Optimizing the Ocular Surface in Glaucoma

Justin Schweitzer, OD, FAAO
Optometric Externship Director
Associate Optometric Residency Director
Vance Thompson Vision, Sioux Falls, South Dakota

Financial Disclosure – Justin Schweitzer, OD, FAAO

- Aerie C/L
- Alcon C/L
- Allergan C/L
- Bausch + Lomb C/L
- Ocular Therapeutix C
- EyePoint C
- Sight Sciences C/L
- Dompe C
- Zeiss C/L
- Visus C
- Science Based Health C
- Kala C
- RVL C
- Santen C

- Sun C/L
- Equinox I
- Reichert C
- J&J C/L
- Glaukos C/L
- Horizon C
- Quidel C
- MediPrint C
- LKC C/L
- Avellino C
- Novartis C
- Iveric bio C
- Ocuphire C
- Tarsus C



The Long Time Glaucoma Patient

"My eyes are red on a daily basis and my vision fluctuates."

"I do miss my drops off and on – and my eyes feel better when I do"

Redefining "Controlled Glaucoma"



IOP/VF/ON



Quality of life

Fluctuating vision
Needing samples
Can't remember the bottle color

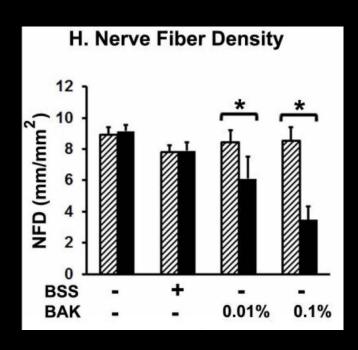


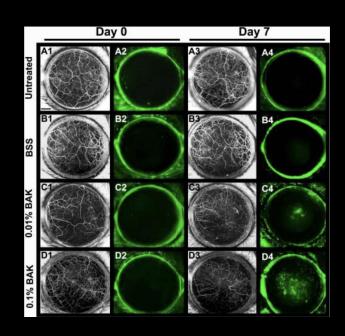
"Not Controlled"

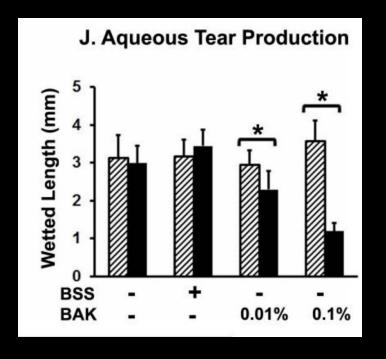
Glaucoma Therapy and the Ocular Surface

Neurotoxicity of BAK

- Exposure to BAK (0.01% or 0.1%) QD x 7 days:
 - Decrease NFD (p=0.02 & 0.001)
 - Decrease aqueous production (phenol red)







Effects on Meibomian Glands

Effect on lids/meibomian glands

Study on glaucoma patients 18mo stable treatment with different medications.

Reduced number of meibomian glands

Reduced numbers of acinae and increased dysfunction in patients

Patients on multiple medications with preservatives = increased dysfunction and reduced number of acinae

Table 3	Clinical	characteristics
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	OSDI score	BUT	STI	Corneal staining	Meibo score	Meibum score
Controls	9.5±4.8*	12.0±2.1*	18.0±5.0*	0.3±1.1*	0.12±0.03*	1.30±0.72*
Group 1	16.4±5.4**	7.2±1.9**	9.3±5.1**	1.9±2.3	0.48±0.32	2.05±0.91
PF drugs	9.4±3.5***	7.7±1.8****	9.1±3.1****	1.9±2.2	0.44±0.41	1.98±0.68
Preserved drugs	18.7±4.1****	6.1±1.9****	9.4±6.1****	1.9±1.8	0.53±0.44	2.12±1.03
Group 2	30.8±6.7	4.1±1.5	7.2±2.7	2.3±2.1	0.54±0.38	2.23±1.15
Group 3	32.6±7.2	3.9±1.5	6.8±2.7	2.2±1.9	0.57±0.63	2.21±1.23

^{*}p<0.05 vs groups 1, 2 and 3.



^{**}p<0.05 vs groups 2 and 3.

^{***}p<0.05 vs group 1 preserved drugs and vs groups 2 and 3.

^{****}p<0.05 vs groups 2 and 3.

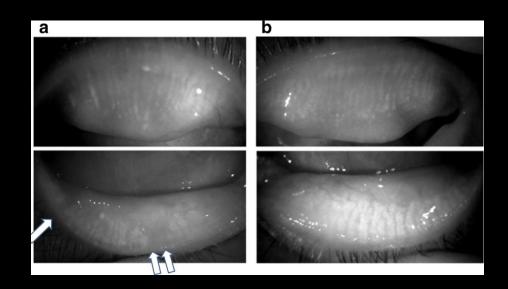
BUT, break-up time; OSDI, Ocular Surface Disease Index; PF, preservative free; STI, Schirmer test I.

Effects on Meibomian Glands

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Arita, et al. 2012; 1 eye treated with glaucoma meds, other eye control. N= 31.
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Mean duration eye drop use 7.9 +/-6.0 years

Significant findings:



Glaucoma Therapy Exacerbated Ocular Surface Disease

101 treated glaucoma/OHTN patients completed OSDI 59% of patients had symptoms of OSD Rate of OSD symptoms increases with number of BAK-containing drops

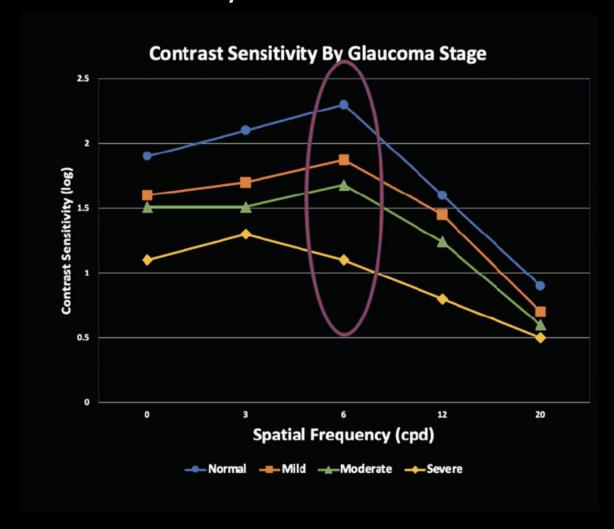
- 1 BAK drop: ~52% of patients with symptoms
- 2 BAK drops: ~62% of patients with symptoms
- 3 BAK drops: ~68% of patients with symptoms

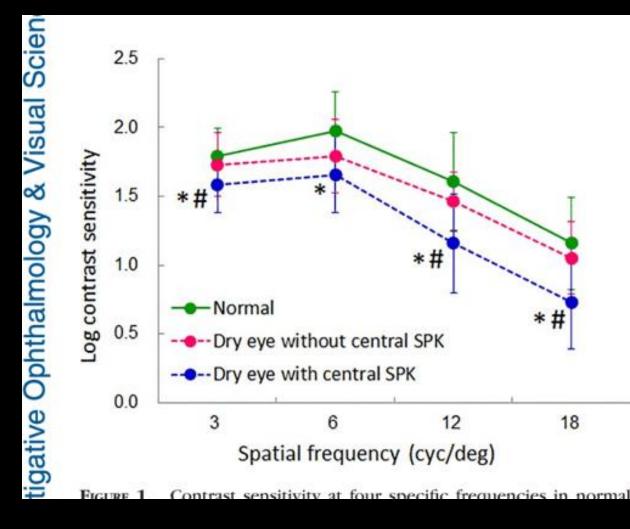
Why Should We Care About the Ocular Surface in our Glaucoma Patients?

Impact of Multiple Glaucoma Medications on Dry Eye Disease

Number of Drops	Incidence of DED among 61 glaucoma patients ¹	Incidence of DED among 19,665 glaucoma patients ²
1	11%	51%
2	39%	55%
3+	40%	60%

Glaucoma and Dry eye – Contrast Sensitivity





Dry eye and glaucoma medication compliance

DED IS A COMMON REASON FOR DISCONTINUATION OR INADEQUATE ADHERENCE/COMPLIANCE TO GLAUCOMA TREATMENT¹,

DED symptoms
were a predictor of
noncompliance in
a study of 74 patients
with glaucoma²

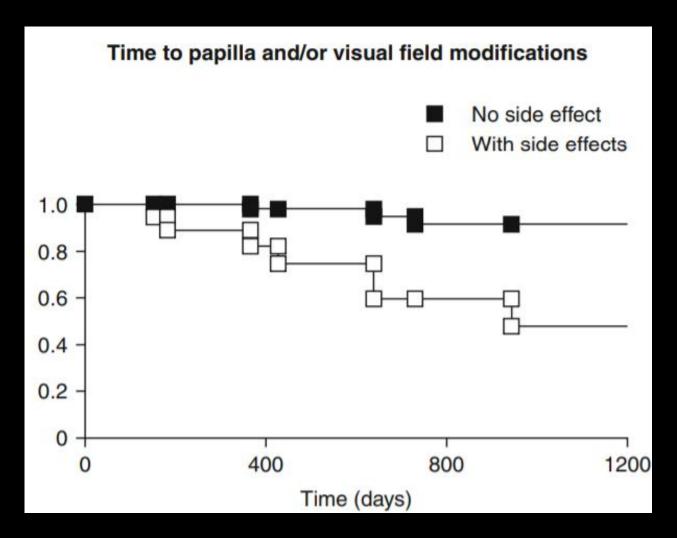
	Compliance rate with glaucoma medications ²
Patients WITHOUT DED symptoms	89%
Patients WITH DED symptoms	63%

BAK has negative effects on Outflow and Surgical Outcomes²

^{1.} Baudouin C. *Acta Ophthalmologica*. 2008;86(7):716–726. 2. Stringham J et al. *Eye & Contact Lens*. 2018;44:50-54.

^{2.} J Glaucoma 2013;22:730-735.

Treatment Challenges



[•] Denis, Philippe, et al Medical outcomes of glaucoma therapy from a nationwide representative survey

Solutions?

Preservative-Free Formulations

N=349, Significant improvement in both signs and symptoms of OSD with switch to PF meds

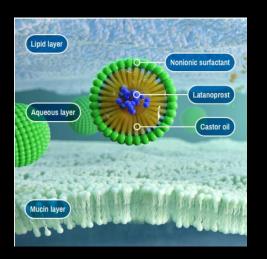
	Visit 1 (preserved)		Visit 2 (preservative free)		
	No*	(%)	No*	(%)	p Value
Patient symptoms					
Discomfort upon instillation	196/340	57.6%	40/343	11.7%	< 0.001
Patients presenting with at least one symptom between instillations	283/342	82.7%	123/344	35.8%	< 0.001
Ocular signs found at the clinical examination (patients presenting with at least one)					
Palpebral sign (Rienharitis)	122/342	35.7%	50/346	14.5%	< 0.001
Palpebral sign (Blepharitis) Conjunctival sign	233/338	68.9%	74/338	21.9%	< 0.001
Superficial punctate keratitis	85/334	25.4%	18/337	5.3%	< 0.001

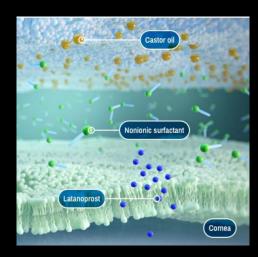
Pisella, P. J., P. Pouliquen, and C. Baudouin. Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication

BAK-Free Latanoprost

Following instillation, micelles mix with the tear film

As the micelles migrate toward the ocular surface, they break apart, releasing latanoprost



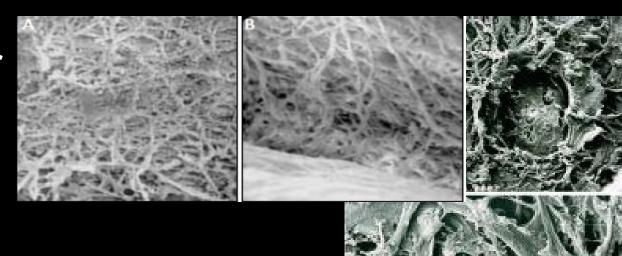


Preservative-Free

SINGLE	LAT (Latanoprost 0.005%)**	7.5mL
SIN	DOR (Dorzolamide 2%)	10mL
	BRIM-DOR ® (Brimonidine 0.15% and Dorzolamide 2%)	10mL
	TIM-LAT® (Timolol 0.5% and Latanoprost 0.005%)**	5mL
ATION	TIM-DOR-LAT® (Timolol 0.5%, Dorzolamide 2%, and Latanoprost 0.005%)**	5mL
COMBINATION	TIM-BRIM-DOR® (Timolol 0.5%, Brimonidine 0.15%, and Dorzolamide 2%)	10mL (2 X 5mL bottles per shipment)
	TIM-BRIM-DOR-LAT® (Timolol 0.5%, Brimonidine 0.15%, Dorzolamide 2%, and Latanoprost 0.005%)**	5mL
TRIPLE/QUAD KIT	TIM-BRIM-DOR® (Timolol 0.5%, Brimonidine 0.15%, and Dorzolamide 2%) TIM-BRIM-DOR-LAT® (Timolol 0.5%, Brimonidine 0.15%, Dorzolamide 2%, and Latanoprost 0.005%)**	5mL
¥		

Selective Laser Trabeculoplasty

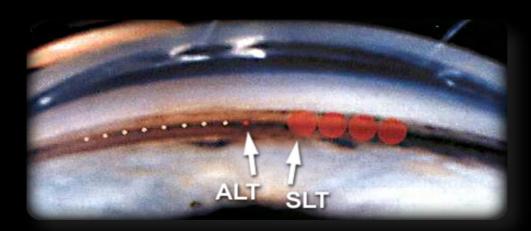
Selectively targets and laser burns pigmented TM cells



Mechanism of Action



SLT uses a Q-switched, 3 nanosecond pulsed, frequency-doubled Nd:YAG; 532 nm wavelength green laser

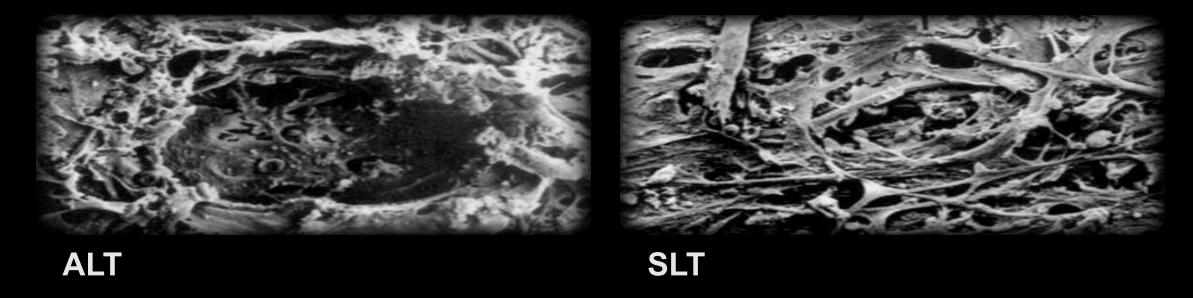


Larger beam diameter with SLT

- Reduces need for focus
- Evenly distributes laser energy

1. Latina MA, Sibayan SA, Shin DH, et al. *Ophthalmology*. 1998;105:2082-2090. 2. Latina MA, Park C. *Exp Eye Res*. 1995;60:359-372. 3. Alvarado JA, Alvarado RG, Yeh RF, Franse-Carman L, et al. *Br J Ophthalmol*. 2005;89:1500-1505. 4. Damji KF, Bovell AM, Hodge WG. *Ophthalmic Pract*. 2003;21:54-58. 5. Kramer TR, Noecker RJ. *Ophthalmology*. 2001;108:773-779.

The Advantages of Selectivity



- ALT causes coagulative damage that leads to scarring of the trabecular meshwork
- SLT treatments do not cause the coagulative damage associated with ALT. Therefore, SLT is believed to improve aqueous outflow and regeneration of the trabecular meshwork

Lancet. 2019 Apr 13;393(10180):1505-1516. doi: 10.1016/S0140-6736(18)32213-X. Epub 2019 Mar 9.

Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial.

Gazzard G¹, Konstantakopoulou E², Garway-Heath D², Garg A², Vickerstaff V³, Hunter R⁴, Ambler G⁵, Bunce C⁶, Wormald R⁷, Nathwani N⁸, Barton K², Rubin G⁹, Buszewicz M⁴; LiGHT Trial Study Group.

Primary Outcome - Quality of Life at 3 years Secondary Outome - Cost, cost-effectiveness, clinical effectiveness, and safety

Conclusions:

No significant difference in QOL

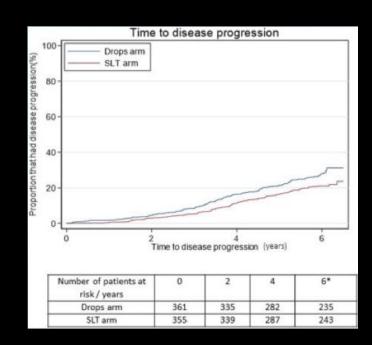
97% probability of SLT as 1st treatment being

more cost-effective

SLT at target IOP 93% of visits vs 91.3% at

target for meds

78.2% of SLT Drop Free @ 3 Years



LiGHT trial: 6-year results of primary selective laser trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension

Gus Gazzard, Evgenia Konstantakopoulou, David Garway-Heath, Mariam Adeleke, Victoria Vickerstaff, Gareth Ambler, Rachael Hunter, Catey Bunce, Neil Nathwani, Keith Barton, on behalf of the LiGHT Trial Study Group

Primary Outcome - Quality of Life at 6 years Secondary Outome - clinical effectiveness and safety

Conclusions:

No significant difference in QOL

26.8% VS 19.6% progressed drops vs SLT

Trab required in 32 eyes in drops arm compared to 13 eyes in the SLT arm 69.8% of SLT Drop Free @ 6 Years

Low-Energy SLT Repeated Annually: Rationale for the COAST Trial

Tony Realini, MD, MPH, Gus Gazzard, MD, Mark Latina, MD, Michael Kass, MD

Newly diagnosed POAG treated with:

- 1. ALT 360 x 1
- 2. Standard SLT 360 as needed
- 3. Low-energy SLT 360 repeated annually

10-year Results
Medication Free Rates

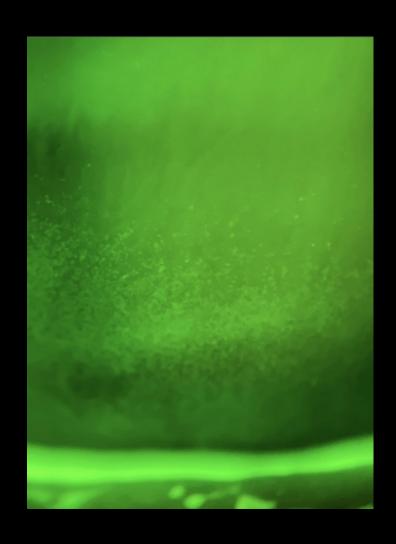
- 1. ALT 22.6%
- 2. Standard SLT -25.0%
- 3. Low-energy SLT 58.3%

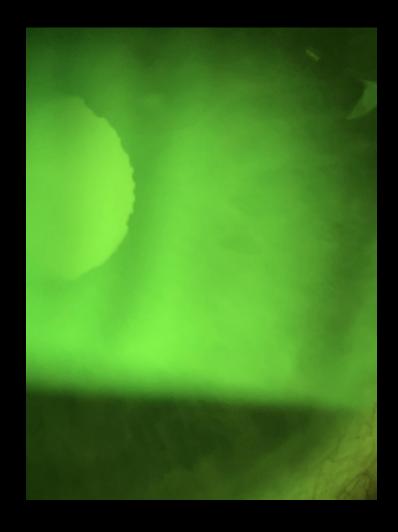
10-year Results

Median Times to Treatment

- 1. ALT 2.8 years
- 2. Standard SLT -3.2 years
- 3. Low-energy SLT 6.2 years

Pre and post SLT





Iridocorneal Angle

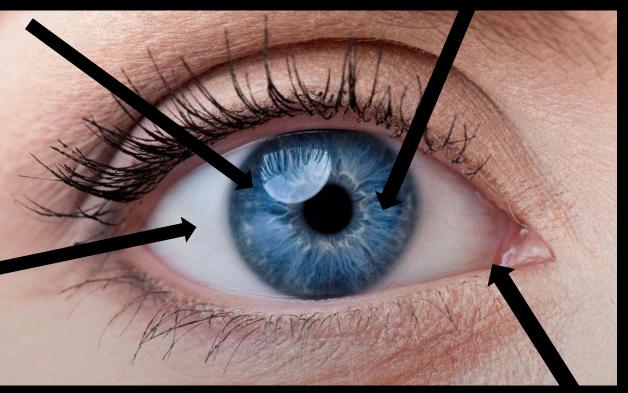
1. Travoprost Intraocular Implant (Glaukos)

Injectable Systems

- 1. Bimatoprost SR (Allergan)
- 2. Travoprost Intracameral Implant (OTX)
- 3. Travoprost Extended Release Implant (Aerie)

Ocular Surface Devices

- 1. Contact Lenses
- 2. Microdose latanoprost
- 3. Iontophoresis



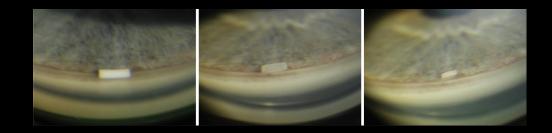
Punctal Plug Devices

- 1. Travoprost Intracanalicular Insert (OTX)
- 2. Latanoprost and Travoprost punctal plug delivery system (Mati)

Glaucoma Drug Delivery

Bimatoprost SR (Allergan) (10-microgram bimatoprost sustained-release implant)

- Biodegradable bimatoprost sustained-release implant
 FDA-approved and indicated to reduce IOP in patients with open angle glaucoma or OHT
- Single intracameral administration
- Phase I/II/III Studies







24 Month Phase I/II Clinical Trial

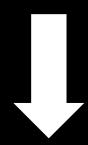
bimatoprost pellet

(6, 10, 15, or 20 micrograms)



24 months – IOP reduction 7.5, 7.3, 7.3, 8.9 mm Hg

topical bimatoprost 0.03%



24 months – IOP reduction of 8.2 mm Hg

No Rescue or Retreatment

68% - 6 mos.

40% - 12 mos.

28% - 24 mos.

Craven ER, Walters T, Christie WC, Day DG, et al. 24-Month Phase I/II Clinical Trial of Bimatoprost Sustained-Release Implant (Bimatoprost SR) in Glaucoma Patients. Drugs. 2020 Feb;80(2): 167-179.

Ocular Surface Disease and Minimally Invasive Glaucoma Surgery



OSD and MIGS



82.4%

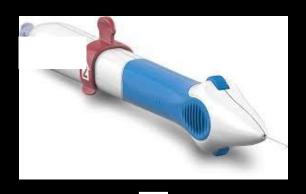
1.7 meds to 0.3 meds

Samuelson TW, et al; HORIZON investigators. A Schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: The HORIZON Study. Ophthalmology. 2019;126(1);29-37.



75% 1.6 meds to 0.4 meds

Samuelson TW, et al; iStent inject Study Group. Prospective, randomized, controlled pivotal trial of an ab interno implanted trabecular micro-bypass in primary open-angle glaucoma and cataract. Ophthalmology. 2019;126(6);811-821.



35% 1.7 meds to 1.1 meds

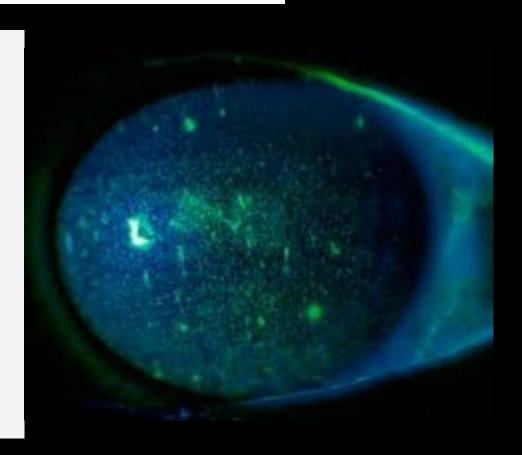
Sarkisian SR, Mathews B, Ding K, Patel A, Nicek Z. 360° ab-interno trabeculotomy in refractory primary open-angle glaucoma. Clin Ophthalmol. 2019;13:161-168.

Prospective Interventional Cohort Study of Ocular Surface Disease Changes in Eyes After Trabecular Micro-Bypass Stent(s) Implantation (iStent or iStent *inject*) with Phacoemulsification

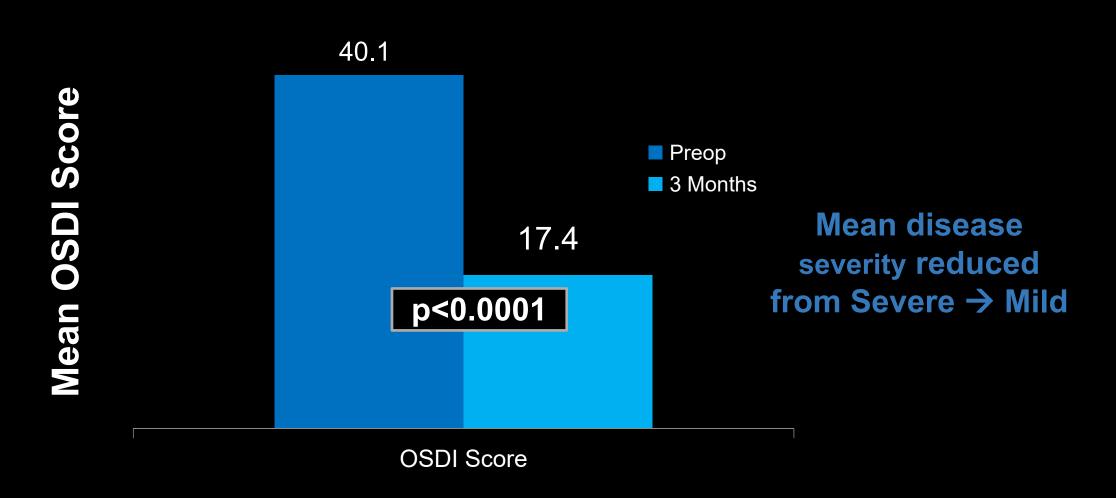
Justin A. Schweitzer, M1 Whitney H. Hauser, Mitch Ibach, Brandon Baartman, Subba R. Gollamudi, Andrew W. Crothers, John E. Linn, and John P. Berdahl

Study Design

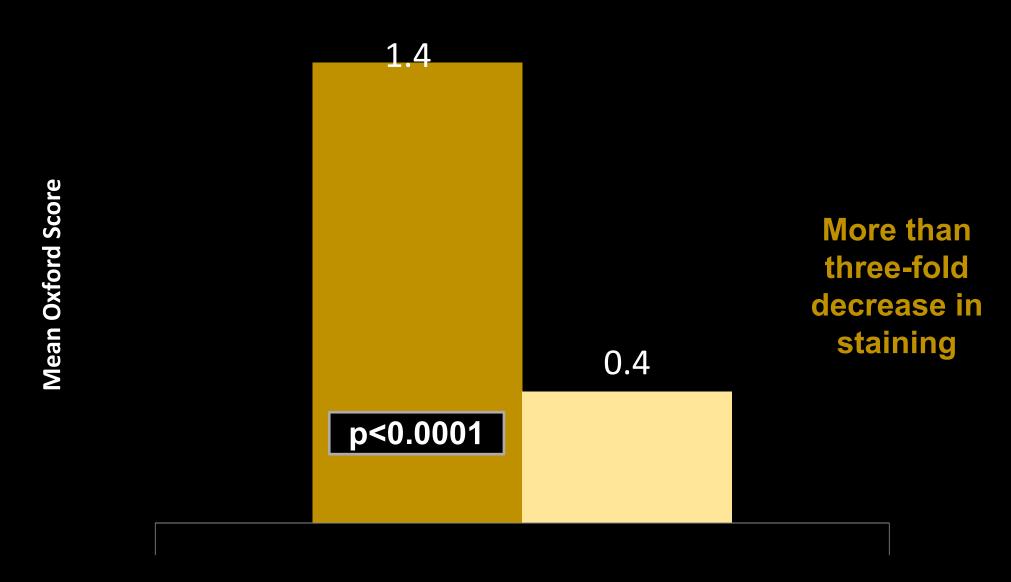
- Prospective multi-surgeon study at 2 U.S. sites
- Trabecular meshwork bypass stent implantation with phaco in 50 eyes with OAG and cataract
- Follow-up through 3 months postop
- Measures:
 - IOP and # topical meds (glaucoma drops, artificial tears, ocular surface meds)
 - Ocular Surface Disease Index (OSDI)
 - Corneal/conjunctival staining (Oxford Scale)
 - Fluorescein tear break-up time (FTBUT)
 - Conjunctival hyperemia (Efron Scale)



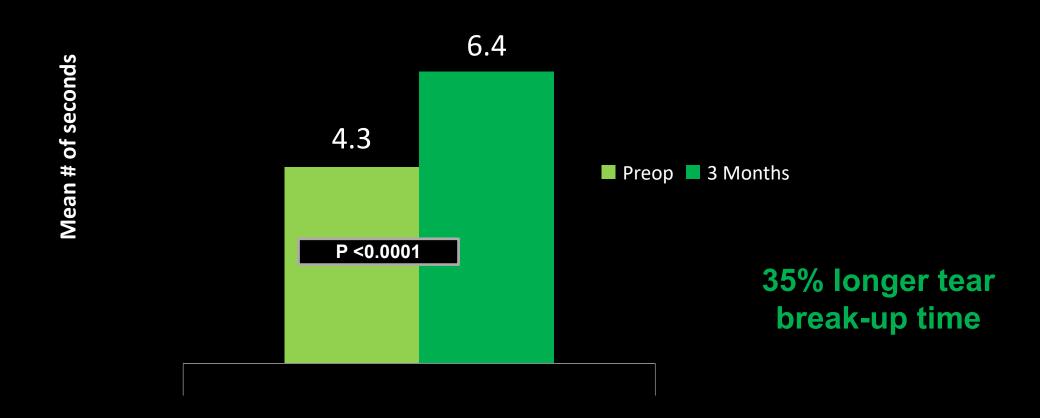
Significant Improvement in Ocular Surface Disease Index



Significantly Reduced Corneal Staining



Significantly Longer Tear Break-Up Time



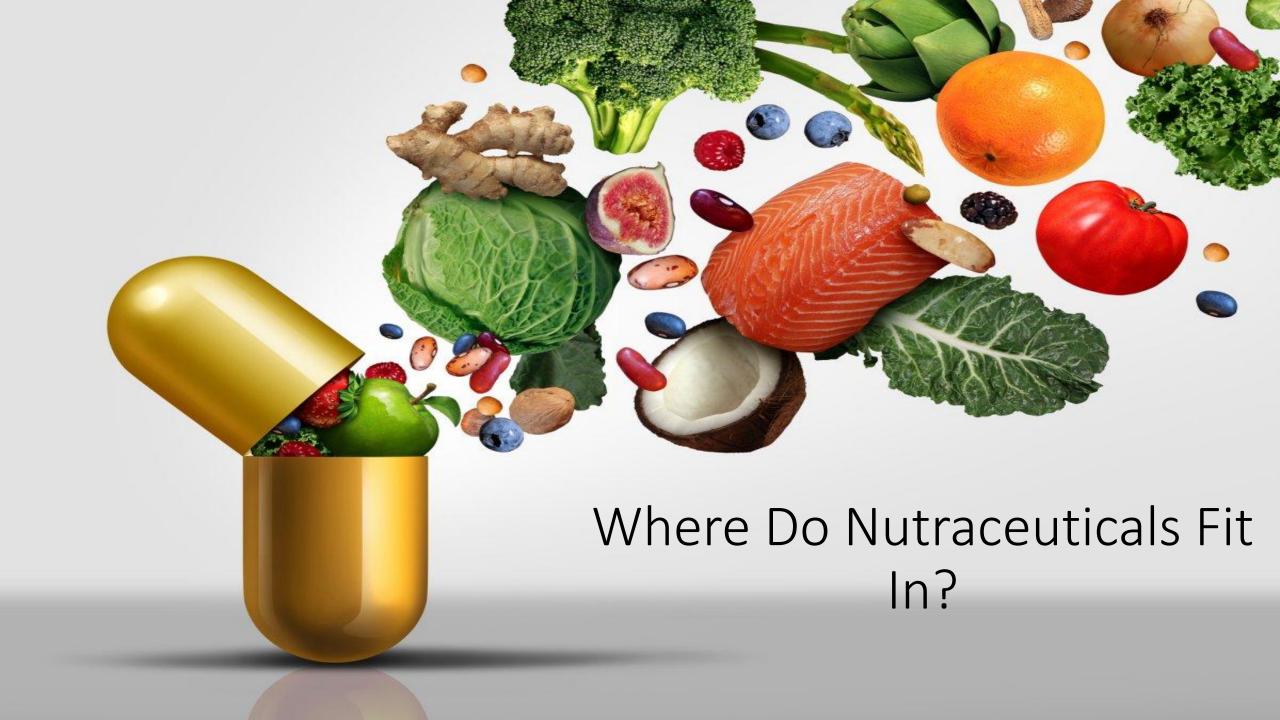
Additional Treatment Considerations



Doxycycline vs Azithromycin

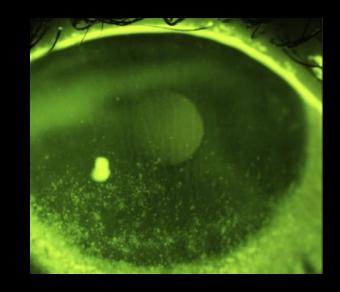
Purpose: To assess the efficacy and safety of oral azithromycin compared with oral doxycycline in patients with MGD who had failed to respond to prior conservative management

Conclusion: Both improved symptoms of MGD, but 5-day oral azithromycin is recommended for its better effect on improving signs, better overall clinical response and shorter duration of treatment.





	te: /				
of Fire Down		Sex: M	F (Circle)	DOB:	/
		Questionnaire, p ne answer per q		er the following	questions by
experience	and when th	ey occur:			
At this	visit	Within past 72 hours		Within past 3 months	
Yes	No	Yes	No	Yes	No
П					
	П		П		
			П		
+	Н		H	7	
\perp	Ш				
en 3=0	Constant				
	Constant ne rating list	below:	3	4	
ms using th	ne rating list		3	4	
ms using th	ne rating list		3	4	
ms using th	ne rating list		3	4	
	At this Yes	At this visit Yes No N	Yes No Yes ptoms using the rating list below:	At this visit Within past 72 hours Yes No Yes No Total Part of the Part of th	At this visit Within past 72 hours Yes No Yes No Yes Person No Yes No Yes Person No Yes Pers

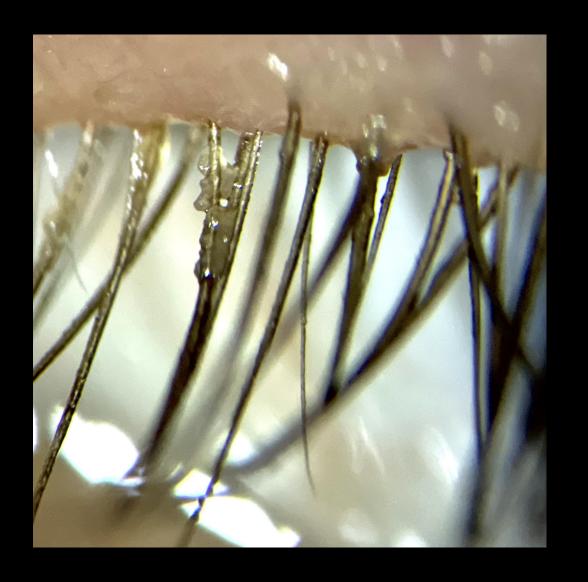




Look Lift Pull Push Look Down

Don't Forget Demodex





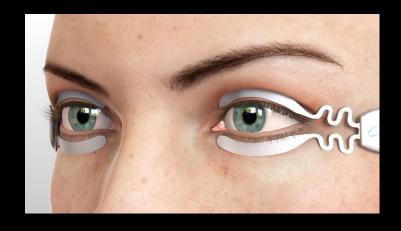
Thermal Pulsation Treatment

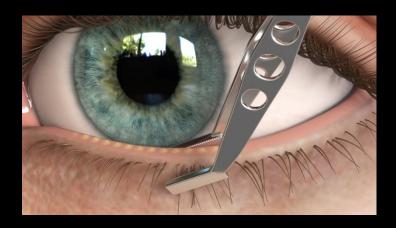




Apply Heat and Manual Expression







Procedure

- 1. Place iLid Devices on patient's lower and upper lids
- 2. Heat delivered to eyelids while patient's eyes remain open and blinking
- 3. Clear: lower and upper lids

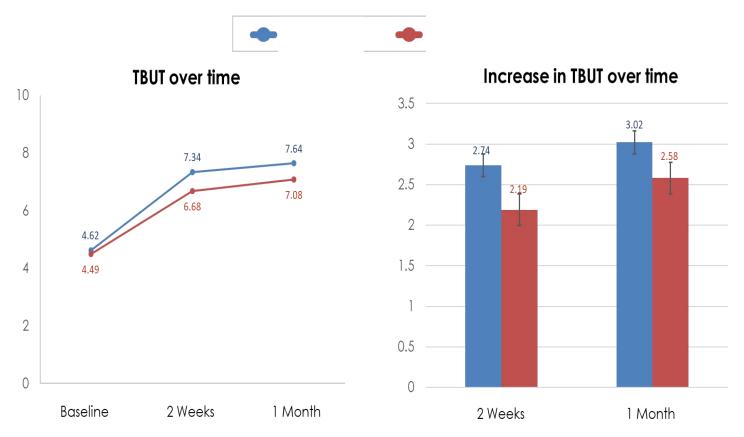
A Novel, Targeted, Open Eye, Thermal Therapy and Meibomian Gland Clearance in the Treatment of Dye Eye:

A Randomized Controlled Investigator masked Trial (OLYMPIA)

Jennifer M. Loh, MD, ABO; William B. Trattler, MD, ABO; Kavita P. Dhamdhere, MD, PhD; Marc R. Bloomenstein, OD; John A. Hovanesian, MD; Mitchell A. Jackson, MD, ABO; Bobby Saenz, OD

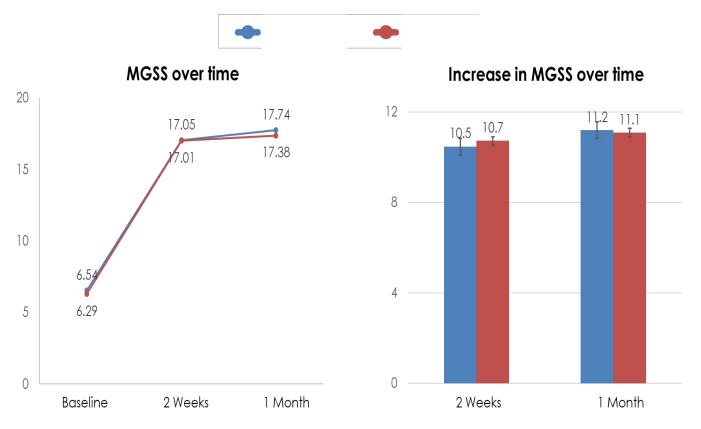
Presented by Jennifer M. Loh, MD, ABO; ASCRS May 16, 2020

Primary Endpoint: Tear Film Break-Up Time (TBUT)



> Statistically significant increase (p<0.0001)in mean TBUT in both groups at all f/u time points

Primary Endpoint: Meibomian Gland Secretion Score (MGSS)

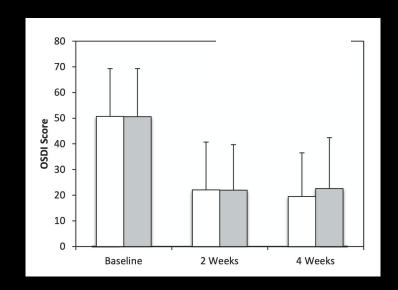


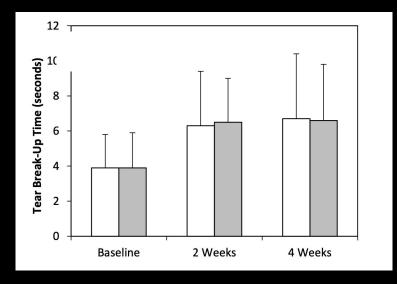
> Statistically significant increase (p<0.0001)in mean MGSS in both groups at all f/u time points

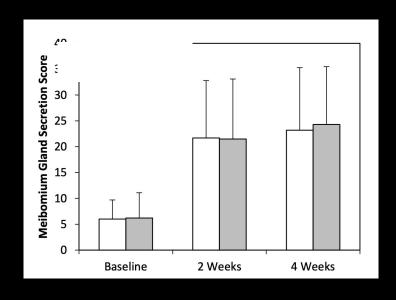
Thermal Pulsation Treatment



Comparison of Two Thermal Pulsation Technologies for the Treatment of MGD and Symptoms: A Randomized Clinical Trial







IPL for Dry Eye?

The specific mechanism of action is not well understood but is believed to be partially due to the thermal heating of the meibum coupled with the therapeutic effects of treating superficial telangiectasia.



Analysis of Cytokine Levels in Tears and Clinical Correlations After Intense Pulsed Light Treating Meibomian Gland Dysfunction



RUIXING LIU, BEI RONG, PING TU, YUN TANG, WENJING SONG, ROLANDO TOYOS, MELISSA TOYOS, AND XIAOMING YAN

- PURPOSE: To investigate the change from baseline of inflammatory markers in tears of dry eye disease (DED) subjects owing to meibomian gland dysfunction (MGD) after intense pulsed light (IPL) treatment and meibomian gland expression (MGE) compared to sham treatment, and the correlations with ocular surface parameters.
- DESIGN: Randomized, double-masked, controlled study.
- METHODS: Those randomized into the active treatment arm received 3 consecutive treatments (14~16 J/cm²) approximately 4 weeks apart in the periocular region. Control eyes received 3 treatments in the same intervals of 0 J/cm2. Tear samples in all eyes were collected and analyzed at baseline, week 12, and/or week 4 for interleukin (IL)-17A, IL-6, and prostaglandin E2 (PGE2). The correlations between cytokines and ocular surface parameters were analyzed before and after IPL treatment. · RESULTS: All of the inflammatory markers declined in value compared to baselines. IL-17A and IL-6 showed statistically significant decreases compared to sham treatment at each measured time point. PGE2 showed statistically significant decreases compared to sham at week 12. Results showed that the expressions of IL-17A and IL-6 correlated well with ocular surface parameters of the lower eyelid before IPL. The changed values of IL-6 and PGE2 in tears correlated with the changed values of partial ocular surface parameters after IPL treatment in study eyes, respectively.
- CONCLUSIONS: The study results suggest that IPL can significantly reduce inflammatory markers in tears of patients suffering with DED owing to MGD after IPL treatment. These findings indicate that IL-17A and IL-6 play roles in the pathogenesis of DED owing to MGD, and the reduction of the inflammatory factors is consistent with the improvement of partial clinical symptoms and signs. (Am J Ophthalmol 2017;183:81-90. © 2017

AIO.com Supplemental Material available at AJO.com. Accepted for publication Aug 23, 2017.

From the Departments of Ophthalmology (R.L., B.R., Y.T., W.S., X.Y.) and Dermatology (P.T.), Peking University First Hospital, Beijing, China; and Toyos Clinic, Germantown, Tennessee (R.T., M.T.).

Inquiries to Xiaoming Yan, Department of Ophthalmology, Peking University First Hospital, Beijing 100034, P. R. China; e-mail: yatuxiaoming/908@163.com

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RY EYE DISEASE (DED) ATTRIBUTABLE TO MEIBOmian gland dysfunction (MGD) represents a common and growing public health issue, particularly in older adults. MGD is a common cause of evaporative dry eye, affecting almost 70% of the population in some parts of the world, especially in Asia. Meibomian glands are the largest sebaceous glands in the human body. Meibomian glands synthesize and secrete a mixture of lipids, termed meibomian oil or meibum, 2,3 which is delivered as a clear liquid via orifices located directly in front of the mucocutaneous junction. MGD produces an abnormal meibum that becomes more stagnant than the usual clear liquid secretions. 4,5 MGD and associated evaporative tear loss is followed by increasing inflammation on the surface of the eye and bacterial overgrowth, as abnormal lipids can provide a rich substrate for the resident bacterial microbiota. The subsequent release of toxic bacterial products, such as lipases, and the production and release of proinflammatory cytokines are pathogenic. This malfunction leads to worsening of abnormal meibum, discomfort, and further derangements of the ocular surface and tear film. Although there are different pathogenic mechanisms responsible for DED owing to MGD, evidence increasingly suggests that all forms of MGD are characterized by varying ocular surface inflammation.^{6,7} Many investigators have reported that the chronic inflammatory status in patients with MGD is associated with high concentrations of tear cytokines.8-12 Currently approved topical medications for dry eye, such as cyclosporine and lifitegrast, target inflammation on the ocular surface. 13,14

Intense pulsed light (IPL) therapy uses light energy to affect the skin surface, and is widely used in dermatology to treat a variety of conditions, including facial rosacea, port wine stains, seborrheic keratosis, and hypertrophic scar. ¹⁵ In addition, the IPL device emits energy in a band from a base of the visible spectrum (580 nm) to near-infrared (1200 nm). ¹⁶ Concurrent ocular surface health improvements have been observed serendipitously in

Results:

- All of the inflammatory markers declined in value compared to baselines.
- IL-17A and IL-6 showed statistically significant decreases compared to sham treatment at each measured time point.
- PGE2 showed statistically significant decreases compared to sham at week 12.
- Results showed that the expressions of IL-17A and IL-6 correlated well with ocular surface parameters of the lower eyelid before IPL.

Conclusion

OSD is common in our glaucoma patients OSD effects QOL, patient outcomes, and maybe IOP BAK is deleterious to the ocular surface

BAK is deleterious to the ocular surface Alternative therapies are safe, effective, and a quickly growing form of treatment

Thank you!!

Justin.Schweitzer@vancethompsonvision.com