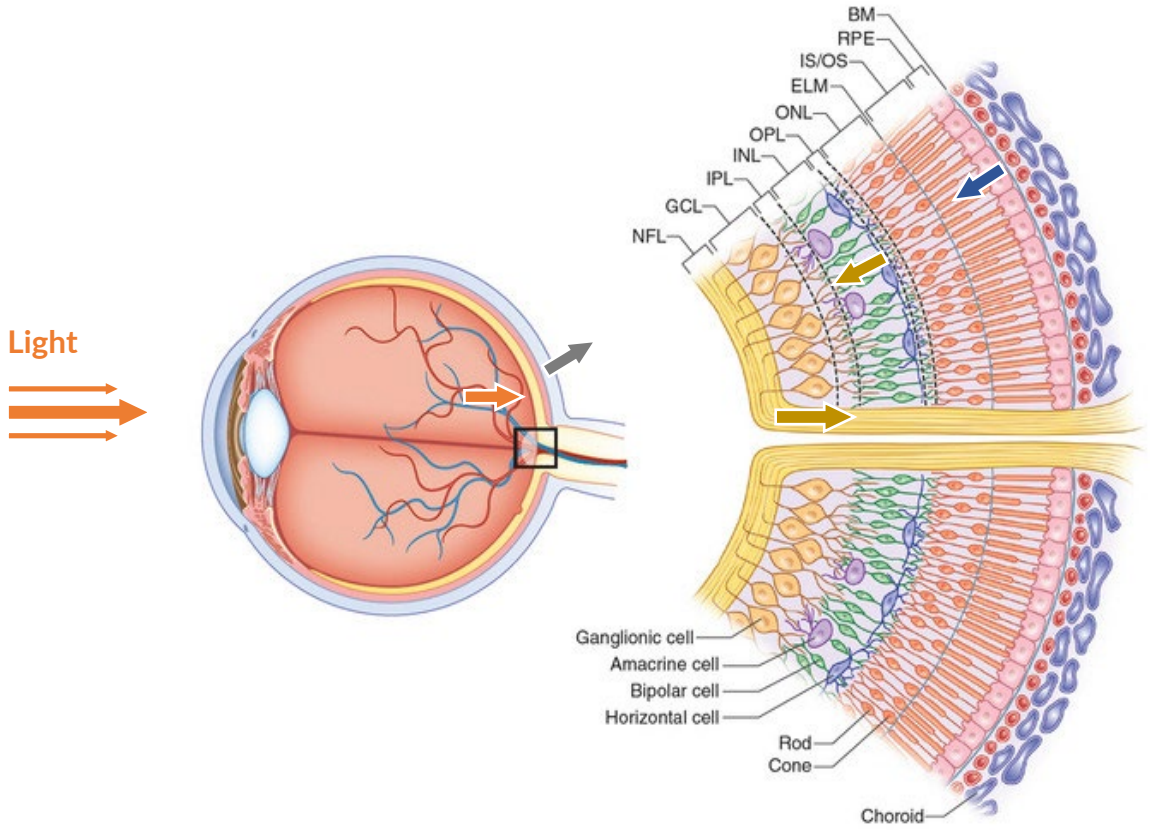
Measures the electrical responses of various cell types in the retina, including the **photoreceptors** (rods and cones), **inner retinal cells** (bipolar and amacrine cells), and the **ganglion cells** in response to a stimulus.







The ERG Waveform

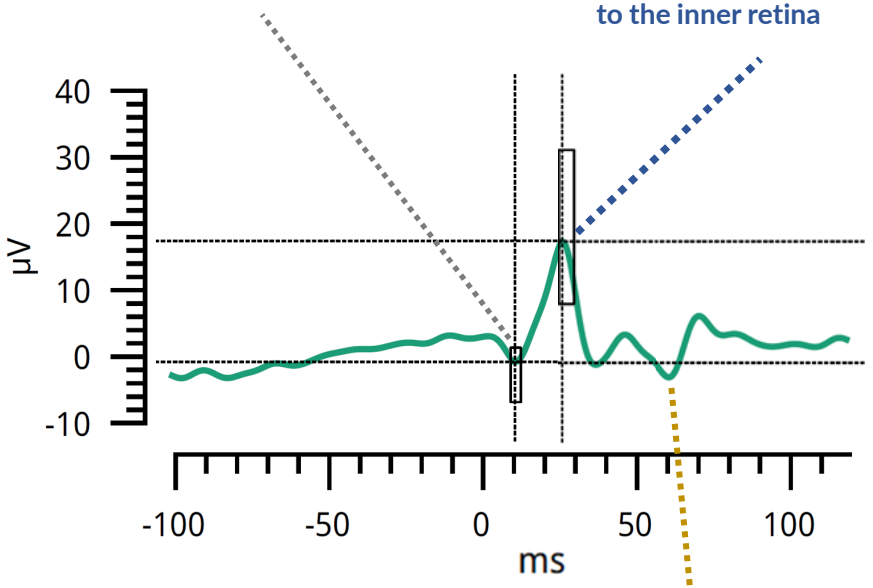


A Wave

Photoreceptor Function, primarily driven by cones

B Wave

Bipolar Cell Function, inverts signal from photoreceptors and transmits to the inner retina

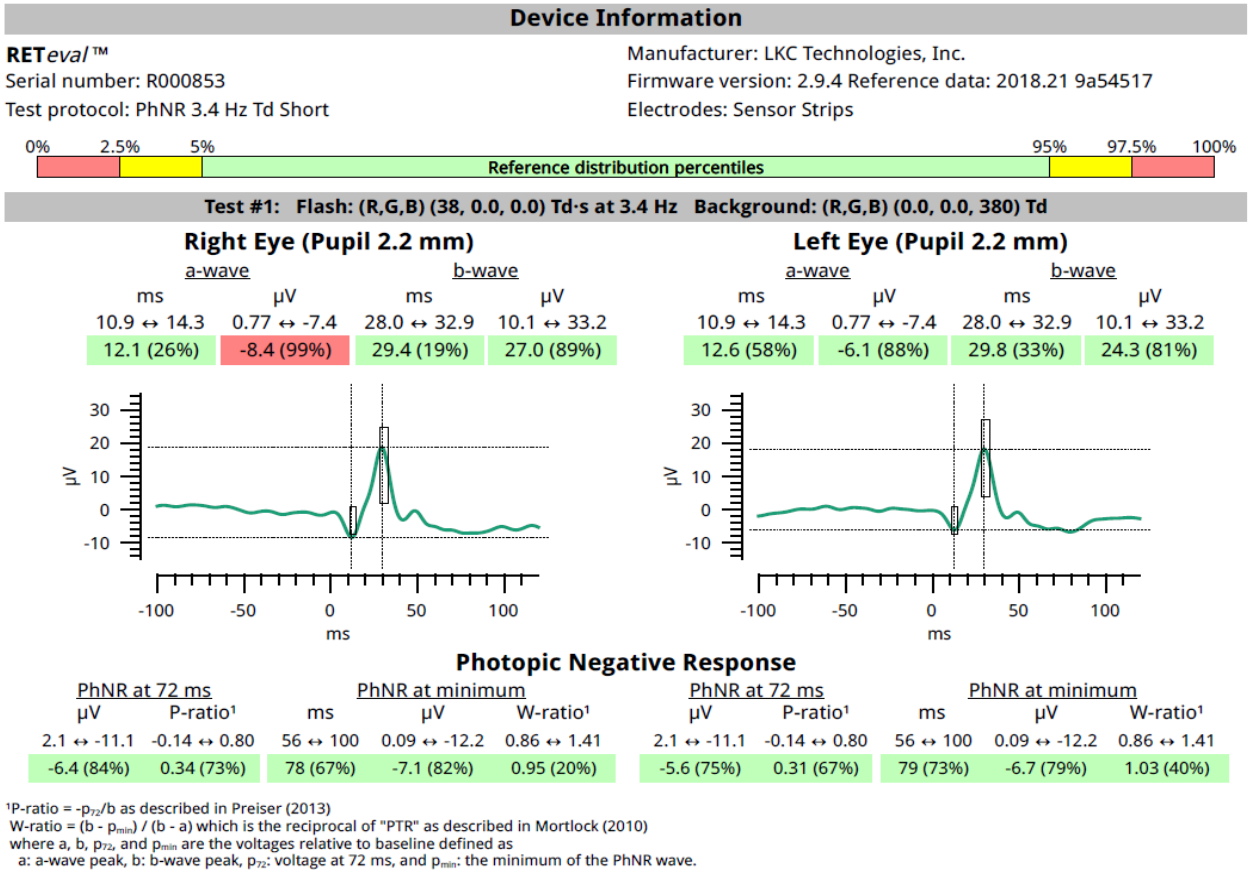


PhNR

Function of the innermost retinal layer, Retinal Ganglion Cell

Mulitple Protocols Provide Information to Help with all Types of Ocular Diseases

For example: PhNR **for glaucoma suspect**



Device Information

RET*eval*™
Serial number: R000853
Test protocol: PhNR 3.4 Hz Td Short

Manufacturer: LKC Technologies, Inc.
Firmware version: 2.9.4 Reference data: 2018.21 9a54517
Electrodes: Sensor Strips

0% 2.5% 5% — Reference distribution percentiles — 95% 97.5% 100%

Test #1: Flash: (R,G,B) (38, 0.0, 0.0) Td·s at 3.4 Hz Background: (R,G,B) (0.0, 0.0, 380) Td

Right Eye (Pupil 2.2 mm)

a-wave		b-wave	
ms	µV	ms	µV
10.9 ↔ 14.3	0.77 ↔ -7.4	28.0 ↔ 32.9	10.1 ↔ 33.2
12.1 (26%)	-8.4 (99%)	29.4 (19%)	27.0 (89%)

Left Eye (Pupil 2.2 mm)

a-wave		b-wave	
ms	µV	ms	µV
10.9 ↔ 14.3	0.77 ↔ -7.4	28.0 ↔ 32.9	10.1 ↔ 33.2
12.6 (58%)	-6.1 (88%)	29.8 (33%)	24.3 (81%)

Photopic Negative Response

PhNR at 72 ms		PhNR at minimum		
µV	P-ratio[1]	ms	µV	W-ratio[1]
2.1 ↔ -11.1	-0.14 ↔ 0.80	56 ↔ 100	0.09 ↔ -12.2	0.86 ↔ 1.41
-6.4 (84%)	0.34 (73%)	78 (67%)	-7.1 (82%)	0.95 (20%)

PhNR at 72 ms		PhNR at minimum		
µV	P-ratio[1]	ms	µV	W-ratio[1]
2.1 ↔ -11.1	-0.14 ↔ 0.80	56 ↔ 100	0.09 ↔ -12.2	0.86 ↔ 1.41
-5.6 (75%)	0.31 (67%)	79 (73%)	-6.7 (79%)	1.03 (40%)

[1]P-ratio = $-p_{72}/b$ as described in Preiser (2013)
W-ratio = $(b - p_{min}) / (b - a)$ which is the reciprocal of "PTR" as described in Mortlock (2010)
where a, b, p_{72}, and p_{min} are the voltages relative to baseline defined as
a: a-wave peak, b: b-wave peak, p_{72}: voltage at 72 ms, and p_{min}: the minimum of the PhNR wave.

- The PhNR reflects generalized activity of retinal ganglion cells and their axons
- Amplitude can be reduced early in diseases that affect the innermost retina, like glaucoma

DR Assessment

Components of the RET*eval* Diabetic Retinopathy Assessment: Biostatistician – Bascom Palmer

DR assessment protocol combines:

implicit time (ERG)

How long it takes the retina to respond

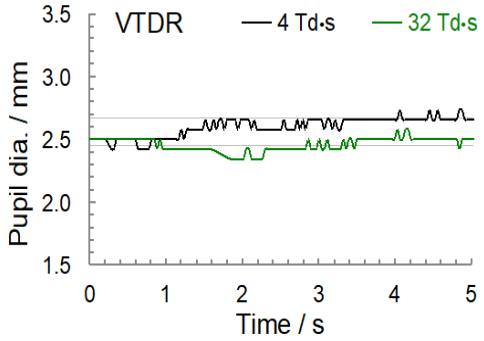
amplitude (ERG)

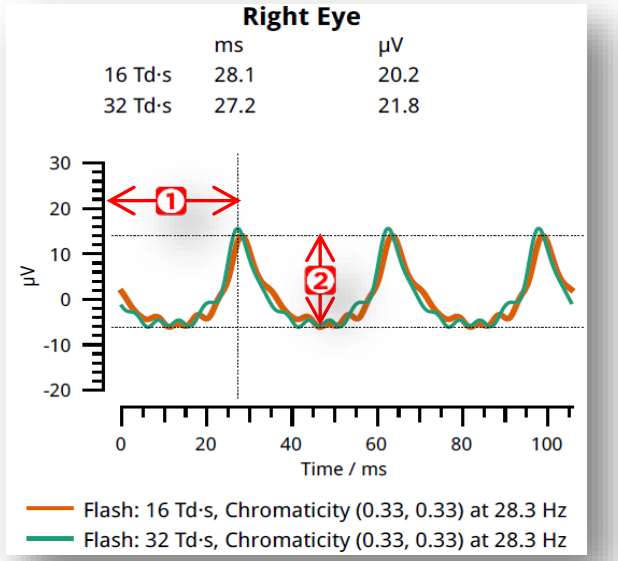
How strong the signal from the retina is

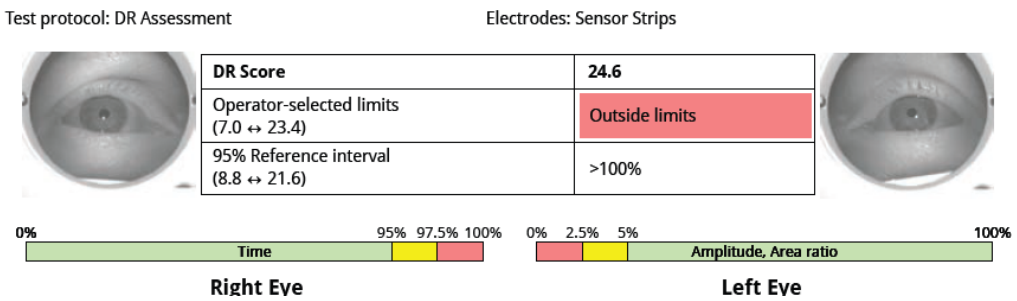
pupil response

Change in pupil diameter–dim vs. bright

patient age



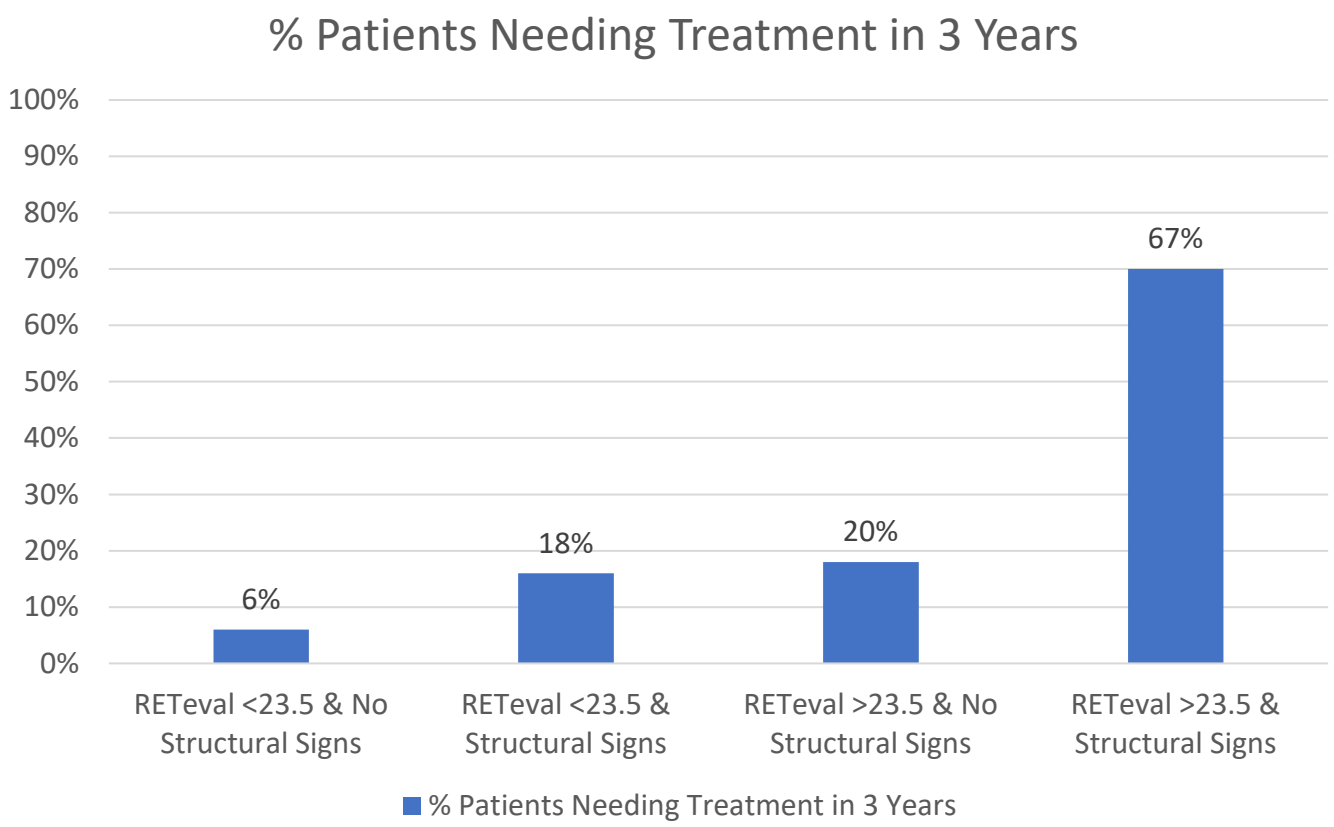




Diabetic Retinopathy

Longitudinal Study Shows Ability of the RET*eval* to Predict Progression

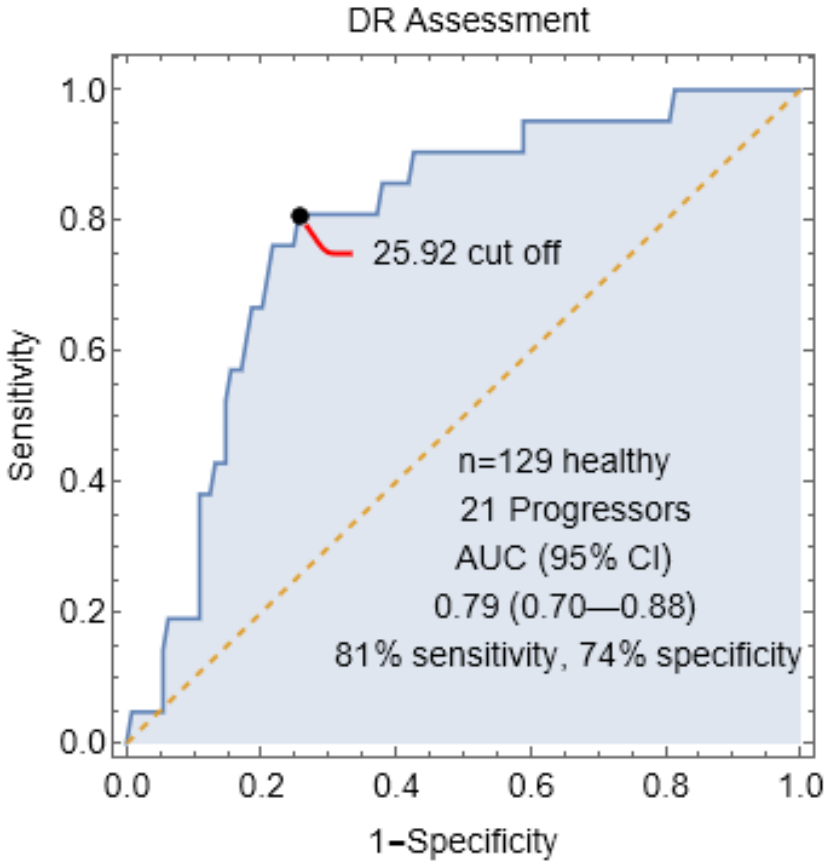
- Longitudinal study with 279 patients
- Conducted in USA
- Primary outcome: treatment conducted in follow up period
- Structure & RET*eval* function were measured to predict progression
- In general: 17% of DR progresses to treatment

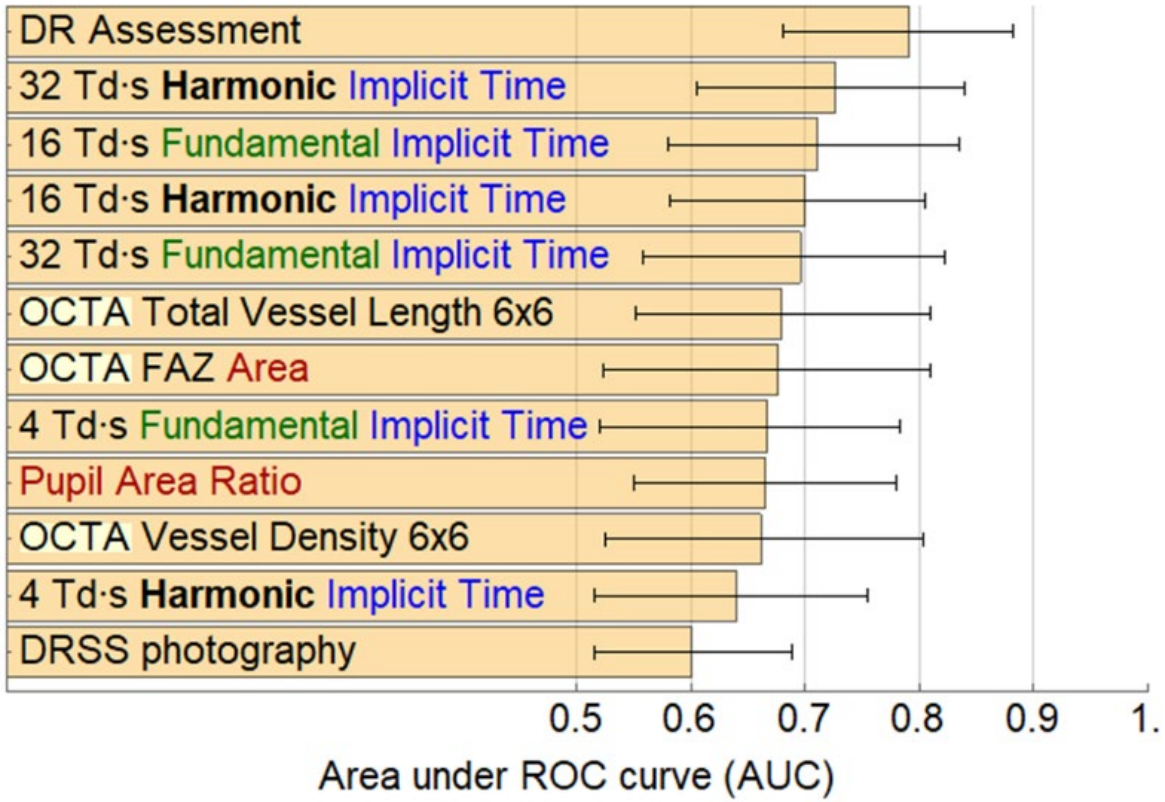


Brigell MG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. *Trans Vis Sci Tech*. 2020;9(9):40-40.

Diabetic Retinopathy

The Predictive Ability of the RETeval Device was Shown to be More Sensitive than Imaging Technologies when Evaluating Patients Needing Treatment in the Next 12 Months





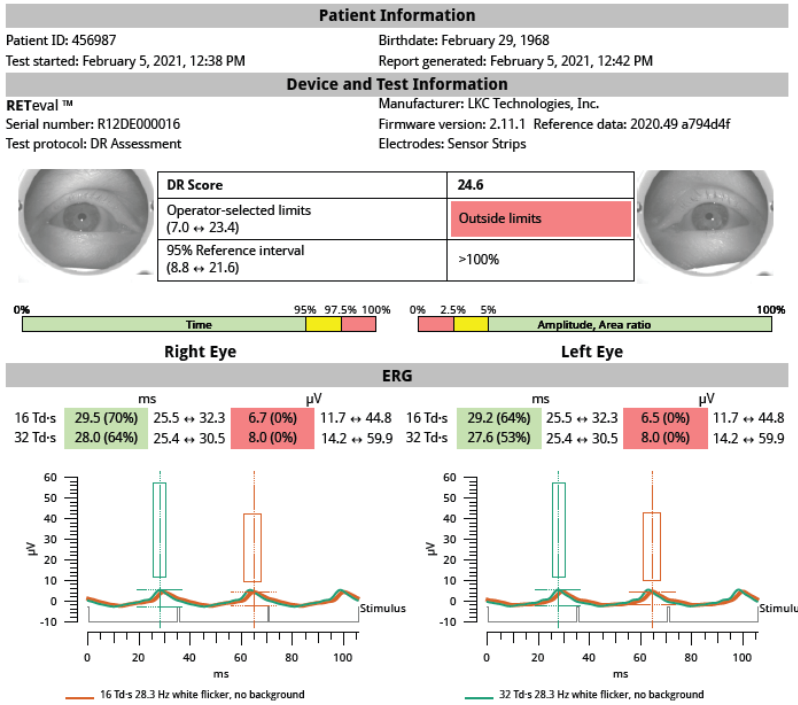
Diabetic Retinopathy

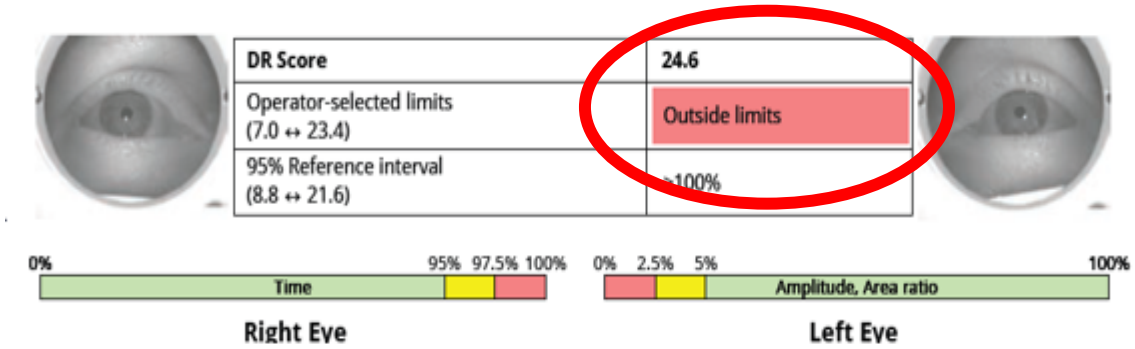
How to Use the DR Score in Practice → Interpretation Guide

Patient test conditions: Test is done always un-dilated. Patient is diabetic with suspected retinopathy or diabetic with existing retinopathy.

Protocol: DR Assessment

Results: If the **Operator Selected limit** is marked red with text Outside Limits, the patient is at the risk to develop vision threatening DR within the coming 36 months.





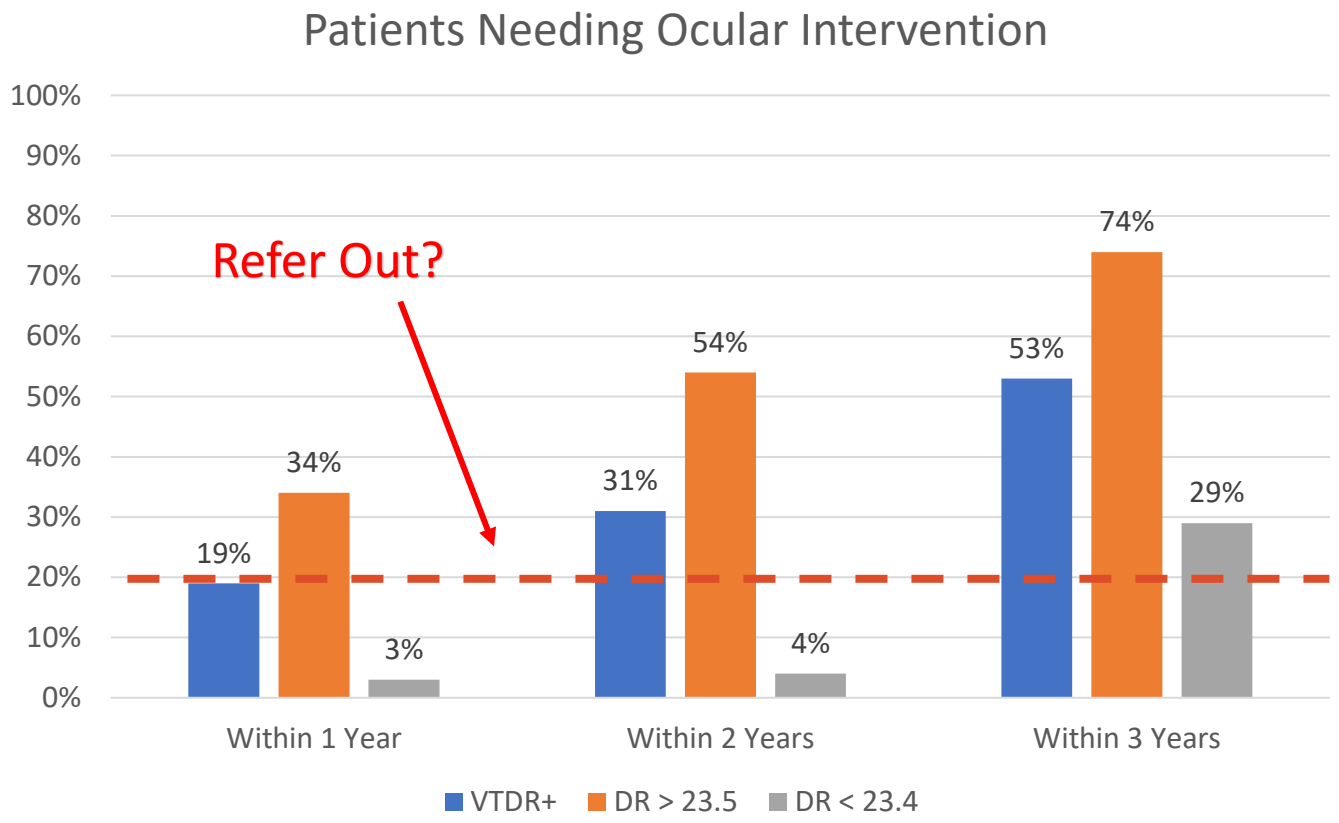
Predicting progression of Diabetic Retinopathy

- **Score <23.5** → Patient is much less likely to progress to needing treatment in the next few years
- **Score >23.5** → high chance of requiring treatment in next 3 years
- **Score >26.0** → predictive of needing treatment in 1 year

Diabetic Retinopathy

Combining Diabetic Structure and Function Gives Us a More Complete Picture for Clinical Decisions

- VTDR+ = positive vision threatening diabetic retinopathy
- VTDR+
- Severe NPDR
- Proliferative DR
- ME
- Would you refer this patient out based on the structural findings?
- Adding in the functional data gives you a more complete picture
- Does this information change your protocols?



Brigell MG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. *Trans Vis Sci Tech*. 2020;9(9):40-40.

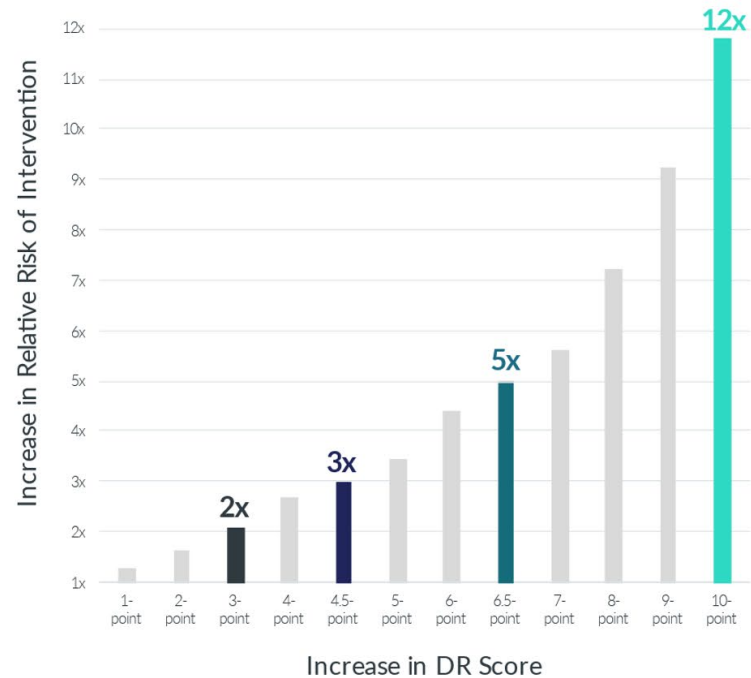
DIABETIC RETINOPATHY

Why the DR Score matters

Each 1-point change in the DR Score increases the probability of ocular intervention over 3 years by 28%

Higher DR Score & change over time dramatically increases risk:

- Risk of intervention **doubles** with a 3-point increase in DR Score (e.g. 20 to 23)
- Risk of intervention **triples** with a 4.5-point increase in DR Score (e.g. 20 to 24.5)
- Risk of intervention **increases 5x** with a 6.5-point increase in DR Score (e.g. 20 to 26.5)
- Risk of intervention **increases 12x** with a 10-point increase in DR Score (e.g. 16 to 26)



Cox proportional hazards analysis (CI = 1.171.40, p < 0.0001)

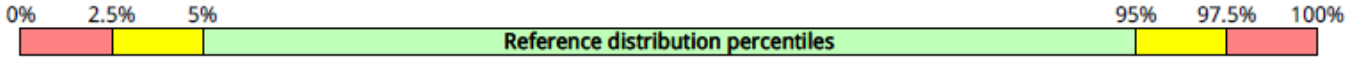
Source:BrigellMG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. Trans Vis Sci Tech. 2020;9(9):4 40.

Patient Information

Patient ID: 6182
Birthdate: February 13, 1932
Test started: January 21, 2019, 8:09 AM
Report generated: January 21, 2019, 8:13 AM

Device Information

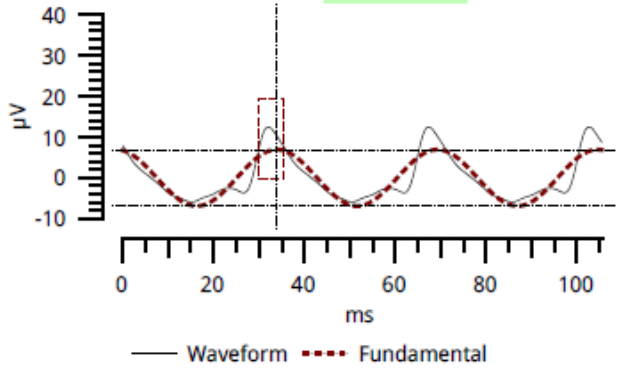
RET*eval*™
Manufacturer: LKC Technologies, Inc.
Serial number: R001133
Firmware version: 2.9.4 Reference data: 2018.21 9a54517
Test protocol: Flicker: 16 Td·s
Electrodes: Sensor Strips



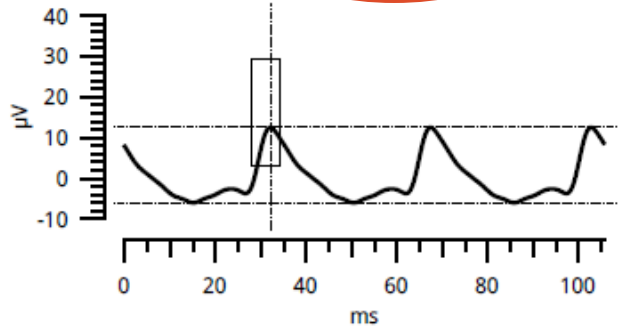
Test #1: Flash: 16 Td·s, Chromaticity (0.33, 0.33) at 28.3 Hz Background: 0.0 Td

Right Eye (Pupil 7.3 mm)

28.3 Hz implicit time (ms) 33.9 (87%) 29.9 ↔ 35.3
28.3 Hz amplitude (μV) 13.9 (46%) 6.5 ↔ 26.1

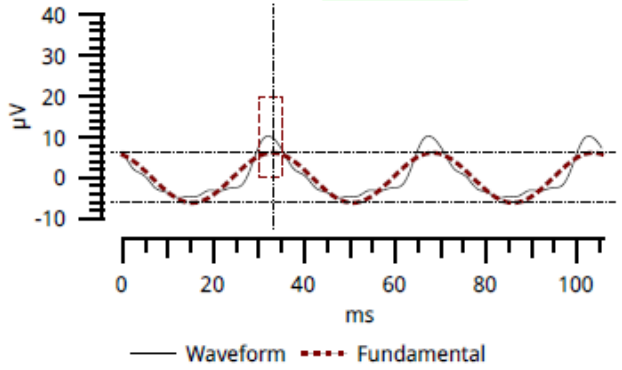


Waveform implicit time (ms) 32.0 (85%) 28.0 ↔ 34.2
Waveform amplitude (μV) 18.5 (44%) 8.9 ↔ 35.1

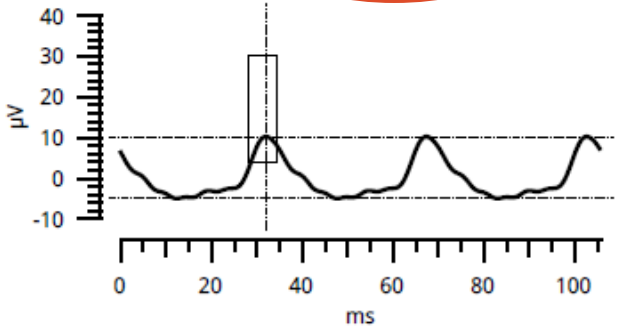


Left Eye (Pupil 5.1 mm)

28.3 Hz implicit time (ms) 33.0 (69%) 29.9 ↔ 35.3
28.3 Hz amplitude (μV) 12.3 (33%) 6.5 ↔ 26.1



Waveform implicit time (ms) 32.0 (84%) 28.0 ↔ 34.2
Waveform amplitude (μV) 15.2 (27%) 8.9 ↔ 35.1



Previous Report

Flicker 16 Tds

Normal

Patient Information

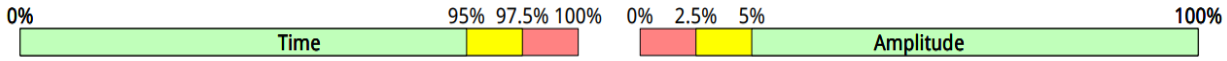
Patient ID [redacted]
Test started: March 1, 2021, 4:15 PM

Birthdate: April 15, 1948
Report generated: March 1, 2021, 4:21 PM

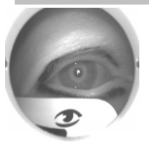
Device and Test Information

RET*eval*™
Serial number: R001634
Test protocol: Flicker: 16 Td·s

Manufacturer: LKC Technologies, Inc.
Firmware version: 2.11.0 Reference data: 2020.49 a794d4f
Electrodes: Sensor Strips

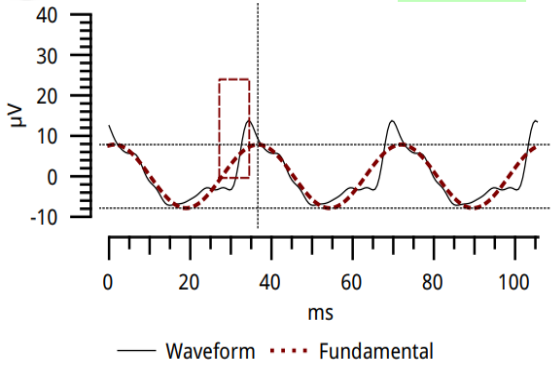


Test #1: Flash: 16 Td·s, Chromaticity (0.33, 0.33) at 28.3 Hz Background: 0.0 Td



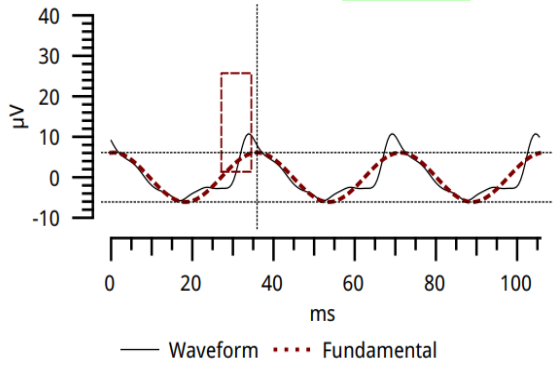
Right Eye (Pupil 2.6 mm)

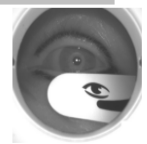
28.3 Hz implicit time (ms) 36.6 (100%) 27.1 ↔ 34.5
28.3 Hz amplitude (μV) 15.7 (53%) 7.5 ↔ 31.8



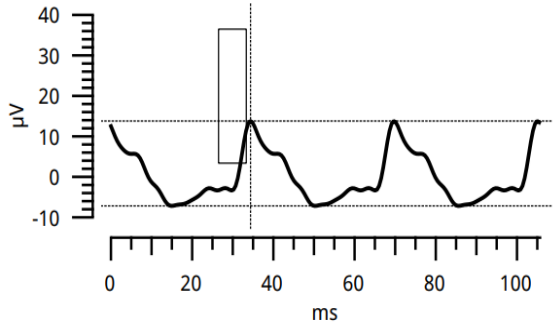
Left Eye (Pupil 2.6 mm)

28.3 Hz implicit time (ms) 36.0 (99%) 27.1 ↔ 34.5
28.3 Hz amplitude (μV) 12.2 (27%) 7.5 ↔ 31.8

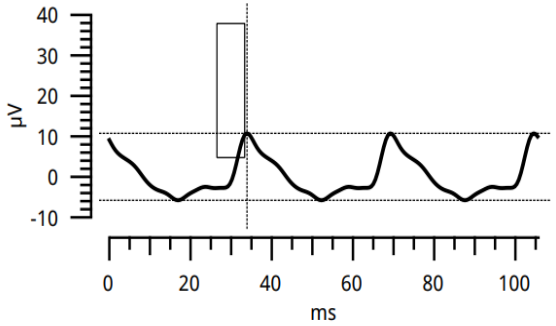




Waveform implicit time (ms) 34.4 (100%) 26.5 ↔ 33.3
Waveform amplitude (μV) 21.0 (50%) 10.6 ↔ 43.7



Waveform implicit time (ms) 33.9 (99%) 26.5 ↔ 33.3
Waveform amplitude (μV) 16.5 (27%) 10.6 ↔ 43.7



New Report
Flicker 16 Tds

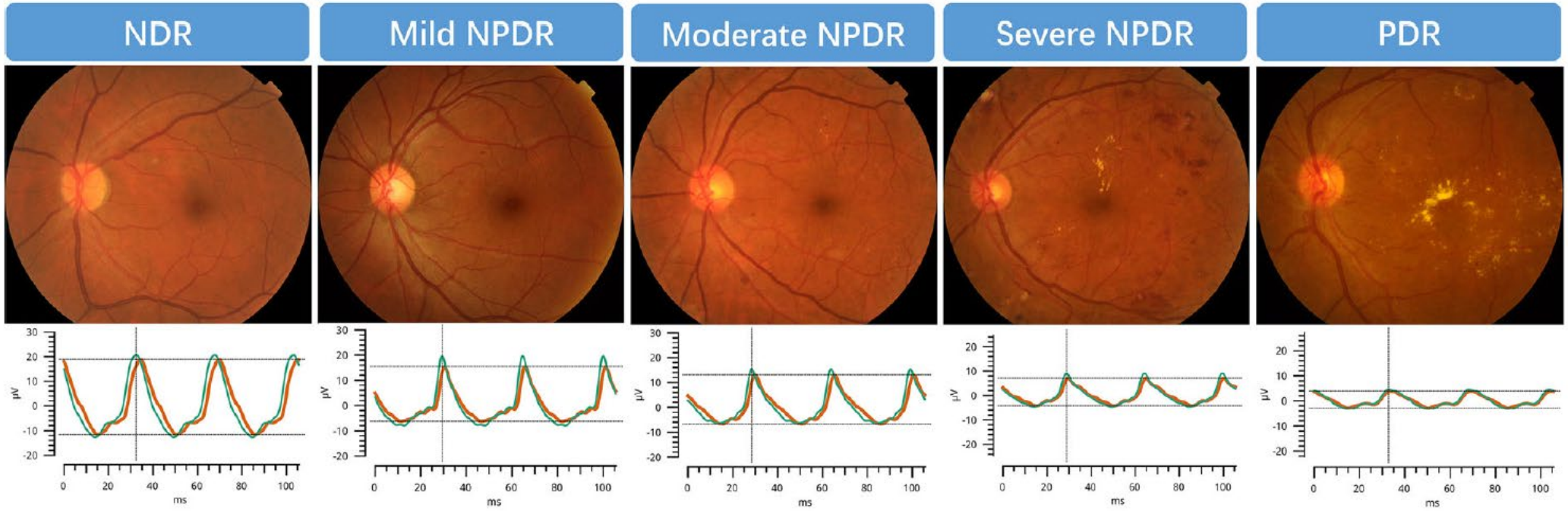
-Significant Stress in both eyes
-No Atrophy

Electroretinograms (ERG) are affected by DR

First published in 1987, results replicated in the North & South America, Europe, and Asia
13 publications using **RET***eval* device

Increasing disease severity →

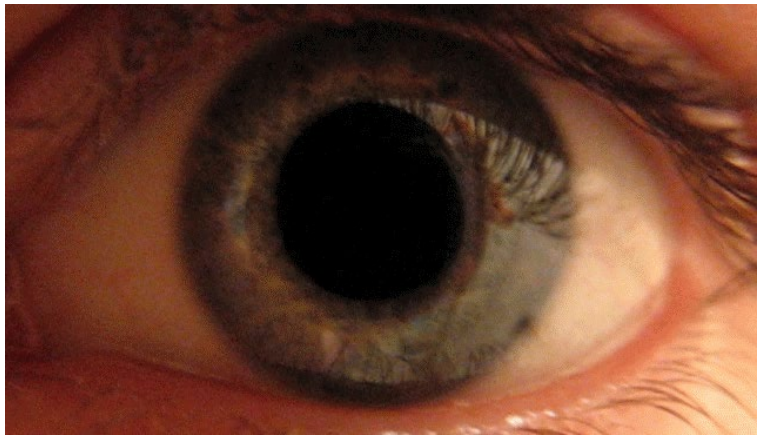
ERG:

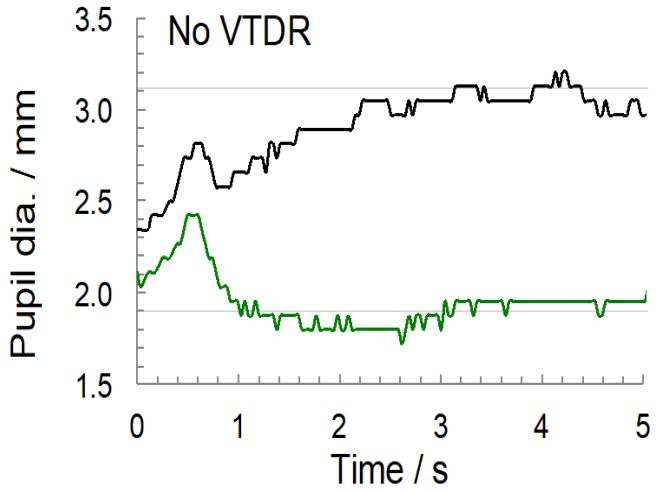


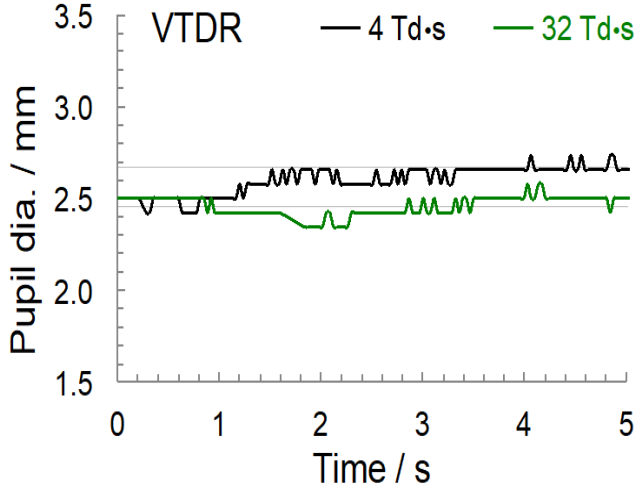
Zeng et al. (2019) "Screening for Diabetic Retinopathy in Diabetic Patients with a Mydriasis-Free, Full-Field Flicker Electroretinogram Recording Device". *Documenta Ophthalmologica*. https://doi.org/10.1007/s10633-019-09734-2.

Pupillary Response is Impacted by Diabetic Retinopathy as Well

Pupil responses are attenuated as diabetic retinopathy gets worse







- 1992 Smith & Smith; Straub, Jeron, & Kerp
- 1994 Straub, Thies, Jeron, Palitzsch, & Scholmerich
- 2001 Nakayama et al.
- 2013 Ortube et al.

Longitudinal study: RET*eval* vs. 7-field photographs

3 YEAR RESULTS

- For patients with VTDR+ the incidence of intervention was 19%, 31%, and 53% after 1, 2, and 3 years of follow-up.
  - In these patients, **intervention incidence increased to 34%, 54%, and 74% the subsequent 1, 2, and 3 years if function was above criterion (RETeval+)**
  - RETeval– results reduced the risk to 3%, 4%, and 29%, respectively, reducing risk to similar levels seen for patients with VTDR– results at baseline.

Brigell et al. (2020) Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure, TVST

Longitudinal study: RET*eval* vs. 7-field photographs

- At baseline, record **RET***eval* DR Assessment test and ETDRS 7-field stereo dilated photographs.
- Wait 3+ years
- Chart review for which subjects had a relevant ocular intervention
  - Anti-VEGF injections
  - Laser
  - Vitrectomy
- Analyze using Kaplan-Meier and relative risks to compare predictive capabilities of **RET***eval* DR Score vs photography

Brigell et al. (2020) Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure, TVST

Components of the RET*eval* DR Score

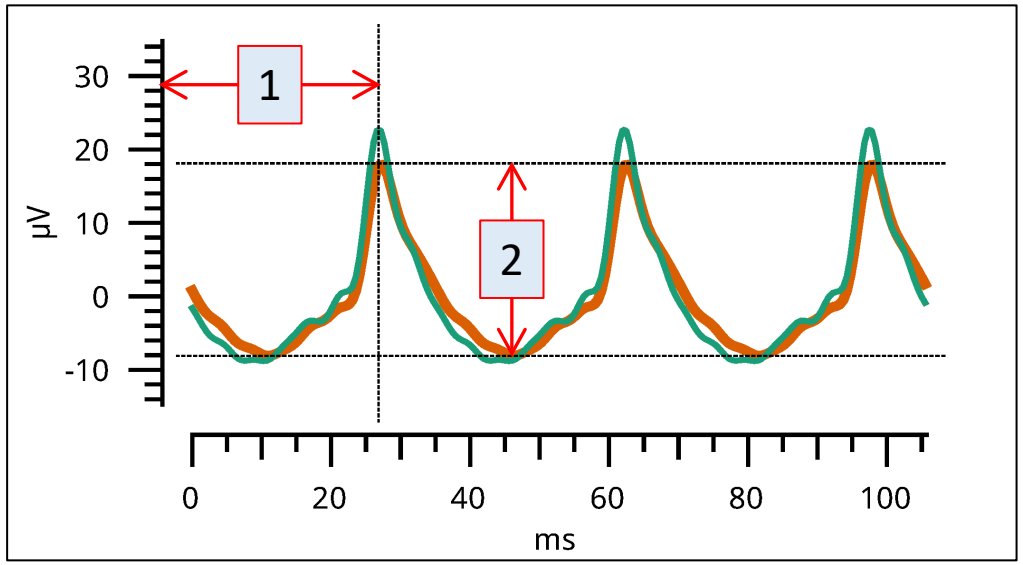
DR Score combines

1. The shorter implicit time between the two eyes
   (How long it takes the retina to respond)

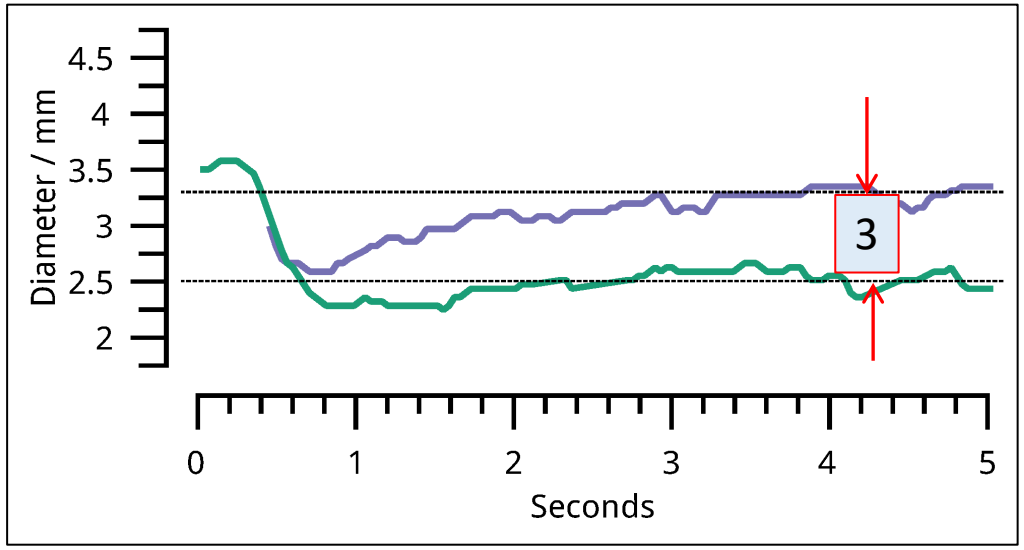
2. The larger amplitude of the two eyes
   (How strong the signal is from the retina)

3. Worst pupil response of the two eyes
   (Change in pupil area from dim to bright light)

4. Age



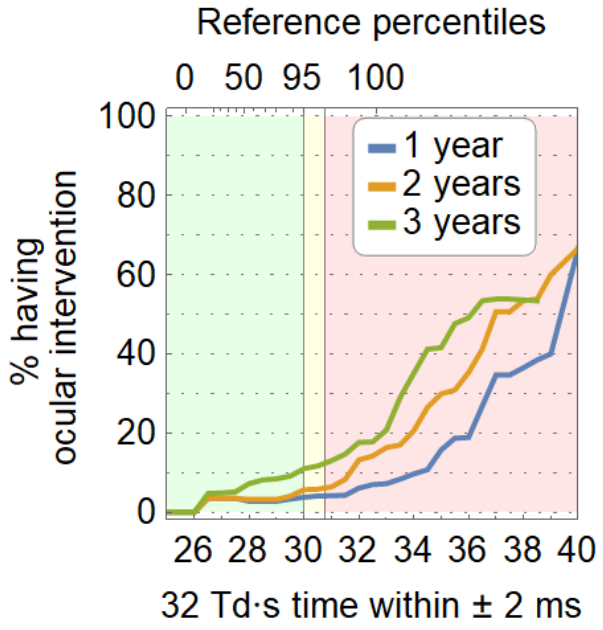
ERG

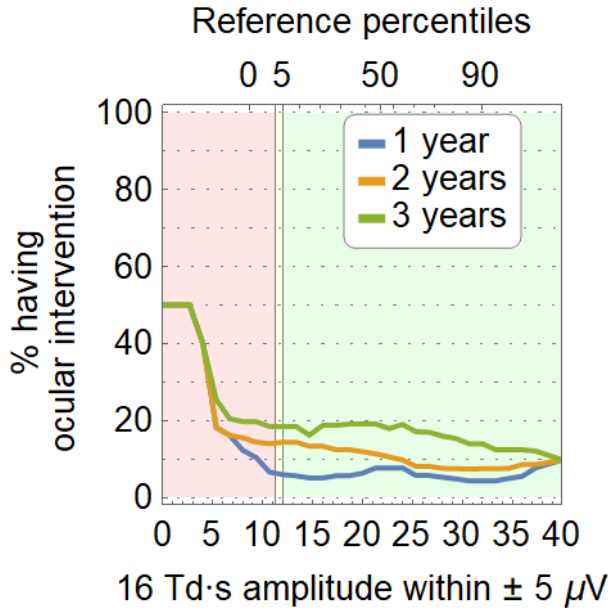


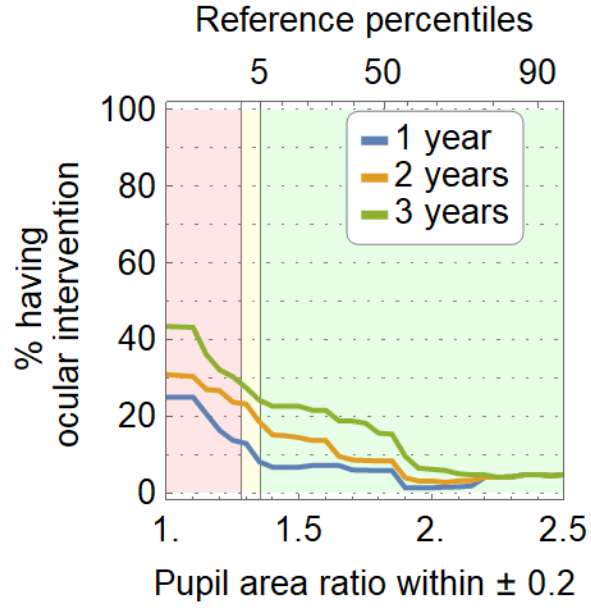
Pupil response

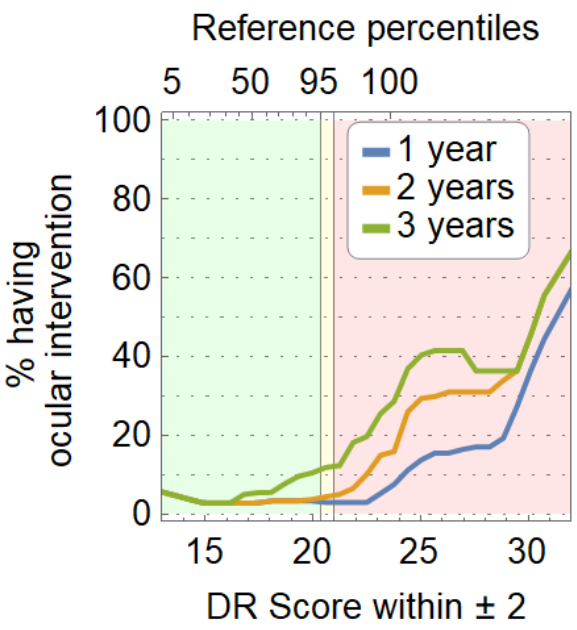
Who is at Risk for an Ocular Intervention within 3 Years?

- Long ERG times
- Small ERG amplitudes
- Small pupil responses
- **Large DR Scores predict disease!!!**



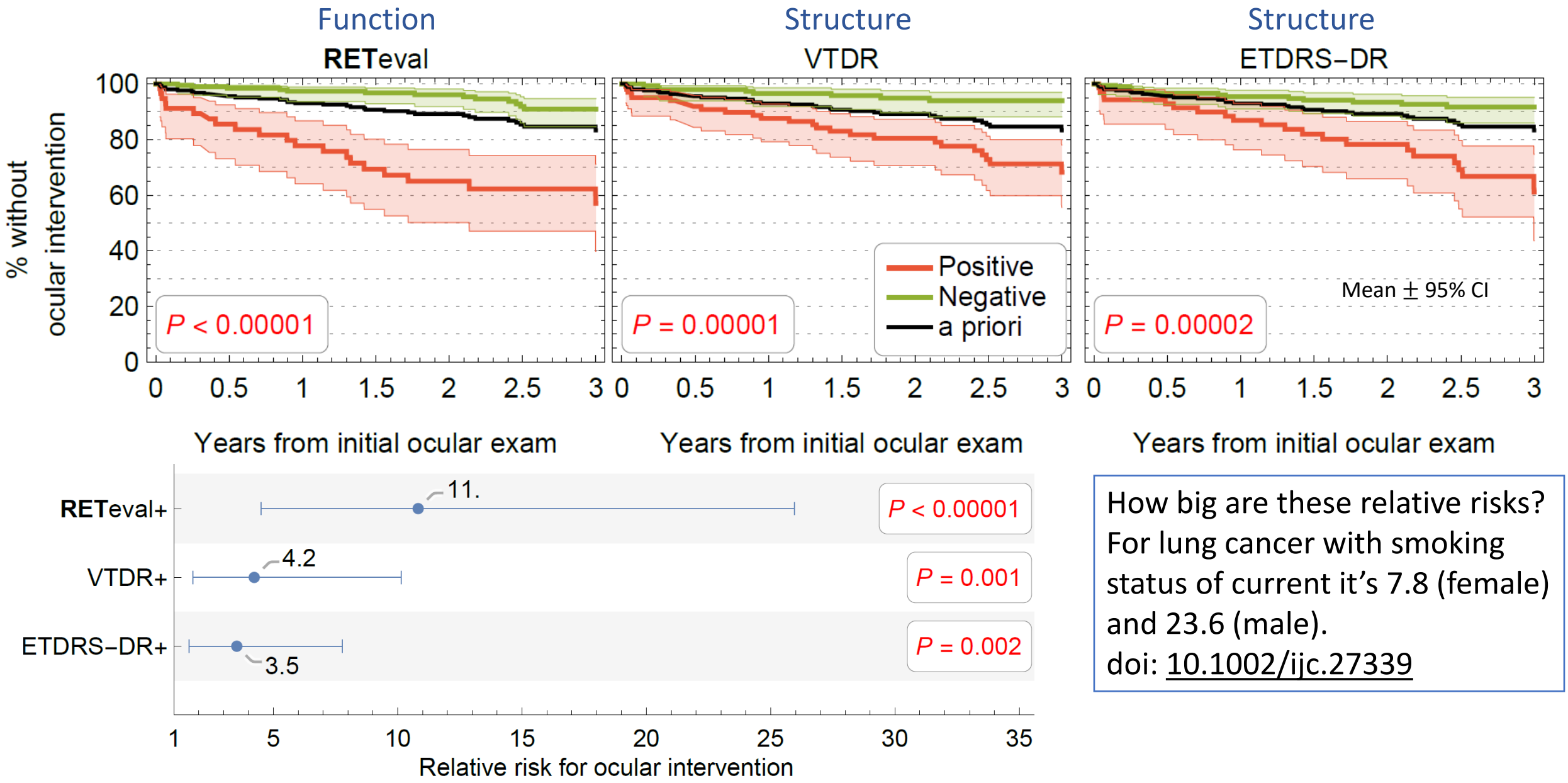






Brigell et al. (2020)

Longitudinal study: RET*eval* (function) vs. 7-field photo (structure)



How big are these relative risks? For lung cancer with smoking status of current it's 7.8 (female) and 23.6 (male).
doi: 10.1002/ijc.27339

Brigell et al. (2020) Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure, TVST

How to set the DR decision limits

Study	Gold standard	Upper clinical decision limit (largest value considered normal)
Maa et al. (2016)	7-field stereo ETDRS photographs on dilated eyes, cross-sectional study	19.9
Degirmenci et al. (2018)	Slit-lamp biomicroscopy and dilated fundus examination by indirect ophthalmoscopy, cross-sectional study	21.9
Zeng et al. (2019)	Slit-lamp biomicroscopy, 7-field stereo ETDRS photographs on dilated eyes, and OCT, cross-sectional study	23.0
Brigell et al. (2020)	Surgical interventions (laser, injections, or vitrectomy) over the subsequent 3 years, longitudinal study	23.4

I recommend 23.4, because I put more weight on longitudinal trials – results are generally more obvious with time. Instead of comparing to a different method of predicting who will have issues, just wait and see.

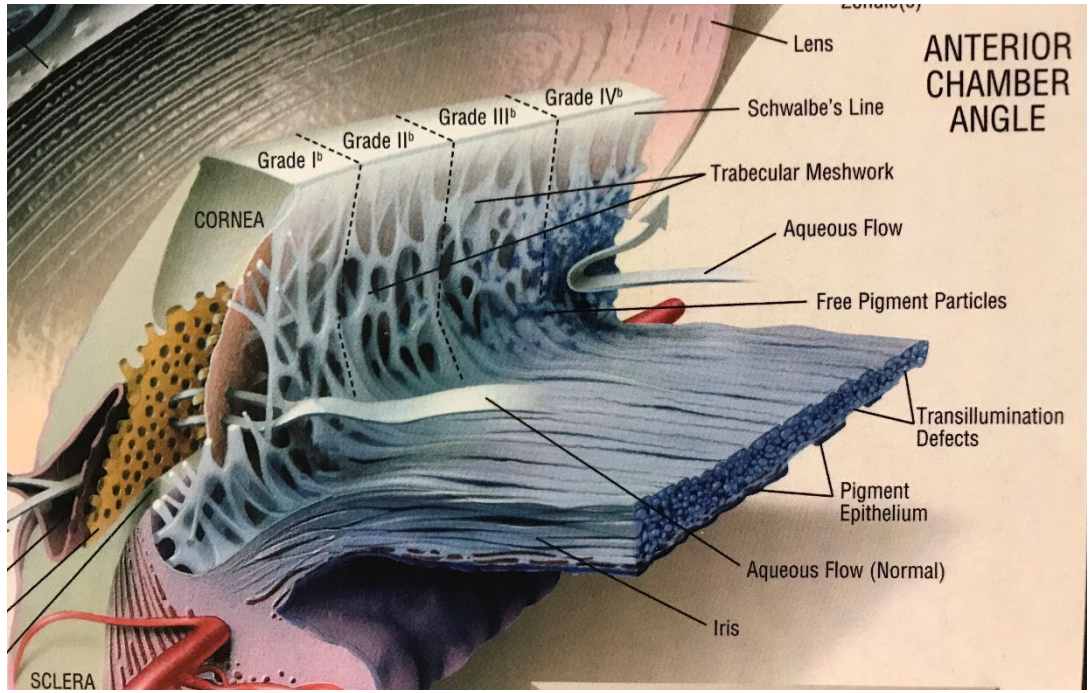
Beyond IOP, Managing Aqueous Outflow

Tonography

Setting a Target Outflow Facility Value

Aqueous Humor Dynamics

Aqueous Humor Outflow Pathway



Is Measuring IOP Alone Enough?

- Does Not Validate Therapeutic Response
- Does Not Predict Risk
- Only Valid if You Obtain Multiple Measurements Over 24 Hours
- Patients with Untreated Glaucoma Can Have Normal IOP

Reference: Baltimore Eye Survey, Johns Hopkins University Study

Aqueous Humor Dynamics

- IOP is directly related to aqueous humor production and inversely related to aqueous humor outflow.
- The rate of aqueous humor production is not constant.
- The rate of aqueous humor outflow is constant.
- IOP varies throughout the day.
- The variability of aqueous humor production is the source of IOP variation.
- Using IOP alone can lead to the incorrect conclusion.
- Eyes with untreated glaucoma may have normal IOP when evaluated.
-

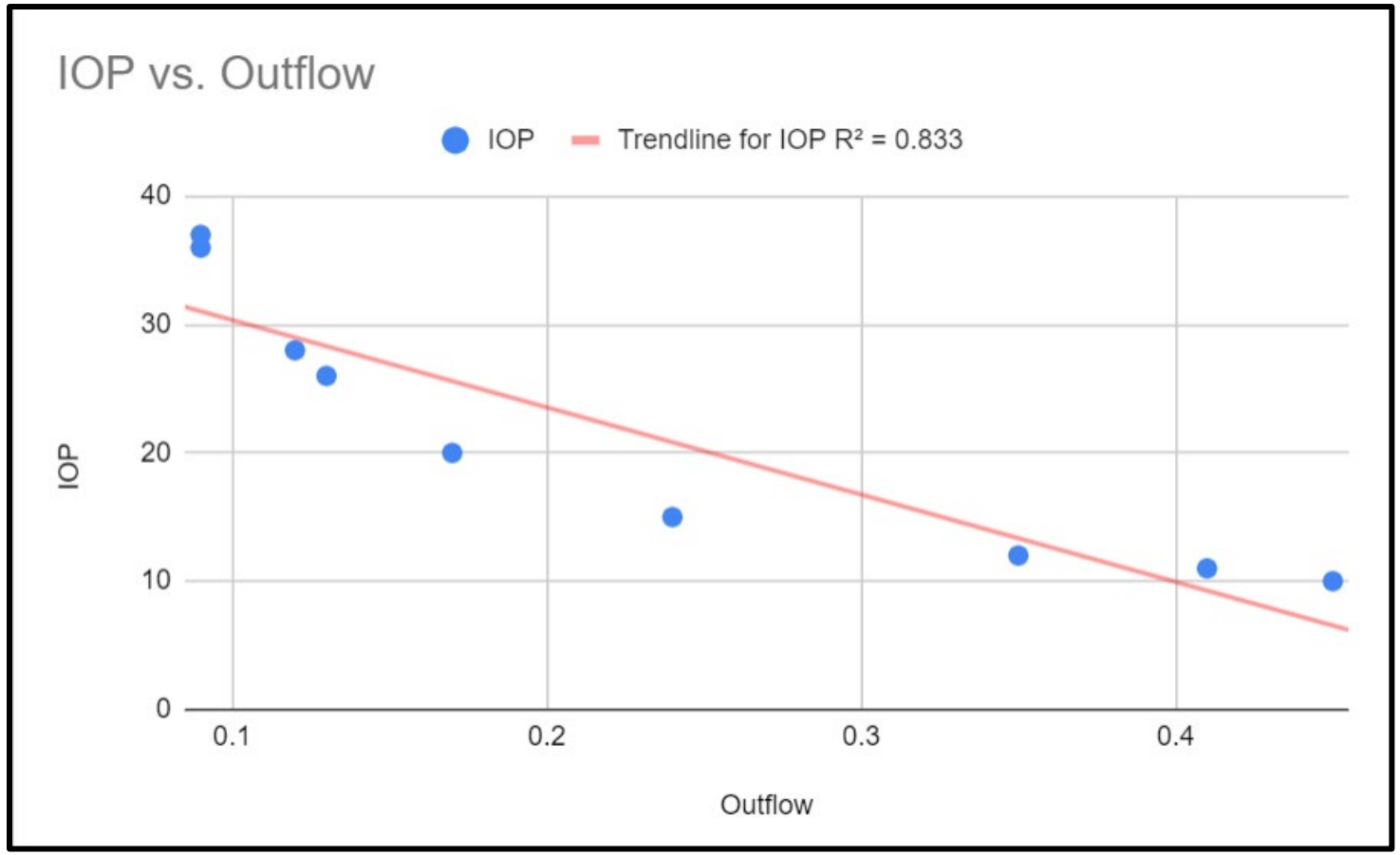
Why Measure Outflow Facility?

- Impaired Outflow Facility is the Primary Cause of Glaucoma
- Outflow Facility Measurements Predict IOP In and Out of the Office
- New Technology Available to Measure Outflow Facility - FMAT1 Tonography
- Outflow Facility Measurements Predict Risk

Reference: Chandler and Grant’s Glaucoma

Outflow Facility Measurements Predict IOP

- FMAT1 FDA Clinical Study Confirms
- IOP = (- 68)(Outflow) + 37, r^2= - 0.83



The Case of the Asymmetric ONH

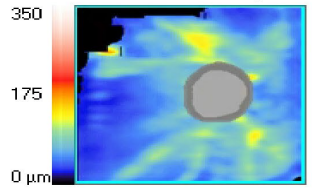
- 63 y/o white male presented for consultation for glaucoma evaluation
- VA: 20/20 OU
- Peak IOP: 25/23 ?
- Ta: 21/19 mmHg
- Tonography: 0.17 OD / 0.24 OS
- Pach: 560/558
- CH: 8.9/9.1

DOB:	5/7/1957	Exam Time:	2:26 PM	2:27 PM
Gender:	Unknown	Serial Number:	5000-20205	5000-20205
Technician:	Stein, Jonathan	Signal Strength:	6/10	9/10

ONH and RNFL OU Analysis:Optic Disc Cube 200x200

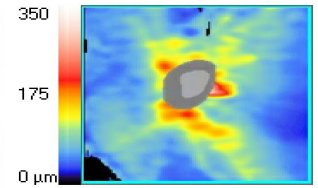
OD ● ● OS

RNFL Thickness Map

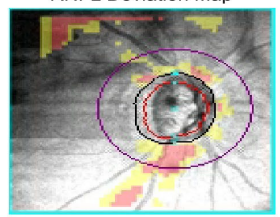


	OD	OS
Average RNFL Thickness	77 µm	86 µm
RNFL Symmetry	17%	
Rim Area	1.12 mm²	1.27 mm²
Disc Area	3.00 mm²	1.87 mm²
Average C/D Ratio	0.78	0.56
Vertical C/D Ratio	0.77	0.55
Cup Volume	0.722 mm³	0.149 mm³

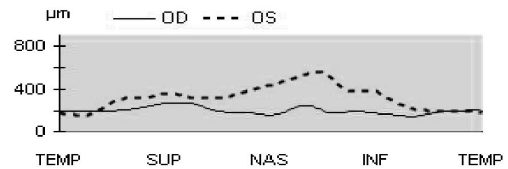
RNFL Thickness Map



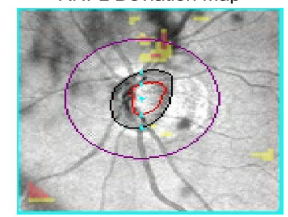
RNFL Deviation Map



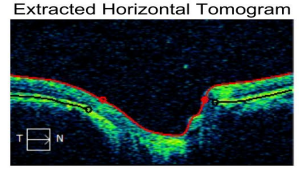
Neuro-retinal Rim Thickness



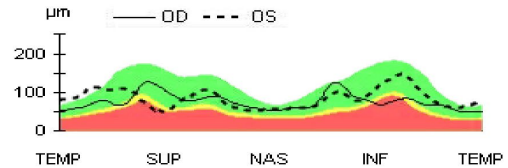
RNFL Deviation Map



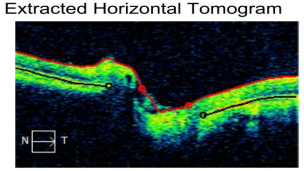
Disc Center(0.72,0.09)mm
Extracted Horizontal Tomogram



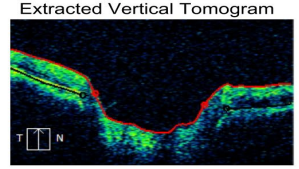
RNFL Thickness

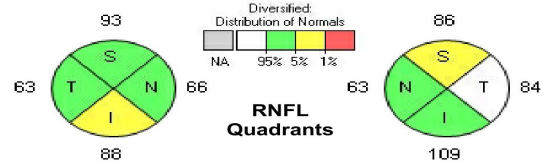


Disc Center(-0.21,0.39)mm
Extracted Horizontal Tomogram

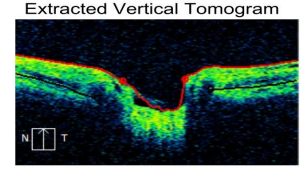


Extracted Vertical Tomogram

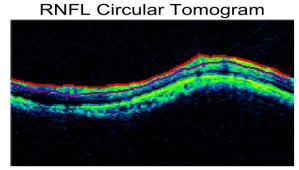


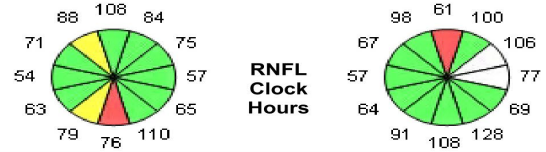


Extracted Vertical Tomogram

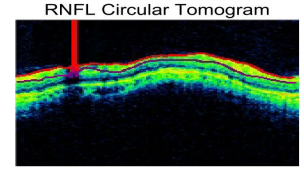


RNFL Circular Tomogram





RNFL Circular Tomogram



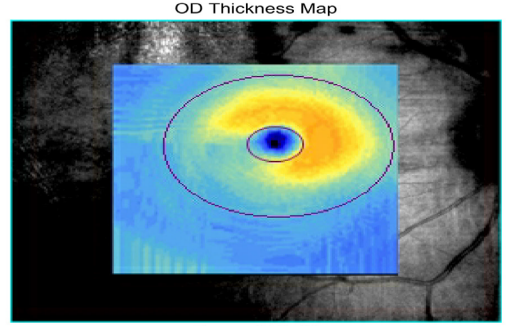
Comments

Doctor's Signature

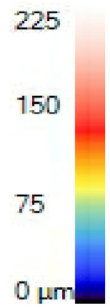
			OD	OS	
Name:	**Barnes, Elizabeth**				
ID:	CZMI1247266039	Exam Date:	9/19/2019	9/19/2019	O.C.C.
DOB:	5/7/1957	Exam Time:	2:23 PM	2:27 PM	
Gender:	Unknown	Serial Number:	5000-20205	5000-20205	
Technician:	Stein, Jonathan	Signal Strength:	10/10	10/10	

Ganglion Cell OU Analysis: Macular Cube 512x128 OD OS

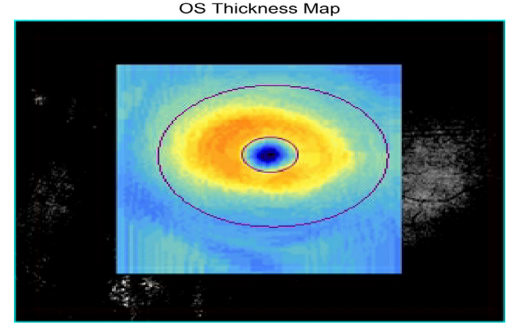
OD Thickness Map



Fovea: 295, 49

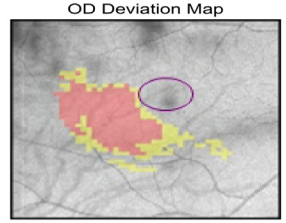


OS Thickness Map

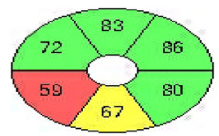


Fovea: 279, 55

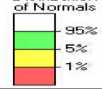
OD Deviation Map



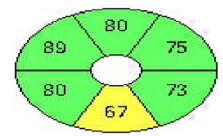
OD Sectors



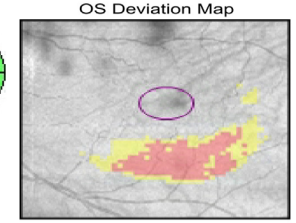
Diversified Distribution of Normals



OS Sectors

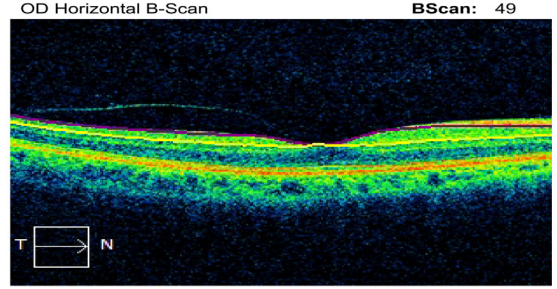


OS Deviation Map

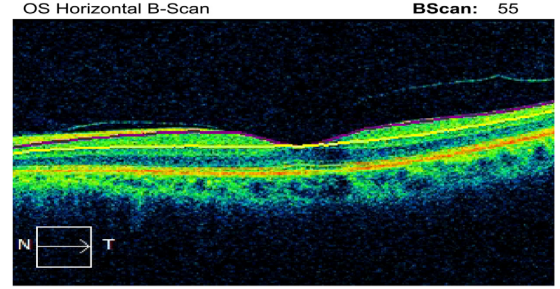


	OD µm	OS µm
Average GCL + IPL Thickness	74	77
Minimum GCL + IPL Thickness	59	70

OD Horizontal B-Scan **BScan:** 49



OS Horizontal B-Scan **BScan:** 55



Comments

Doctor's Signature

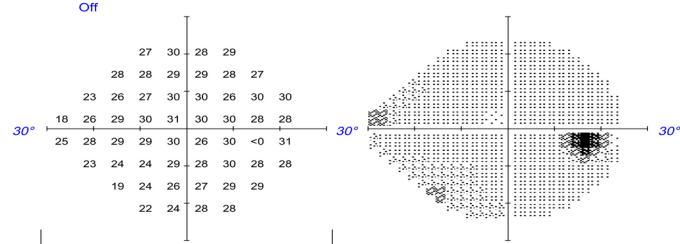
SW Ver: 9.5.2.19038

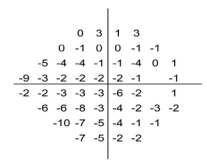
Patient: **barnes, elizabeth**
Date of Birth: **May 07, 1957**
Gender: **Female**
Patient ID: **05071957**

Ophthalmic Consultants of Connecticut
1375 Kings Highway, Ste 301
(203) 366-8000

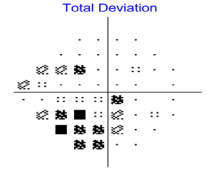
OD Single Field Analysis — Central 24-2 Threshold Test

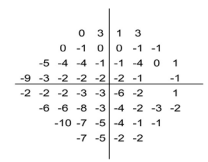
Fixation Monitor:	Gaze Monitor	Stimulus:	III, White	Date:	Oct 10, 2019
Fixation Target:	Central	Background:	31.5 asb	Time:	11:14 AM
Fixation Losses:	0/0	Strategy:	SITA Faster	Age:	62
False POS Errors:	6%	Pupil Diameter:	5.1 mm *		
False NEG Errors:	Off	Visual Acuity:			
Test Duration:	02:46	Rx:	+3.25 DS		
Fovea:	Off				



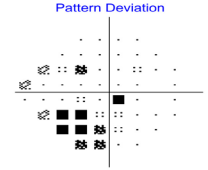


Total Deviation





Pattern Deviation



GHT: Outside Normal Limits

VFI: 94%
MD24-2: -2.85 dB P < 1%
PSD24-2: 2.75 dB P < 2%

:: P < 5%
P < 2%
P < 1%
P < 0.5%

Comments

The Case of the Asymmetric ONH

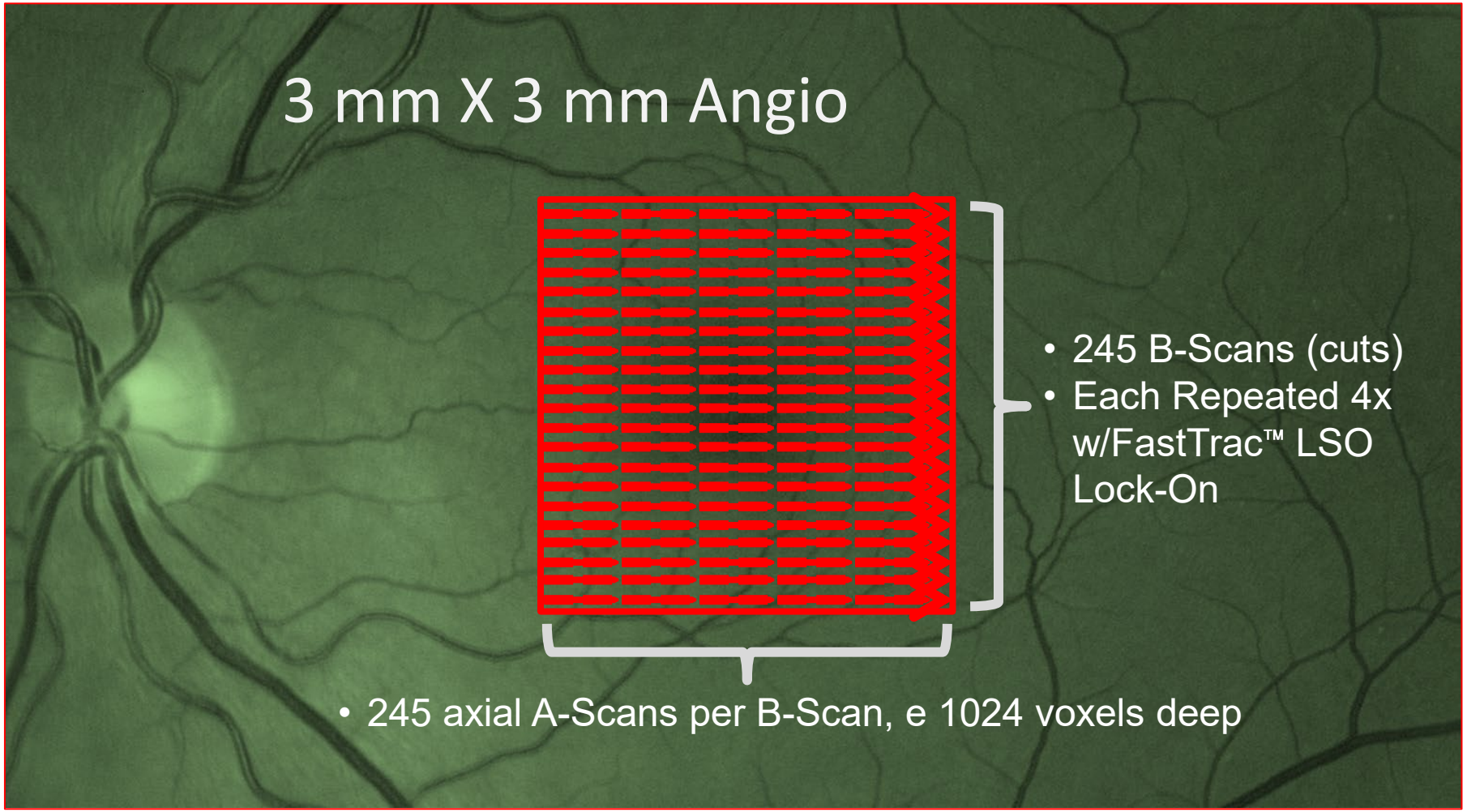
- Tx: Vyzulta 1 gtt qhs OU
- Follow up: 3 weeks
- IOP post Tx:
  - OD 17
  - OS 15
  - Tonography: OD 0.25 / OS 0.29
- Next step?

Outflow Facility Measurements Predict IOP

- Example : Outflow 0.10 ul/mmHg = IOP of 30 mmHg
- Example: Outflow 0.20 ul/mmHg = IOP of 23 mmHg
- What must the Outflow be to never exceed an IOP of 12 mmHg outside the office ? Answer 0.37 ul/mmHg
- Manage Outflow for Optimum IOP Control

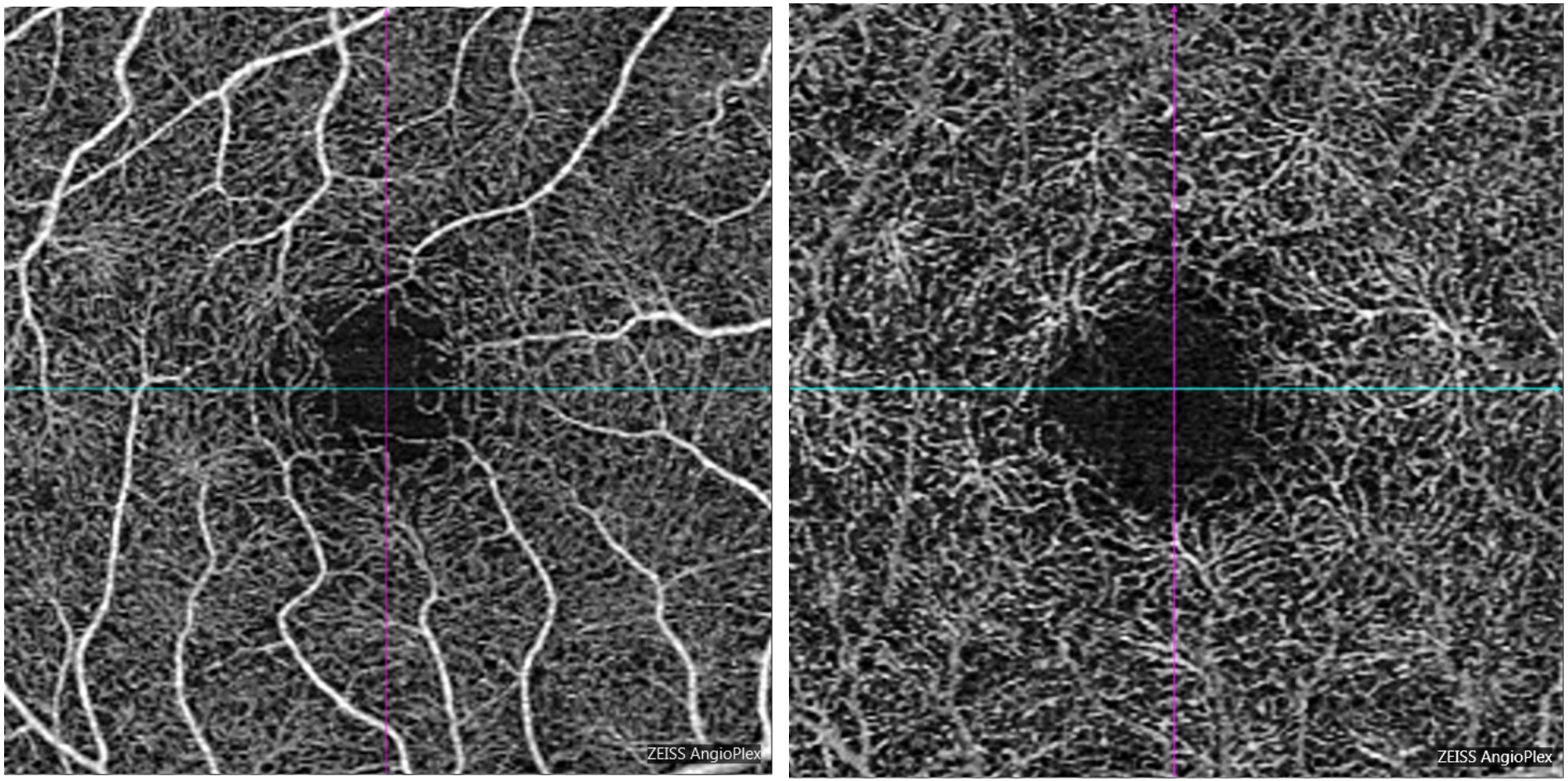
OCTA: Has The Time Come

Zeiss AngioPlex™ = One Fast Cubic Scan x4

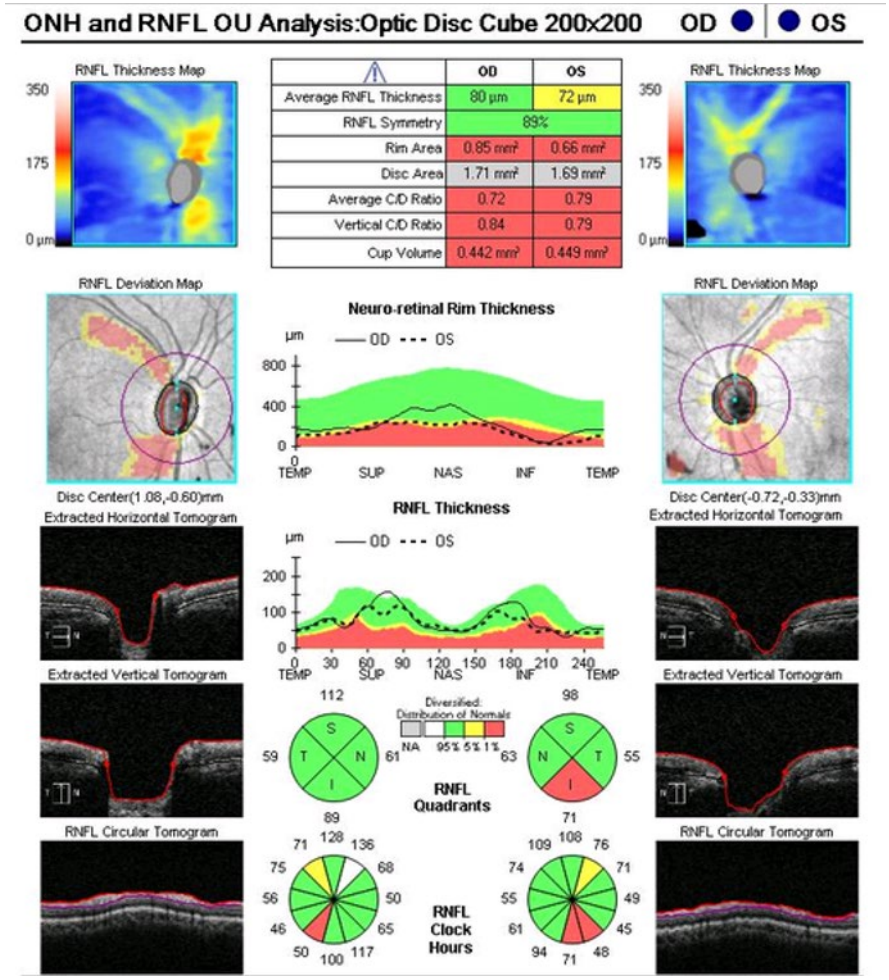


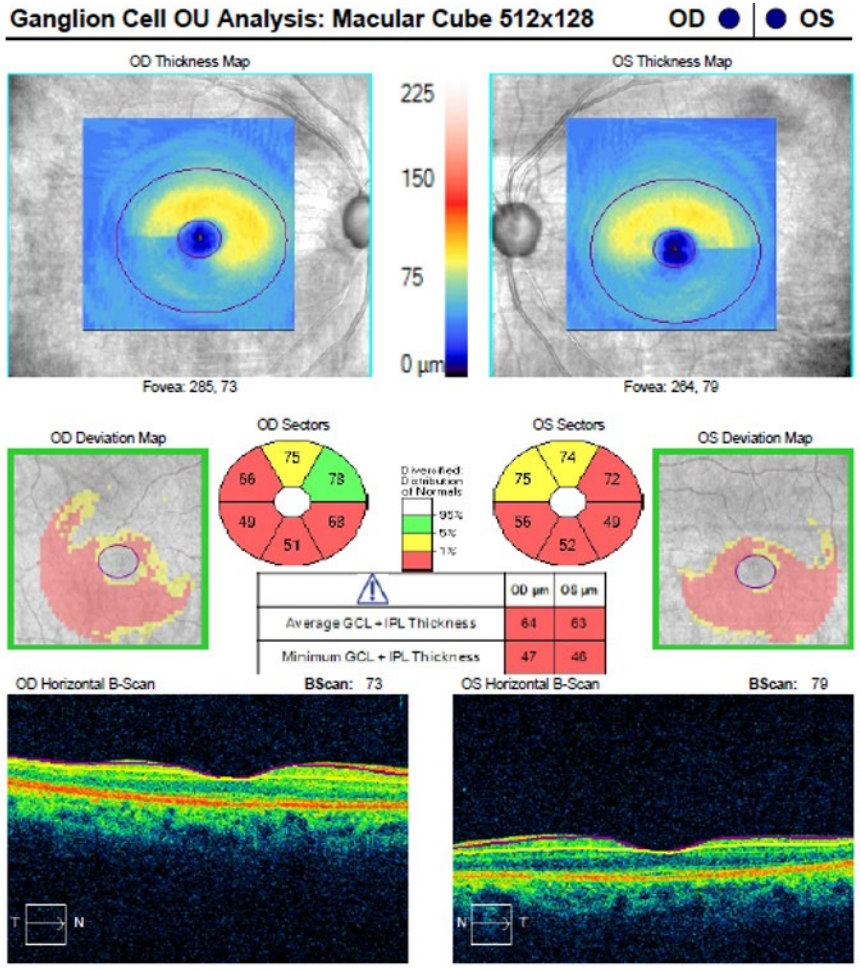
Total = **240,000 A-scans,** ~ 5.0 secs

Normal 3x3 Angio Cube OD - Full Retina (L) and Deep Plexus (R)

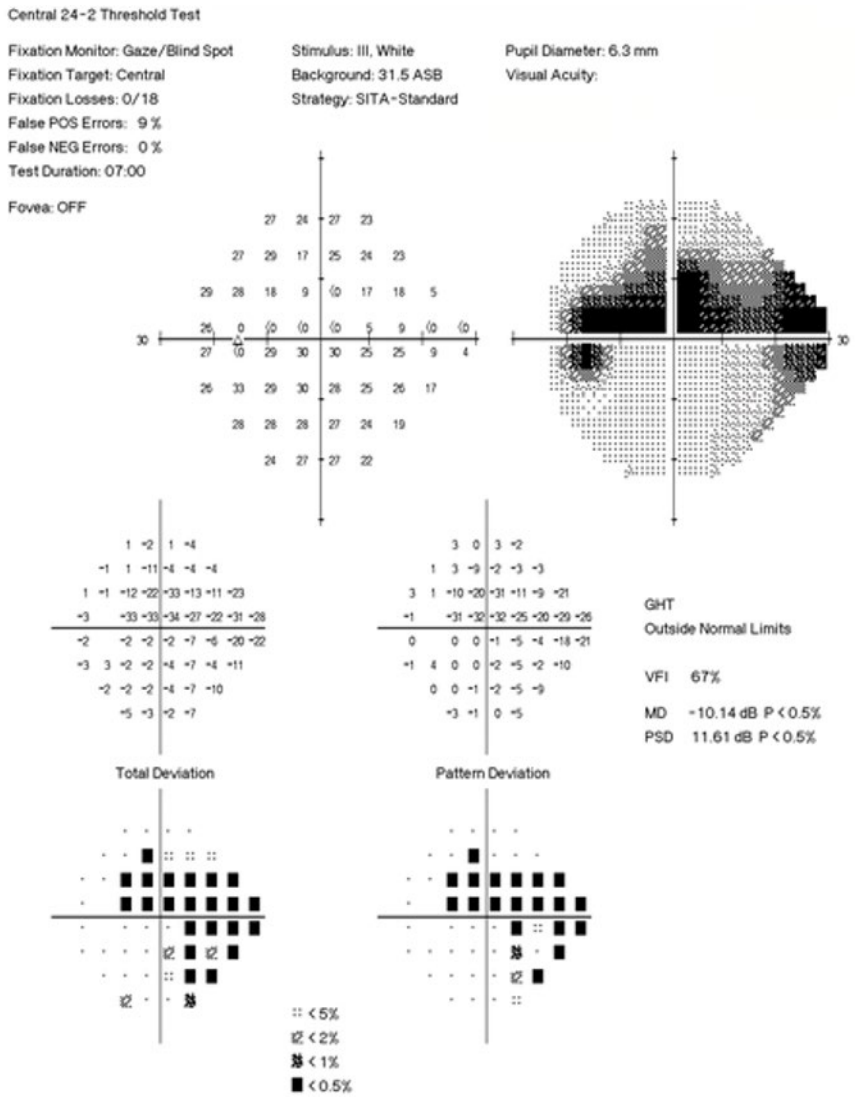


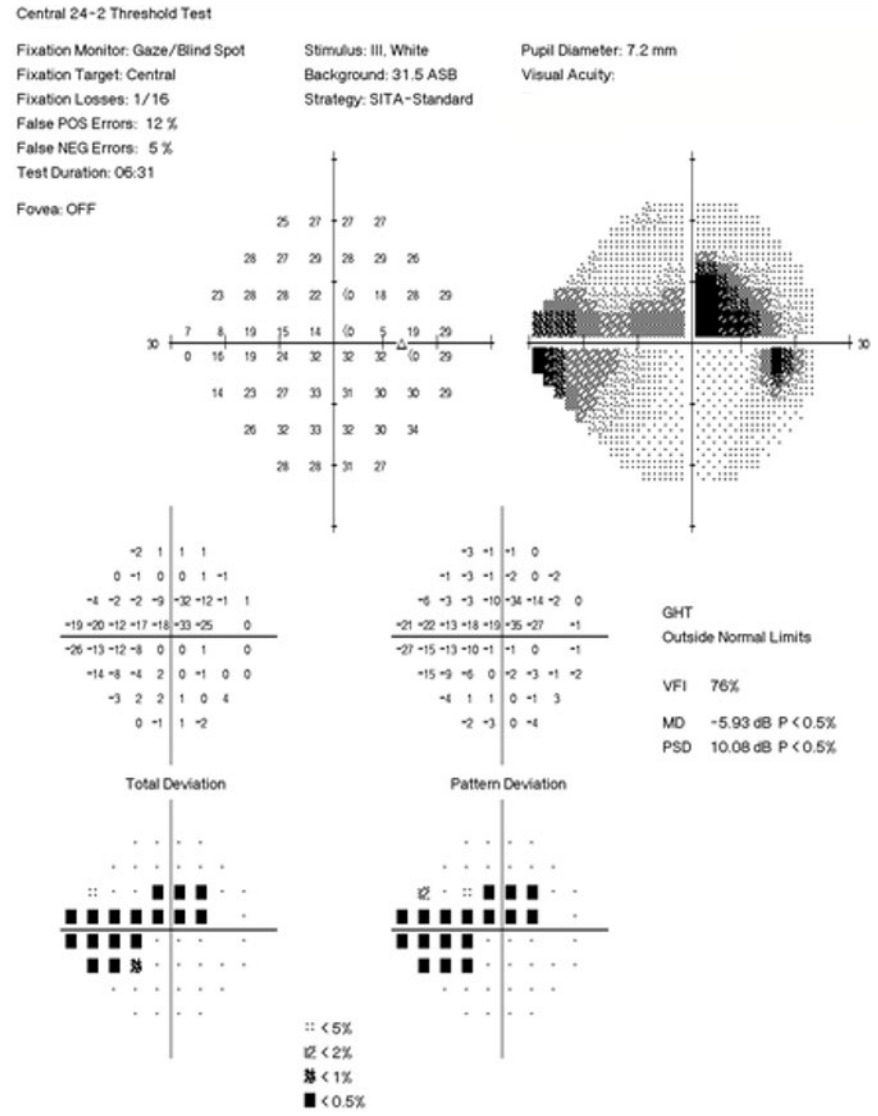
Glaucoma


ONH and RNFL OU Analysis:Optic Disc Cube 200x200
OD
OS
RNFL Thickness Map
350
175
0 µm
Average RNFL Thickness 80 µm 72 µm
RNFL Symmetry 89%
Rim Area 0.85 mm² 0.66 mm²
Disc Area 1.71 mm² 1.69 mm²
Average C/D Ratio 0.72 0.79
Vertical C/D Ratio 0.84 0.79
Cup Volume 0.442 mm³ 0.449 mm³
RNFL Deviation Map
Neuro-retinal Rim Thickness
µm
OD
OS
800
400
0
TEMP
SUP
NAS
INF
TEMP
Disc Center(1.08,-0.60)mm
Disc Center(-0.72,-0.33)mm
Extracted Horizontal Tomogram
RNFL Thickness
200
100
0 30 60 90 120 150 180 210 240
Extracted Vertical Tomogram
Diversified Distribution of Normals
NA 95% 5% 1%
RNFL Quadrants
S
T
N
I
112
59
61
89
98
55
63
71
RNFL Circular Tomogram
RNFL Clock Hours
71 128 136
75 68
56 50
46 65
50 100 117
109 108 76
74 71
55 49
61 45
94 71 48


Ganglion Cell OU Analysis: Macular Cube 512x128
OD
OS
OD Thickness Map
OS Thickness Map
225
150
75
0 µm
Fovea: 285, 73
Fovea: 264, 79
OD Deviation Map
OD Sectors
OS Sectors
OS Deviation Map
75
66
78
49
68
51
74
75
72
56
49
52
Diversified Distribution of Normals
95%
5%
1%
OD µm
OS µm
Average GCL + IPL Thickness 64 63
Minimum GCL + IPL Thickness 47 46
OD Horizontal B-Scan
BScan: 73
OS Horizontal B-Scan
BScan: 79
T
N

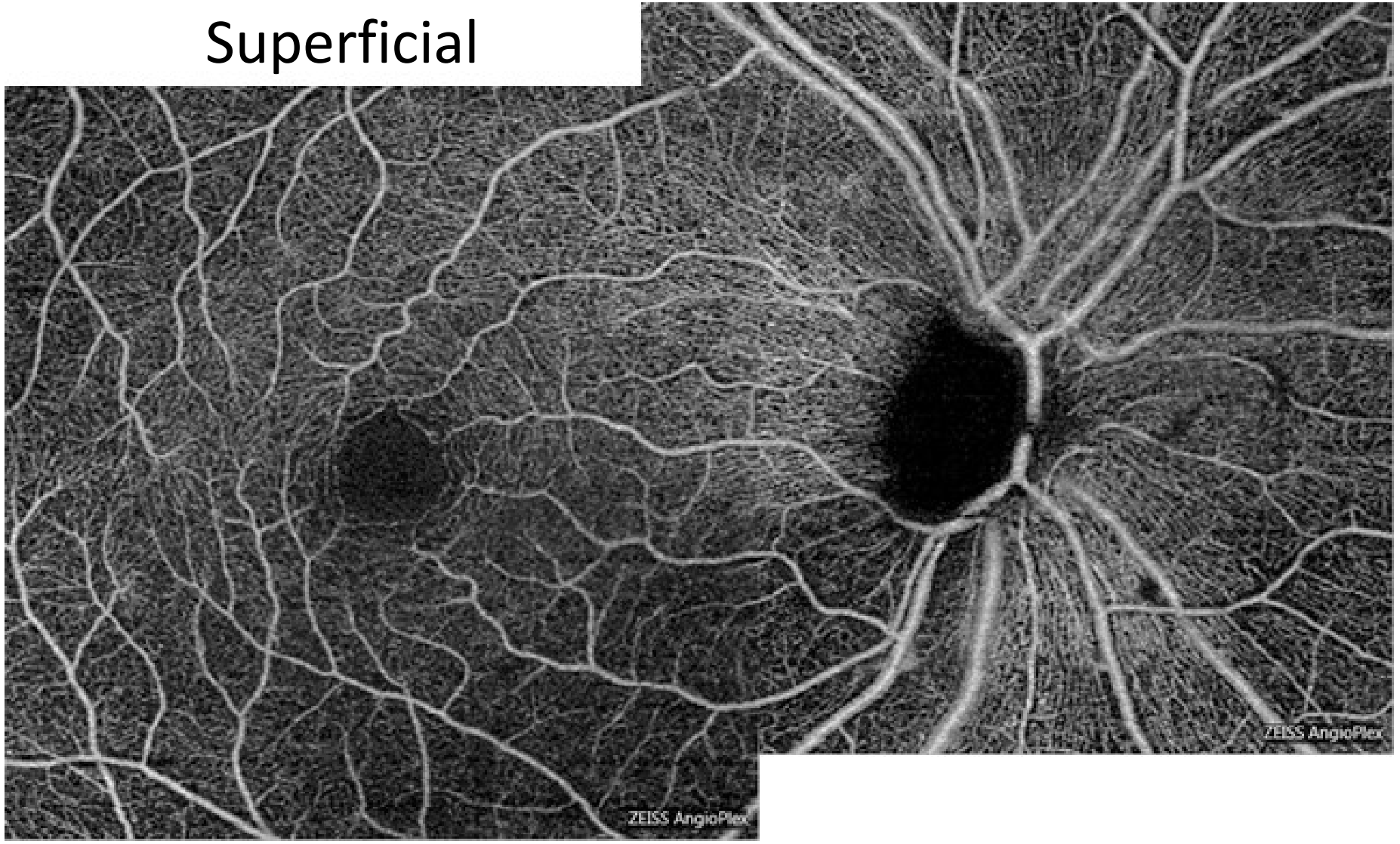
Glaucoma


Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/18
False POS Errors: 9 %
False NEG Errors: 0 %
Test Duration: 07:00
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 6.3 mm
Visual Acuity:
GHT
Outside Normal Limits
VFI 67%
MD -10.14 dB P < 0.5%
PSD 11.61 dB P < 0.5%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
< 1%
< 0.5%


Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 1/16
False POS Errors: 12 %
False NEG Errors: 5 %
Test Duration: 06:31
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 7.2 mm
Visual Acuity:
GHT
Outside Normal Limits
VFI 76%
MD -5.93 dB P < 0.5%
PSD 10.08 dB P < 0.5%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
< 1%
< 0.5%

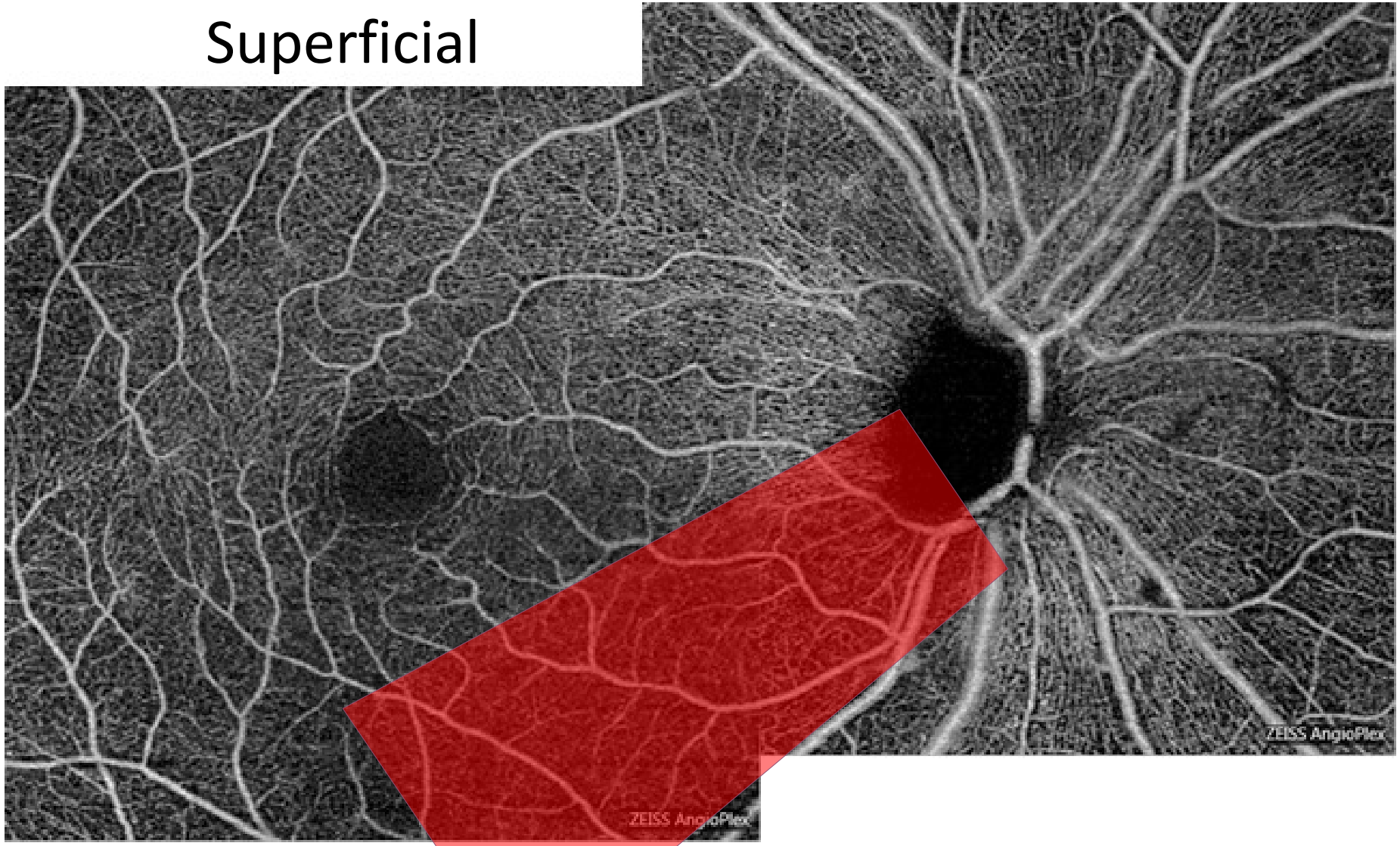
Glaucoma

Superficial

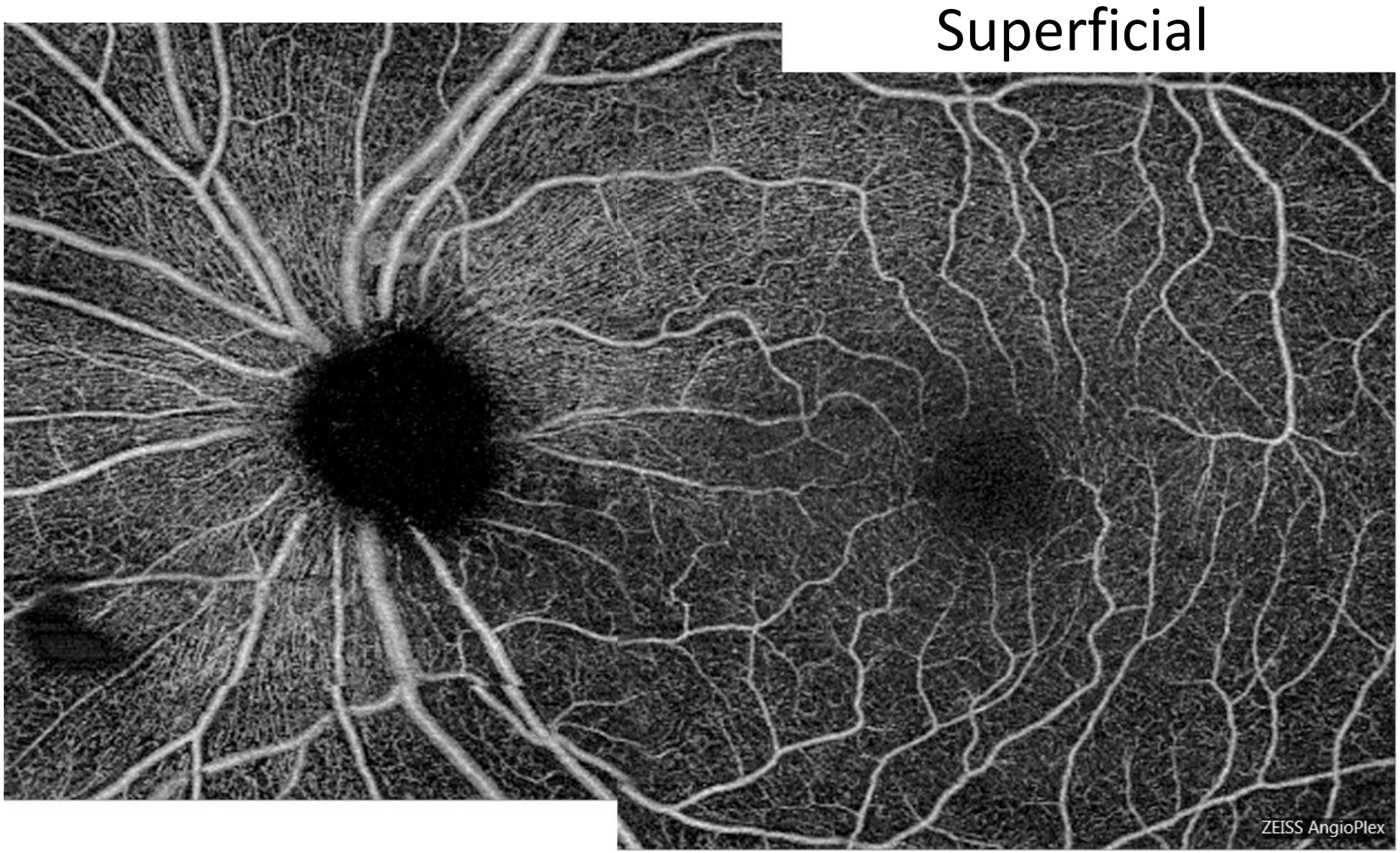


Glaucoma

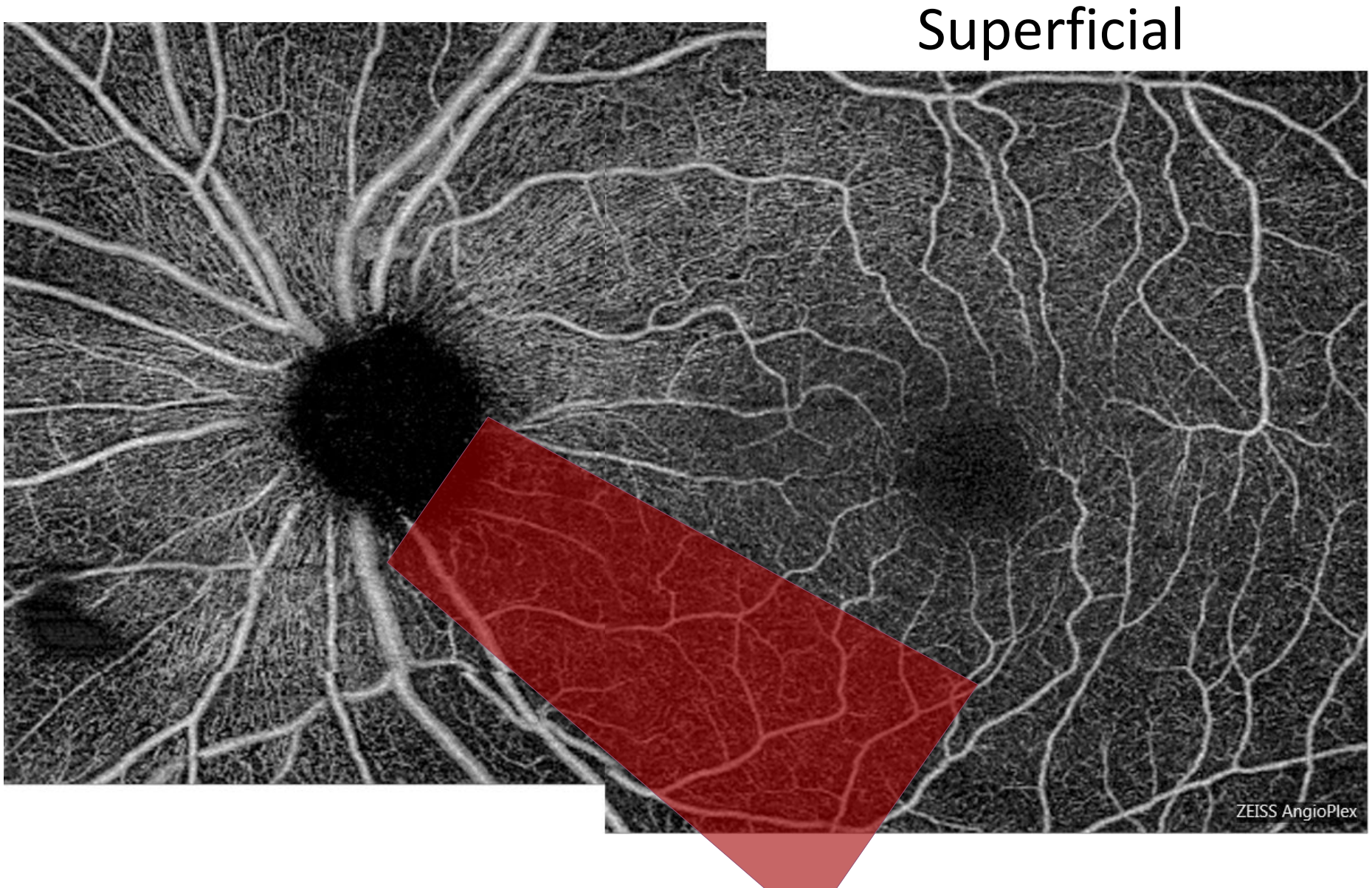
Superficial



Glaucoma



Glaucoma



OPHTHALMOLOGY VOLUME 127, ISSUE 4

Measuring Glaucomatous Focal Perfusion Loss in the Peripapillary Retina Using OCT Angiography

David Huang, MD et al

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Participants

A total of 47 patients with primary open-angle glaucoma (POAG) and 36 normal participants were analyzed.

Methods

One eye of each subject was scanned using an AngioVue (Optovue, Fremont, CA) 4.5-mm OCTA scan centered on the disc.

En face nerve fiber layer (NFL) plexus angiogram was generated. With the use of custom software, a capillary density map was obtained by computing the fraction of area occupied by flow pixels after low-pass filtering by local averaging 21×21 pixels.

The low-perfusion map is defined by local capillary density below 0.5 percentile over a contiguous area above 98.5 percentile of the normal reference population. The LPA parameter is the cumulative area, and the FPL is the percent capillary density loss (relative to normal mean) integrated over the LPA.

Measuring Glaucomatous Focal Perfusion Loss in the Peripapillary Retina Using OCT Angiography

David Huang, MD et al

- Main Outcome Measures
- Peripapillary retinal LPA and FPL.
- Results
- Among patients with POAG, 3 had preperimetric glaucoma and 44 had perimetric glaucoma, with visual field (VF) mean deviation (MD) of −5.14±4.25 decibels (dB). The LPA was 3.40±2.29 mm^2 in those with POAG and 0.11±0.18 mm^2 in normal subjects ($P < 0.001$). The FPL was 21.8%±17.0% in those with POAG and 0.3%±0.7% in normal subjects ($P < 0.001$).
- The diagnostic accuracy as measured by the area under the receiver operating curve was 0.965 for both LPA and FPL, with a sensitivity of 93.7% at 95% specificity. The repeatability as measured by intraclass correlation coefficient was 0.977 for LPA and 0.958 for FPL.
- The FPL had excellent correlation with VF MD (Spearman's rho = −0.843), which was significantly ($P = 0.008$) better than the correlation between NFL thickness and VF MD (rho = 0.760). The hemispheric difference correlation between FPL and VF (Spearman's rho = 0.770) was significantly ($P < 0.001$) higher than the hemispheric difference correlation between LPA and VF (rho = 0.595).

Measuring Glaucomatous Focal Perfusion Loss in the Peripapillary Retina Using OCT Angiography
David Huang, MD et al

- Conclusions
- The low-perfusion map and LPA and FPL parameters are able to assess the location and severity of focal glaucoma damage with good agreement with VF.

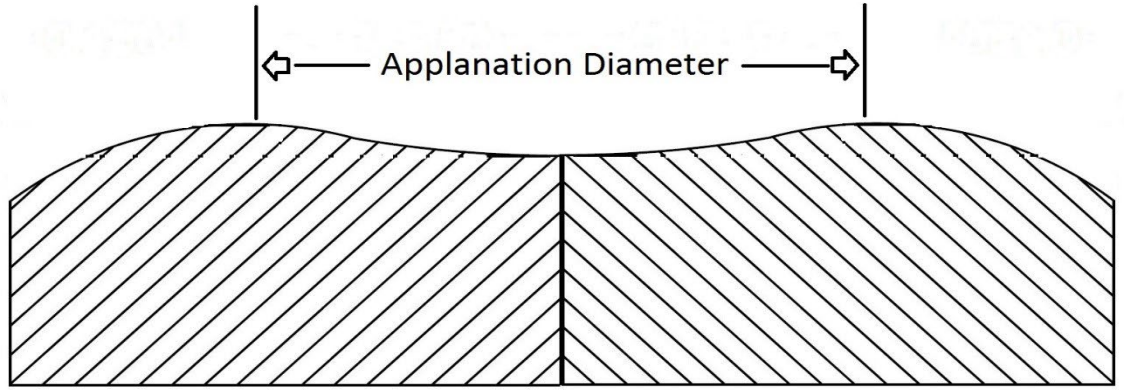
CATS: Correcting Applanation Tonometry Surface

Inventor Sean McCafferty MD

Sean McCafferty is an Ophthalmologist with a degree in Mechanical Engineering and a Master of Science in optical engineering. This unique combination of skills equipped him to envision the CATS™ Tonometer Prism design in 2011.

After years of work, the device became FDA cleared in October 2018.

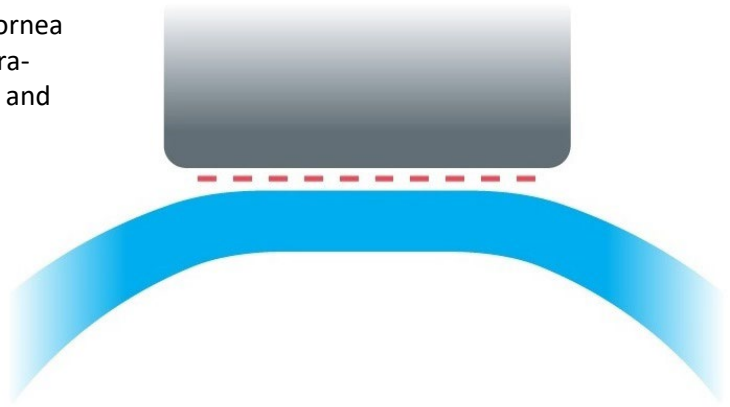
CATS is simply a replacement prism for any Goldmann applanation or Perkins tonometer. The CATS Tonometer Prism™ utilizes a concave contact surface to minimize mechanical bending resistance of the cornea. The device also features a tapered edge, which helps to reduce the influence of tear-film adhesion.



CATS: Correcting Applanation Tonometry Surface

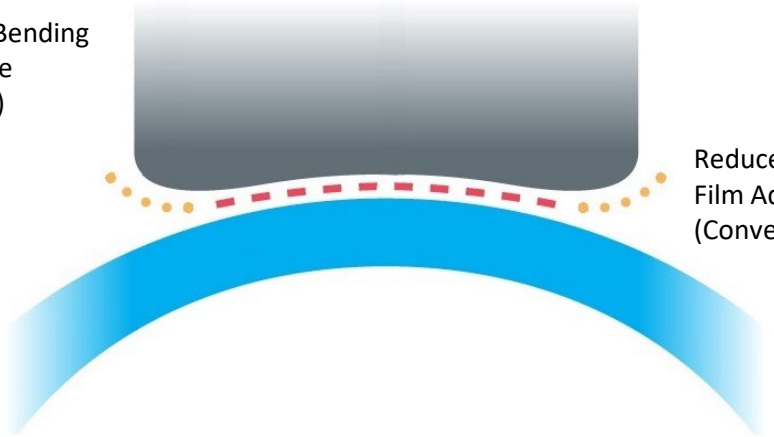
Traditional GAT Prism – No change in 65 Years

Flattens the Cornea Amplifying Intra-Corneal Stress and IOP errors



CATS™ Tonometer Prism – the New Shape of IOP

Reduces Bending Resistance (Concave)



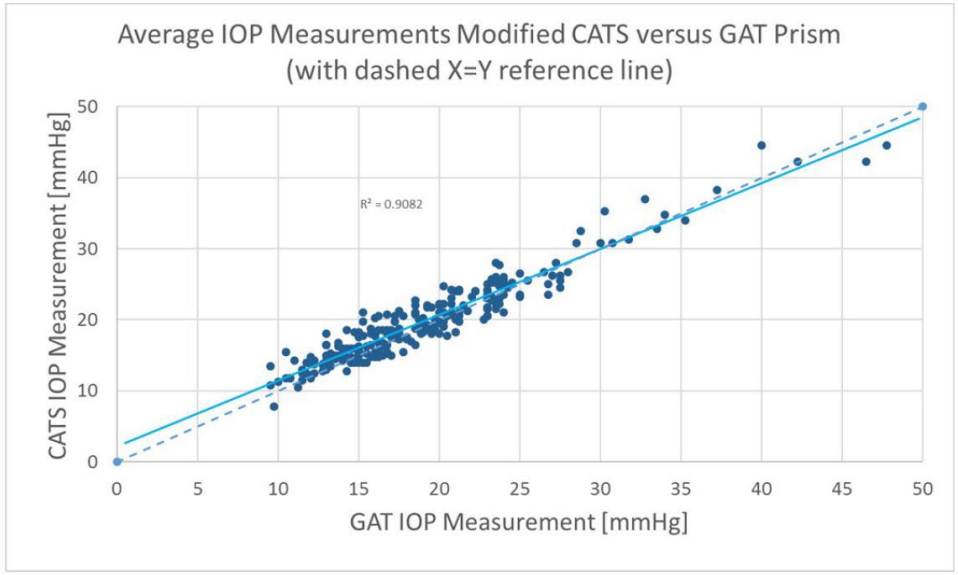
Reduces Tear Film Adhesion (Convex)

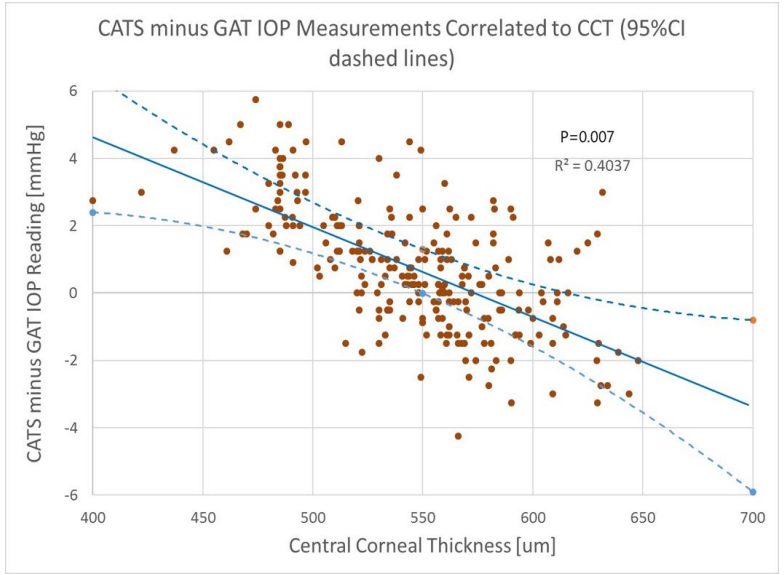
CATS: Compare CATS to GAT in Normal Eyes

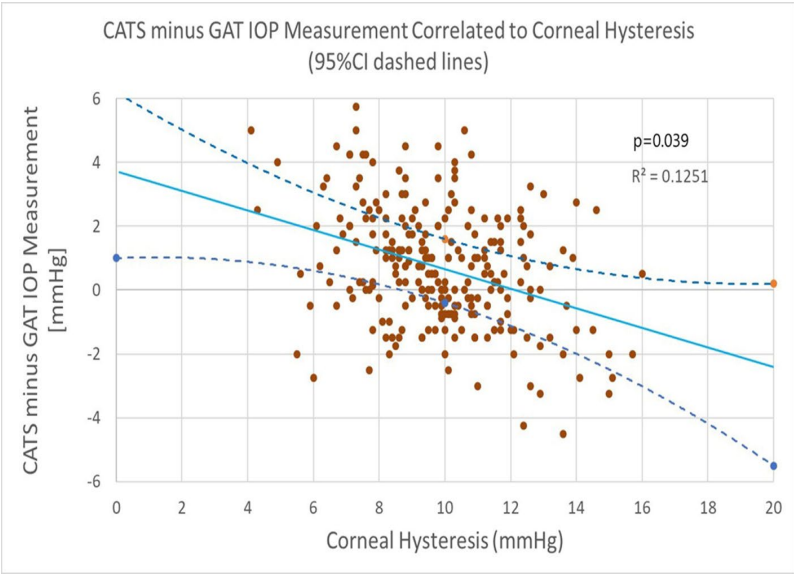
Purpose:

1. Compare CATS to GAT in 243 Normal Eyes with Central Corneal Thickness between 400 – 650 Microns

2. Evaluate the impact of corneal properties on GAT and CATS





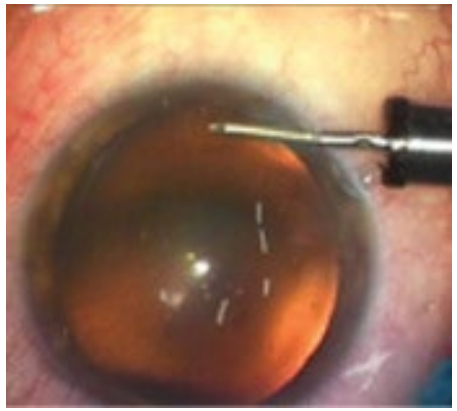


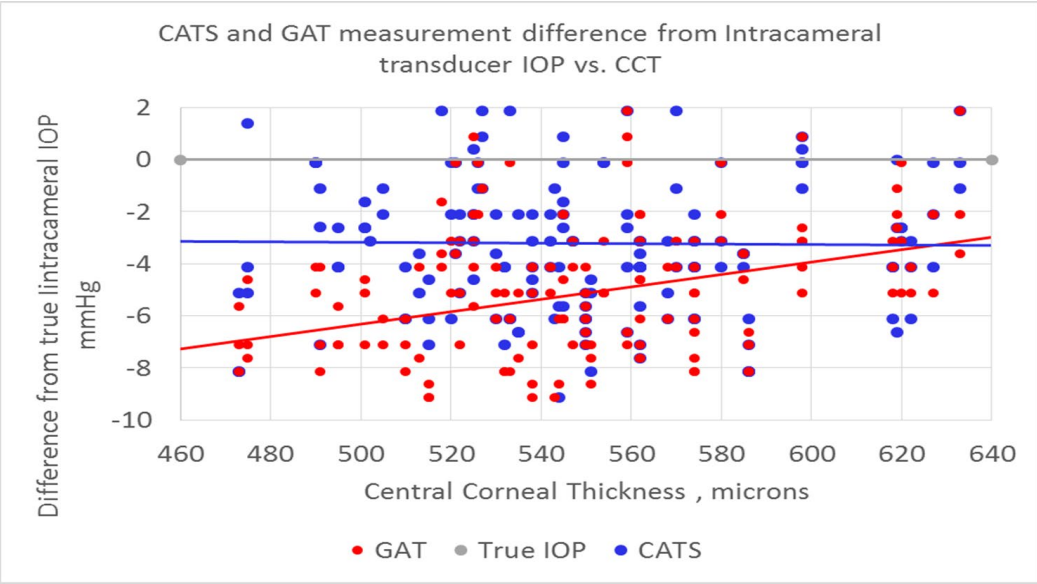
A significant reduction in CATS prism's sensitivity to CCT and CH was demonstrated compared with the traditional GAT prism

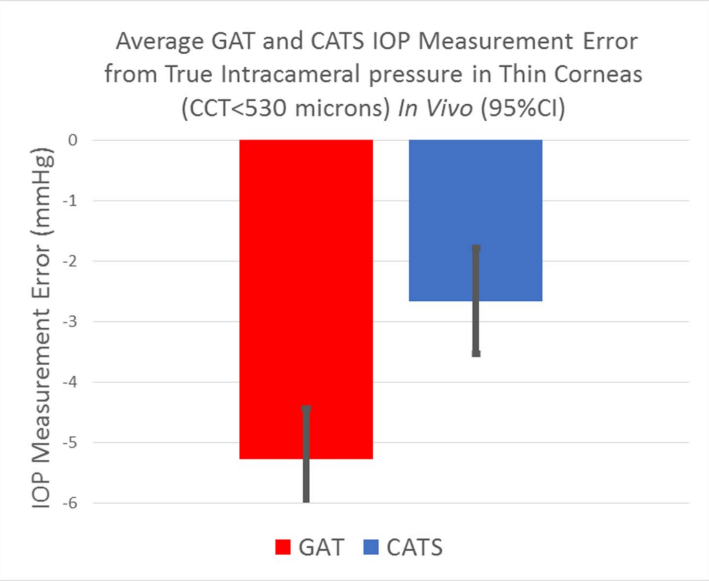
CATS Intercameral Pressure Validation

Methods:

- Intracameral IOP measured on 58 eyes undergoing cataract surgery
- IOP manometrically modulated to 10, 20, and 40 mmHg
- Difference between the CATS and GAT IOP measurements from true intracameral pressure correlated to the error parameters







The CATS prism is significantly more accurate compared to the GAT prism compared to true intracameral pressure, and is unaffected by CCT.

Preservative Free Latanoprost

Preservatives in IOP lowering medications

BRAND NAME	ACTIVE INGREDIENT	PRESERVATIVE
EYE DROPS WITH BENZALKONIUM CHLORIDE (BAK)		
Iopidine	Apraclonidine 0.5%, 1%	BAK 0.01%
Betoptic S	Betaxolol 0.25%	BAK 0.01%
Betoptic	Betaxolol 0.5%	BAK 0.01%
Lumigan	Bimatoprost 0.01%	BAK 0.02%
Lumigan	Bimatoprost 0.03%	BAK 0.005%
Lumify	Brimonidine 0.025%	BAK 0.01%
Alphagan	Brimonidine 0.2%	BAK 0.005%
Combigan	Brimonidine 0.2%/timolol 0.5%	BAK 0.005%
Azopt	Brinzolamide 1%	BAK 0.01%
Simbrinza	Brinzolamide 1%/brimonidine 0.2%	BAK 0.003%
Trusopt	Dorzolamide 2%	BAK 0.0075%
Cosopt	Dorzolamide 2%/timolol 0.5%	BAK 0.0075%
Xalatan	Latanoprost 0.005%	BAK 0.02%
Rocklatan	Latanoprost 0.005%/netarsudil 0.02%	BAK 0.02%
Vyzulta	Latanoprostene 0.024%	BAK 0.02%
Betagan	Levobunolol 0.25%, 0.5%	BAK 0.004%
Rhopressa	Netarsudil 0.02%	BAK 0.015%
Isopto Carpine	Pilocarpine 1%	BAK 0.01%
Timoptic	Timolol 0.25%, 0.5%	BAK 0.01%

EYE DROPS CONTAINING ALTERNATIVE PRESERVATIVES		
Alphagan P	Brimonidine 0.1%, 0.15%	Purite® (stabilized oxychloro complex) 0.005%
Xelpros	Latanoprost 0.005%	Potassium sorbate
Timoptic-XE	Timolol-XE 0.25%, 0.5%	Benzododecinium bromide 0.012%
Travatan Z	Travoprost 0.004%	sofZia®

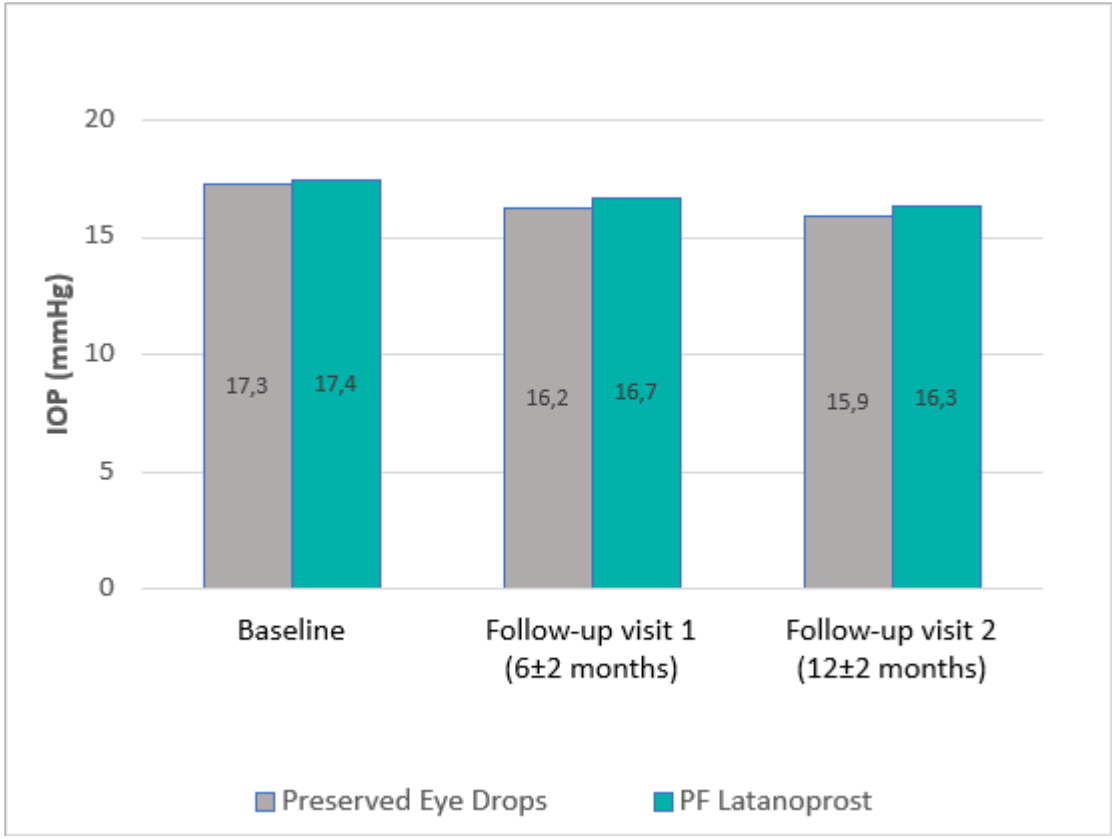
PRESERVATIVE-FREE EYE DROPS		
Cosopt PF	Dorzolamide 2%/timolol 0.5%	Preservative-free
PF Latanoprost	**Latanoprost 0.005%**	**Preservative-free**
Zioptan	Tafluprost 0.0015%	Preservative-free
Timoptic in Ocudose	Timolol 0.25%, 0.5%	Preservative-free

BAK is the most used preservative in topical ophthalmic formulations

PF-Latanoprost has been approved by the FDA for use in the United States.

IOP Lowering: PF-latanoprost vs. Preserved glaucoma medications*[1]

PF-latanoprost vs. preserved glaucoma medication at 6 months and 12 months



The most common preserved glaucoma treatments were:

- preserved beta-blockers (21.2%)
- preserved latanoprost (20.7%)
- preserved travoprost (9.8%)
- preserved bimatoprost 0.01% (5.6%).

*Multicenter, international, prospective, noninterventional real-life study conducted in France, the Netherlands, Norway, Poland, and Sweden

1. Economou et al. Clinical Ophthalmology 2018: 12; 2399-2407.

CORNEAL HYSTERESIS:
The Newest Disruptive Technology
In Glaucoma

CH: Average Values in Normal Subjects

CH Values in Normals around the world	N	CH*
Brazil[1]	105	10.1 ± 1.8
UK[2]	272 pairs	10.2 ± 1.2
China[3]	125	10.9 ± 1.5
Japan[4]	204	10.2 ± 1.3
Spain[5]	88	10.8 ± 1.5
USA[6]	44	10.5 ± 1.2

*CH units are mmHg

1. Fontes BM J Refract Surg. 2008 Nov;24(9):941-5.
2. Carbonaro. The Heritability of Corneal Hysteresis and Ocular Pulse Amplitude A Twin Study doi:10.1016/j.ophtha.2008.02.011
3. Lam A. Et Al. Optom Vis Sci. 2007 Sep;84(9):909-14
4. Kamiya Et Al. J Refract Surg. 2009 Oct;25(10):888-93
5. Ortiz Et Al. J Cataract

Clinical Evidence – Study 1

Corneal Hysteresis found to be associated with progression

- The first observational study to investigate the relationship of Corneal Hysteresis to a variety of other parameters in a glaucoma population

- 230 POAG or suspected POAG patients were included in the study
  - POAG was defined by a reliable visual field that was abnormal according to OHTS criteria, with an optic nerve image, photo, or CDR thought to be consistent with the field damage by a fellowship-trained glaucoma specialist.
  - GAT, ORA, CCT and Axial Length measurements (IOL master) were recorded
  - Among persons with three or more reliable fields over three or more years, or with five reliable fields in less than three years, progression was defined as having achieved the OHTS standard of “conversion” (if previously normal), or (if previously damaged as evidenced by an abnormal GHT or PSD) having worsened by 1 dB or greater per year in either MD or PSD.
  - A stepwise model was not used nor were any hypotheses about interactions made.

POAG Primary Open Angle Glaucoma; GAT Goldmann Applanation Tonometry; IOP intraocular pressure; ence limit.

CCT Central Corneal Thickness; CH Corneal Hysteresis

Congdon NG et al. *Am J Ophthalmol.* 2006;141:868-875.

Clinical Evidence – Study 1

Corneal Hysteresis found to be associated with progression

	OR	LCL	UCL	*P*-value
Age per year <65	1.12	1.01	1.24	.03
Age per year >65	1.08	1.01	1.15	.02
GAT IOP per mmHg	1.22	0.95	1.58	.12
Treatment	1847.6	3.16	10^6	.02
IOP by treatment interaction	0.79	0.61	1.03	.08
CCT per 100 microns	1.65	0.66	0.98	.30
Years with glaucoma	1.00	0.96	1.04	.98
Baseline IOP	0.99	0.93	1.06	.79
CH per mmHg	0.81	0.66	0.98	**.03**

Conclusions: Corneal Hysteresis was the parameter most associated with progressive field worsening

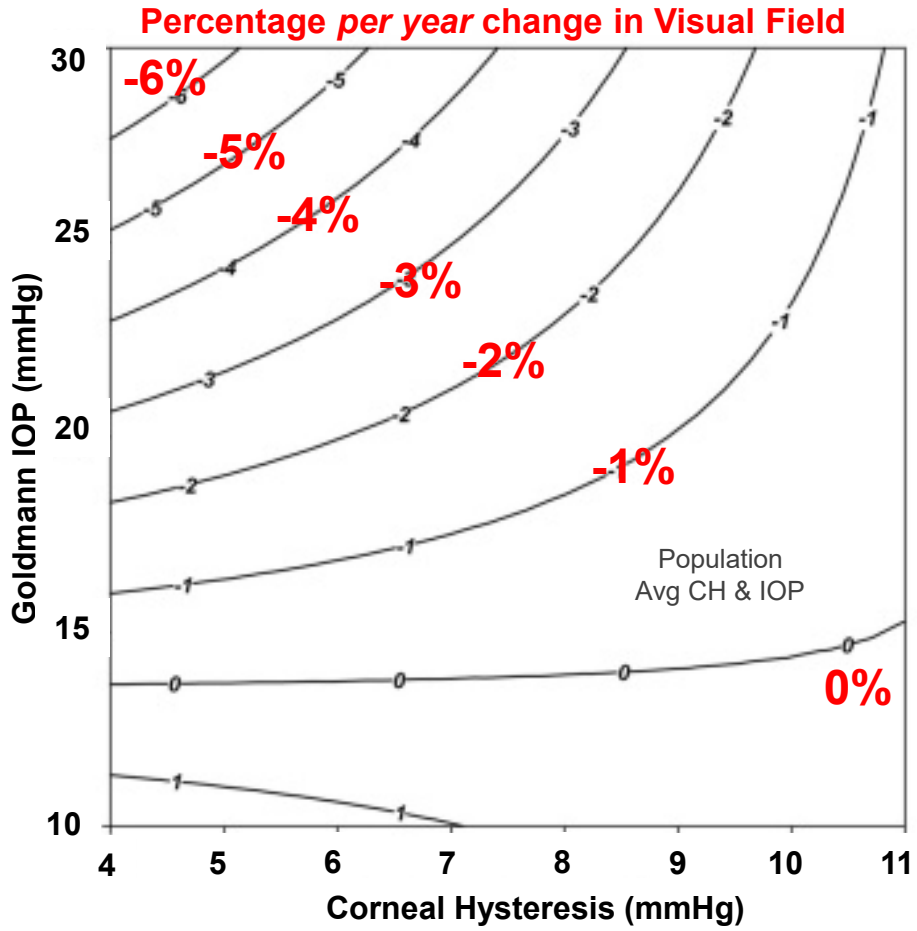
GAT Goldmann Applanation Tonometry; IOP intraocular pressure; OR odds ratio; LCL lower confidence limit; UCL upper confidence limit.

CCT Central Corneal Thickness

Congdon NG et al. *Am J Ophthalmol*

Corneal Hysteresis in Glaucoma

Predictive of Progression in Prospective, Longitudinal Study (DIGS)



Medeiros FA et al.
Ophthalmology. 2013;120:1533-1540.

"The Effect of IOP on rates of progression was dependent upon Corneal Hysteresis"

- For eyes with lower CH, the impact of IOP on VF loss was significantly greater
- **IOP of 30** is not so bad with a CH of 11.
- **IOP of 20** is very bad with a CH of 6

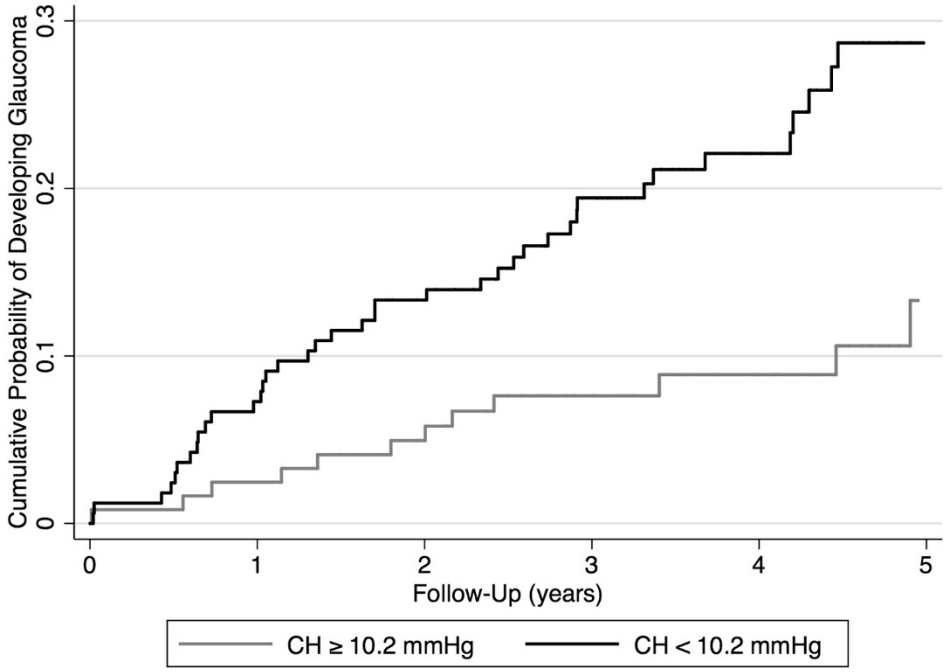
Corneal Hysteresis in Glaucoma

Predictive of conversion to Glaucoma in pre-perimetric Glaucoma Suspects

Purpose: To investigate the role of CH as a risk factor for **development** of glaucoma in a prospective longitudinal study.

Results: Fifty four (19%) of the 287 eyes developed repeatable visual field defects during a 4 year follow-up.

CH was *independently* predictive of conversion to glaucoma even when adjusted for age, IOP, and CCT.



Each 1mmHg lower CH was associated with an increase of 21% in the risk of developing glaucoma during follow up

A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor for Predicting Development of Glaucoma
AJOPHT 10365 – in press
Author Block: Feilin Zhu , Alberto DinizFilho, Linda M. Zangwill , Felipe A. Medeiros

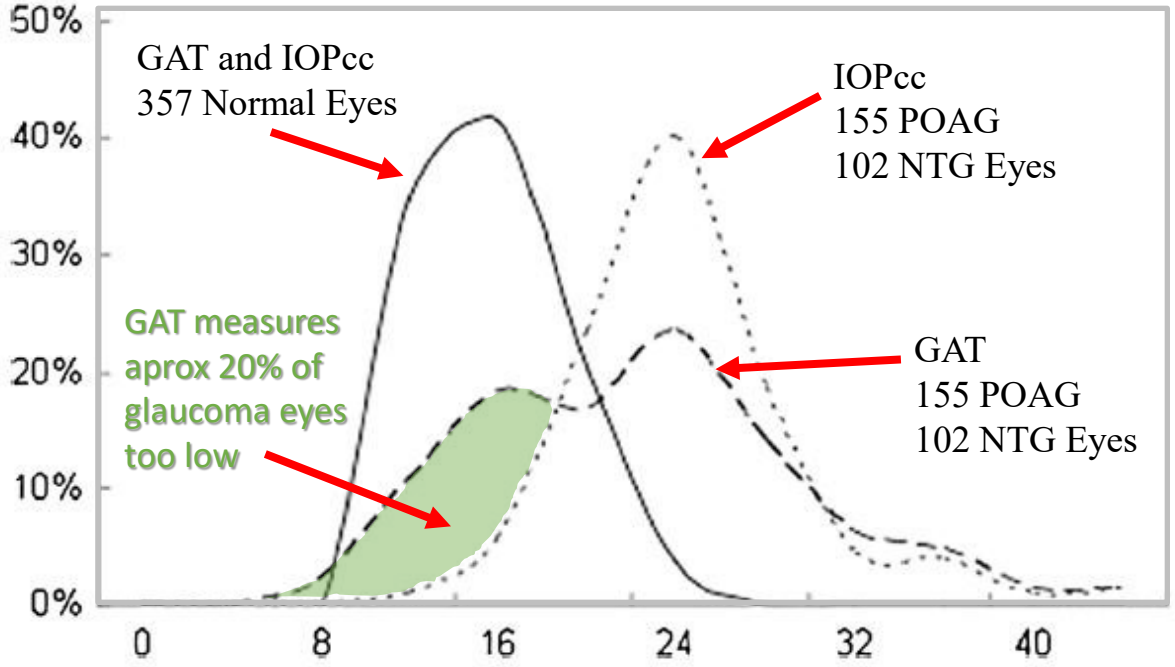
Corneal Compensated IOP

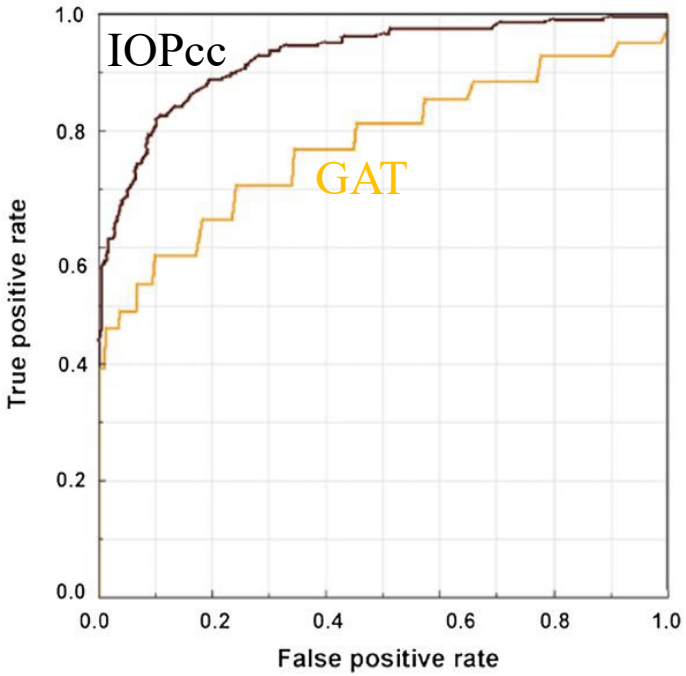
- Superior to Goldmann in all forms of post Refractive Surgery IOP measurements

IOPcc Key Benefit #2
IOPcc is superior for glaucoma risk assessment

IOPcc is clinically superior to GAT, other NCTs, and iCare because it is more associated with Glaucoma risk, status of glaucoma, and glaucoma progression

"the results of this study suggest that IOPcc may represent a superior test for the evaluation of glaucoma"





AUC .93 for IOPcc vs .78 for GAT

Not shown here from this study:

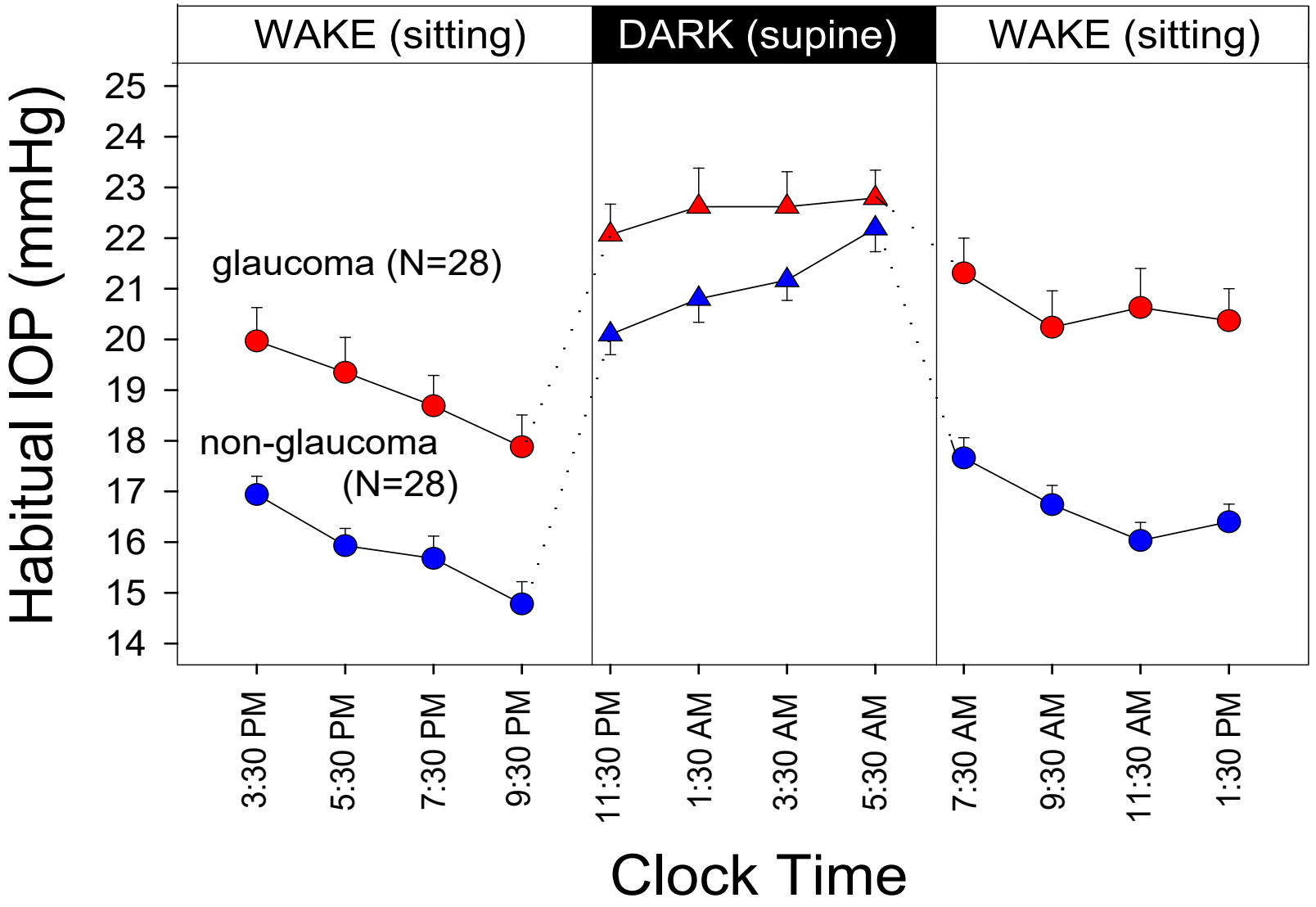
- **39%** of NTG eyes would be re-classified as POAG with IOPcc
- Average IOPcc was **5 mmHg higher** than GAT in NTG eyes

Goldmann applanation tonometry compared with corneal-compensated intraocular pressure in the evaluation of primary open-angle Glaucoma
Joshua R Ehrlich, Nathan M Radcliffe, and Mitsugu Shimmyo

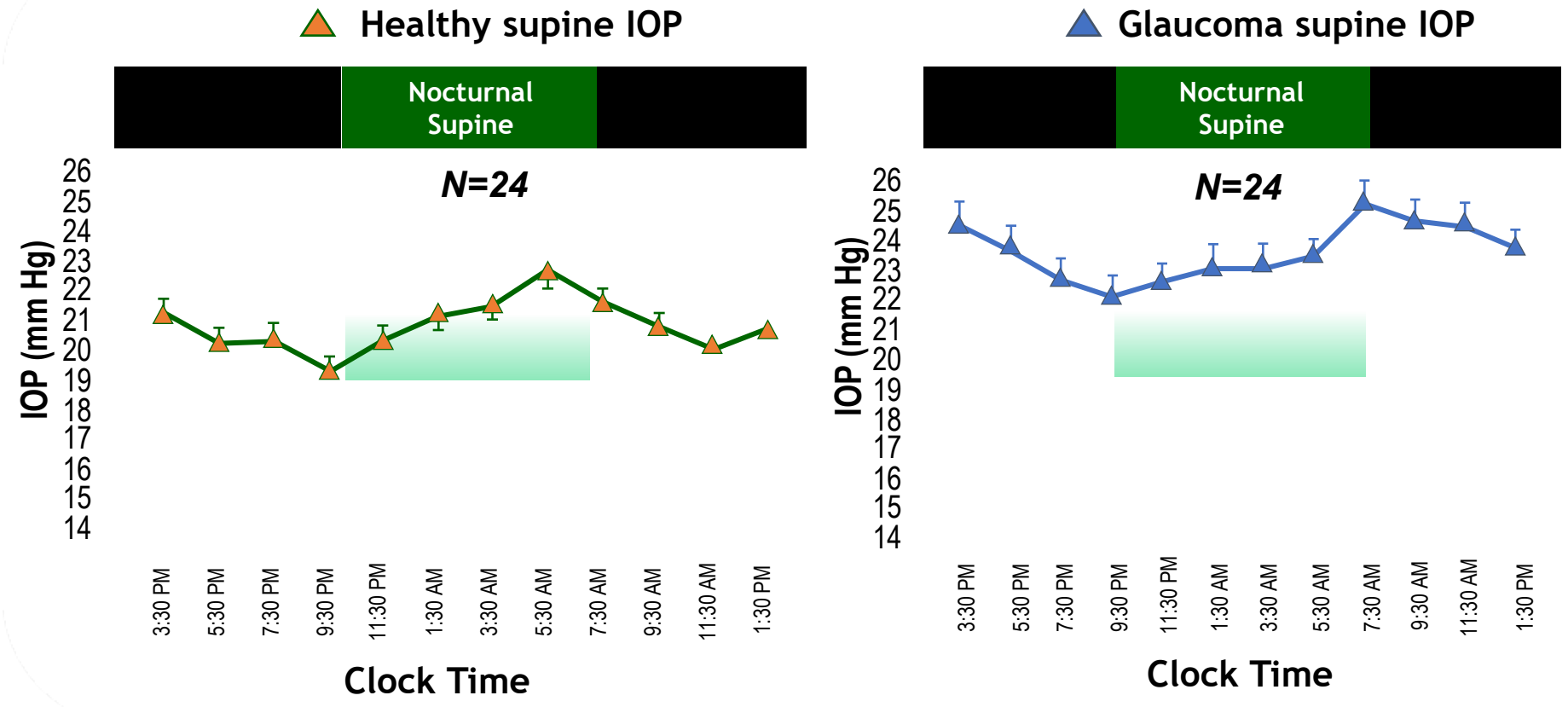
24-Hour IOP Monitoring

- How do we evaluate IOP if we are only measuring it briefly in office?
- Currently we make decisions based upon single in-office IOP but patient's IOP may vary at other times
  - With 24 hour IOP measurement, will be able to determine our treatment target based upon IOP peak, 24-hour mean or fluctuation over 24 hours
  - New 24-hour devices may be able to synchronize drug release with peaks of IOP
- 24-hour IOP monitoring systems
  - Better define target IOPs leading to better therapies
  - Personalize glaucoma care
- Three approaches to measure IOP over 24 hour period
  - Self tonometry
  - Permanent continuous IOP monitoring
  - Temporary continuous IOP monitoring

24-hour IOP pattern (ages 40-80)
glaucoma vs. non-glaucoma

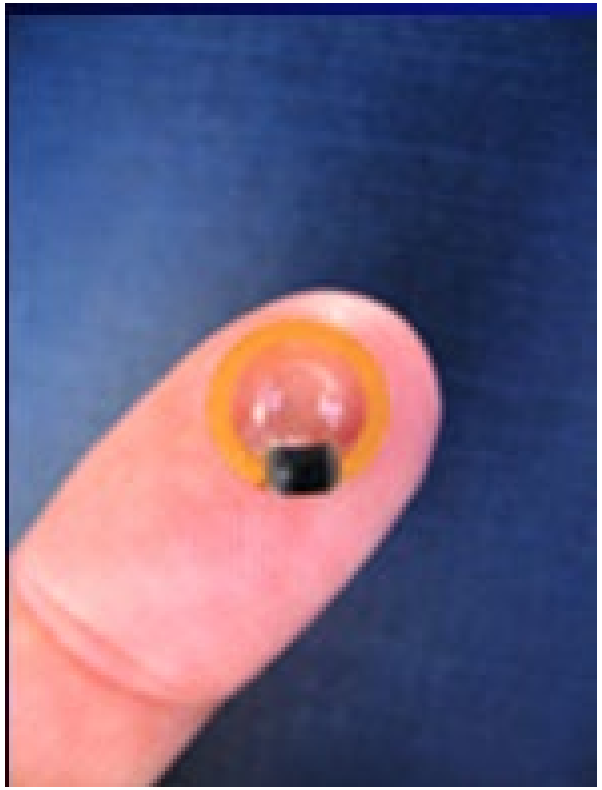


IOP Is Higher At Night



Liu, Zhang, Kripke, Weinreb. *Invest Ophthalmol Vis Sci*. 2003;44:1586-1590.

Implantable IOP monitor



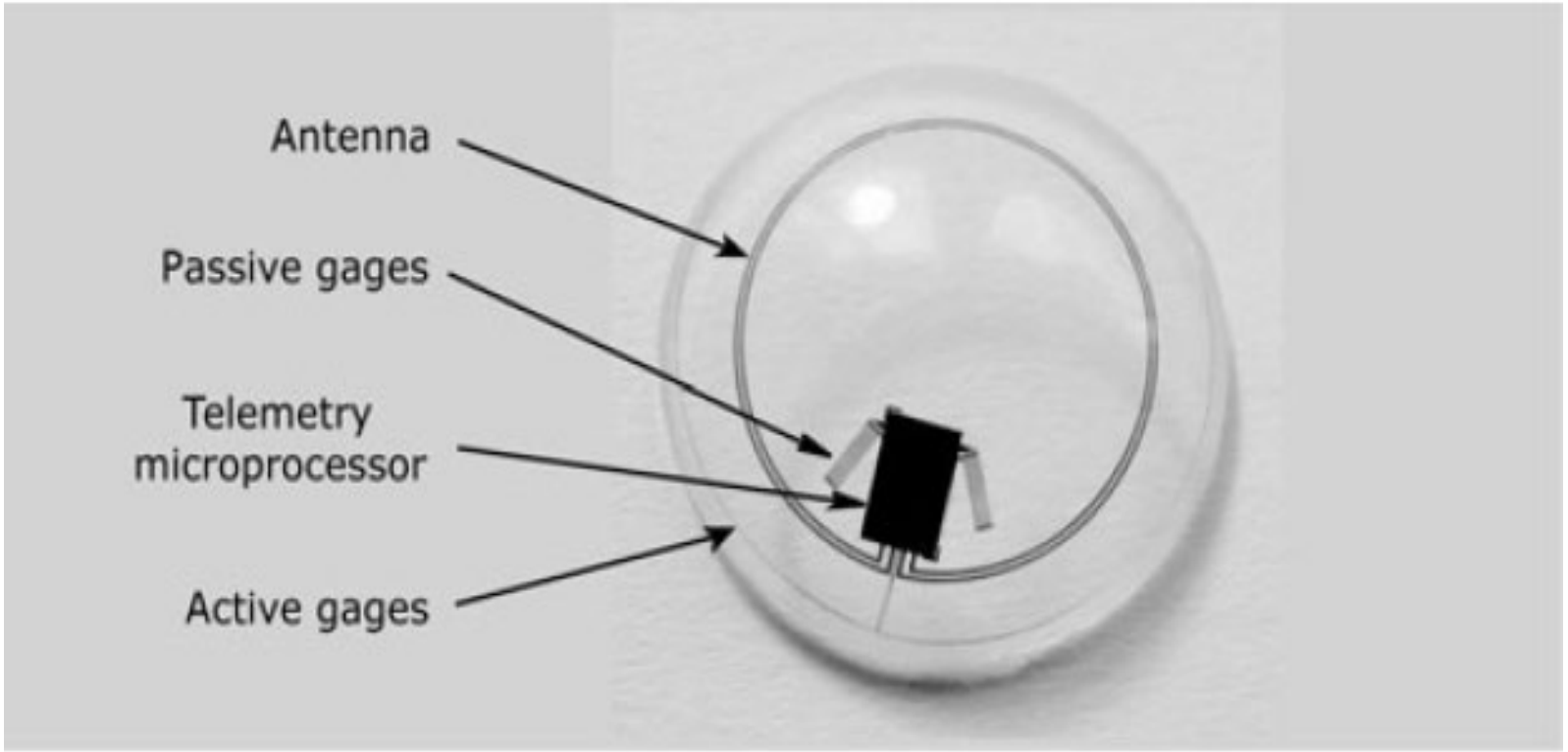
Temporary Continuous IOP Monitoring

- Triggerfish contact-lens system
  - FDA approved March 2016 but not available for sale in US
  - Measures changes in corneal curvature as surrogate for IOP

Triggerfish Contact Lens Monitor

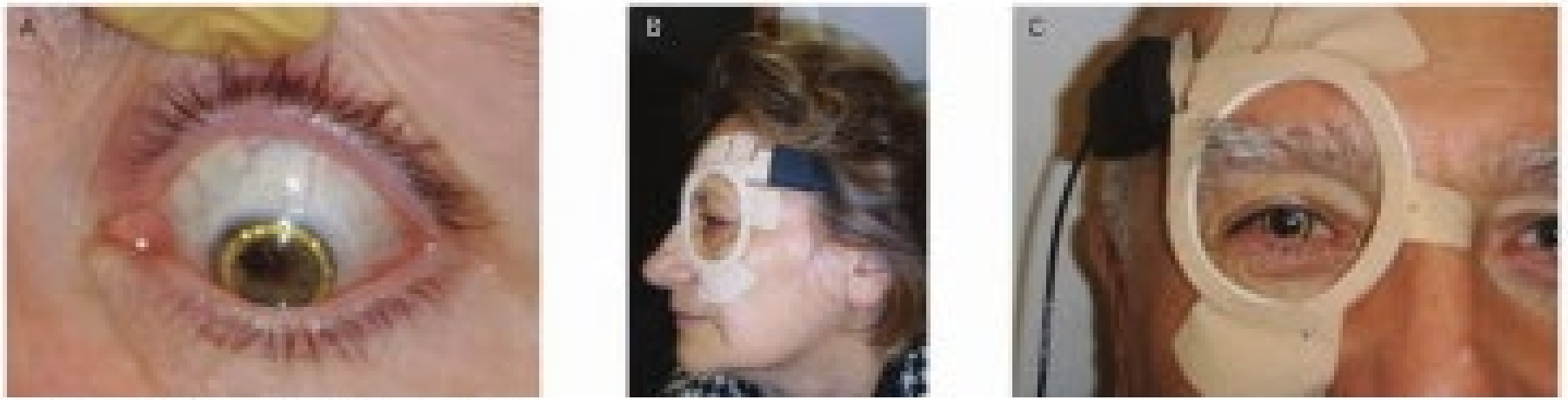
- Provides 24 hour IOP monitoring, including the sleep period
- Takes measurement every five minutes
  - 288 times per day
- At the five minute measurement, obtains 300 data points
  - 10 Hz for 30 seconds
- Main concern is that instrument does not provide IOP measurement
  - Provides change in corneal curvature, based upon peripheral corneal measurement that correlates with change in IOP
  - Detect fluctuations in IOP

Triggerfish Contact Lens 24-Hour IOP Monitoring Device

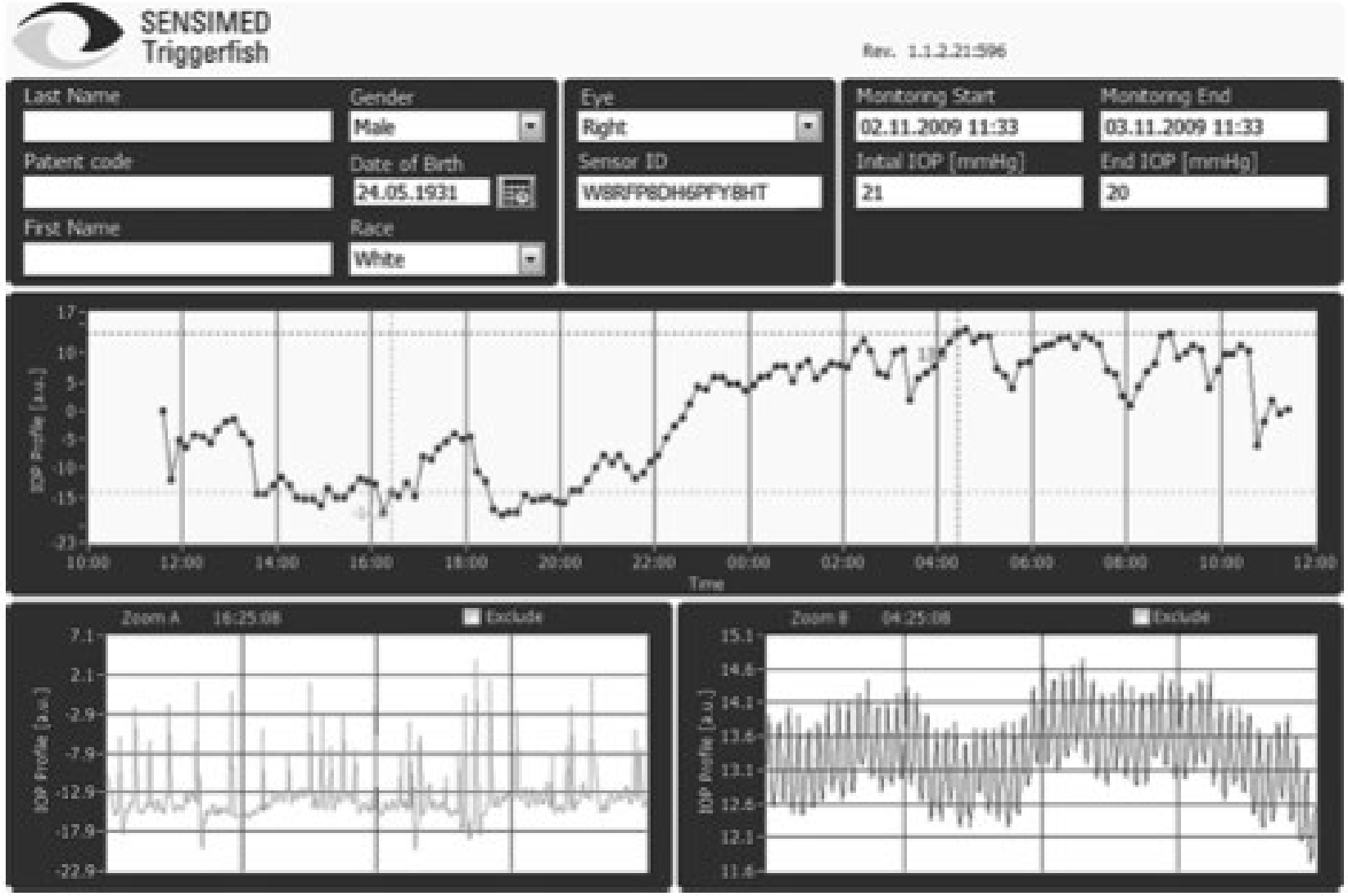


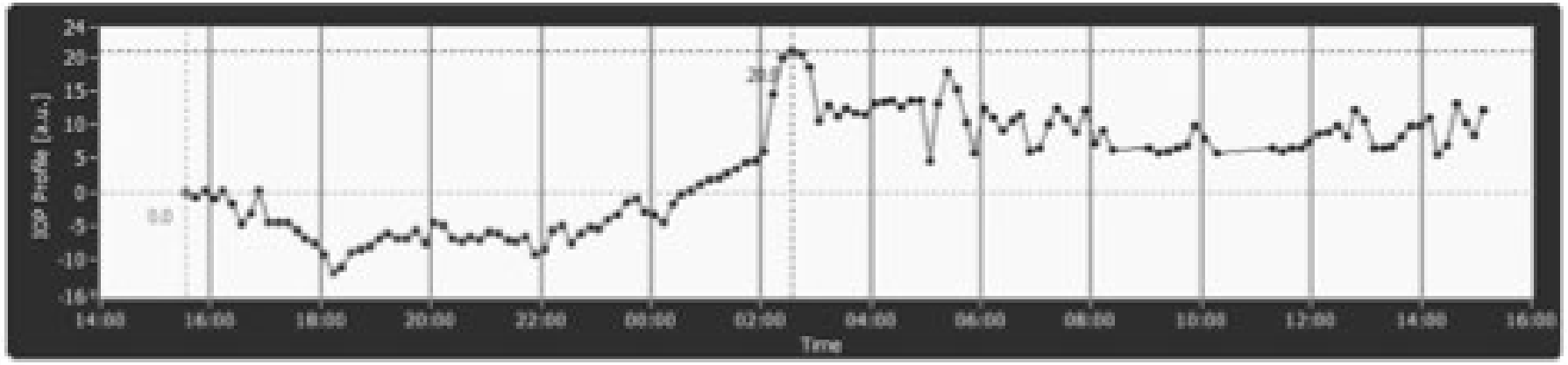
Leonardi M, et al. Wireless contact lens sensor for intraocular pressure monitoring: assessment on enucleated pig eyes. Acta Ophthalmol. 2009: 87: 433–437

Figure 1: Placement of the Sensimed Triggerfish® and Antenna



A: Well-positioned contact lens; B: Lateral view; C: Frontal view.


SENSIMED
Triggerfish
Rev. 1.1.2.21:596
Last Name
Patient code
First Name
Gender
Male
Date of Birth
24.05.1931
Race
White
Eye
Right
Sensor ID
W8RFP8DH6PPYBHT
Monitoring Start
02.11.2009 11:33
Intial IOP [mmHg]
21
Monitoring End
03.11.2009 11:33
End IOP [mmHg]
20
IOP Profile [a.u.]
Time
Zoom A 16:25:08
Exclude
Zoom B 04:25:08
Exclude


ICP Profile [a.u.]
24
20
15
10
5
0
-5
-10
-15
0.0
20.0
14:00
16:00
18:00
20:00
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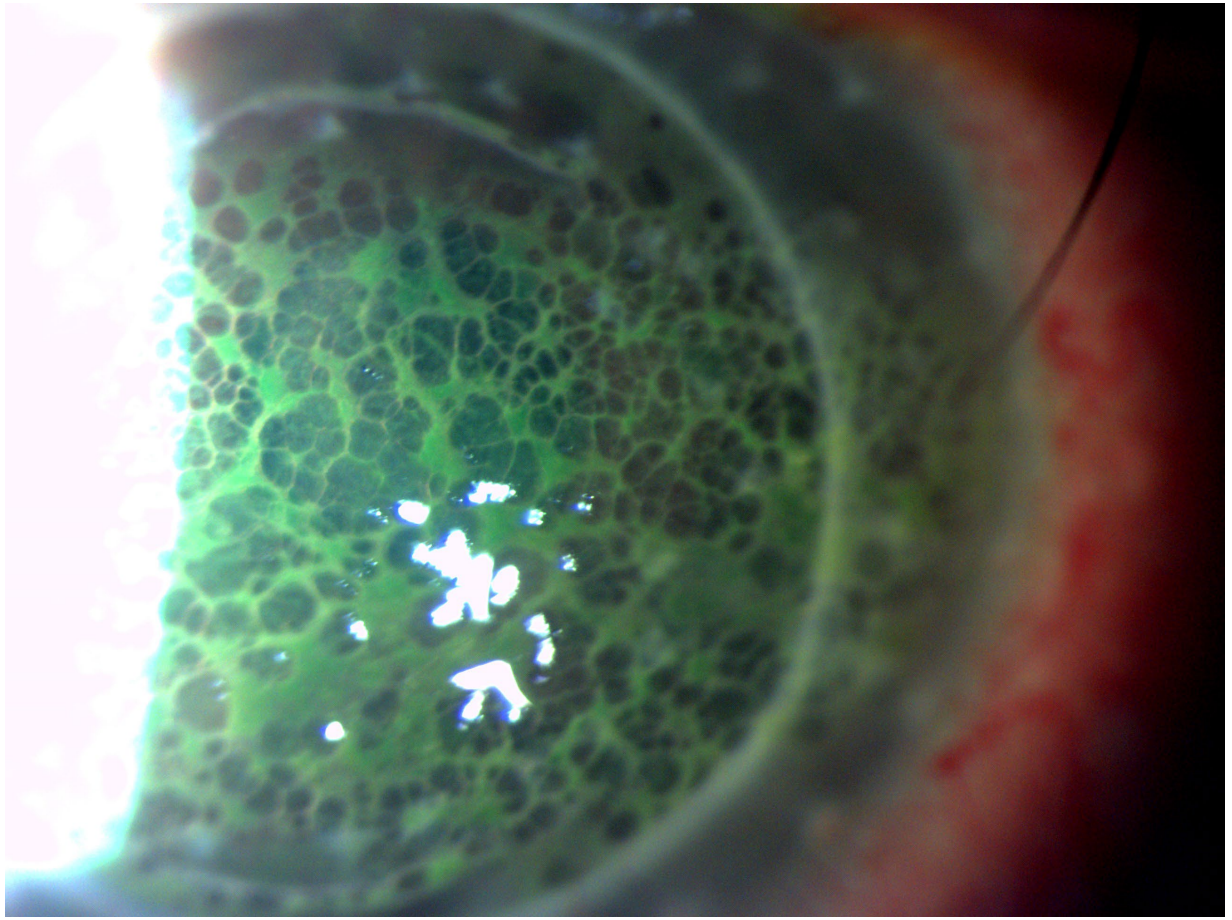
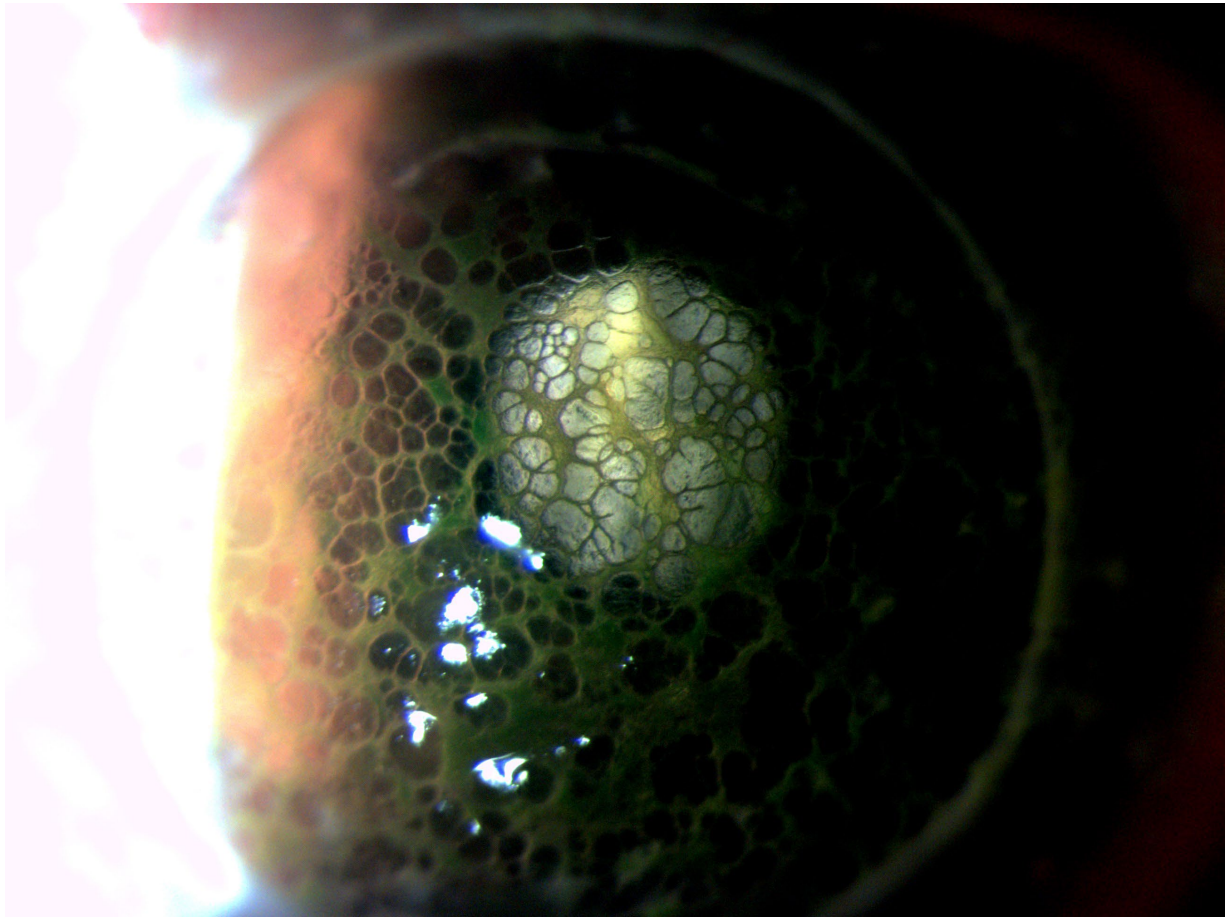
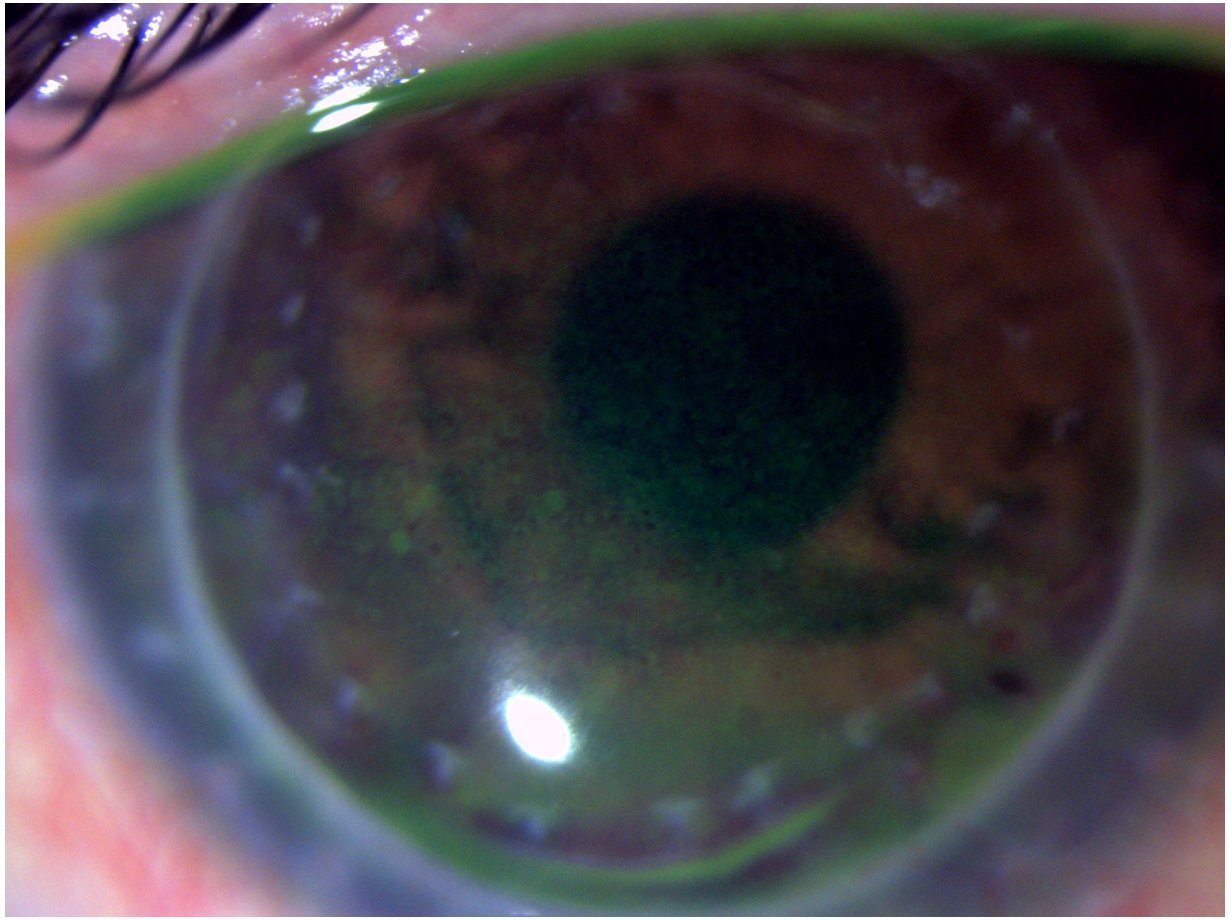
16:00
Time

Bonus Case







VERSÉA
OPHTHALMICS

Building a dedicated and experienced ophthalmics division

Focusing on complete ocular diagnostic and therapeutic solutions

Providing rapid point-of-care (POC) testing that guides clinical management and therapeutic interventions, such as novel biologics, to improve patient care for those afflicted with ocular surface disease

OCULAR SURFACE DISEASE TREATMENT OPTIONS & LIMITATIONS: THE IMPORTANCE & VALUE OF SYMPTOM RELIEF & PATIENT SATISFACTION

Artificial tears, lubricants, tear duct plugs, steroids, antibiotics, cyclosporine, scleral lenses, and serum tears do not fully address the underlying disease process or promote mechanisms that facilitate long-term wound repair.

Patients suffer pain, scarring, vision loss, and require frequent regimen of topical medication, which often leads to severe ocular side effects. Corneal staining persists in the majority of patients despite aggressive treatment.

25%

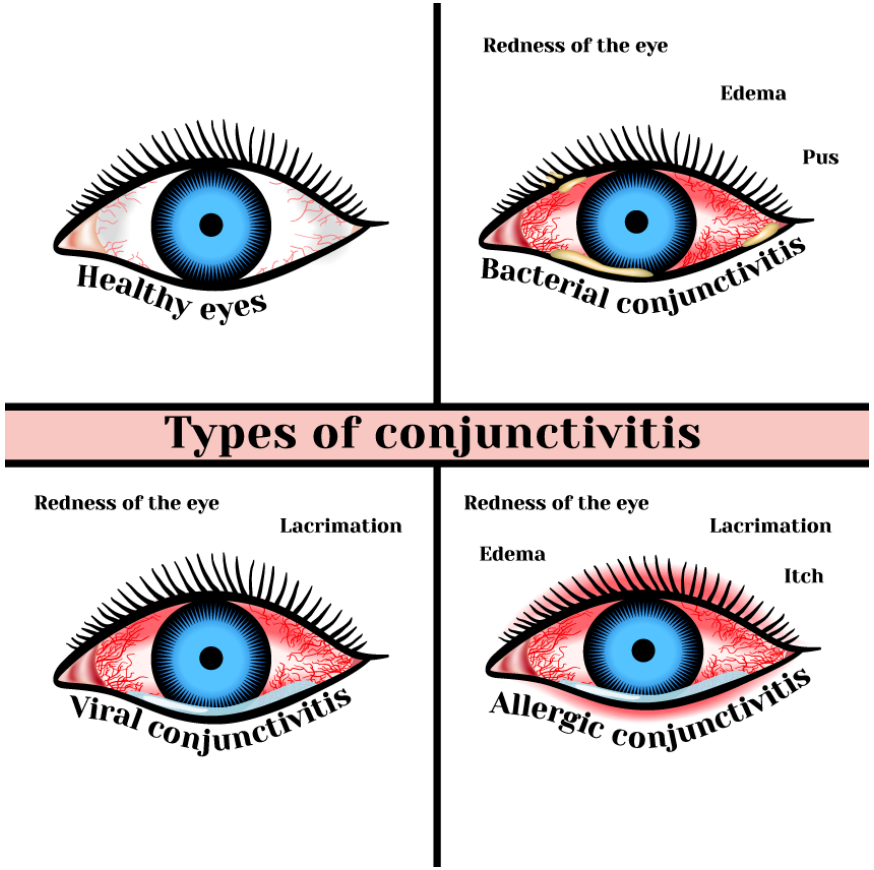
of patients are somewhat dissatisfied or dissatisfied with their current medication.

37%

of patients report ineffective symptom relief.

White DE, Zhao Y, Jayapalan H, Machiraju P, Periyasamy R, Ogundele A. Physician Satisfaction with Anti-Inflammatory Topical Medications for the Treatment of Dry Eye Disease. Clin Ophthalmol. 2020;14:931-938. Published 2020 Mar 25. doi:10.2147/OPTH.S237832.

Infectious Conjunctivitis (Red Eye)

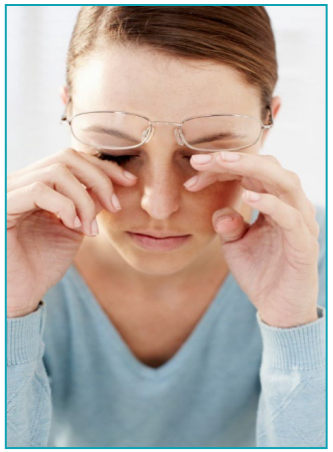


- Can be caused by virus, bacteria, or allergy
- Affects approximately 2% of the population annually in the U.S.[1]
- 1-2% of all office visits[2]
- ~50% of patients clinically misdiagnosed using symptoms and signs[3]

[1] Thomson Reuters Medstat Marketscan Data, 2005. [2] Shields T, Sloane PD. Fam Med. 1991 Sep-Oct;23(7):544-6 [3]] LeibowitzHW, Pratt MV, Flagstad IJ, et al. Human conjunctivitis. I. Diagnostic evaluation. *Arch Ophthalmol*. 1976;94:1747-9. [4] Cheung D, Bremner J, Chan JT. Epidemic kerato-conjunctivitis--do outbreaks have to be epidemic? *Eye*. 2003;17:356-63. [5] O'Brien TP, Jeng BH, McDonald M, Raizman MB. Acute conjunctivitis: truth and misconceptions. *Curr Med Res Opin*. 2009; Jun 25.

Incorporating Tear-Based Diagnostics into Practice

Point-of-Care testing can be used on these types of patients:



Symptomatic Ocular Surface Disease

- Patients presenting with complaints of sandy/gritty, burning, stinging, foreign body sensation, itching, eye fatigue, fluctuating vision, or tearing should be considered for routine tear-based testing

Contact Lens Fittings

- Contact lens intolerance and dropout frequently caused by underlying ocular surface disease

Pre-operative Testing

- Testing all pre-operative LASIK and cataract surgery patients for ocular allergy and dry Eye will help determine who may benefit from more aggressive treatment to optimize the ocular surface prior to surgery

Meeting the Ideal Criteria for Tear-based POC Testing

Feature	T-POC TOTAL IgE	T-POC LACTOFERRIN	Osmolarity	Adenovirus	MMP-9
Objective	X	X	X	X	X
Quantitative	X	X	X		
Rapid	X	X	X	X	X
Specific	X	X	X	X	
Reproducible	X	X		X	X
Inform/Guide tx decisions	X	X		X	X
Simple & efficient workflow	X	X	X	X	X

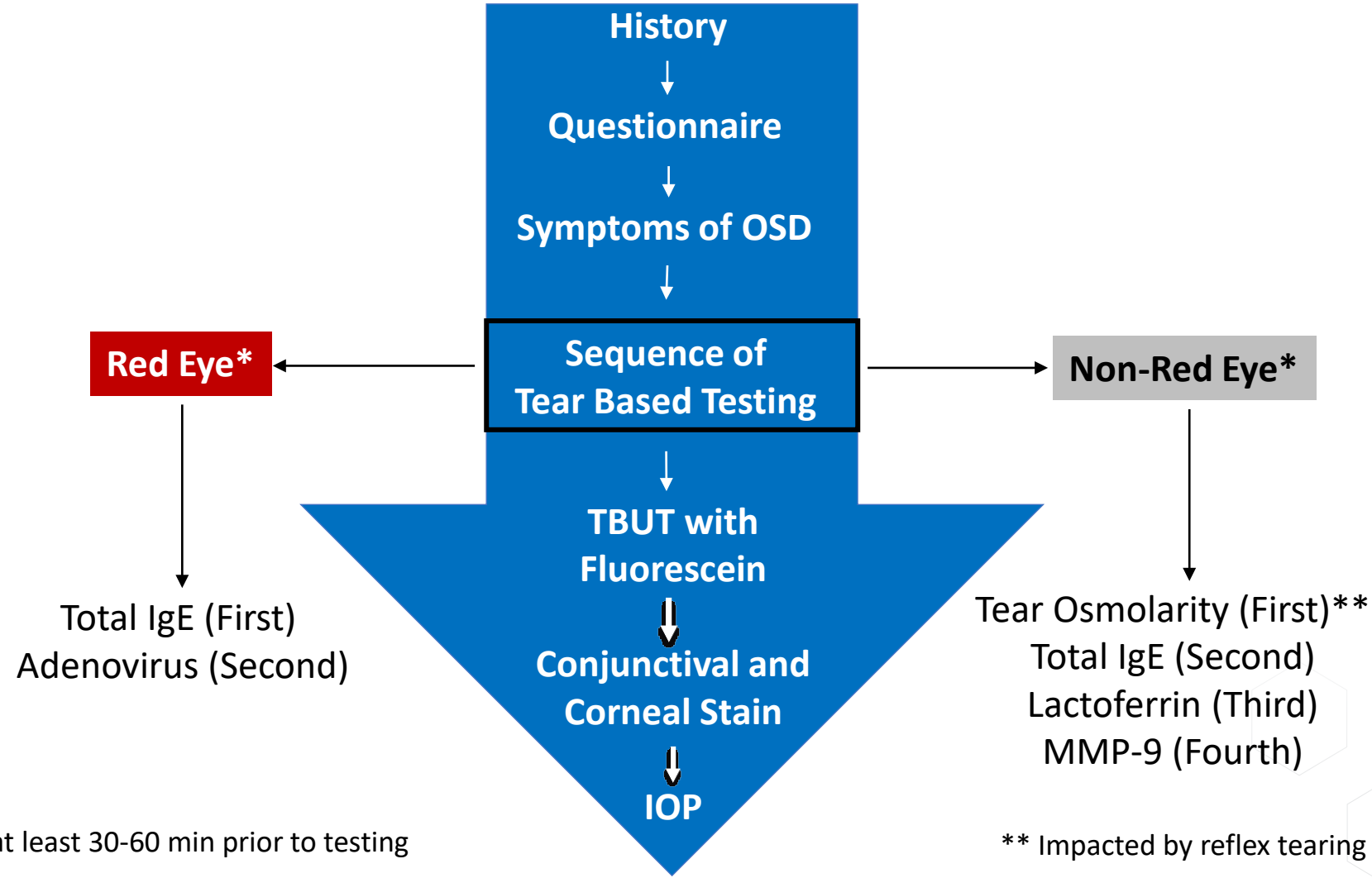
Lin H, Yiu SC. Dry eye disease: A review of diagnostic approaches and treatments. Saudi J Ophthalmol. 2014 Jul;28(3):173-81.

Ocular Surface Disease Advanced Tear Testing

Device Characteristic	T-POC IgE	T-POC LACTOFERRIN	InflammaDry (MMP-9)	TearLab (Osmolarity)
Sensitivity (Positive Agreement)	93%	78-83%	81-85%	64-73%
Specificity (Negative Agreement)	96%	79%-95%	94-98%	71-92%
Requires testing before receiving ocular drops	Yes	Yes	Yes	Yes
Requires implementation of a practice protocol	Yes	Yes	Yes	Yes
Biomarker/analyte detected	**Total IgE Increased**	**Lactoferrin reduced**	**MMP-9 Increased**	**Tear Osmolarity Increased**
Helps differentiate aqueous from evaporative DED	**Yes (Indirect)**	**Yes (Direct)**	No	No
Directly confirms the presence of inflammation	**Yes (Indirect)**	No	**Yes**	No
Guides therapeutic management	Yes	Yes	Yes	**No**
Affected by reflex tearing	No	No	No	**Yes**
Variability in testing	No	No	No	**Yes**
Results	**Quantitative**	**Quantitative**	**Qualitative (yes/no)**	**Quantitative**
Dedicated reimbursement code	Yes	Yes	Yes	Yes

1] InflammaDry positive agreement and negative agreement was compared to clinical truth in RPS clinical study: protocol #12-0615. [2] Sambursky R, Davitt WF 3rd, Latkany R, et al. Sensitivity and specificity of a point-of-care matrix metalloproteinase 9 immunoassay for diagnosing inflammation related to dry eye. JAMA Ophthalmol. 2013 Jan;131(1):24-8. [3] FDA Section 510(k) number k083184 for TearLab™ Osmolarity System; May 5, 2009. [4] Lemp MA,Bron AJ, Baudouin C, et al. Tear osmolarity in the diagnosis and management of dry eye disease. Am J Ophthalmol. 2011 May;151(5):792-798. 5] Foulks, G. N., Baratz, K., & Ferrone, P. (1994). Rapid measurement of selected tear proteins in health and disease using the touch tear microassay system. Advances in experimental medicine and biology, 350, 371-3756] Nomura K, Takamura E. Tear IgE concentrations in allergic conjunctivitis. Eye (Lond) 1998; 12:296 – 298. 7] Thomas Chester, Sumit (Sam) Garg, Josh Johnston, Brandon Ayers & Preeya Gupta (2023) How Can We Best Diagnose Severity Levels of Dry Eye Disease: Current Perspectives, Clinical Ophthalmology, 17:, 1587-1604, DOI: 10.2147/OPTH.S388289

Potential POC Testing Workflow



* No drops at least 30-60 min prior to testing

** Impacted by reflex tearing

T-POC TOTAL IgE TESTING
Is There An Allergic Component?

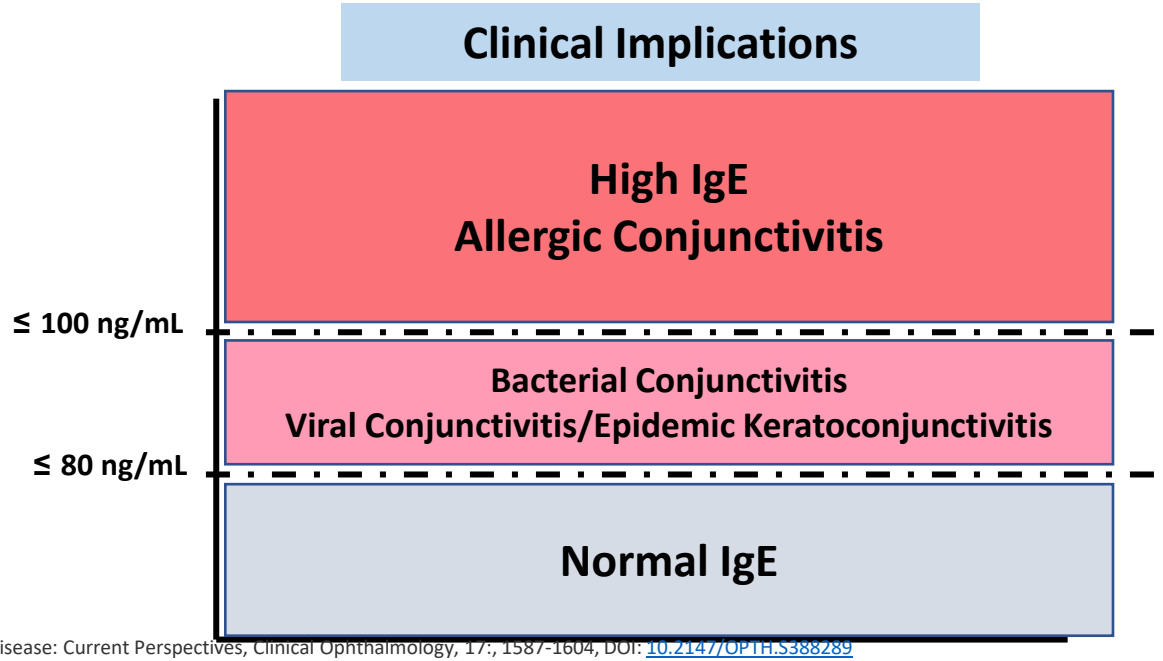
Benefits of testing IgE levels in the tear film:

- Presence of IgE indicates the diagnosis of allergic conjunctivitis (seasonal, perennial, atopic, and vernal)
- Levels of IgE increase with severity
- IgE testing can help differentiate allergic conjunctivitis from dry eye and viral conjunctivitis
- Elevated IgE causes tear film instability
- Changes in IgE levels may show the efficacy of prescribed treatment

If IgE value is < 80 ng/mL (33 kIU), there is a 95.7% probability that the patient does not have an ocular allergy

If IgE value is ≥ 80 ng/mL, there is a 92.9% probability that this elevated IgE is indicative of an ocular allergy

Sensitivity: 93%
Specificity: 96%
Dynamic range: 20 ng/mL - 2,000 ng/mL
Coefficient of variation: < 9%



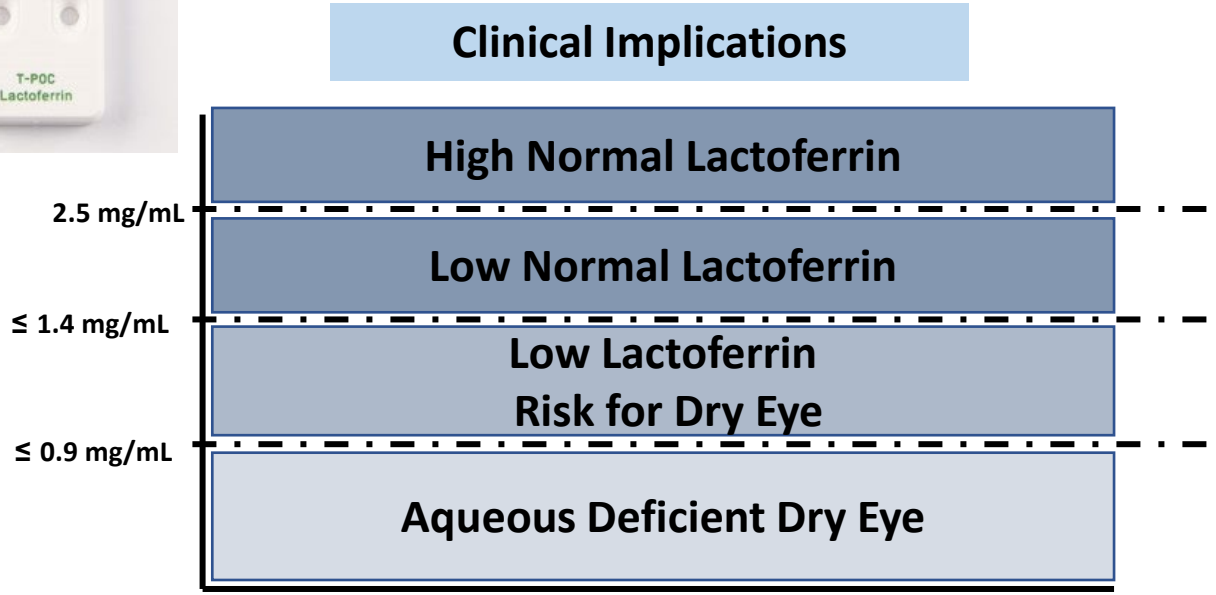
Thomas Chester, Sumit (Sam) Garg, Josh Johnston, Brandon Ayers & Preeya Gupta (2023) How Can We Best Diagnose Severity Levels of Dry Eye Disease: Current Perspectives, Clinical Ophthalmology, 17:, 1587-1604, DOI: 10.2147/OPTH.S388289
. Nomura K, Takamura E. Tear IgE concentrations in allergic conjunctivitis. Eye (Lond). 1998;12 (Pt 2):296-8.

T-POC LACTOFERRIN TESTING
Is it Aqueous Deficient or Evaporative Disease?

Benefits of testing Lactoferrin levels in the tear film:

- Low Lactoferrin levels less than 1.4 mg/mL) directly correlate to DED caused by aqueous deficiency
- Severity of DED can be determined by the Lactoferrin level
- Lactoferrin ≤ 0.9 mg/mL has 72% sensitivity and 95% specificity for Sjogren's Disease for further testing
- Low Lactoferrin levels indicate DED with increased surgical risk
- Low Lactoferrin levels may indicate the cause of contact lens intolerance
- Changes in Lactoferrin levels may show the efficacy of the prescribed treatment
- Lactoferrin levels are normal, and not reduced, in the setting of meibomitis-related rosacea

Sensitivity: 83%
Specificity: 99%
Dynamic range: 0.4 mg/mL – 2.5 mg/mL
Coefficient of variation: < 9%



Thomas Chester, Sumit (Sam) Garg, Josh Johnston, Brandon Ayers & Preeya Gupta (2023) How Can We Best Diagnose Severity Levels of Dry Eye Disease: Current Perspectives, Clinical Ophthalmology, 17:, 1587-1604, DOI: 10.2147/OPTH.S388289
McCollum CJ, Foulks GN, Bodner B, Shepard J, Daniels K, Gross V, Kelly L, Cavanagh HD. Rapid assay of lactoferrin in keratoconjunctivitis sicca. Cornea. 1994 Nov;13(6):505-8

T-POC TESTING GUIDES THERAPEUTIC DECISIONS

Positive SPEED Test/OSDI

IgE < 80 ng/ml

Lactoferrin < 1.4 mg/ml

AQUEOUS DEFICIENT DRY EYE

Low Inflammation
MMP-9 < 40 ng/ml OR
Lactoferrin ≥ 1.0 mg/ml

- PF tears
- Punctal occlusion

High Inflammation
MMP-9 ≥ 40 ng/ml OR
Lactoferrin ≤ 0.9 mg/ml

- PF tears
- Immunomodulator
  - Cyclosporine
  - Lifitegrast

IgE ≥ 80 ng/ml

Lactoferrin < 1.4 mg/ml

ALLERGY & AQUEOUS DEFICIENT DRY EYE

Low Inflammation
MMP-9 < 40 ng/ml OR
Lactoferrin ≥ 1.0 mg/ml

- Mast cell stabilizer
- Antihistamine
- PF tears
- Punctal occlusion

High Inflammation
MMP-9 ≥ 40 ng/ml OR
Lactoferrin ≤ 0.9 mg/ml

- Mast cell stabilizer
- Antihistamine
- PF Tears
- Steroids
- Immunomodulator

Amniotic membrane grafts, serum tears, and scleral lenses for treatment failures

Thomas Chester, Sumit (Sam) Garg, Josh Johnston, Brandon Ayers & Preeya Gupta (2023) How Can We Best Diagnose Severity Levels of Dry Eye Disease: Current Perspectives, Clinical Ophthalmology, 17:, 1587-1604, DOI: 10.2147/OPTH.S388289

T-POC TESTING GUIDES THERAPEUTIC DECISIONS

Positive SPEED Test/OSDI

IgE < 80 ng/ml

Lactoferrin > 1.4 mg/ml

EVAPORATIVE DRY EYE

Low inflammation
MMP-9 < 40 ng/ml

- PF tears
- Omega 3 FAs
- Warm Compress
- Thermal therapy
- Intense light therapy

High inflammation
MMP-9 ≥ 40 ng/ml

- Warm compress
- Immunomodulator
  - Cyclosporine
  - Lifitegrast
- Omega 3 FAs
- Thermal therapy
- Intense light therapy

IgE ≥ 80 ng/ml

Lactoferrin > 1.4 mg/ml

ALLERGY & EVAPORATIVE DRY EYE

Low inflammation
MMP-9 < 40 ng/ml

- Mast cell stabilizer
- Antihistamine
- Warm compress
- Thermal therapy
- Intense light therapy

High inflammation
MMP-9 ≥ 40 ng/ml

- Mast cell stabilizer
- Antihistamine
- Warm compress
- Steroid
- Immunomodulator
- Thermal therapy
- Intense light therapy

Amniotic membrane grafts, serum tears, and scleral lenses for treatment failures

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RED EYE PROTOCOL

IDENTIFICATION & EVALUATION
History, symptoms, and signs

↓

POC differential diagnostic testing
Total IgE & Adenoviral Testing

↓

READ & INTERPRET test results

POSITIVE Adenoviral Test
Negative IgE (IgE < 80 ng)

↓

MANAGEMENT PLAN

- Education: hygiene and hand washing
- Supportive care: artificial tears, cool compresses, and antihistamines
- No antibiotics
- No work, school, or daycare for 5-7 days
- No contact lens use while symptomatic
- Consider antiviral medication

↓

DECONTAMINATE
the exam room

NEGATIVE Adenoviral Test

IgE < 80 ng/ml
Significant discharge/eyelash matting or crusting

↓

MANAGEMENT PLAN

- Consider topical antibiotics
- Return to school or work in 24 hours

↓

Positive IgE ≥ 80 ng/ml

↓

MANAGEMENT PLAN

- Consider topical antihistamines

→

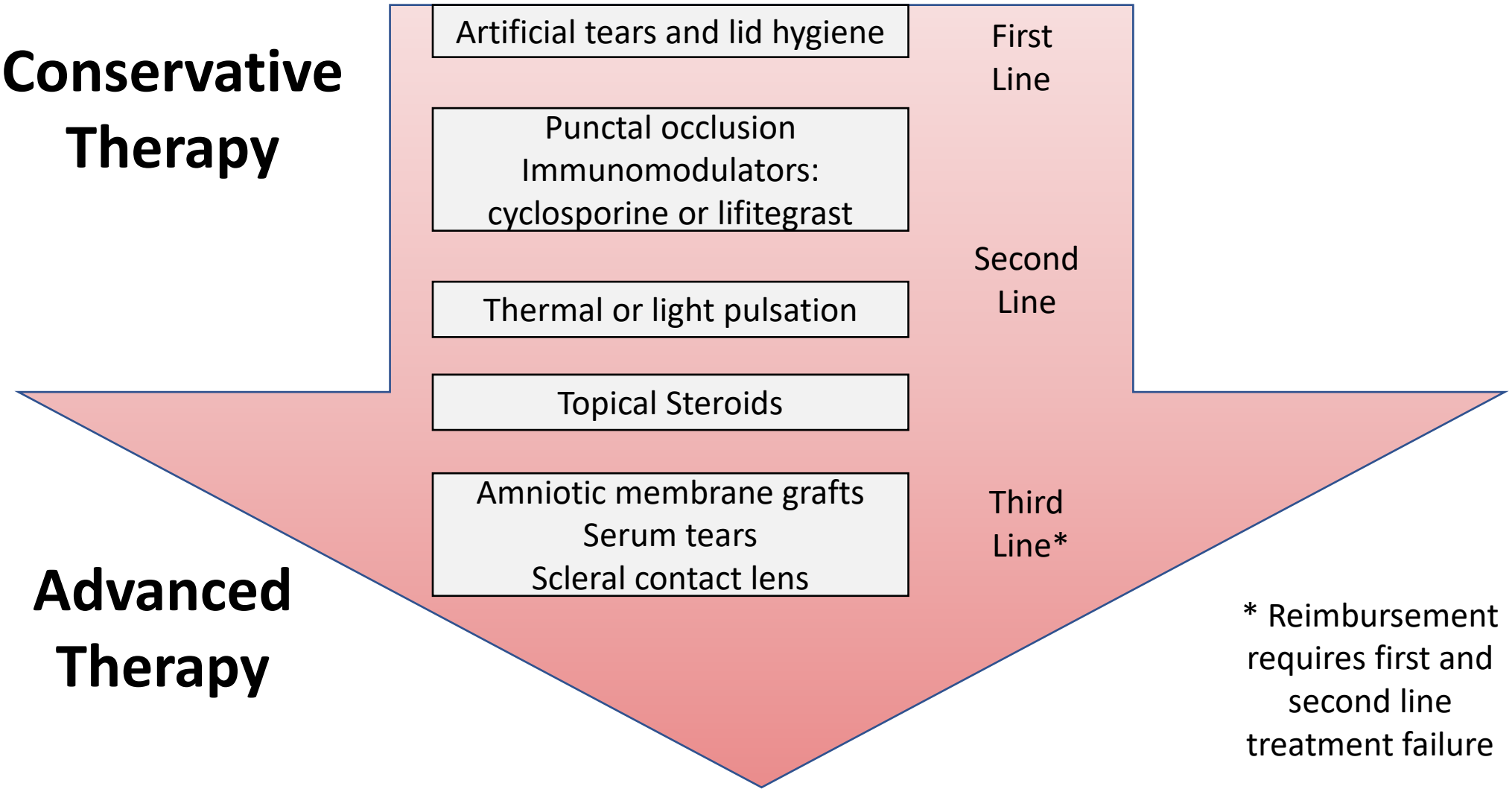
IgE Specific Allergy Panel Testing

Sublingual Desensitization Therapy

↓

REFER to eye care professional for vision loss or no improvement in 7 days

Ocular Surface Disease Treatment Plan



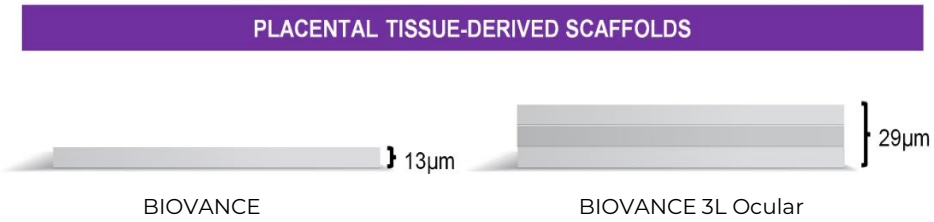
* Reimbursement requires first and second line treatment failure

CORNEAL DEFECTS

- Corneal epithelial defects are focal areas of epithelial loss most frequently caused by mechanical trauma, corneal dryness, neurotrophic keratitis, post-surgical changes, or infection (ref 10)
- Amniotic membrane graft applications as a cover or barrier may include, but are not limited to, corneal and conjunctival related injuries or defects such as corneal epithelial defects, pterygium repair, fornix reconstruction and other procedures
- Common diagnoses resulting in or associated with corneal defects include:

BIOVANCE 3L OCULAR

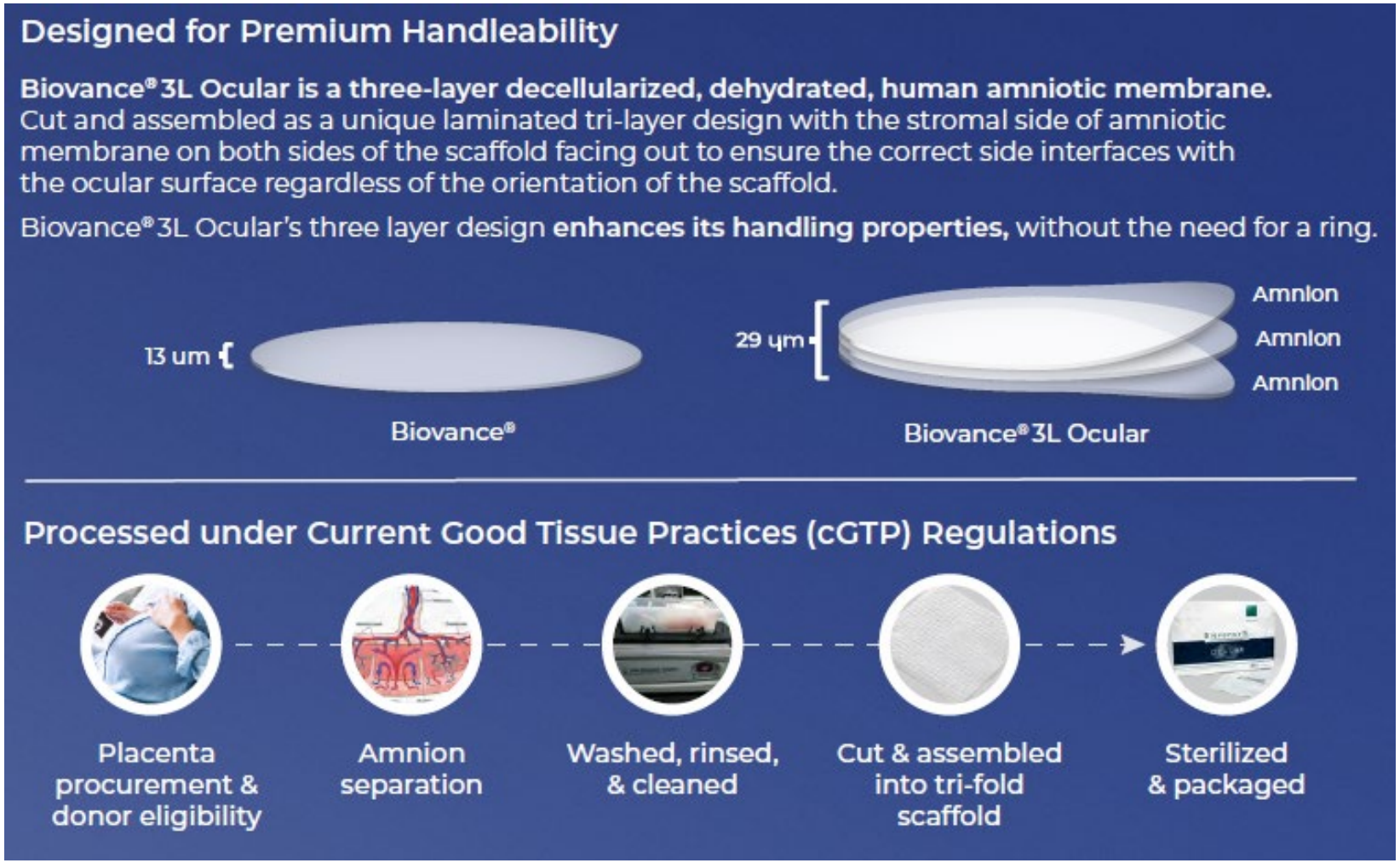
- Request for Designation (RFD) as a 361 biological product granted
- Unique 3-layer amnion basement membrane construction
- Decellularized Dehydrated Human Amniotic Membrane (DDHAM)
- Designed for superior handling while optimizing a ringless design
- ***Cell attachment is a natural stimulus for the orderly release of growth factors and cytokines***[1]
- A benchtop study showed*[2,3]
  - Cell viability
  - Cell adhesion
  - Cell proliferation



***An in vitro test was conducted to measure viability, adhesion, and proliferation of human corneal and conjunctival epithelial cells at days 1, 4, and 7**

1. Bhatia M, Pereira M, Rana H, Stout B, Lewis C, Abramson S. The mechanism of cell interaction and response on decellularized human amniotic membrane: Implications in wound healing. 2007;19(8):207-217. 2. Diaz V. et al; ARVO 2022 Poster; A Comparison Study of the Effects of Ocular Scaffolds on Human Ocular Epithelial Cells. 3. Mao Y, Protzman NM, John N, et al. An in vitro comparison of human corneal epithelial cell activity and inflammatory response on differently designed ocular amniotic membranes and a clinical case study. J Biomed Mater Res. 2022;1-17. doi:10.1002/jbm.b.35186

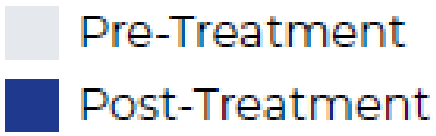
PROCESSED UNDER cGTP REGULATIONS & DESIGNED FOR PREMIUM HANDLEABILITY

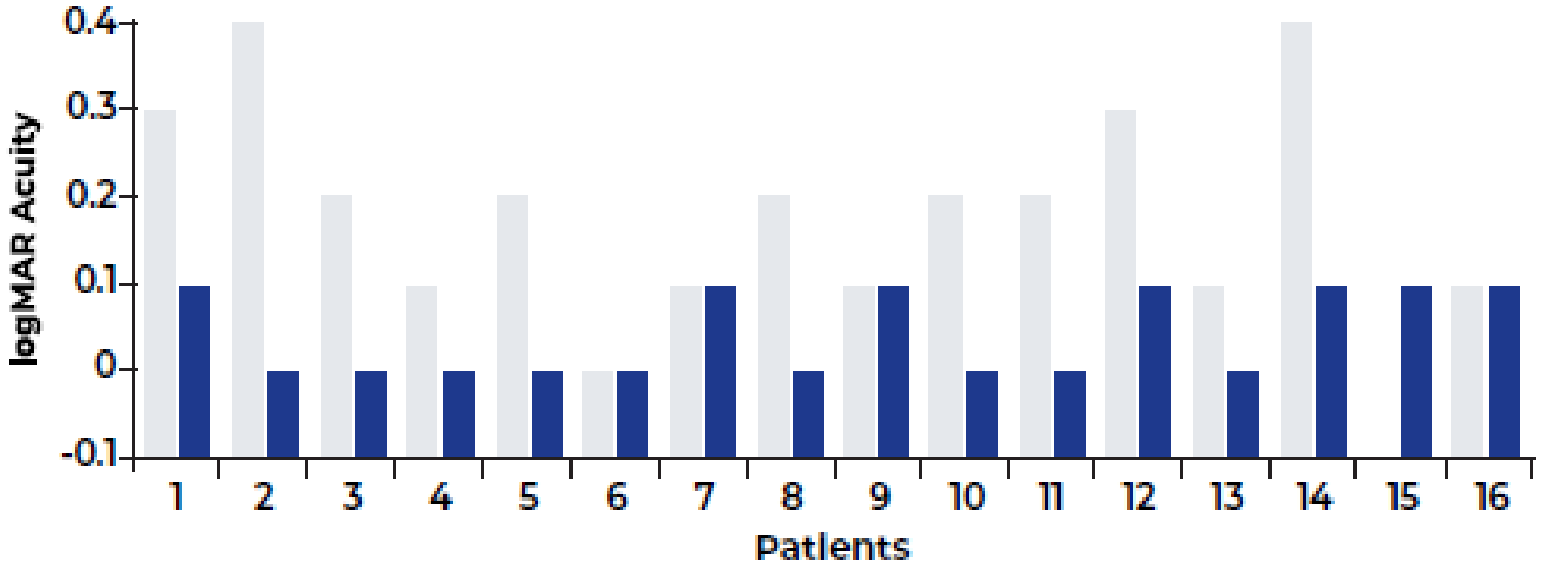


REDIRECT THE CURRENT TO IMPROVED BCVA

Post procedure BCVA improved in all patients with an initial BCVA less than 20/25.[14]

BCVA: Best Corrected Visual Acuity





Chima H. Cianciolo M. Pilot Evaluation of Biovance® 3-Layer Amniotic Membrane Graft for Ocular Surface Disease. American Optometric Association Meeting 2023.

Comparative Benchtop Study Findings:

Biovance® 3L (DDHAM) / Ambio2® (DHAM) / AmnioGraft® (CHAM)

An in vitro test was conducted to measure viability, adhesion, and proliferation of human corneal and conjunctival epithelial cells at days 1, 4, and 7

DDHAM (Biovance 3L Ocular) = Decelluarized, Dehydrated human amniotic membrane
ChAM (AmnioGraft) = Cryopreserved human amniotic membrane
DhAM (Ambio2) = Dehydrated human amniotic membrane

Ocular epithelial **cell viability** significantly greater than ChAM and DhAM ($p<0.001$)

Ocular epithelial **cell adhesion** significantly greater as compared to ChAM ($p<0.001$) and DhAM ($p<0.011$)

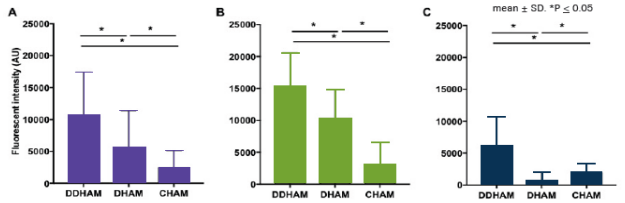
Ocular epithelial **cell proliferation** rate significantly greater than ChAM ($p<0.001$)

Corneal and Conjunctival Cells

Corneal Cells

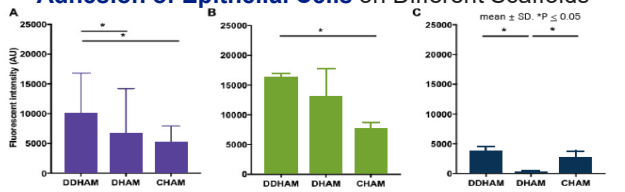
Conjunctival Cells

Epithelial Cell Viability by Cell Type and Scaffold



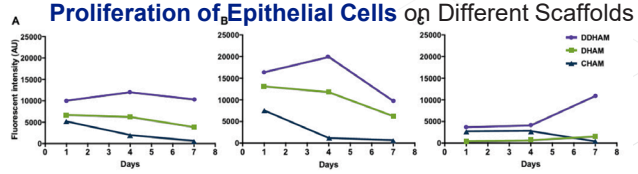
Human corneal epithelial cells and human conjunctival epithelial cells (A), human corneal epithelial cells (B), and human conjunctival epithelial cells (C). The viability of adhered cells was detected using the alamarBlue assay.

Adhesion of Epithelial Cells on Different Scaffolds



Human corneal epithelial cells and human conjunctival epithelial cells were seeded onto scaffolds and incubated for 24H. Adhesion of human corneal epithelial cells and Human conjunctival epithelial cells (A), Human corneal epithelial cells (B), and Human conjunctival epithelial cells (C).

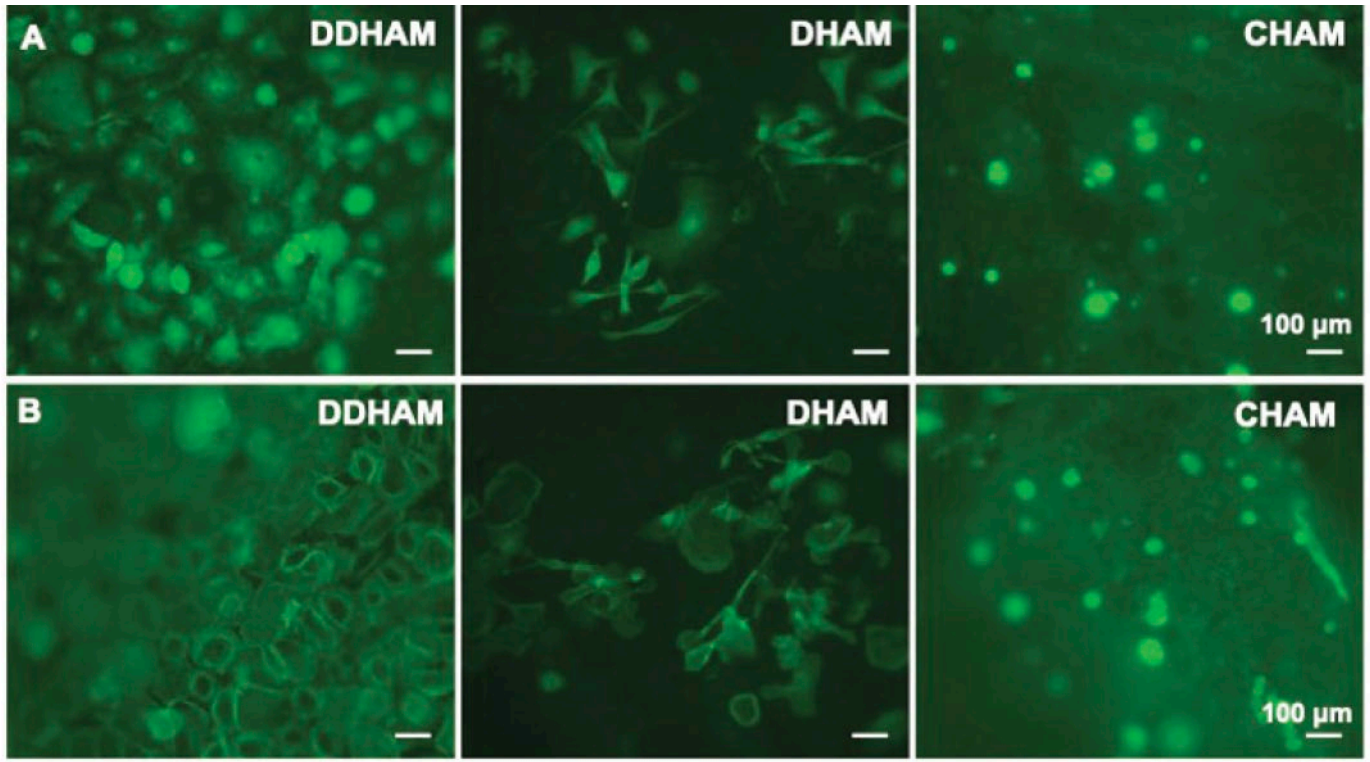
Proliferation of Epithelial Cells on Different Scaffolds



Proliferation of human corneal epithelial cells and human conjunctival epithelial cells (A), human corneal epithelial cells (B), and human conjunctival epithelial cells (C)

1. Diaz V. et al; ARVO 2022 Poster; A Comparison Study of the Effects of Ocular Scaffolds on Human Ocular Epithelial Cells; 2. Rutgers Benchtop Data Report: Biovance 3L Ocular;

BENCHTOP STUDY FINDINGS:
BIOVANCE 3L OCULAR WITH CALCIEN AM STAINING AT DAY 4



Human corneal epithelial cells were seeded on the different scaffolds, cultured, and stained with Calcein AM to visualize viable cells at Day 4 (A).

The morphology of Human corneal epithelial cells on scaffolds was monitored by actin staining on Day 4 (B).

DDHAM (Biovance 3L Ocular) = Decelluarized, Dehydrated human amniotic membrane
ChAM (AmnioGraft) = Cryopreserved human amniotic membrane
DhAM (Ambio2) = Dehydrated human amniotic membrane

Ocular epithelial **cell viability significantly greater than ChAM and DhAM**

1. Diaz V. et al; ARVO 2022 Poster; A Comparison Study of the Effects of Ocular Scaffolds on Human Ocular Epithelial Cells; 2. Mao Y, Protzman NM, John N, et al. An in vitro comparison of human corneal epithelial cell activity and inflammatory response on differently designed ocular amniotic membranes and a clinical case study. J Biomed Mater Res. 2022;1-17. doi:10.1002/jbm.b.35186

BANDAGE CONTACT LENS CONSIDERATIONS

CLINICAL APPLICATION PROCESS

Required materials

Anesthetic drops, sterile gloves, Weck-Cel tip applicator, antibiotic drops, sterile toothless forceps, eyelid speculum (optional)

Clinical application process

- Place unopened tissue, contact lens case, toothless forceps, Weck-Cel or cotton tip applicator and other materials needed on workspace. Keep Biovance 3L Ocular covered until ready for placement.
- If using an eye lid speculum, place it now.
- Instill one drop of topical anesthetic to eye, followed by one non-viscous topical antibiotic drop.
- Use Weck-Cel sponge to dry corneal surface.
- Carefully open pouch.
- Use smooth tip forceps and remove Biovance 3L Ocular from pouch (grooved forceps can damage the product).
- Place graft centrally on to the cornea using toothless forceps and use a damp Weck-Cel to smooth Biovance 3L Ocular to corneal surface.
- Place a drop of antibiotic or preservative-free tears on to the Biovance 3L Ocular graft to hydrate.
- Remove bandage contact lens (BCL) from case and place over the graft*.
- Place a drop of antibiotic or preservative-free tears on to the bandage contact lens.
- Instruct patient to keep eyes closed for 2-3 minutes without rubbing eyes.
- Instruct patient to continue with antibiotic and lubrication eye drops, as directed. Plan to see patient in 5-7 days; sooner if there is discomfort / redness / swelling.

- Access Clinical Application Process Video at www.versea.com/ophthalmics/resources

BANDAGE CONTACT LENS (BCL) PEARLS

Potential Complication

- All BCLs induce some level of edema, including silicone hydrogels, which have extremely high DK/T values
- Underlying dry eye predisposes to contact lens discomfort
- CLs restrict corneal oxygen availability, creating a hypoxic environment at the anterior corneal surface[1]
    - Cornea edema
    - Anterior chamber reaction
    - Sterile mid-peripheral infiltrates

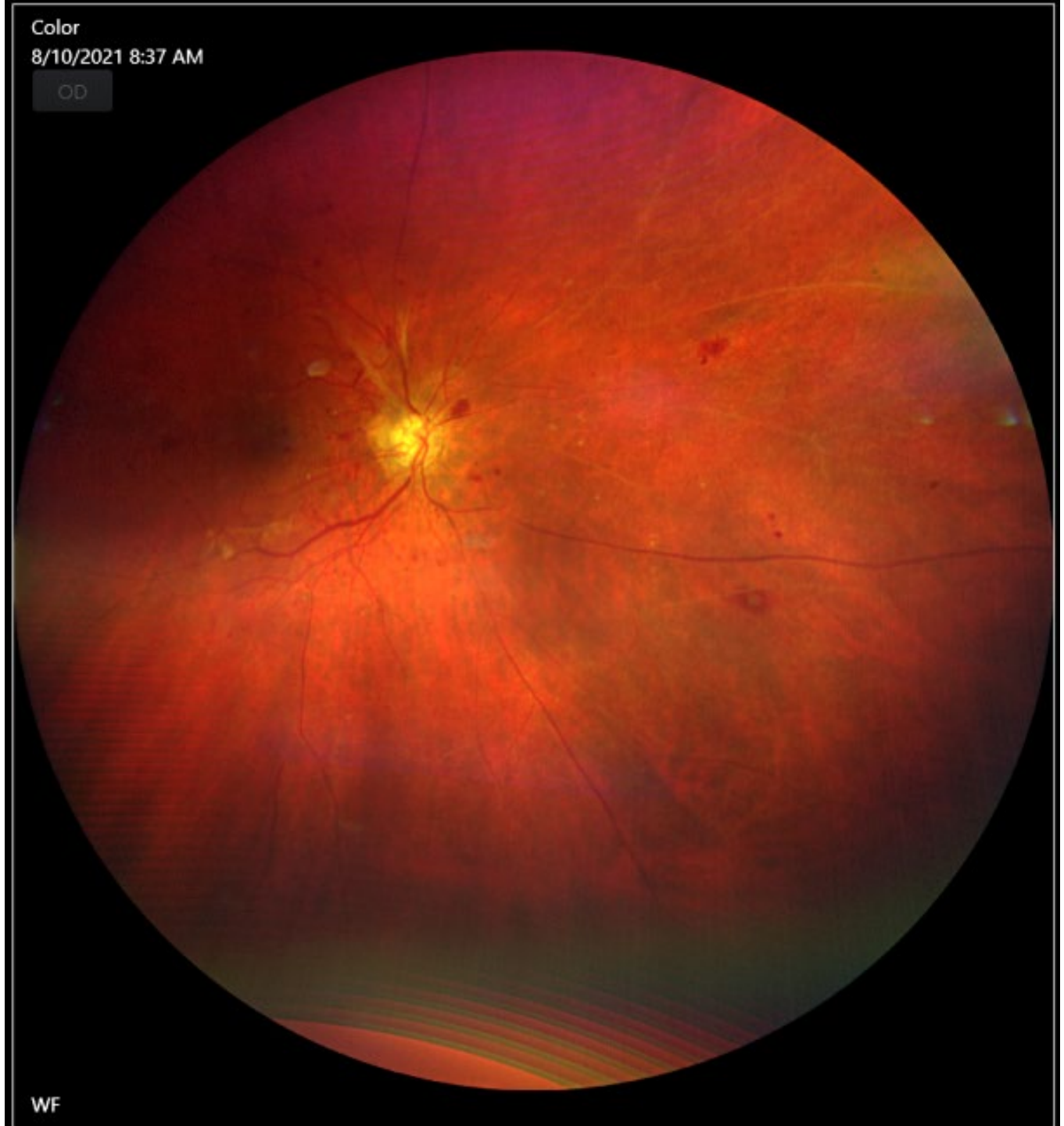
Mitigation Strategy

- Pressure patch in lieu of BCL
- Use keratometry to fit BCL with an AMG flatter than average K value[2]
- Use topical antibiotic/steroid combination or immunomodulator to reduce inflammation produces favorable outcomes in terms of pain management and epithelial healing[3-4]
- Frequent lubrication

1] Nathan Efron, Lyndon Jones, Anthony J. Bron, Erich Knop, Reiko Arita, Stefano Barabino, Alison M. McDermott, Edoardo Villani, Mark D. P. Willcox, Maria Markoulli; The TFOS International Workshop on Contact Lens Discomfort: Report of the Contact Lens Interactions With the Ocular Surface and Adnexa Subcommittee. Invest. Ophthalmol. Vis. Sci. 2013;54(11):TFOS98-TFOS122. 2] Lim L, Lim EWL. Therapeutic Contact Lenses in the Treatment of Corneal and Ocular Surface Diseases-A Review. Asia Pac J Ophthalmol (Phila). 2020 Dec;9(6):524-532. 3] Gicquel JJ, Bejjani RA, Ellies P, Mercie M, Dighiero P. Amniotic membrane transplantation in severe bacterial keratitis. Cornea. 2007;26(1):27–33. 4] Lee SH, Tseng SC. Amniotic membrane transplantation for persistent epithelial defects with ulceration. Am J Ophthalmol. 1997;123(3):303–312

Wide Field Imaging

- **Clarus**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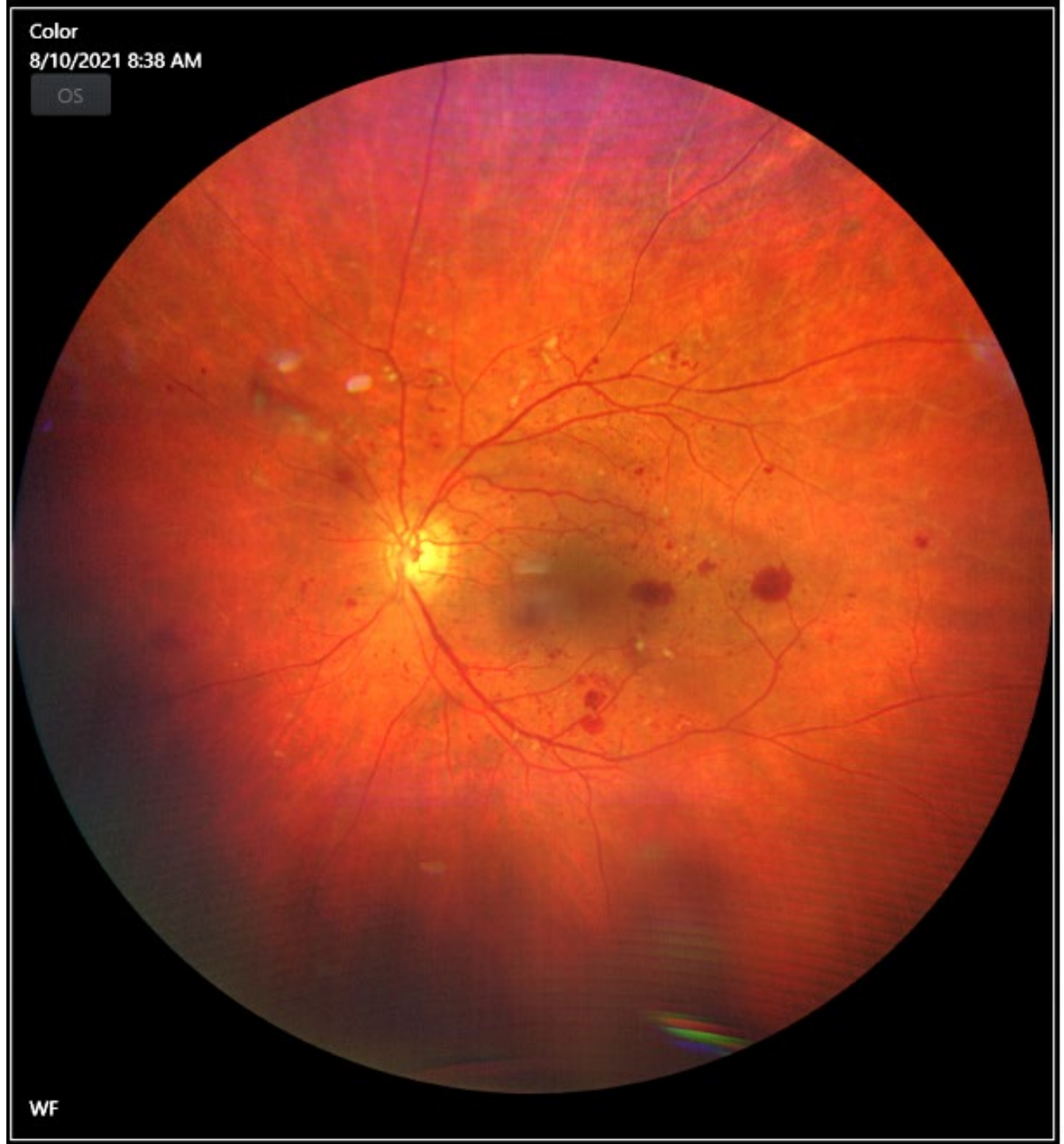
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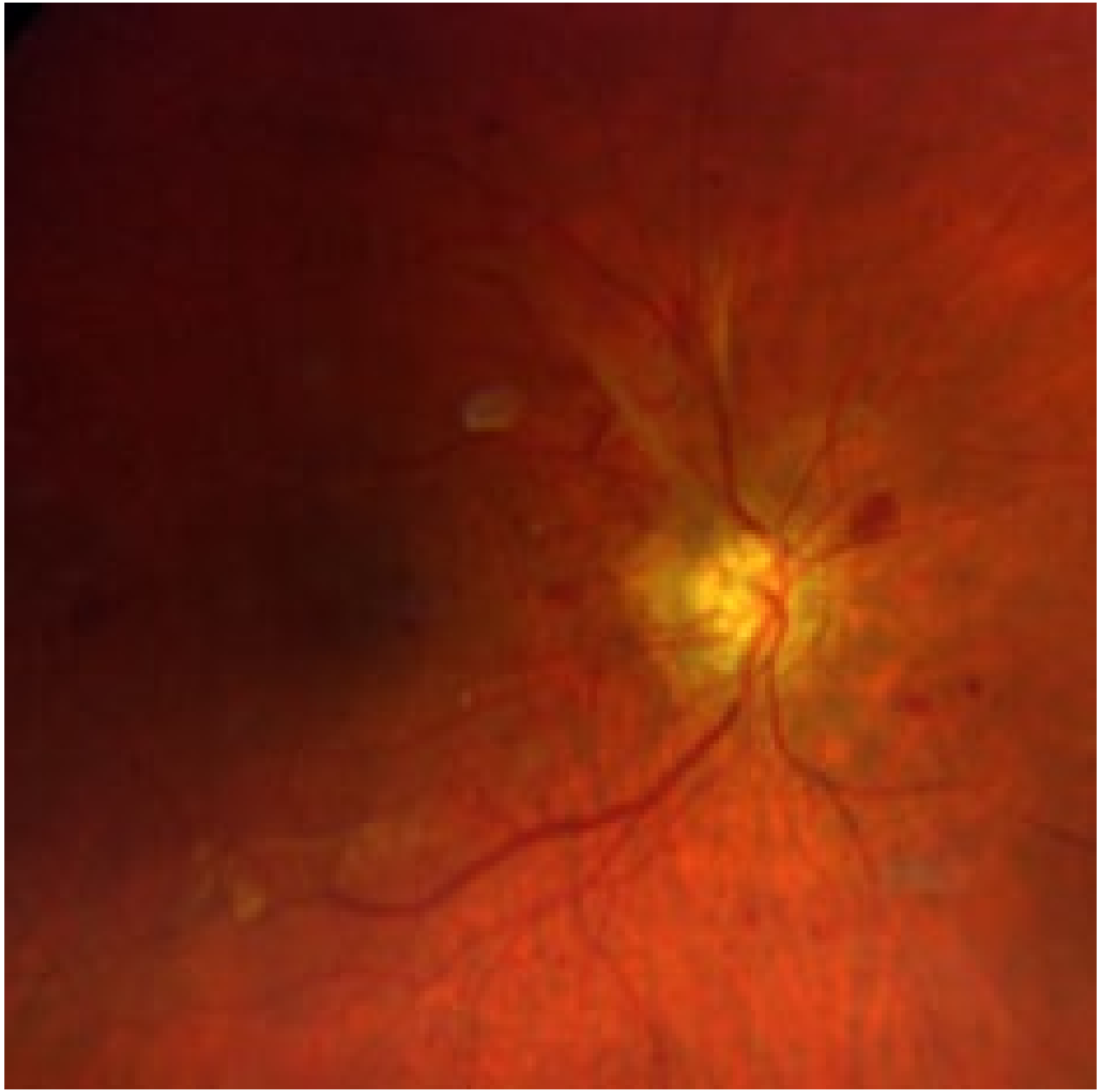

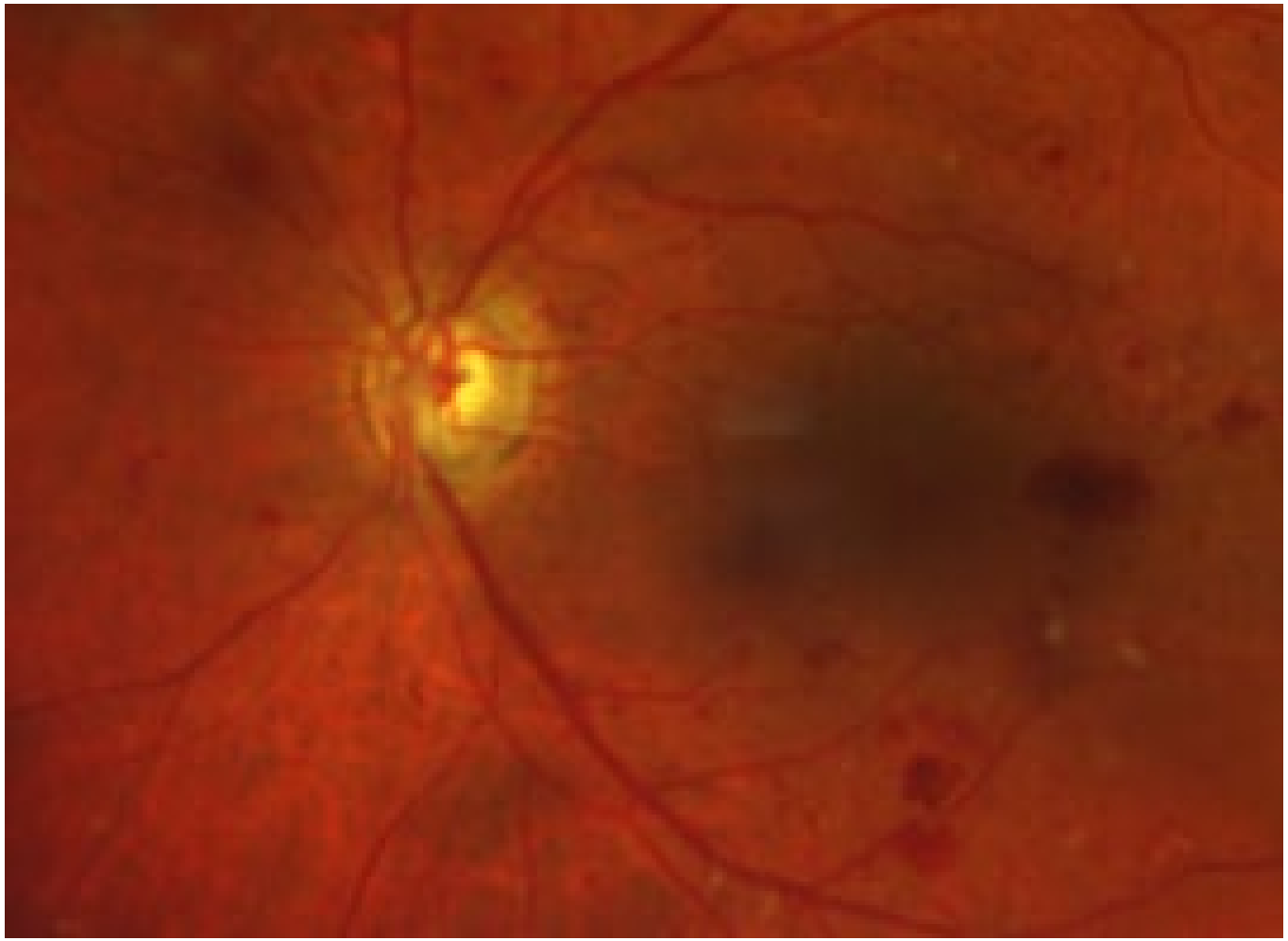

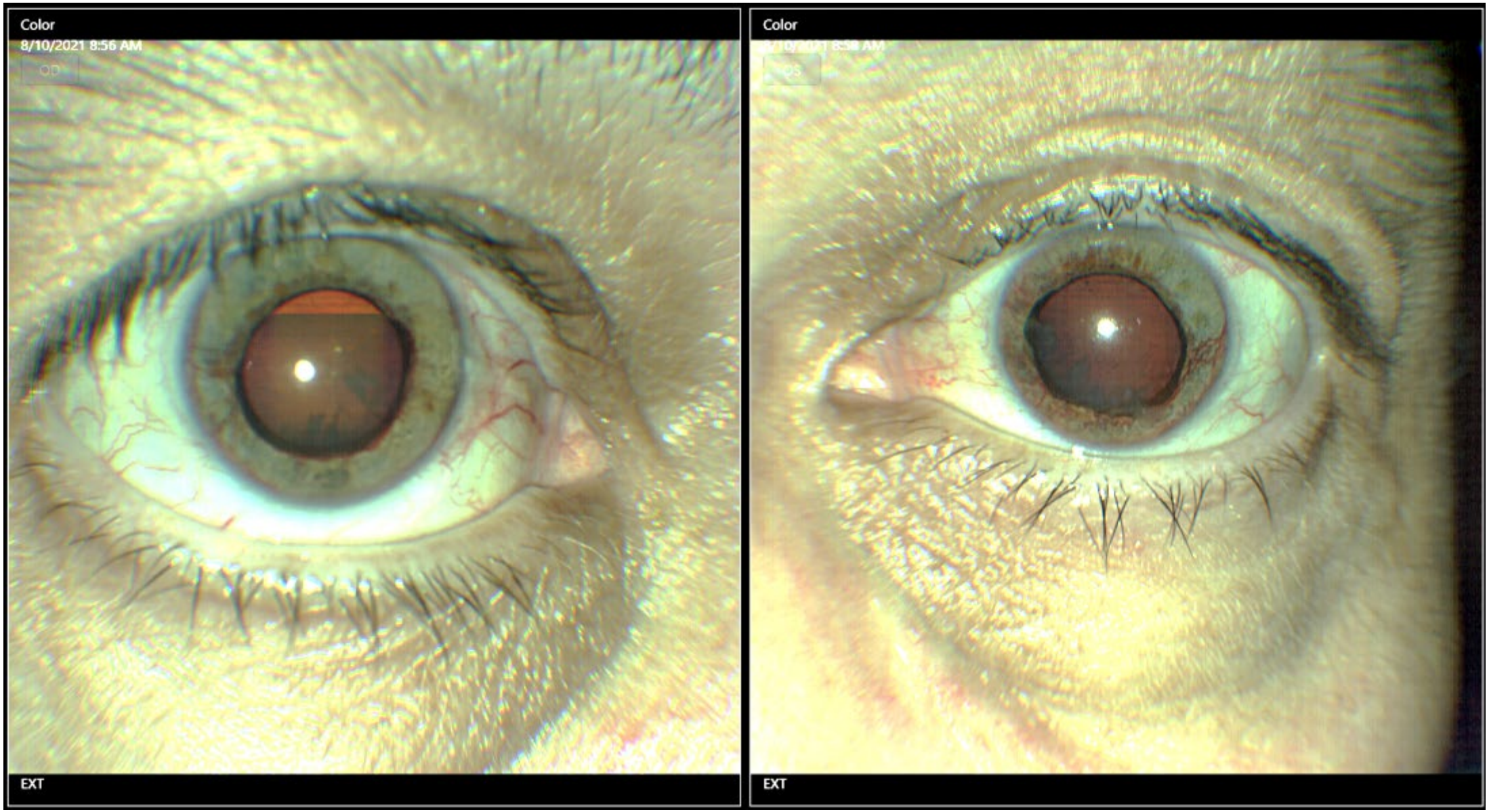
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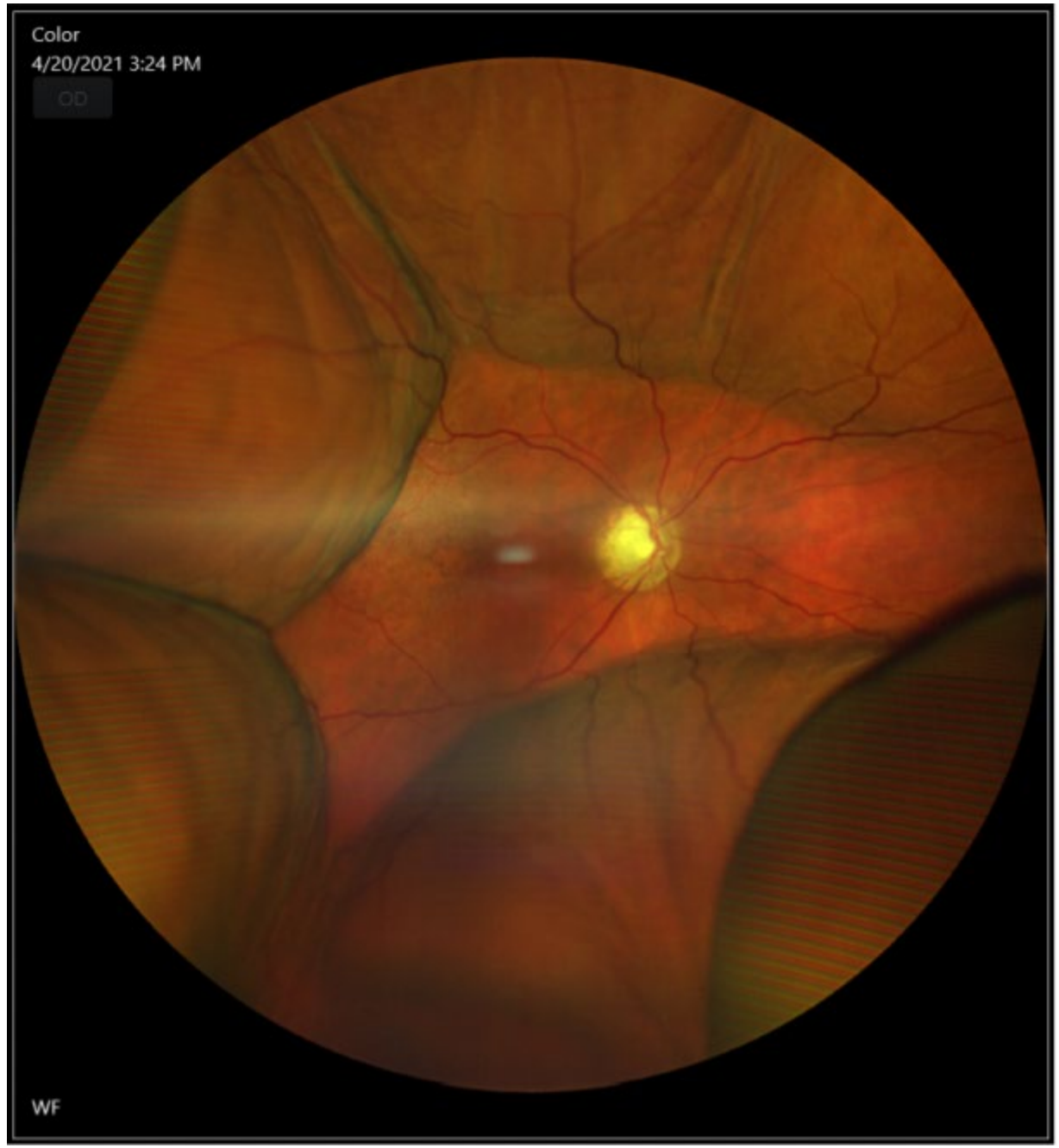
Bonus Case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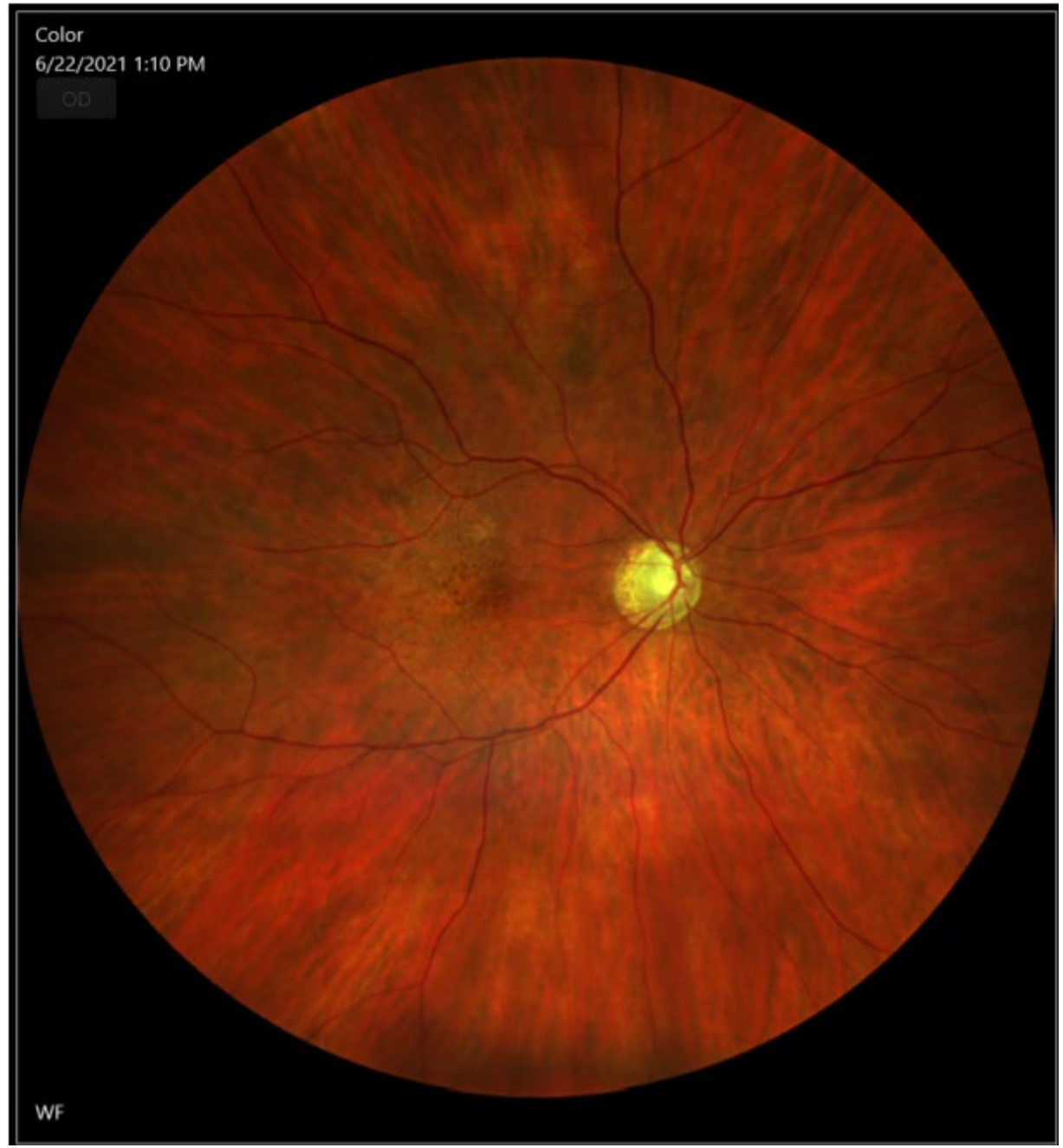
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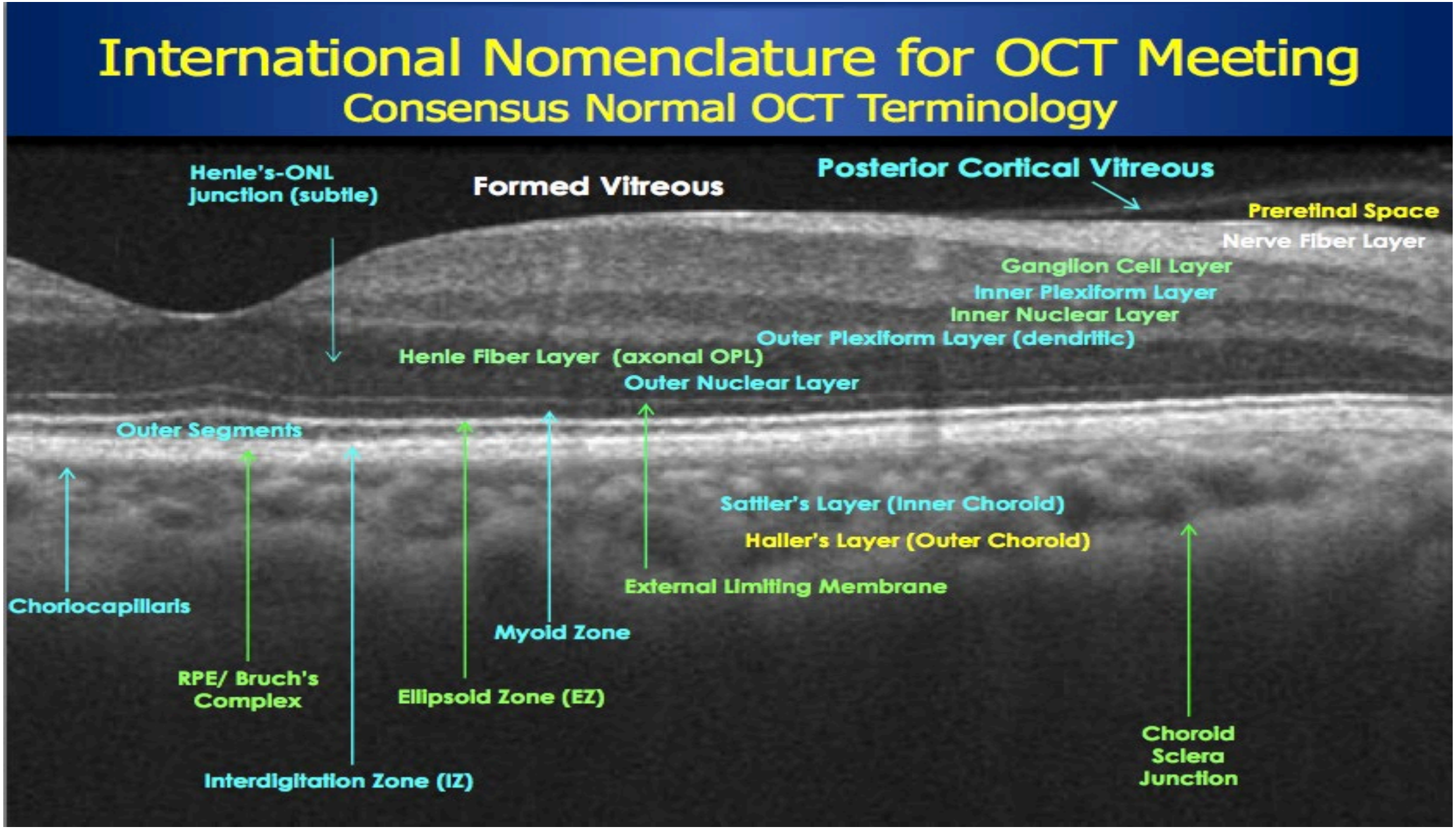
Advances in OCT Technology: Automated Intelligence for the ECP

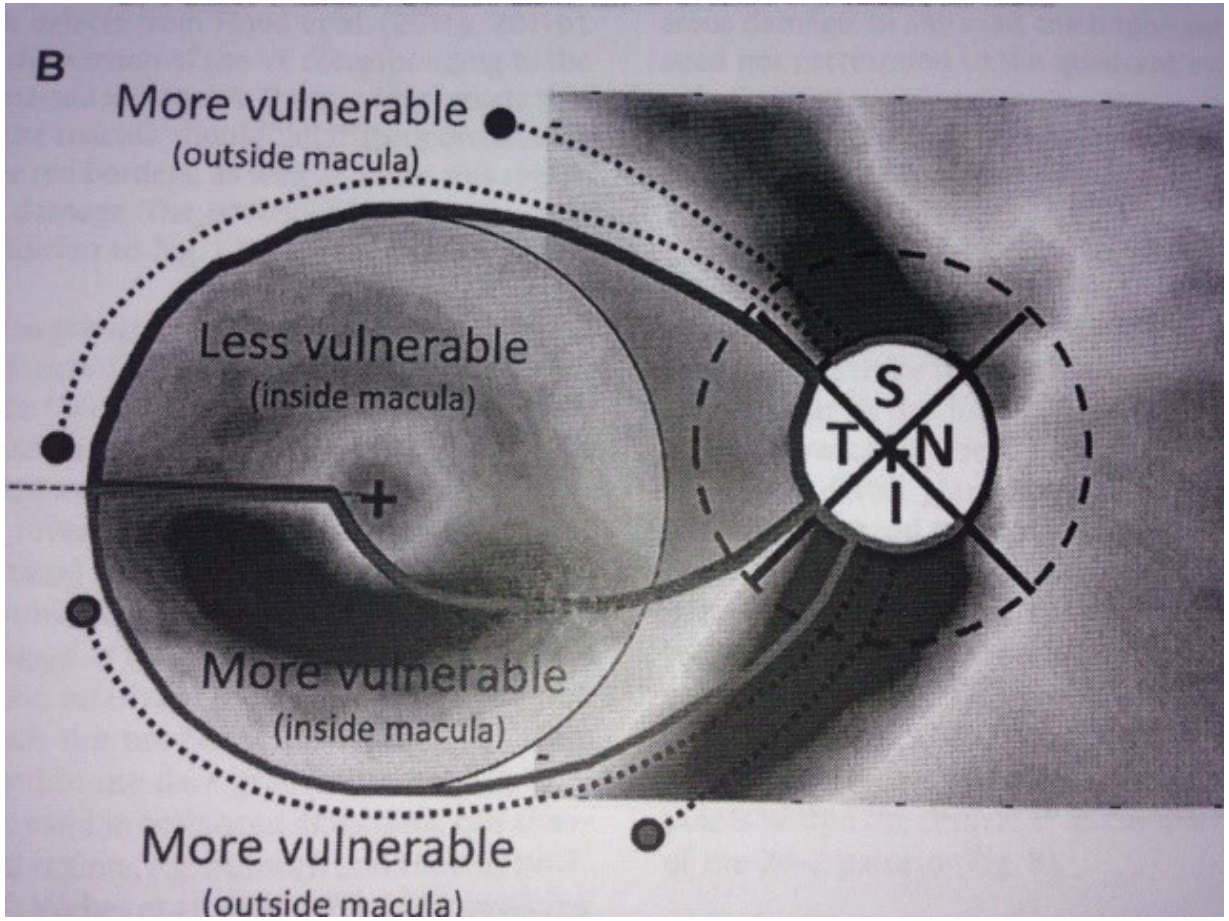
- Ganglion Cell Analysis: A New Horizon in Primary Care
- HD SD/OCT Anterior Segment
- OCT Angiography in Glaucoma

International Nomenclature for OCT Meeting

Consensus Normal OCT Terminology



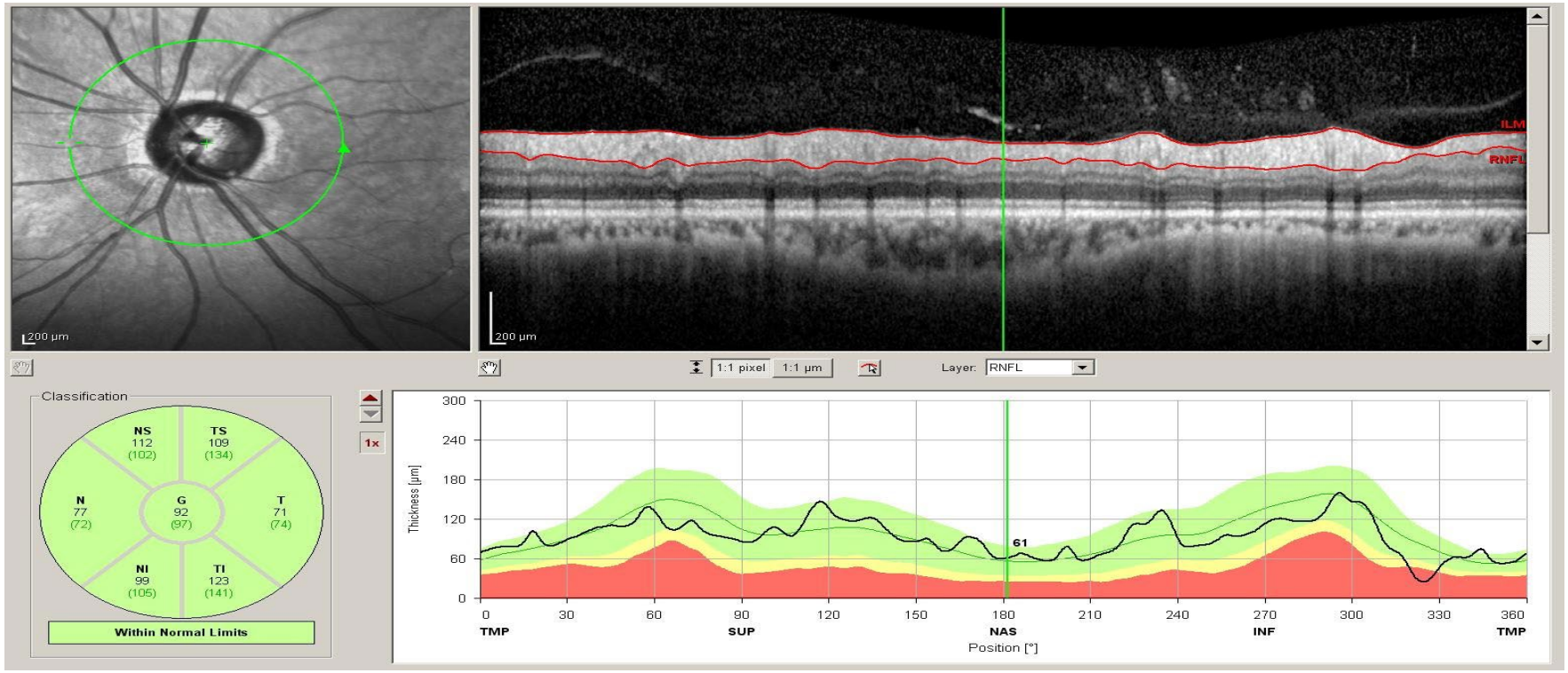
Ganglion Cell Anatomy

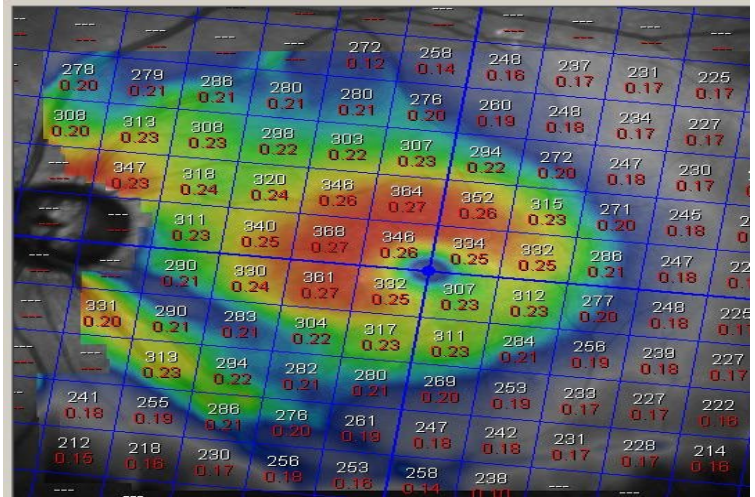


Ganglion Cell Anatomy

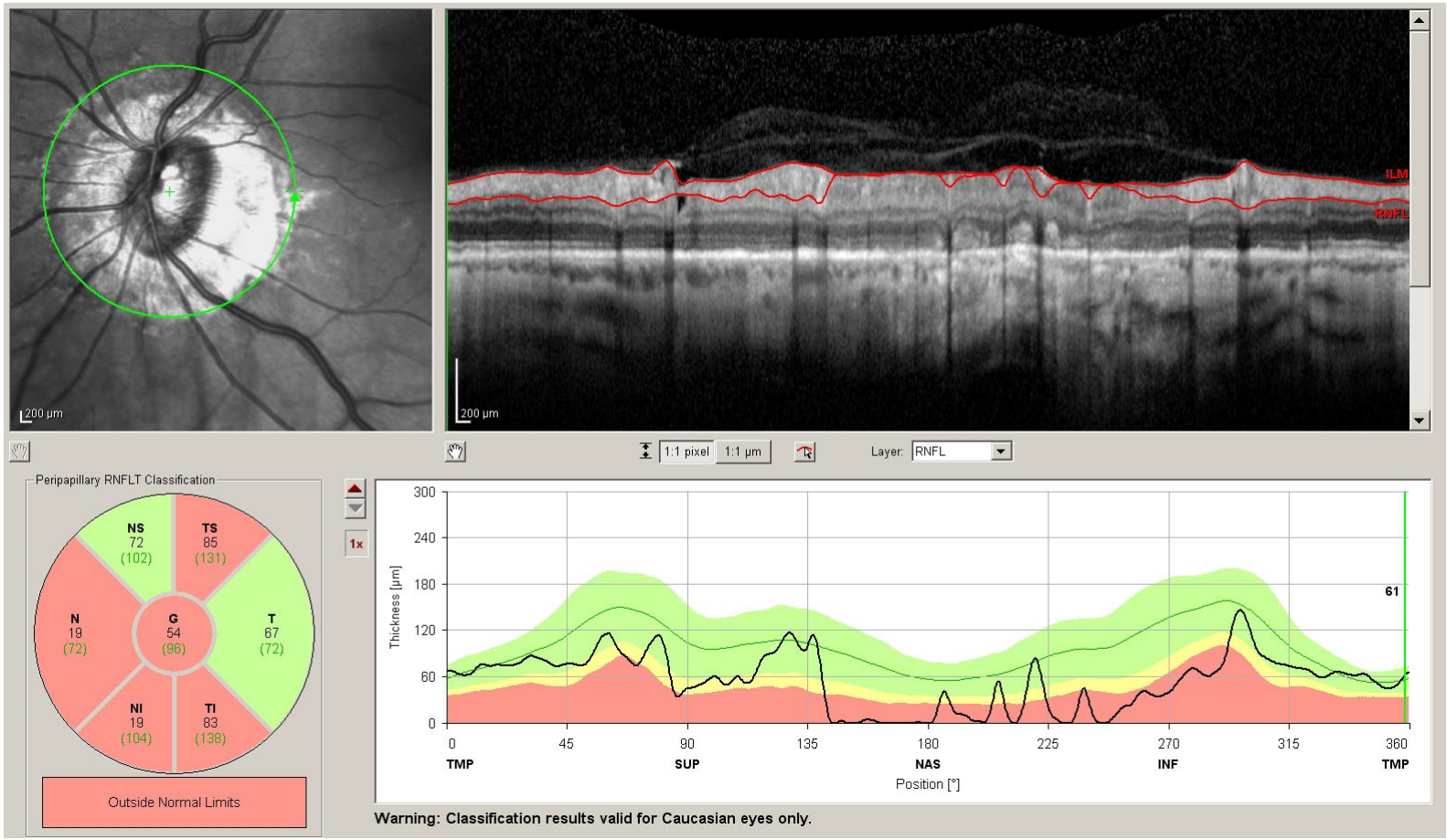
- Analysis of VF in RGC loss in Glaucoma
  - 24-2 protocol has 6 degrees separation allowing for thinning the RGC to be missed to due point placement
    - Drazdo t al: Vision Research 2007
  - 10-2 testing substantially improves correlation with RGC analysis
    - Hood and Raza; Vis Science 2011
  - Stamper(1984) identified the relationship between NTG and macular damage with typically near fixation visual field loss.
  - Heijl & Lundqvist 1984
    - 45 patients followed from normal to abnormal VF's using test points at 5,10,15 & 20 degrees from fixation
    - Largest number at 15 degrees but a surprising number at 5 degrees confirming Hood's work showing that early damage occurs in the macula as well as more traditional arcuate zones

“Green Disease”





Myopia = “Red Disease”

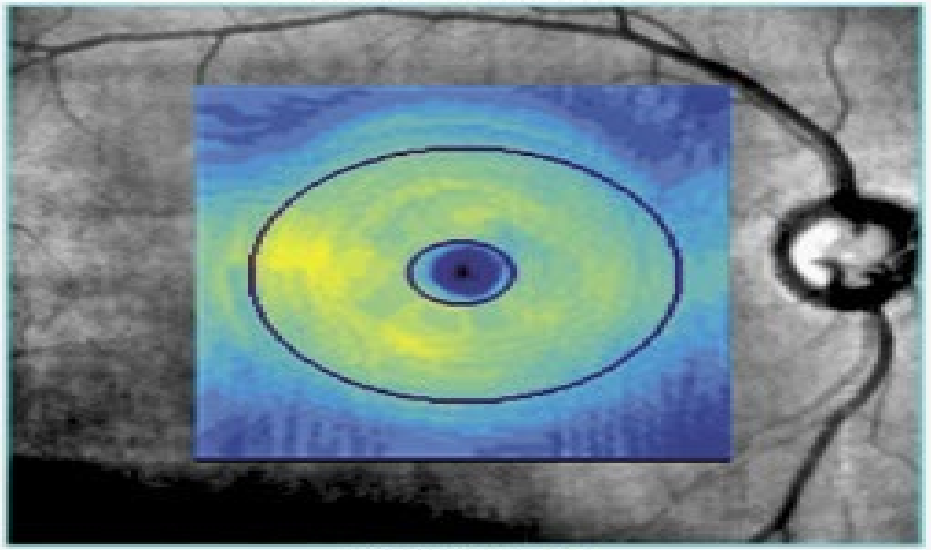


Optical Coherence Tomography as a Biomarker for Diagnosis, Progression, and Prognosis of Neurodegenerative Diseases
Satue, etal AJO 2016

- Recent research using the latest SD OCT imaging technology has demonstrated that an early damage of the anterior visual pathway occurs in MS, PD, and AD and that the ganglion cell layer is the ultimate biomarker for disease diagnosis, severity, and progression.
- Thus, OCT technology should be used as a common and very useful clinical complement in the diagnosis and control of neurodegenerative disorders.
- 85 Citations

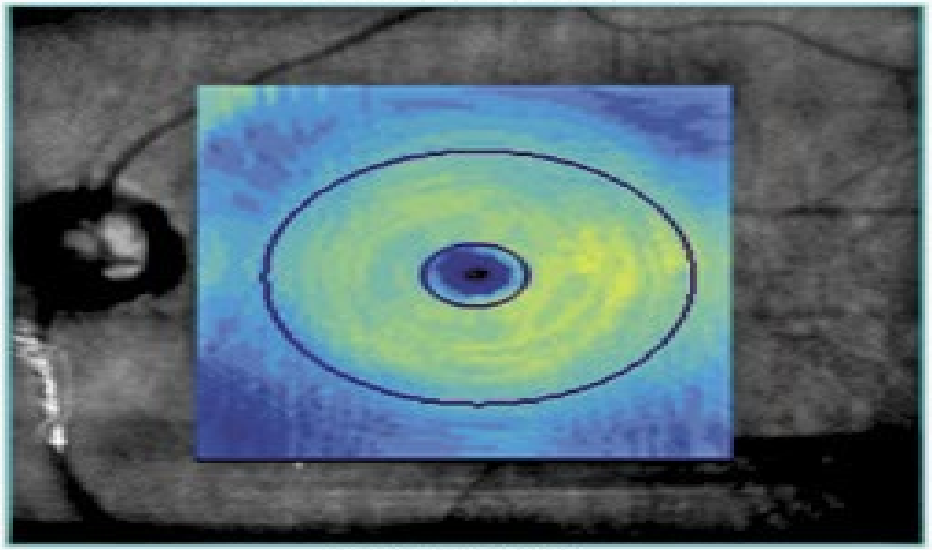
Ganglion Cell OU Analysis: Macular Cube 512x128 — OD ● | ● OS

OD Thickness Map



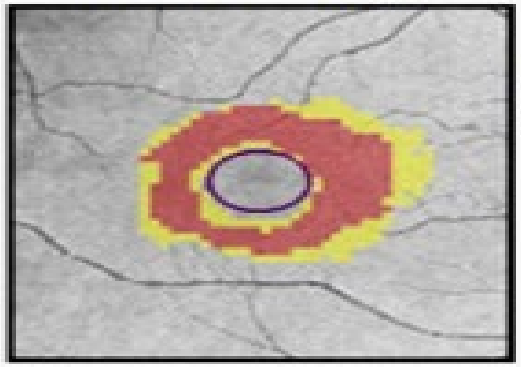
Fovea: 256, 64

OS Thickness Map

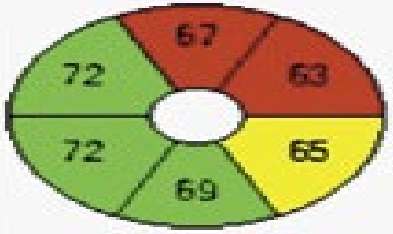


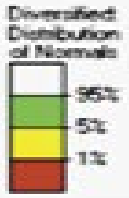
Fovea: 268, 65

OD Deviation Map

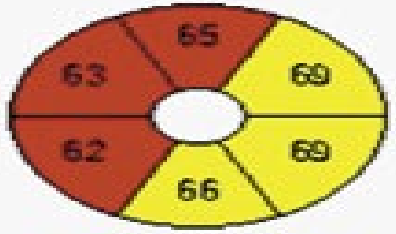


OD Sectors

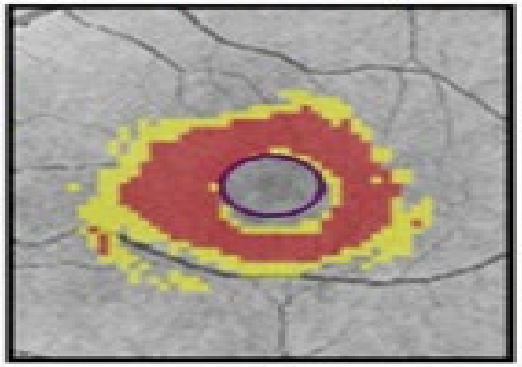




OS Sectors



OS Deviation Map



	OD µm	OS µm
Average GCL + IPL Thickness	68	66
Minimum GCL + IPL Thickness	62	61

American Journal of Ophthalmology
December 2016

Baseline Fourier-Domain Optical Coherence Tomography Structural Risk Factors for Visual Field Progression in the Advanced Imaging for Glaucoma Study

David Huang, MD etal

AIG/ 2016

- A total of 277 eyes of 188 participants were followed up for 3.7 ± 2.1 years.
- VF progression was observed in 83 eyes (30%).
- Several baseline NFL and GCC parameters, but not disc parameters, were found to be significant predictors of progression on univariate Cox regression analysis.
- The most accurate single predictors were the GCC focal loss volume (FLV), followed closely by NFL-FLV. An abnormal GCC-FLV at baseline increased risk of progression by a hazard ratio of 3.1

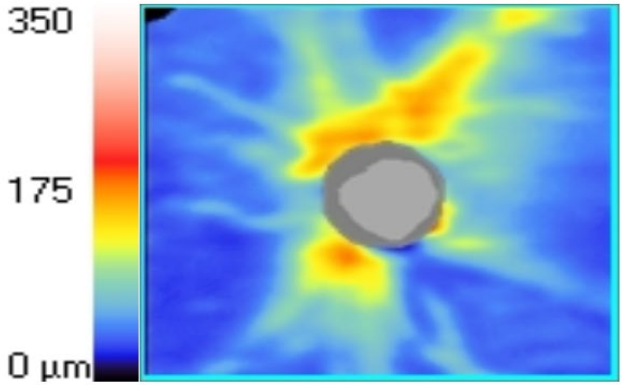
New Perspectives on Disease Management

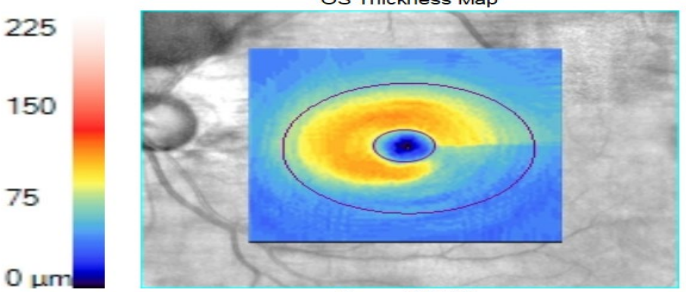
- SD-OCT is superior in identifying progression in glaucoma suspects, pre-perimetric glaucoma, mild glaucoma and early moderate disease compared with SAP are superior in identifying progression, after an initial VF to set baseline.
- Average time to identification of statistically significant progression is 2-3 years with SD-OCT and up 6 years with SAP
- Intra-test variability is up to 10x less with OCT(3%) than VF(20%)

New Perspectives on Disease Management

- RNFL “Floor” limits usefulness in late moderate to advanced glaucoma (50-60 microns)
- GCC progression analysis can continue to be useful in late moderate to advanced glaucoma due to density of fibers in the macula and the later involvement of central vision in the disease

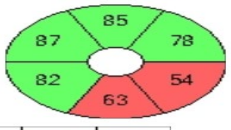
RNFL Thickness Map



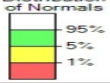


Fovea: 257, 65

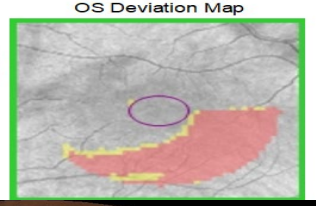
OS Sectors



Diversified Distribution of Normals

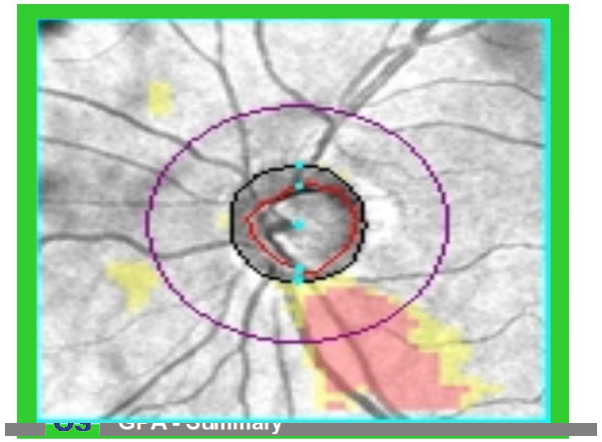


OS Deviation Map



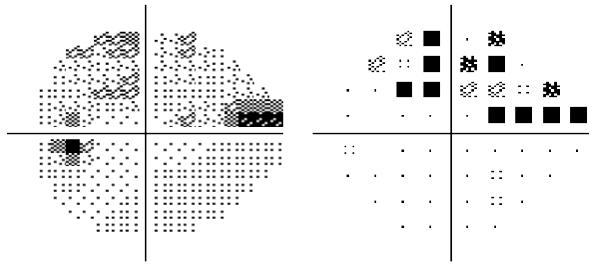
	OD µm	OS µm
+ IPL Thickness	84	75

RNFL Deviation Map



Graytone Pattern Deviation

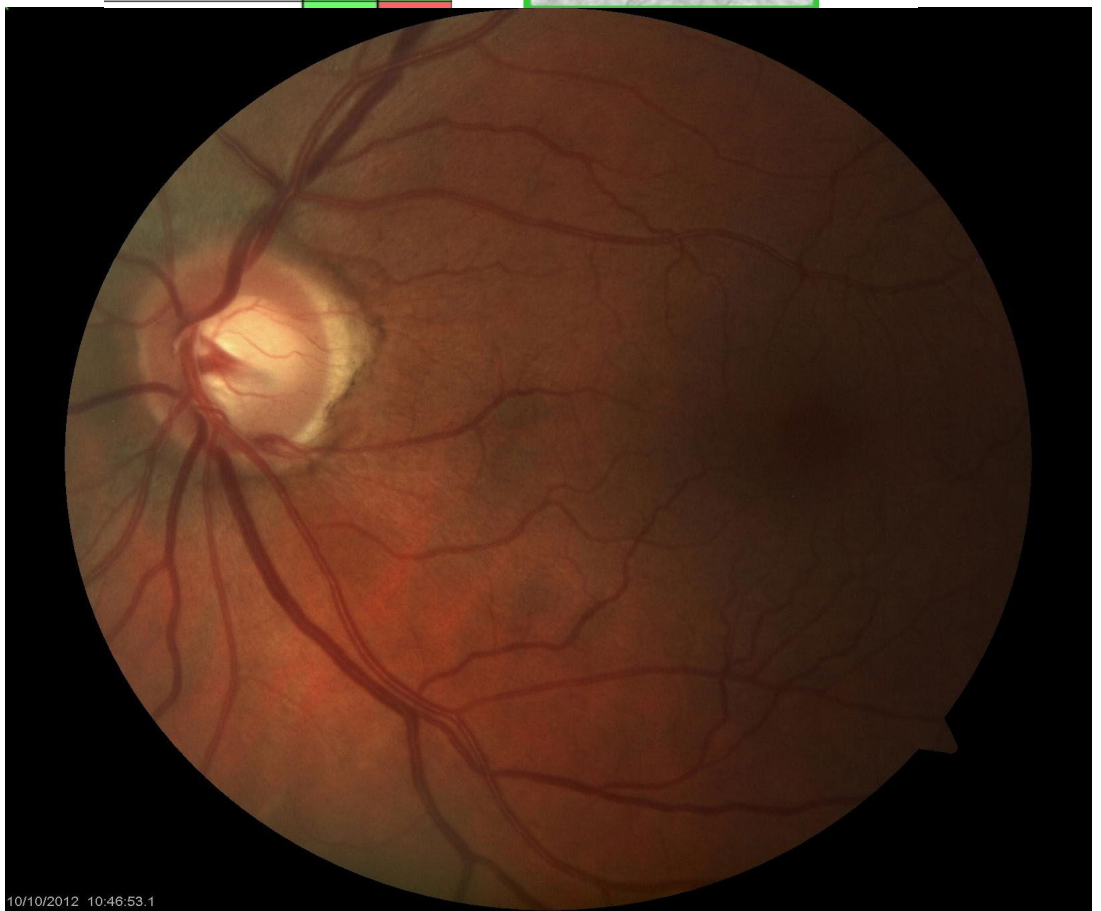
Sep 18, 2012 GHT: Outside Normal Limits
SITA-Standard



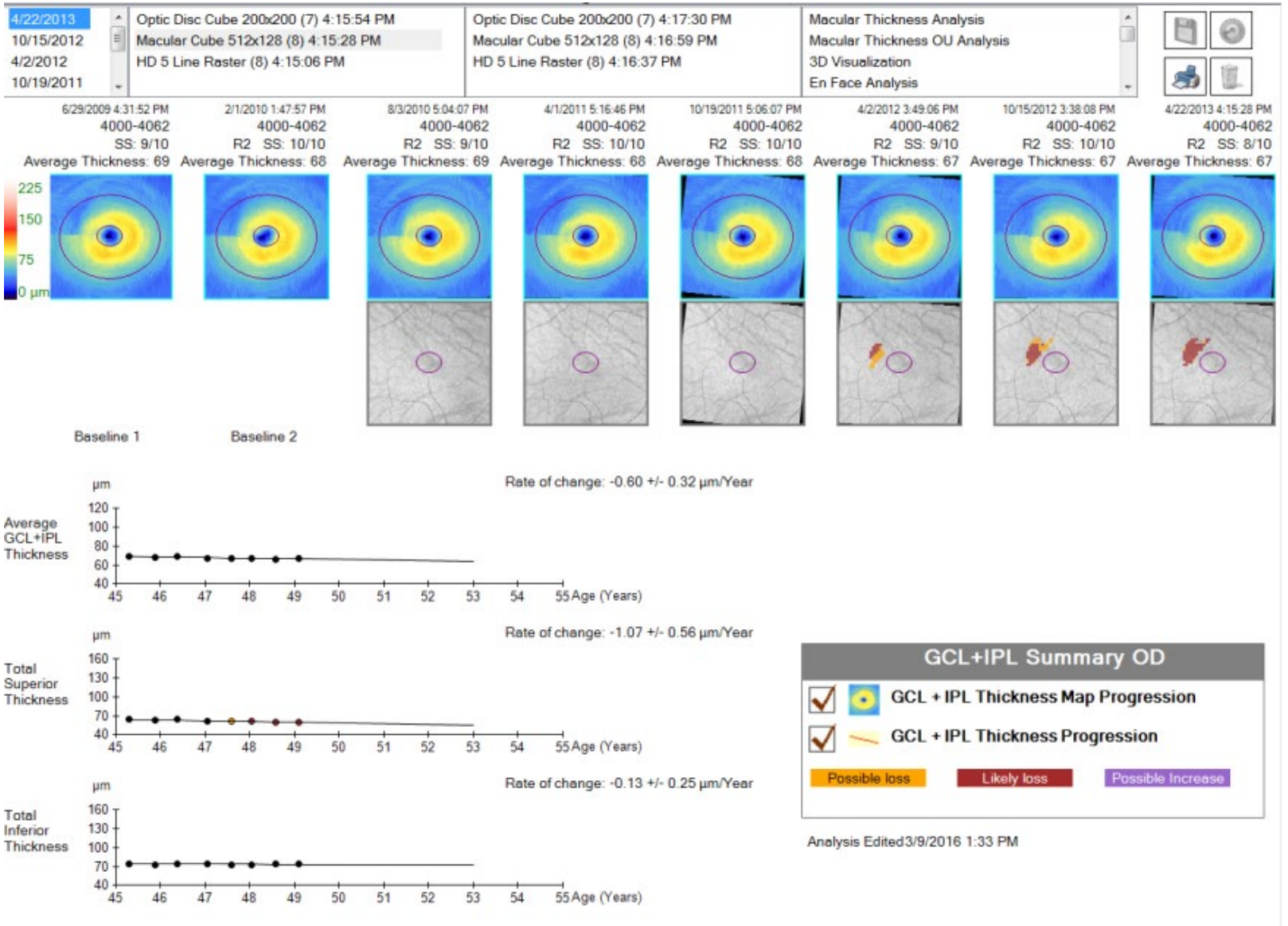
FL: 0/15
Fovea: Off
VFI: 91%

FN: 0%

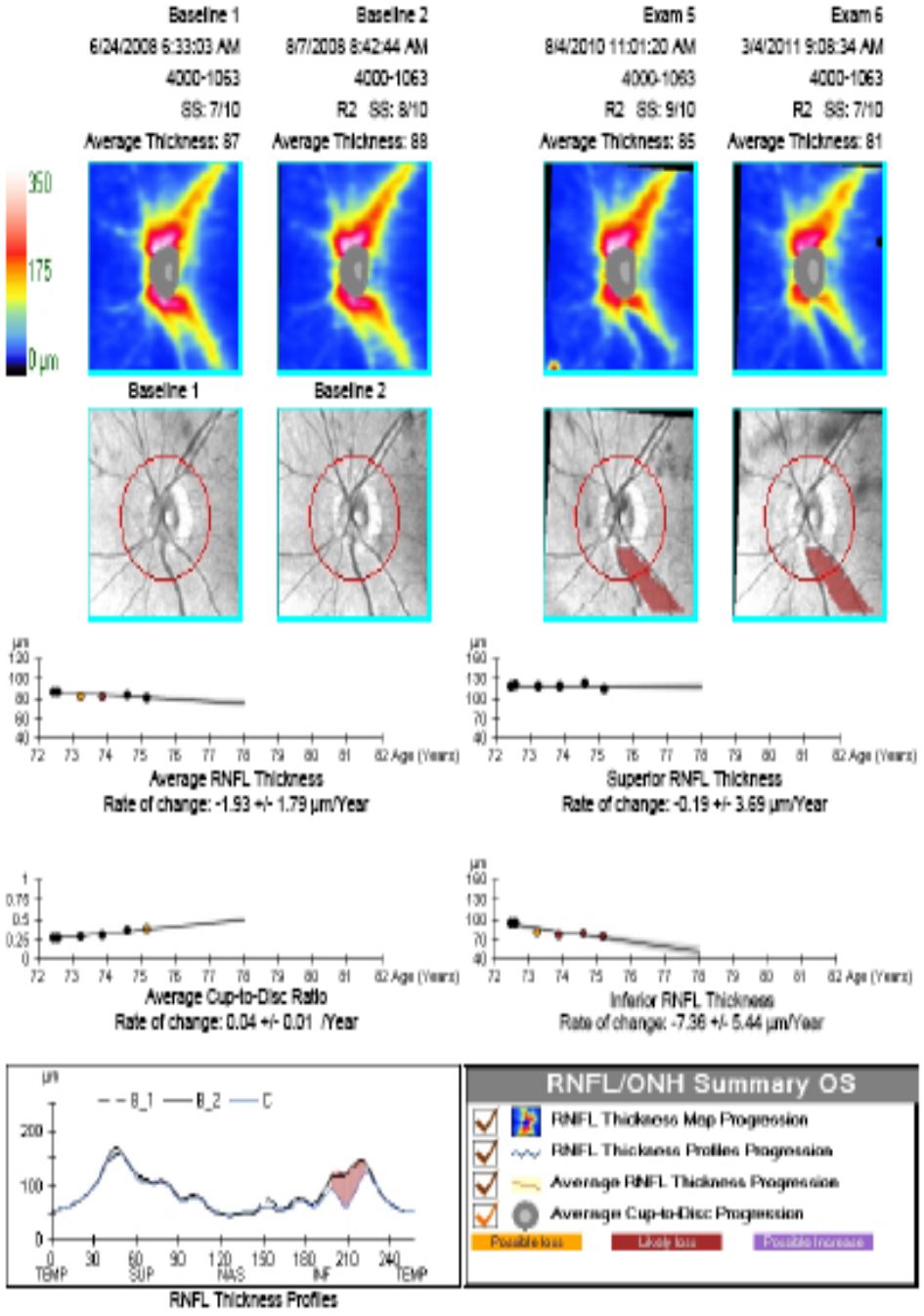
FP: 0%
MD: -3.93 dB P < 1%
PSD: 5.51 dB P < 0.5%



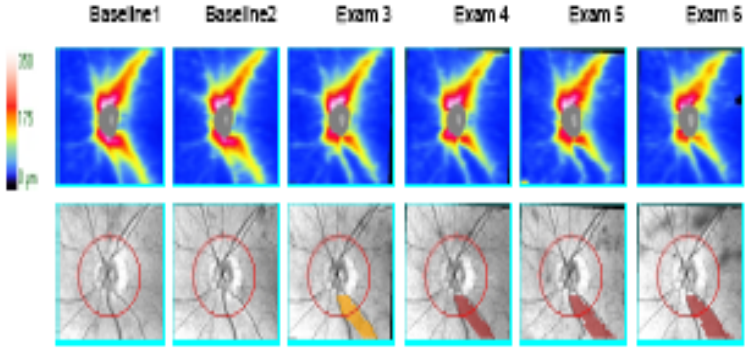
GCC Progression Analysis



Guided Progression Analysis: (GPA™) OD ○ ● OS



Guided Progression Analysis: (GPA™) OD ○ ● OS



RNFL and ONH Summary Parameters

		Exam Date/Time	Serial Number	Registration Method	SS	Avg RNFL Thickness (µm)	Inf Quadrant RNFL (µm)	Sup Quadrant RNFL (µm)	Rim Area (mm²)	Average Cup-to-Disc Ratio	Vertical Cup-to-Disc Ratio	Cup Volume (mm³)
Baseline1:	1	6/24/2008 6:33:53 AM	4000-1063		6/10	87	97	123	1.32	0.30	0.33	0.028
Baseline2:	2	8/7/2008 8:42:44 AM	4000-1063	R2	8/10	87	97	120	1.28	0.28	0.29	0.025
	3	4/2/2009 3:44:24 PM	4000-1063	R2	7/10	83	82	118	1.25	0.34	0.39	0.040
	4	11/18/2009 2:27:57 PM	4000-1063	R2	7/10	83	79	119	1.23	0.31	0.33	0.030
	5	8/4/2010 11:01:20 AM	4000-1063	R2	9/10	84	81	125	1.24	0.37	0.42	0.036
Current:	6	3/4/2011 9:08:34 AM	4000-1063	R2	7/10	81	76	116	1.20	0.39	0.44	0.053

Registration Methods
R2 - Registration based on translation and rotation of OCT fundus
R1 - Registration based only on translation of disc center

Likely Loss
Possible Loss

Compared to baseline, statistically significant loss of tissue detected. For Average RNFL, Superior RNFL, Inferior RNFL, Rim Area the values have decreased. For Cup-to-Disc Ratios and Cup Volume values have increased.

Possible Increase

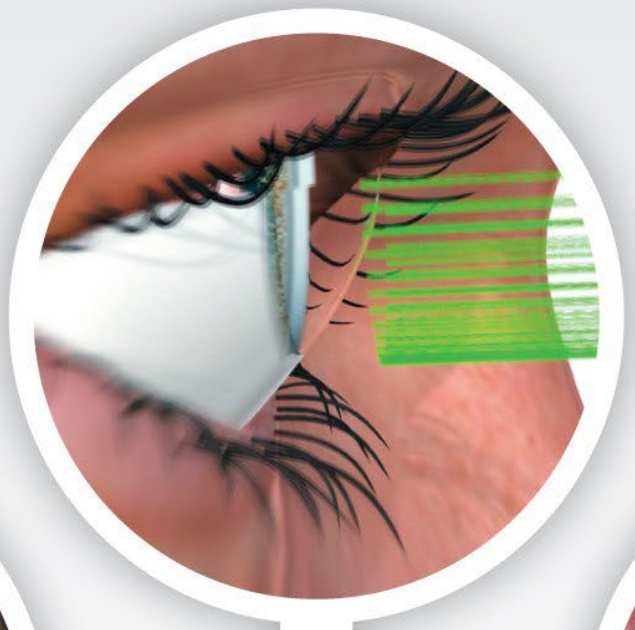
Compared to baseline, statistically significant increase detected. For Average RNFL, Superior RNFL, Inferior RNFL, Rim Area values have increased. For Cup-to-Disc Ratios and Cup Volume values have decreased.

1

Camera-guided system enables precise **non-contact procedure**

Advanced image-processing algorithm **locates exact treatment area**

2

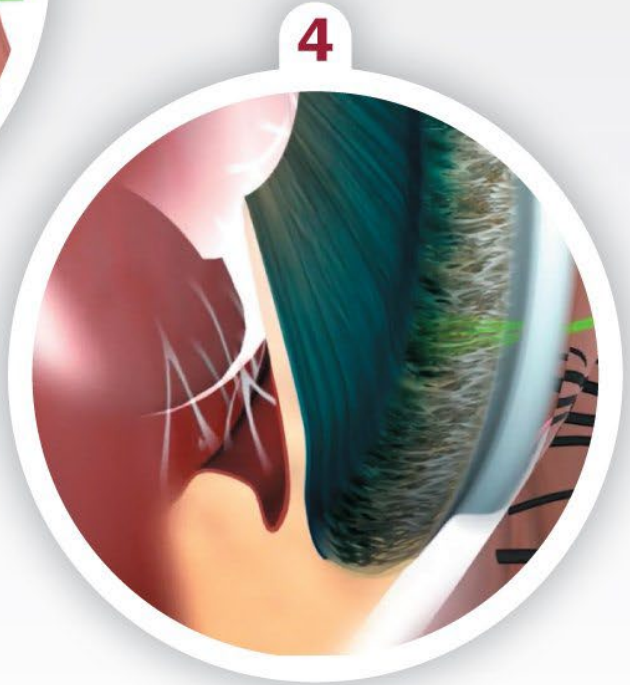


3

100 laser beams are directed to the trabecular meshwork

Delivery in **1.2 seconds**

4



IN VIEW: The investigational non-invasive, non-contact procedure is performed with automated laser technology that delivers 100 spots to the trabecular meshwork through the limbus in just 1.2 seconds. *(Images courtesy of BELKIN Laser Ltd.)*

WATCH THE PROCEDURE Go to OphthalmologyTimes.com/1Second

Belkin DSLT

- An investigational IOP-lowering modality, direct selective laser trabeculoplasty (DSLT) (BELKIN Laser), is being developed for its potential as a first-line treatment for ocular hypertension (OHT) open-angle glaucoma (OAG) and possibly for angle-closure glaucoma (ACG) that overcomes the limitations of current initial therapeutic options.
- The non-invasive, non-contact procedure is performed with automated laser technology that delivers 100 spots to the trabecular meshwork through the limbus in just 1.2 seconds.
- A proof-of-concept study provided evidence for the efficacy and safety of the transscleral approach to laser beam delivery using a conventional SLT instrument, and studies are under way outside of the United States using the external automatic glaucoma laser device itself

Belkin DSLT

- **Results**: In the trial group (N=16), IOP decrease from an average of 20.21 mmHg before treatment to 15.50 at 6 months.
- The corresponding numbers for the control group (n=16), were 21.14 mmHg and 15.00. There was no statistical difference between the two groups in IOP reduction.
- Complications rate was significantly higher in the control group ($p<0.0001$, OR 6.881, 95% CI 1.676/28.248).
- Anterior chamber inflammation and superficial punctate keratitis rates were significantly higher in the control group and compared to the study group ($p=0.006$).

Durysta-Brimatoprost Implant

Cannabinoids

Marijuana & Glaucoma

TABLE 1. MARIJUANA SIDE EFFECTS*[5,14]

OCULAR	SYSTEMIC
• Conjunctival hyperemia	• Tachycardia
• Decreased lacrimation	• Decreased blood pressure
• Photophobia	• Orthostatic hypotension
• Ptosis	• Euphoria or dysphoria
• Blepharospasm	• Impaired coordination
• Nystagmus	• Difficulty with concentration, problem solving, memory
• Impairment of accommodation	• Decreased testosterone
	• Impaired immunity

**Any route of administration*

Marijuana & Glaucoma Therapy

American Glaucoma Society:

“Although marijuana can lower the intraocular pressure, its side effects and short duration of action, coupled with a lack of evidence that its use alters the course of glaucoma, preclude recommending this drug in any form for the treatment of glaucoma at the present time.”

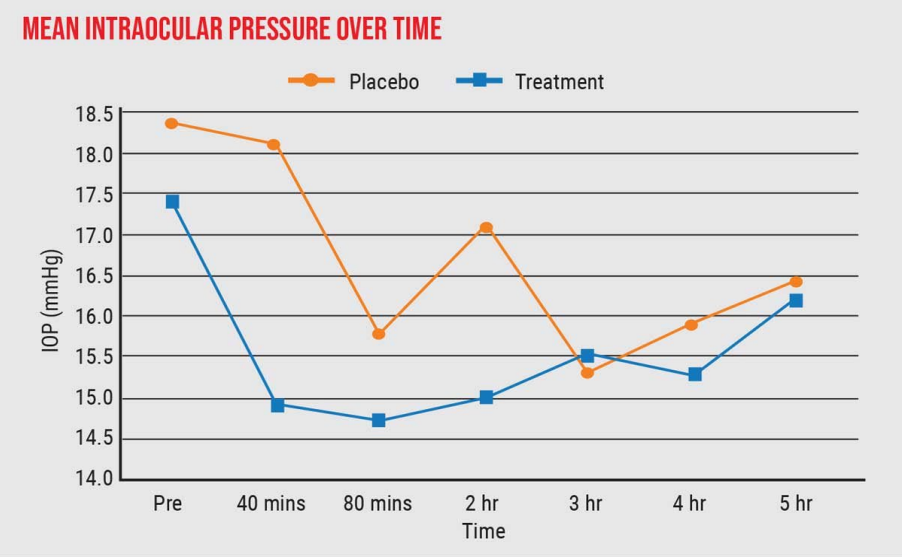
Cannabis, Glaucoma and Intraocular Pressure

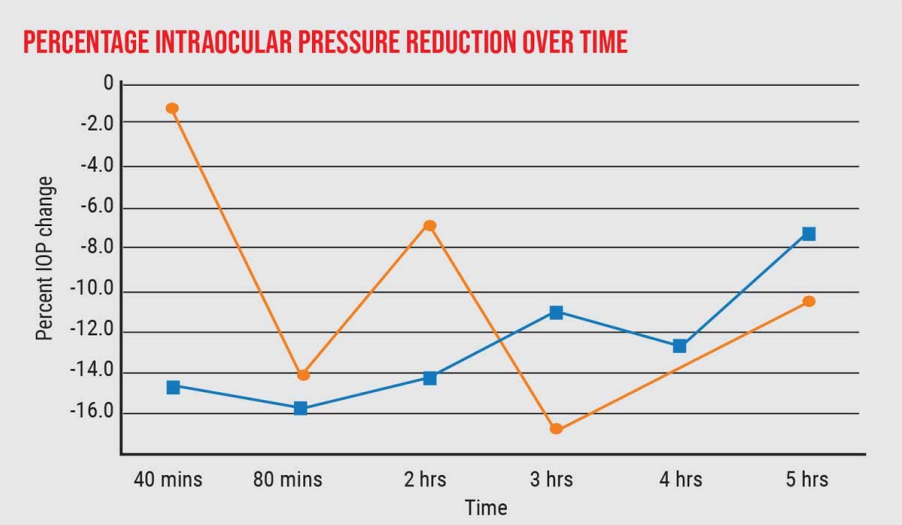
- Because of the Schedule I status and the stigma associated with it, all research on cannabis basically ceased in the 1980s; it was just too difficult to get around the regulations.
- Among other things, limited high-quality data has impacted the current American Academy of Ophthalmology and American Glaucoma Society positions on the use of cannabis to treat glaucoma.
- They don't support it, largely because there's too little information to justify such support.
- Sameh Mosaed, Etal (Review of Ophthalmology 2022)

Cannabis, Glaucoma and Intraocular Pressure

Sameh Mosaed, MD / Review of Ophthalmology

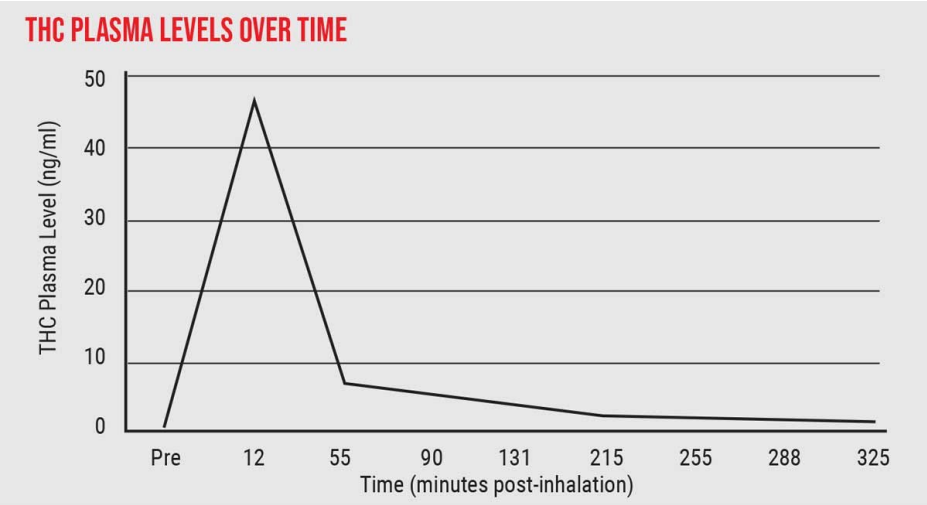
Dr. Mosaed is a professor of ophthalmology and director of the Glaucoma Division of the Gavin Herbert Eye Institute at UC Irvine.
.Dr. Singh is a professor of ophthalmology and chief of the Glaucoma Division at Stanford University School of Medicine.
Dr. Netland is Vernah Scott Moyston Professor and Chair at the University of Virginia in Charlottesville.

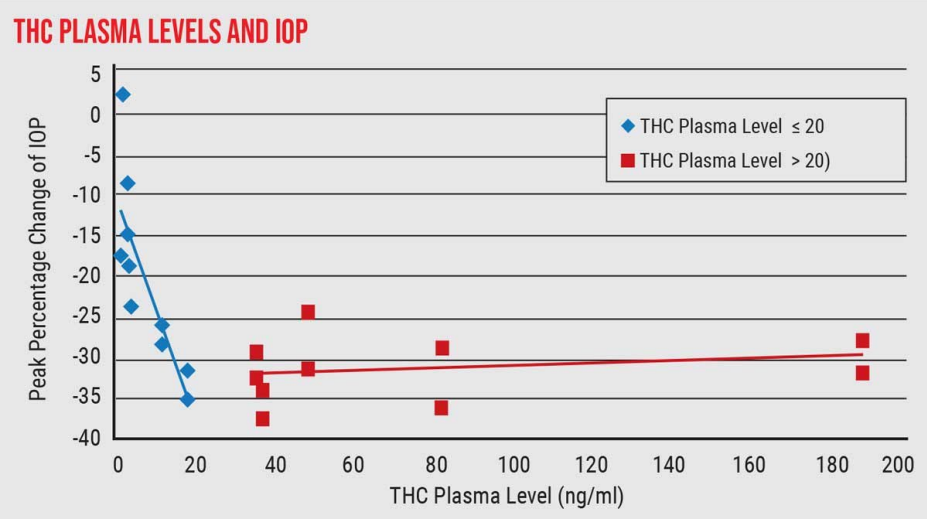




One of the author's studies found a substantial and significant decrease in IOP in subjects smoking cigarettes with THC, compared to placebo. The patients went from a mean IOP of 17.5 mmHg prior to smoking down to lower than 15 mmHg, 15 percent below baseline.

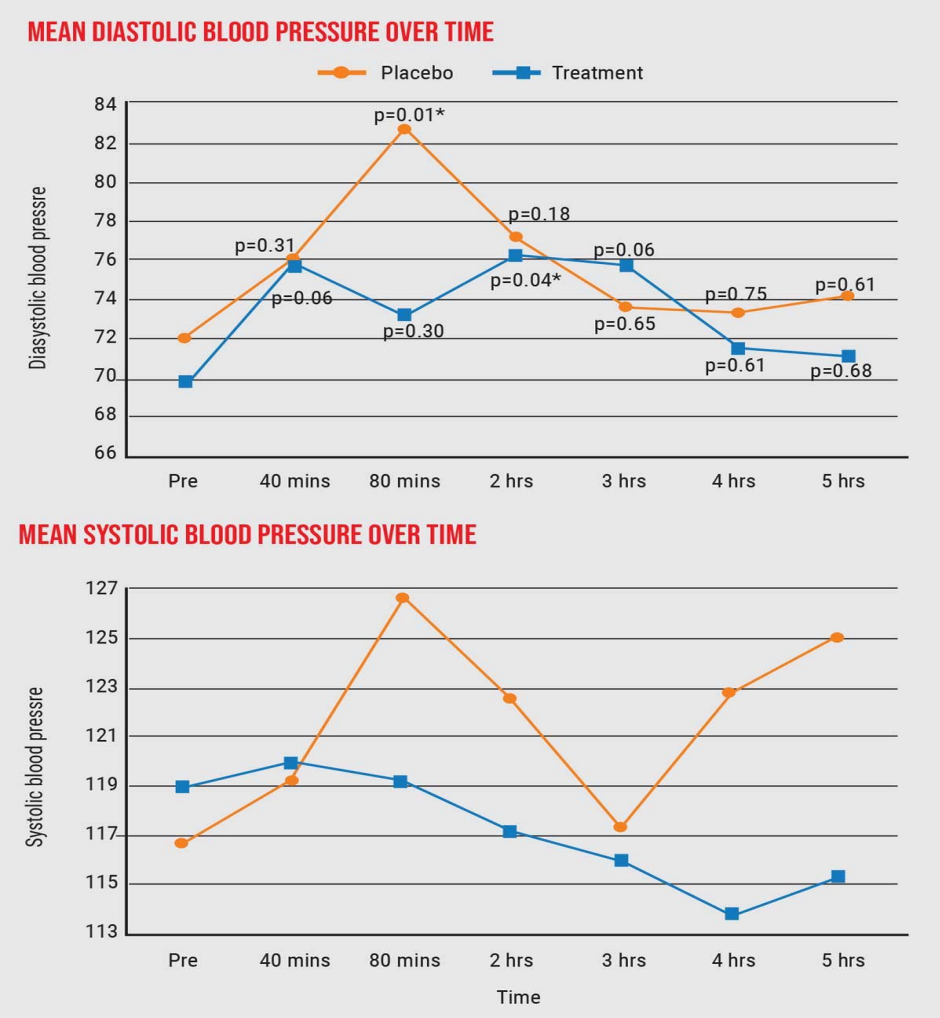
Cannibis, Glaucoma and Intraocular Pressure





THC is metabolized quickly, soon disappearing from the bloodstream. (Top graph) Decline in IOP paralleled rising THC plasma levels up to 20 ng/ml; above that, IOP did not decline. (Bottom graph) This suggests that a limited intake of THC—possibly a small enough amount to avoid psychotropic effects—could accomplish significant IOP lowering

Cannabis, Glaucoma & Intraocular Pressure



The data revealed only one point of statistically significant difference between the placebo group and cannabis group in diastolic or systolic blood pressure (asterisk).

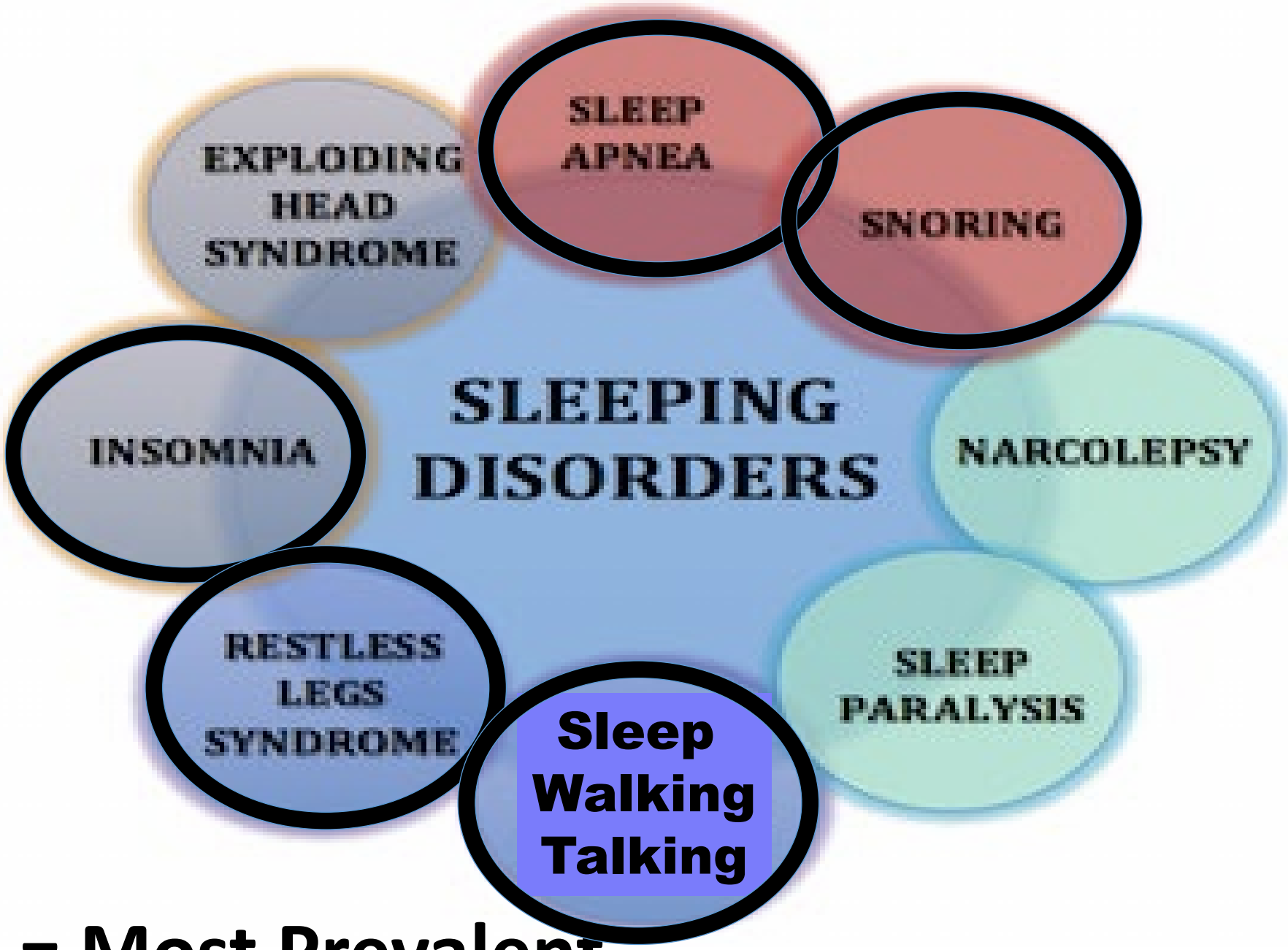
Cannabis, Glaucoma and Intraocular Pressure

- Many people talk about marijuana when they really should be discussing *cannabis*.
- Cannabis is a genus of flowering plants in the *Cannabaceae* family, which consists of three primary species: *Cannabis sativa*; *Cannabis indica*; and *Cannabis ruderalis*.
- The term marijuana has negative connotations; it's used to refer to specific varieties of cannabis that contain more than 0.3 percent THC. CBD, on the other hand, has no psychotropic effects.
- Cannabis contains multiple compounds—more than 480, of which about 65 have been identified as phytocannabinoids (including CBD and THC).
- Cannabis also contains about 120 compounds that give it its characteristic aroma—mainly volatile terpenes and sesquiterpenes. Not surprisingly, most patients don't know much about cannabis; many don't even understand the distinction between THC and CBD.

Cannabis, Glaucoma & Intraocular Pressure

- We found a substantial and significant decrease in IOP in subjects smoking cigarettes with THC compared to placebo. The patients went from an average IOP of 17.5 mmHg prior to smoking, down to lower than 15 mmHg, 15 percent lower than baseline.
- A 15-percent reduction, when you start out with normal pressure, is quite significant—on a par with what you'd see with a single-agent IOP-lowering eye drop.
- The lower pressure was sustained for up to three hours.
- In terms of systolic and diastolic blood pressure, we found no statistically significant differences between the placebo group and cannabis group. There were some differences, as the graphs show *(graph below)*, but the differences were only statistically significant at a single time point (marked with an asterisk).
- We confirmed that THC is metabolized very quickly; it gets absorbed into tissues and disappears from the bloodstream very quickly.
- There was a linear correlation between THC level in the blood plasma and IOP reduction, up to about 20 ng/ml of THC. Additional elevation of plasma THC, however, didn't correlate with further IOP lowering. *(See graph above.)* In other words, achieving 20 ng/ml of blood plasma level of THC was all that was required to achieve the maximum IOP-lowering effect.

Sleep Apnea:
It’s Role in Glaucoma Management



= Most Prevalent

Sleep Apnea

- **Most case are Obstructive (OSAS)**
  - **22% of men / 17% of women → 22 million Americans**
  - **Rates increase with age & obesity →** **80% unDx**
- **< 10% are Central - <1% of population**
  - **Decreased or absent ventilatory effort (neurologic)**

- **Apnea: temporary cessation of breathing (≥ 10 seconds) during sleep with reduced O_2 saturation [≥ 4% drop]**
- **Hypopnea: decreased airflow ≥ 10 sec with reduced O_2 saturation (≥3% or ≥ 4%) (partial obstruction)**
  - **Elevated Apnea-Hypopnea Index (AHI)**

J Thorac Dis. 2015 Aug; 7(8): 1311–1322

Is POAG Prevalence Higher in OSAS?

- 2023 Systematic review and meta-analysis of 46 studies (n= 4+ million patients), OSAS was associated with a 40% increased risk of POAG after adjusments for age, gender, diabetes, HTN, CV disease/dyslipidemia ($p < 0.01$)

Cheong AJY, Wang SKX, Woon CY, Yap KH, Ng KJY, Xu FWX, Alkan U, Ng ACW, See A, Loh SRH, Aung T, Toh ST. Obstructive sleep apnoea and glaucoma: a systematic review and meta-analysis. Eye (Lond). 2023 Oct;37(15):3065-3083.

Higher Prevalence of OSAS in Patients with Dx Glaucoma?

- 2021 meta-analysis of of 10 studies with 966 subjects
- **35% of glaucoma patients had OSAS**
  - → compared to 20% of the adult population

Yu BE, Cheung R, Hutnik C, Malvankar-Mehta MS. Prevalence of Obstructive Sleep Apnea in Glaucoma Patients: A Systematic Review and Meta-analysis. J Curr Glaucoma Pract. 2021 Sep-Dec;15(3):109-116.

Treating OSA

- CPAP is the **gold standard**, but compliance rates are low (50% discontinue within the first year and another 25% by year 3)
- Females, > 55 yo and improved daytime sleepiness (ESS) predict compliance past 6 mos

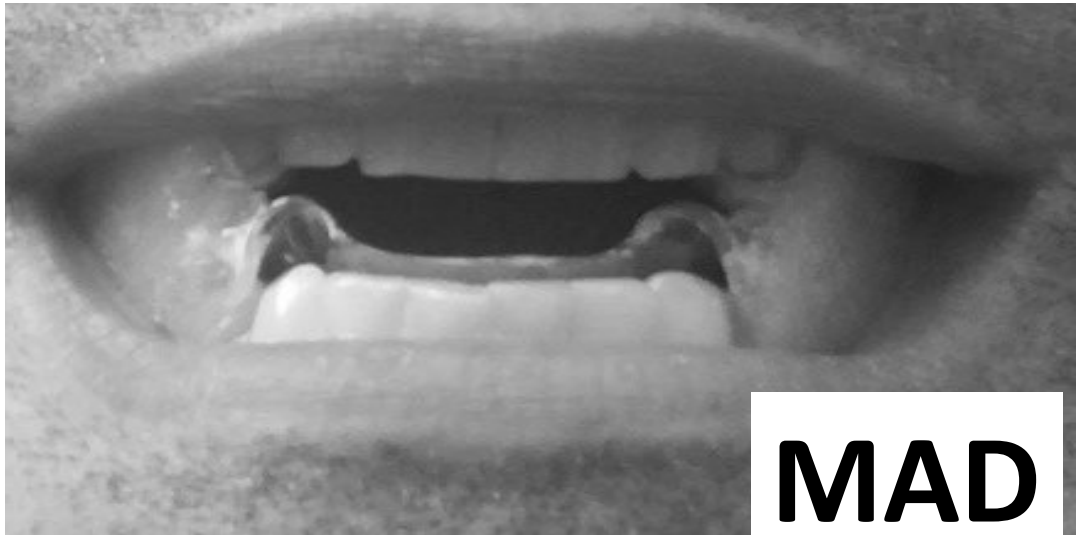
Respir Care. 2010 Sep;55(9):1230-9

- CPAP did NOT improve MACE or mortality in pts with established CVD (mean nightly use only 3.3 hrs on 70% of nights)

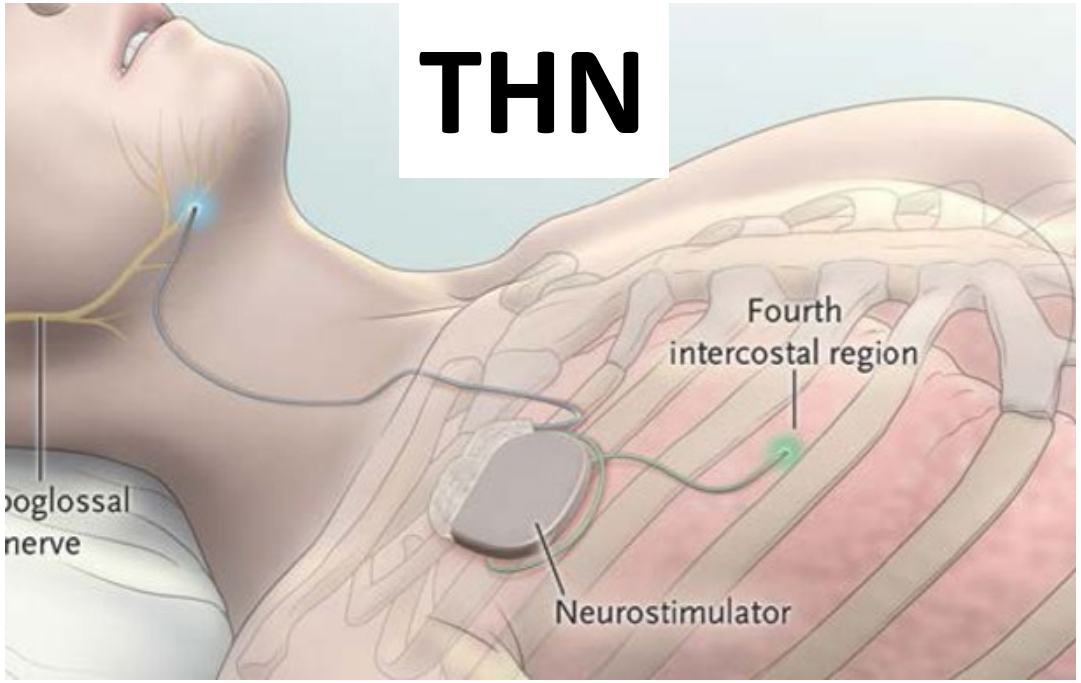
Sleep Apnea. N Engl J Med. 2016 Sep 8;375(10):919-31

Other OSA Tx Options NOT ↑ EVP

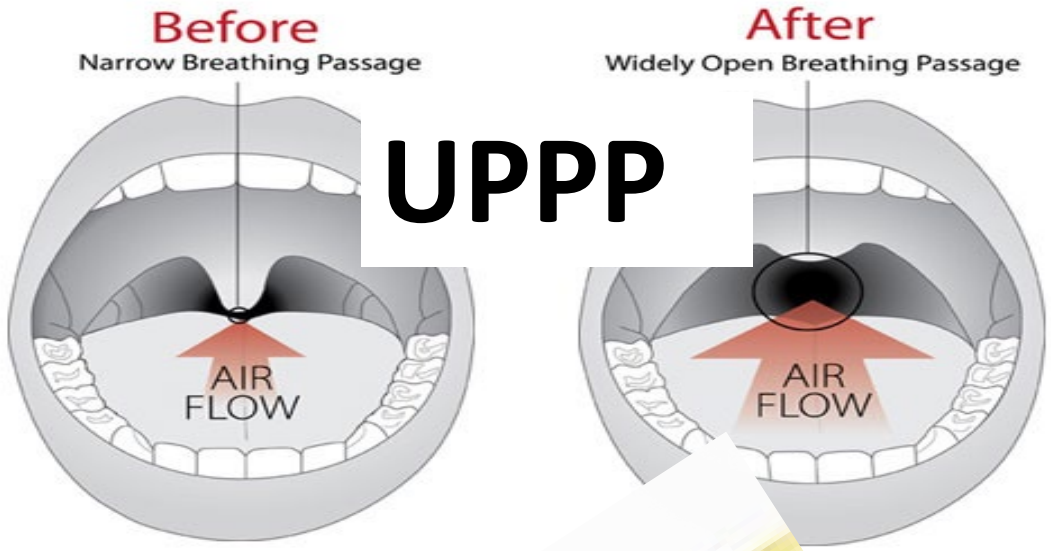
- **Mandibular Advancement Devices (MAD)**
  - comparable to CPAP for mild OSA (50-60% lower AHI)
- **Uvulopalatopharyngoplasty (UPPP)**
  - removal of tonsils, posterior soft palate, uvula
- **Targeted Hypoglossal Neurostimulation**
  - improves tongue muscle tonus
- **Playing a double-reed instrument (e.g. an oboe)**
  - lower prevalence of OSA
- **Play didgeridoo - comparable to CPAP for mild-moderate OSA**
- **Weight Loss**



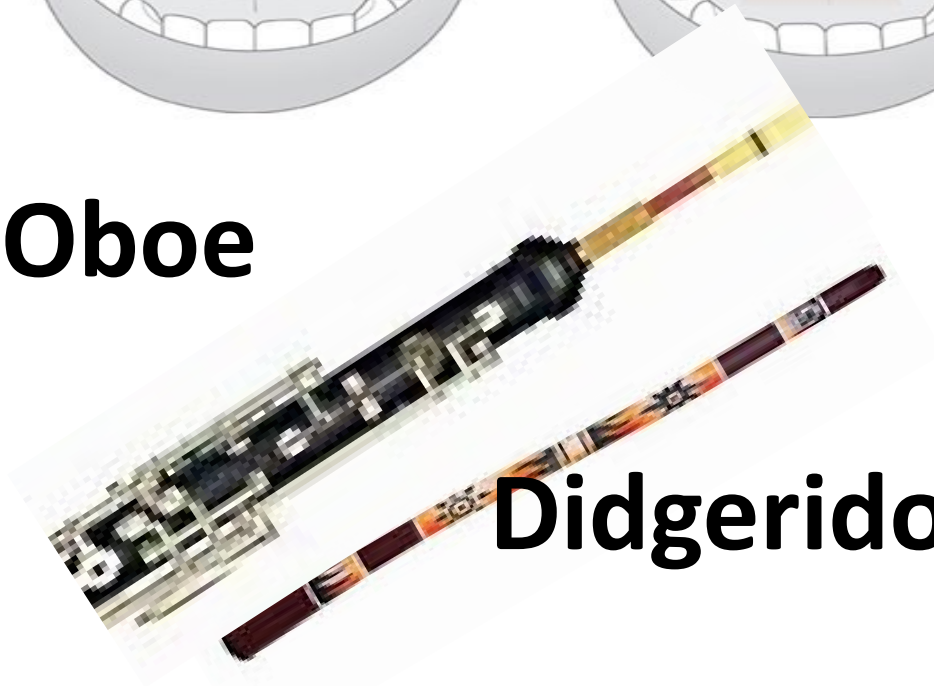
MAD



THN



UPPP



Oboe

Didgeridoo

Dtsch Arztebl Int. 20[illegible]Mar; 115(12): 200–207
Mayo Clin Proc. 2009 Sep; 84(9): 795–800.
Sleep. 2015 Oct 1; 38(10): 1593–1598
J Clin Sleep Med. 2012 Jun 15; 8(3): 251–255
BMJ. 2006 Feb 4; 332(7536): 266–270

Targeted Hypoglossal Neurostimulation

- **Minimally invasive surgery**
- **Intercostal pacemaker with a multi-contact electrode to CN XII**
  - **43% with significant improvement in AHI & O_2 saturation at 6 mos**
  - **BMI < 35 and AHI < 65 predicted good response**
  - **At 1 year, 'responders' had mean AHI decrease from 28.6 to 9.5 events/hour**
  - **> 50% reduction in AHI at 5 years**

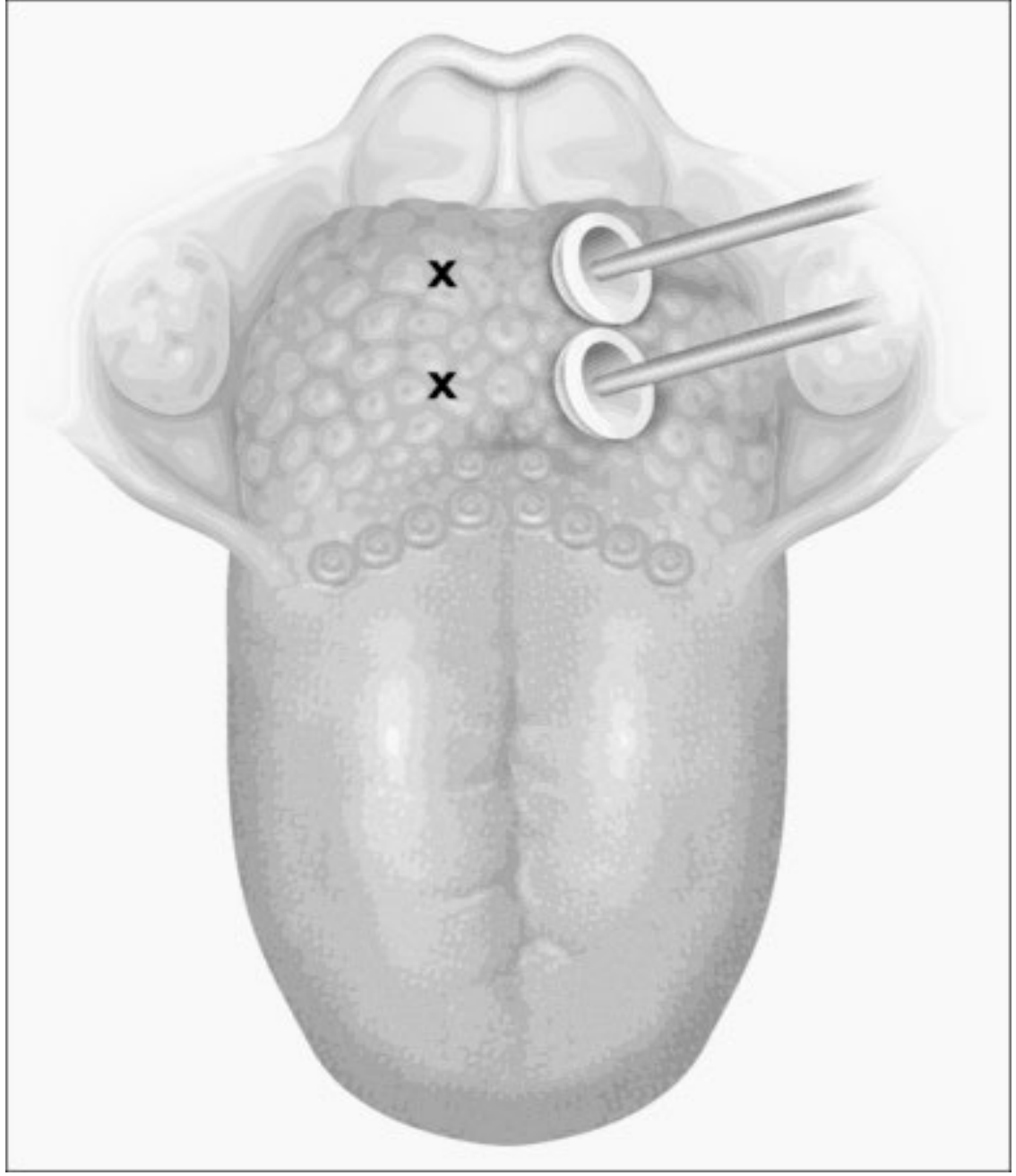
Laryngoscope. 2016 Nov;126(11):2618-2623
Laryngoscope. 2018 Feb;128(2):509-515
Otolaryngol Head Neck Surg. 2018 Jul;159(1):194-202

Mandibular Advancement Devices (MAD)

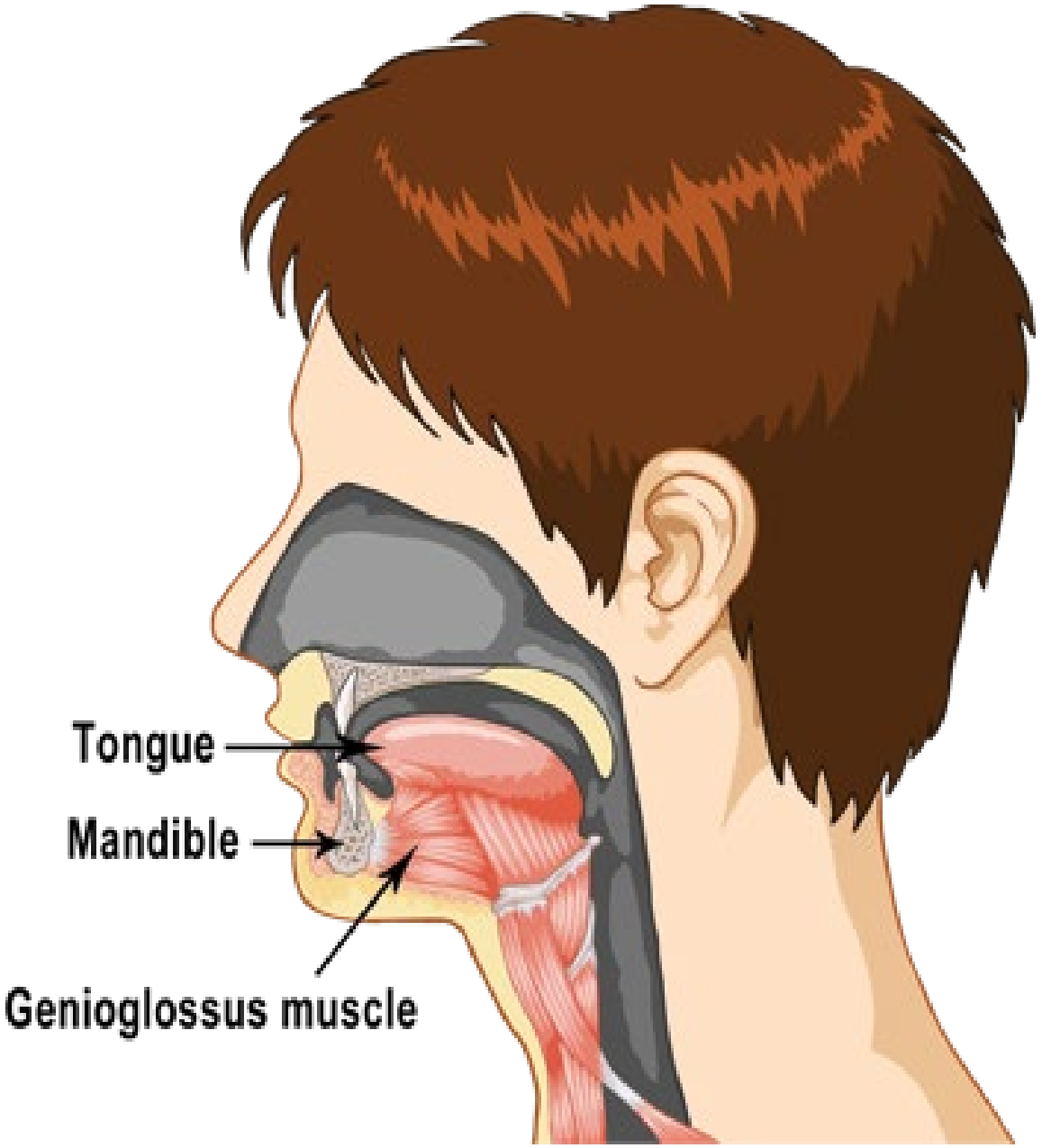
- Reduce required positive airway pressure when used in combination with CPAP
- Combo Tx better tolerated by many patients
- **Patients without severe upper airway collapsibility and with a weaker reflex of throat muscles were more likely to benefit from MAD** (measured by PSG)
  - 93 adults with moderate to severe OSA
  - **OSAS severity & BMI did NOT predict response to MAD**

PLoS One. 2017 Oct 26;12(10):e0187032.

Annals of the American Thoracic Society, 2019; DOI: 10.1513/AnnalsATS.201903-190OC



Tongue Base Radiofrequency



Genioglossus Advancement