

How Low Can We Go?

Disc Hemorrhages, NTG, and 24-hour Control

ROMA PATEL, MD MBA
BAYLOR COLLEGE OF MEDICINE
ASSOCIATE PROFESSOR
CHIEF OF OPHTHALMOLOGY & MEDICAL DIRECTOR,
BEN TAUB HOSPITAL & HARRIS HEALTH EYE CLINICS

Case Presentation

- ▶ 51 yo Caucasian female presents for glaucoma evaluation
- ▶ No know IOP range, but mother recently diagnosed with advanced glaucoma
- ▶ Denies any ocular complaints including pain, discomfort, trauma, flashes

History

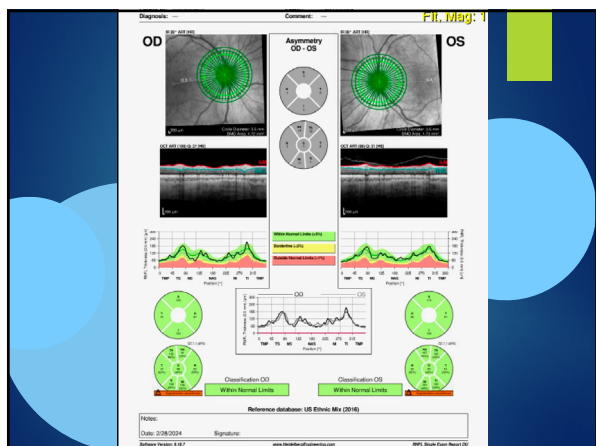
- ▶ PMHX
None
- ▶ Medications
Flaxseed Oil
MVI
Calcium
- ▶ Allergies
PCN
- ▶ Family History
+Mother diagnosed with severe glaucoma needing surgery
+ DM, HTN
- ▶ Social History
Denies ETOH, Tob

Examination

- ▶ BCVa
20/20 c -5.25 sph
20/20 c -4.50 sph
- ▶ Pupils
5mm→3mm, 3+
No RAPD
- ▶ Ta
17
16
- ▶ CCT- 504 OD, 491 OS
- ▶ Motility - Full OU
- ▶ External - WNL
- ▶ SLE
Unremarkable, No TID, PXE material
- ▶ Gonio
CBB 360, no PAS
- ▶ DFE
Normal Vessels, Macula,
periphery

0.55 CDR 0.5 CDR

Visual field plots for Right Eye and Left Eye. Each plot includes a grid of visual field points, a central fixation point, and associated data such as Mean Deviation (MD) and Index of Individual Ictus (IIT).

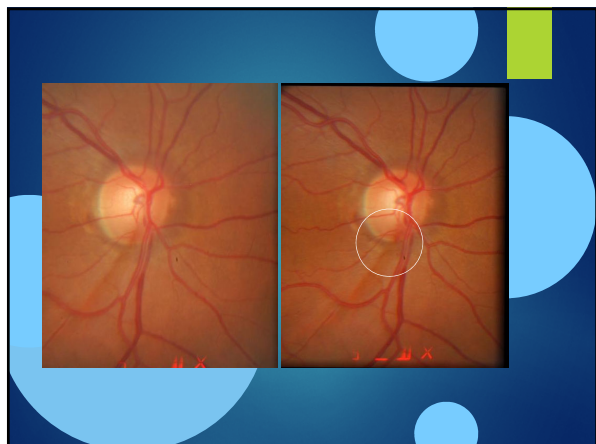


Recommendation

- ▶ Glaucoma Suspect
- ▶ Opted to follow patient off drops
- ▶ Return visit in 4 months:
- ▶ VA unchanged; IOP 20 OD, 16 OS
- ▶ Undilated exam: unchanged
- ▶ Return in 8 months

Returns at 8 months

- ▶ No new subjective complains
- ▶ Exam unchanged
- ▶ TA- 18 OU
- ▶ ONH exam- see photos



Other Causes of Disc Heme

<u>OCULAR CAUSES</u>	<u>SYSTEMIC CAUSES</u>
▶ Posterior Vitreous Detachment	▶ Hypertension
▶ Vascular occlusive event	▶ Diabetes
▶ Optic Disc Drusen	▶ SLE
▶ Non-Glaucomatous Optic Neuropathies	▶ Leukemia
	▶ Medications

OHTS Study & Disc Heme

- ▶ Presence of Disc Heme ?
- ▶ 6X risk of patient developing POAG
- ▶ (median time 13 months)

Badriz et al. Detection and Prognostic Significance of Optic Disc Hemorrhage during the Ocular Hypertension Treatment Study. Ophthalmology, 113(12) December 2006; 2137-2143.

What comes first, the RNFL Loss or the Disc Heme?

- ▶ 25 patients with OHTN with Disc Heme followed for ~6 years (33 months before & 38 months after)
- ▶ 8 out of 25 developed glaucomatous damage
- ▶ Serial photos documented disc heme before RNFL loss in all patients.
- ▶ Location of disc heme correlated to RNFL defect.
- ▶ 4 patients developed perimetric changes 1-2 years following event. 3 had normal fields.

Airaksinen PJ et al., Optic Disc Haemorrhages Precede Retinal Nerve Fiber Layer Defects in Ocular Hypertension. Acta Ophthalmologica, 1981; 59:627-641

OCT Role in correlating RNFL thickness and Disc Hemorrhage

- ▶ 32 eyes with POAG/NTG (19%/81%)
- ▶ "Disc Hemorrhage is associated with RNFL thinning measured by Optical Coherence Tomography"
- ▶ Negative Correlation between the number of recurrent hemorrhages and RNFL thickness

Choi, Jin et al. Retinal Nerve Fiber Layer Thickness Evaluation Using Optical Coherence Tomography in Eyes With Optic Disc Hemorrhage. Ophthalmic Surgery and Lasers. 38(2), March/April 2007. 118-125

Hemorrhage in glaucomatous eyes

- ▶ most commonly seen in inferotemporal and superotemporal quadrants
- ▶ Found in 8.2% of glaucoma cases

Disc Hemorrhages in nonglaucomatous eyes

- ▶ More common in the temporal hemisphere
- ▶ Found in 0.2% in nonglaucoma cases

OCT - Use sector analysis

Location	RNFL Thickness (microns)	P ^a
At the sector with disc hemorrhage	81.7 ± 32.9	
At the superior or inferior symmetrical sector	100.7 ± 34.5	.005 ^b
At the equivalent sector of the contralateral eye	92.8 ± 31.7	.092 ^c

Location	RNFL Thickness (microns)	P ^a
At the quadrant with disc hemorrhage	102.4 ± 30.8	
At the counter quadrant (superior or inferior)	105.7 ± 30.4	.591 ^b
At the same quadrant of the contralateral eye	104.2 ± 31.3	.784 ^c

RNFL = retinal nerve fiber layer.
^aObtained using the paired-sample t test.
^bP value was obtained by comparing the RNFL thickness in the hemorrhagic sector with the RNFL thickness in the superior or inferior symmetrical sectors.
^cP value obtained by comparing the RNFL thickness in the hemorrhagic sector with the RNFL thickness in the equivalent sector in the contralateral eye.

RNFL = retinal nerve fiber layer.
^aObtained using the paired-sample t test.
^bP value obtained by comparing the RNFL thickness of the hemorrhagic quadrant with the RNFL thickness of the superior or inferior counter quadrants.
^cP value obtained by comparing the RNFL thickness of the hemorrhagic quadrant with the RNFL thickness of the same quadrant in the contralateral eye.

Choi, Jin et al. Retinal Nerve Fiber Layer Thickness Evaluation Using Optical Coherence Tomography in Eyes With Optic Disc Hemorrhage. Ophthalmic Surgery and Lasers. 38(2), March/April 2007, 118-125

What groups are susceptible?

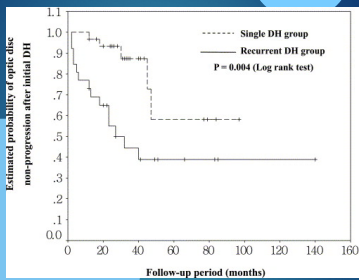
- ▶ 13,965 photos were reviewed in Japan
- ▶ Disc Heme more common in normotensive (IOP<20) elderly (>60 yo) females
- ▶ Incidence
 →8.2% in patients with glaucoma
 →0.2% in non glaucoma cases

Watanabe, Tetsuya et al. Optic Disc Hemorrhages Detected in a Large-Scale Eye Disease Screening Project. Journal of Glaucoma, Volume 13(8) Oct. 2004, 356-360

Is Recurrent Disc Hemorrhage worse than a single episode of disc hemorrhage?

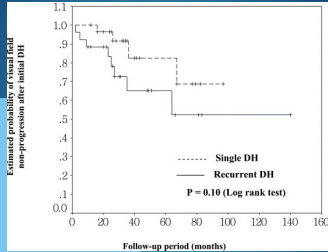
- ▶ 57 eyes with DH reviewed
 - 26 eyes with recurrent disc hemorrhage
 - 31 eyes with single episode

Seok Hwan Kim MD and Ki Ho Park MD, The Relationship between Recurrent Optic Disc Hemorrhage and Glaucoma Progression, Ophthalmology, 2006, 113:598-602.



Optic Disc Progression after Disc Hemorrhage

Seok Hwan Kim MD and Ki Ho Park MD, The Relationship between Recurrent Optic Disc Hemorrhage and Glaucoma Progression, Ophthalmology, 2006, 113:598-602.



Visual Field Progression after Disc Hemorrhage

Seok Hwan Kim MD and Ki Ho Park MD, The Relationship between Recurrent Optic Disc Hemorrhage and Glaucoma Progression, Ophthalmology, 2006, 113:598-602.

Optic Disc Hemorrhages and Other Diseases

	OR	95% CI	P value
Platelet aggregation inhibitors	3.16	1.97 5.06	<0.0001
Antihypertensive agents	1.10	0.82 1.47	0.5241
Cholesterol-lowering agents	0.94	0.23 3.80	0.9286
Triple combination	2.20	0.89 5.40	0.0865
Warfarin	0.94	0.38 2.31	0.8925
Diabetes	0.78	0.38 1.58	0.4872
Gender (male)	0.78	0.60 0.99	0.0446
Age	1.10	1.07 1.13	<0.0001

n, number of individuals; OR, odds ratio; CI, confidence interval.

Older Age & platelet aggregation inhibitors were more common in patients with disc hemorrhage

Godwin, Kelly et al. Optic Disc Hemorrhage and Optic Atrophy in Glaucoma. Volume 118, June 2022
© 2022 American Academy of Ophthalmology

Clinician Considerations

► Patient context:

- (1) Am I meeting pressure goals?
- (2) Is the patient compliant?
- (3) Do I need to more intensively follow the patient?
- (4) Escalate treatment?
- (5) Am I missing other disease processes?

Back to Our Patient

- No other causes for disc hemorrhage
- New Diagnosis – Normal Tension Glaucoma
- Patient was offered PGA vs SLT
- Elected for SLT OD
- After SLT – IOP 13 OD


Normal Tension Glaucoma

- ▶ **Diagnosis of exclusion**
- ▶ Glaucomatous optic neuropathy: cupping
- ▶ Characteristic patterns of visual field loss
- ▶ IOP < 21mmHg – check diurnal patterns
- ▶ **Progressive disease**

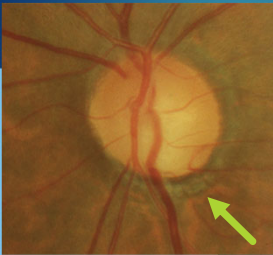
Percentage of POAG Patients with NTG

Japan	92%
Singapore	84.6%
China	51.43% - 83.58%
Netherlands	38.9%
United States	31.7%
Italy	30%

1/3 of your patients!



Common Clinical Findings




- ▶ Features of cupping:
 - ▶ Notch
 - ▶ Diffusely shallow

Beta zone atrophy – absent RPE & photoreceptors

65-year-old F, NTG

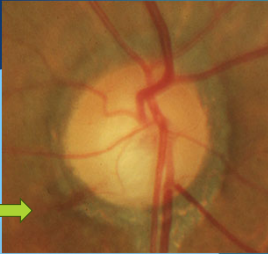
Clinical Findings



Absence of RPE seen as peripapillary crescents or halos

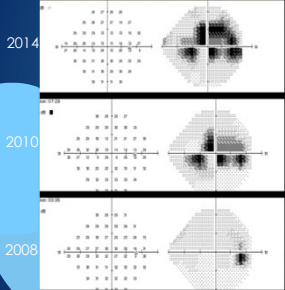
Seen more often in NTG

Disc hemorrhage



- ▶ More frequent in NTG
- ▶ Indicates progression
- ▶ Poor IOP control

NTG HVF



- ▶ VF deficit near fixation
- ▶ Progression within the paracentral VF was more common
- ▶ Alternate 10-2 and 24-2 HVF

Glaucomatous paracentral scotomas originate from blind spot


61 yo, M

NTG requires investigation!



Make sure NTG fits!

- ▶ History: lower BMI, cold hand/feet, migraines, childhood motion sickness, ?Type A personality
- ▶ Family History of 1st degree relative - (96% specific)
- ▶ Color vision (typically normal until late)
- ▶ Pachymetry, IOP with diurnal curve
- ▶ Blood work: CBC, B12/folate levels, Neurosyphilis



Associated Systemic Diseases

TABLE 3.
Systemic Metrics: An Odds Ratio > 1 Indicates a Higher Frequency in the LTG Group, Whereas an Odds Ratio of <1 Indicates a Higher Frequency in the Control Group


Systemic Factors	Odds Ratio	Confidence Interval (95%)	P
DM2	0.98	0.95-1.01	0.3
BMI < 25 vs. > 30	1.20	0.97-1.44	0.7
BMI < 25 vs. > 30	1.69	1.09-2.61	0.02
Systemic hypertension	1.64	1.17-2.31	0.004
Dyslipidemia	1.29	0.92-1.82	0.1
Diabetes mellitus	3.01	1.93-4.67	< 0.001
Obstructive sleep apnea	0.91	0.59-1.40	0.7
Coronary artery disease	1.16	0.89-1.48	0.2
Peripheral vascular disease	2.61	1.17-5.14	< 0.009
Cerebrovascular disease	1.46	0.72-2.96	0.3
Carotid stenosis	1.52	0.53-4.32	0.4
Migraines	2.12	1.11-4.04	0.02
Lupus	3.02	0.31-29.23	0.3
Raynaud syndrome	3.09	0.98-9.70	0.05
Anemia	2.18	1.31-3.61	0.003
Systemic hypotension/syncope	4.43	2.44-8.04	< 0.001
Alcohol use	0.97	0.69-1.3	0.9
Smoking history	1.00	0.70-1.43	1

Significant findings:
 BMI <25 or > 30
 Systemic HTN
 Diabetes Mellitus
 Peripheral Vasc Dz
 Migraines
 Raynaud
 Anemia
 Systemic hypotension
 Syncope

Punk et al. Multiple Systemic Vascular Risk Factors Are Associated with Low Tension Glaucoma. J Glaucoma 2022

Other causes for cupping

- ▶ 50% of GCA developed cupping vs 10% NAION
- ▶ Demyelinating optic neuritis
- ▶ Hereditary optic neuropathy
 - ▶ Leber's hereditary optic neuropathy
 - ▶ Autosomal Dominant Optic Atrophy
- ▶ Traumatic optic neuropathy
- ▶ Methanol toxicity
- ▶ Shock optic neuropathy
- ▶ Compressive lesion



Rule these out first:

- ▶ Past Steroid Use
- ▶ "Burned Out" Pigment Dispersion
- ▶ Compressive Lesion
- ▶ Vascular Cause- hypotension, anemia
- ▶ Optic Nerve Congenital Abnormality
- ▶ h/o of Uveitis
- ▶ Hypotensive Event

Who needs a MRI?

- ▶ Age < 50 years old
- ▶ Visual acuity worse than 20/40
- ▶ Color vision deficits (Dyschromatopsia)
- ▶ Atypical visual field for glaucoma
 - ▶ Dense central or cecocentral losses
 - ▶ Scotomas respect vertical meridian, temporal hemianopia
- ▶ Atypical rate of VF loss despite IOP control
- ▶ Unilateral disease
- ▶ Pallor > cupping
- ▶ Presence of HA or other neurological symptoms

Greenfield DS et al. The cupped disc: Who Needs Neuroimaging. Ophthalmology 1998; 105 (10). 1866-1874.

Collaborative NTG Study Key Findings

- ▶ Imperfect study
- ▶ Lowering IOP by 30% impacted progression: 35% of untreated vs 12% treated
- ▶ Risk factors for progression:
 - ▶ Female patient
 - ▶ Migraine
 - ▶ Disc heme

Treatment Goals

- ▶ Aim for 30% IOP reduction
- ▶ More aggressive for Females, Vasospasm or Disc heme
- ▶ Avoid certain systemic medications:
 - ▶ beta-blockers or Viagra
 - ▶ Reduce PM antihypertensives
- ▶ Check home BP when laying down

SLT and NTG

J Glaucoma. 2013 Nov 16

- ▶ 20% IOP lowering (13.5 -> 11)
- ▶ Decreases nocturnal IOP fluctuations
- ▶ In Japan: effective initial treatment for NTG

Medical treatment

- ▶ **Prostaglandins - #1**
 - ▶ good at Normotension range, 15-30% IOP reduction
 - ▶ consistent coverage over 24hrs, particularly in the nocturnal period
- ▶ **Carbonic Anhydrase Inhibitors**
 - ▶ 10 % reduction in NT, less potent
 - ▶ Good nocturnal efficacy, adjunctive to PGs
- ▶ **Brimonidine**
 - ▶ reduces 10-20% in NTG but no nocturnal control
 - ▶ LoGTS Trial Outcome : At 30 months, brimonidine group had less VF loss (9% vs 39.2%) compared to Timolol despite similar IOP

Rhopressa

- ▶ Rho Kinase (ROCK) inhibitor drugs potentially able to lower IOP from normal EVP levels (<10-12)
- ▶ Targets both TM outflow, lowers EVP & reduces aqueous production
- ▶ My experience - Amazing for 50% of patients; can't predict who

For NTG, I will try after SLT and PGA



Surgical Interventions

- ▶ Ultimately many need Trabeculectomy
- ▶ Some do well with Xen gel stents
 - ▶ I will try Xen first in those patients who are IDEAL bleb makers
- ▶ Phaco disrupts Bleb function
- ▶ Consider Phaco / OMNI or Phaco/iTrack if cataract present
- ▶ Then bleb procedure

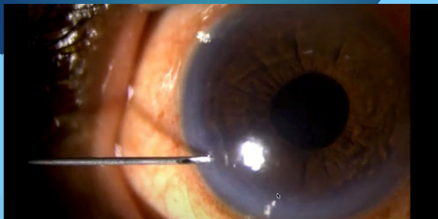
Refer early if paracentral losses

Doc, What Else Can I Do?

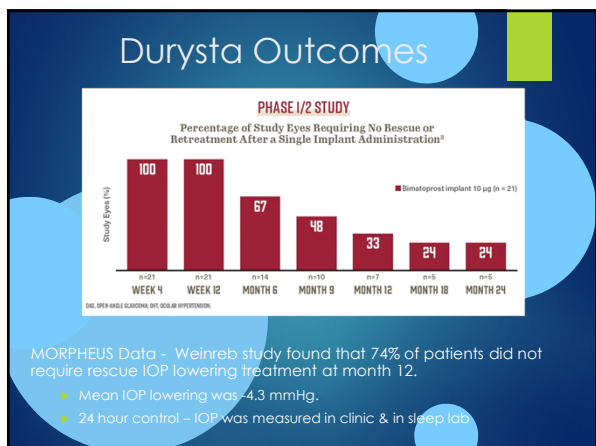
- ▶ Discuss adherence – cell phone reminders
- ▶ No Nocturnal hypotension – including Viagra
- ▶ Aim for Average BMI
- ▶ Avoid inversion/yoga/wind instruments
- ▶ Discuss sleep position – unilateral worsening w/ side sleepers
- ▶ Ginkgo biloba & Resveratrol
- ▶ Memantine – worked in animals, no effect in human RCTs
- ▶ Switch to Calcium channel blockers vs BB for HTN

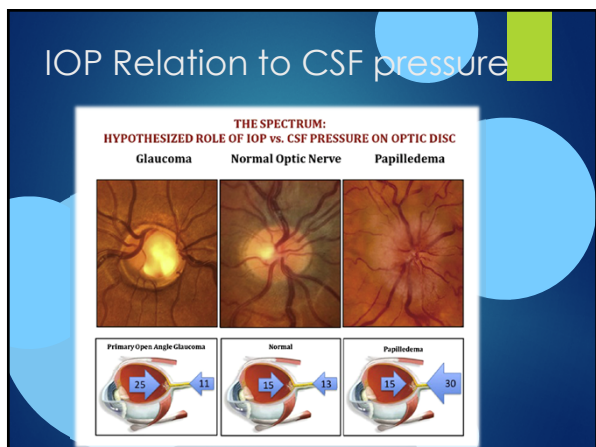
24 Hour Control – Options?

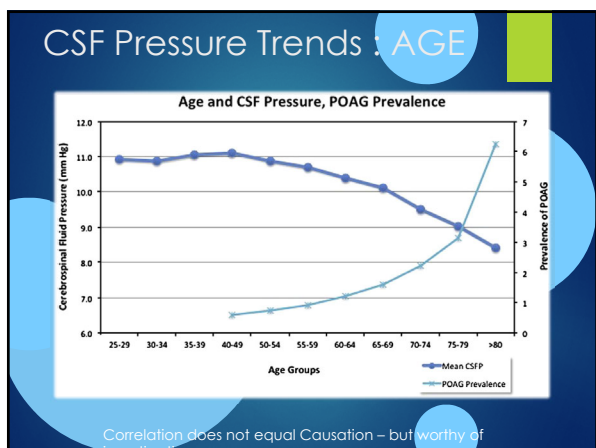
Durysta sustained bimatoprost implant



Illinois Eye Ahmad A. Aref
Video courtesy of Dr. Ahmad Aref of Illinois Eye



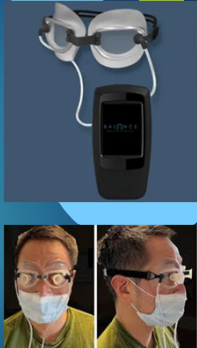




Ocular Pressure Adjusting Pump "OPAP"

Programmable pressure-modulating pump

- ▶ Designed to be compact and portable
- ▶ Two mini diaphragm pumps for creating negative pressure levels in each eye
- ▶ Each pump exerts up to -40 mmHg relative atmospheric pressure (limited to -20 mmHg)



OPAP

FDA clears for medical marketing:

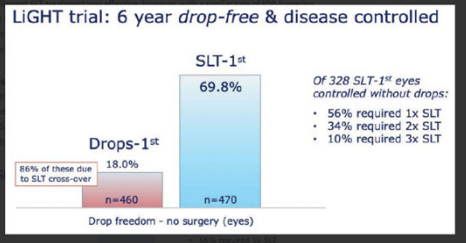
- ▶ "the data demonstrated a reasonable assurance of effectiveness as an adjunctive therapy for the indicated patient (ie: NTG/OAG) population"

Multiple studies - Data from CONFIRM Pivotal

- ≥20% IOP reduction by Week 52
- 58.1% of study eyes & (1% of control) → clinic visit (daytime)
- 63.4% of study eyes & (3% of control eyes) → sleep lab visit (night)

▶ Side effects: Eyelid edema 12%
3-5% → Dry eyes, Conjunctival hyperemia, and Eye pain

LiGHT trial: 6 year drop-free & disease controlled



Group	Drop freedom - no surgery (eyes)	SLT-1st
Percentage	18.0%	69.8%
n	n=460	n=470

Of 328 SLT-1st eyes controlled without drops:

- 56% required 1x SLT
- 34% required 2x SLT
- 10% required 3x SLT

86% of these due to SLT cross-over

By 6 years, 979 laser procedures had been performed.
Only 10 eyes has IOP rise more than 5mmHg post SLT

Less disease progression & greater time to surgery in the SLT arm than in the drops arm (drops arm had access to SLT, just not first)

LIGHT trial

- ▶ 700+ mild to moderate glaucoma patients
- ▶ 50/50 RCT - treat to target IOP
- ▶ 360 degree SLT

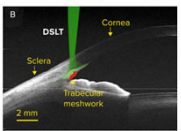
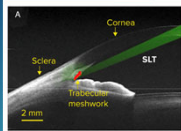
- ▶ 78% of SLT first eyes were drop/surgery free @ 3 years
- ▶ 77% only needed 1 treatment
- ▶ SLT was repeated if needed and of them, 60% met target

Belkin Direct SLT (DSL) - "Eagle" Acquired by Alcon

- ▶ FDA clearance December 2023
- ▶ May 2022 – available in the European Union (EU) and the United Kingdom (UK)
- ▶ Q-switched, 532 nm-wavelength, frequency-doubled, (Nd:YAG) laser device



- ❖ 120 pulses of 1.8 mJ
- ❖ 400 micron diameter
- ❖ 7 nanosecond pulse



- ❖ Circular & consecutive pattern
- ❖ Automated algorithm w/ eye tracking
- ❖ No Gonioscopy Lens Non Contact
- ❖ Set up patient
- ❖ Adjust target treatment
- ❖ Press the button

