

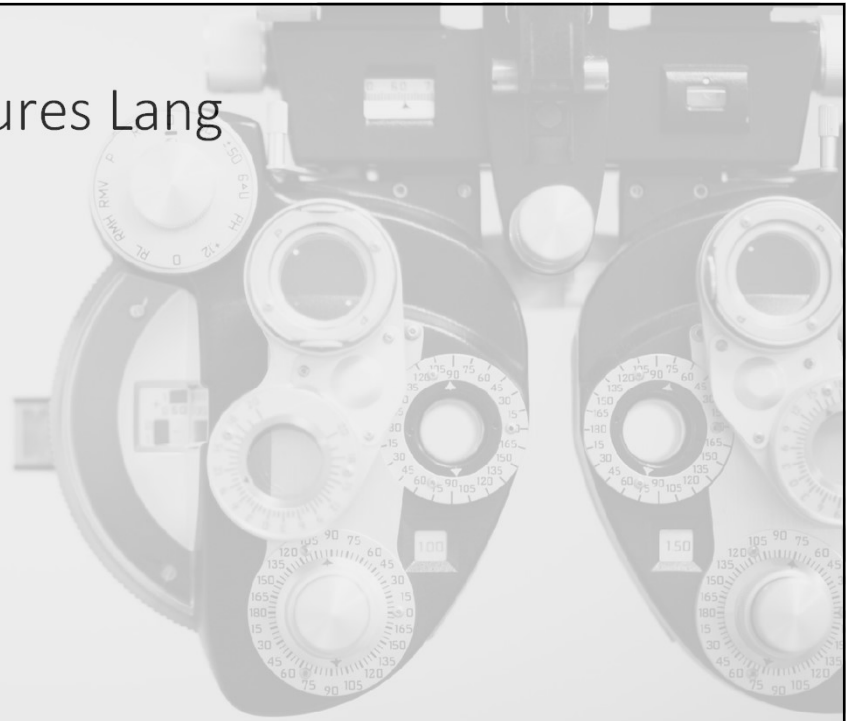
Ocular Surface Mythbusters

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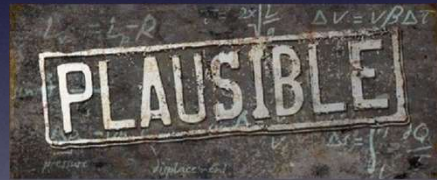
Financial Disclosures Lang

- Allergan
- Avellino
- Aldeyra
- Dompe'
- Kala
- Novartis
- AOS
- Scope
- Sun Pharma
- Tarsus
- Quidel
- Horizon
- Aerie
- Ocular Therapeutix
- Orasis
- Oyster Point



MythBusters?

- You Pick!



Myth;

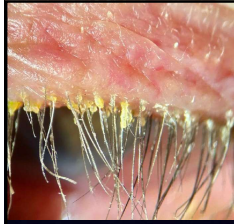
- Ocular Surface Disease Patients have an **“Infection”**
- VS “Inflammation”

OSD Infections

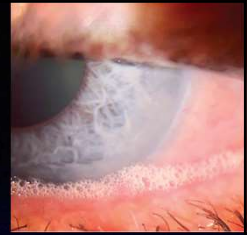
- What common pathogens might be associated with OSD/Dry Eye/ MGD?

OSD Infections

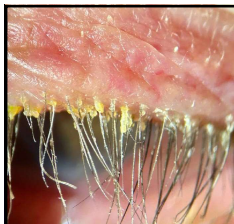




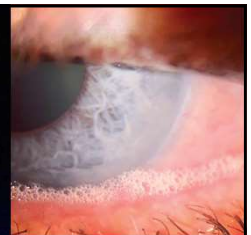
OSD Infections



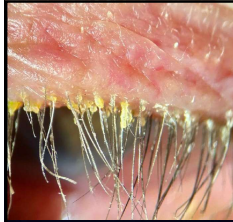
- Do Staph. sp. cause OSD?
 - Marginal Ulcers
 - Ulcerative Blepharitis
 - Inflammation
 - Hyperosmolarity and Hyper-Evaporative States?



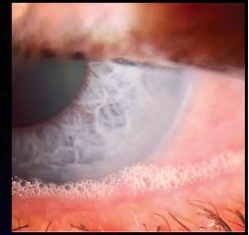
OSD Infections



- Do Demodex sp. cause OSD?
 - There are two species of Demodex mites
 - Demodex folliculorum and Demodex brevis.
 - Folliculorum are generally larger and call the base of the eyelash follicles their home, while brevis are smaller and reside in the sebaceous glands.
 - These mites are specific to humans. In fact, Demodex are a normal part of the lid environment and are the most common ectoparasite of human skin.



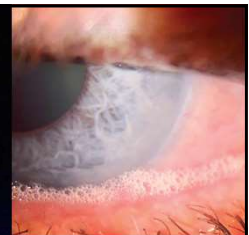
OSD Infections



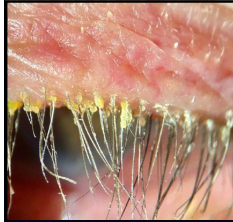
- Do Demodex sp. cause OSD?
- Infestation has been implicated in a variety of dermatologic and anterior segment conditions.
- Many of the consequences of demodicosis are thought to occur due to immune response and inflammatory reactions.
- Demodex has also been found to act as a mechanical blockage in sebaceous glands and is associated with hordeolum and chalazia formation.



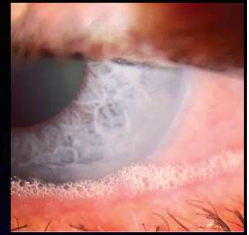
OSD Infections



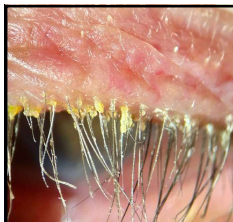
- Do Demodex sp. cause OSD?
- Demodex makes its living by eating sebum with its pin-like mouthparts.
- Although the mites have no excretory orifice, their digestion occurs internally, driven by lipase enzymes. Waste is regurgitated externally through the “mouth.”
- The death and breakdown of the chitinous exoskeletons has been shown to induce an inflammatory immune response.
- Demodex hosts several types of bacteria, including Staphylococcus and Bacillus oleronius, which may perpetuate inflammatory processes or responses on their own accord.



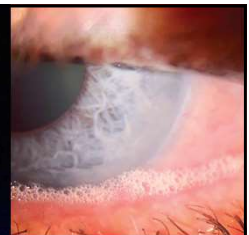
OSD Infections



- Do Demodex sp. cause OSD?
- Undigested waste, lipids, keratin, Demodex eggs, and dead Demodex mites migrate out of the eyelash follicle and accumulate around the base of the eyelashes to form the pathognomonic sign of Demodex blepharitis, described as collarettes or cylindrical dandruff (Figure).



OSD Infections



- Do Demodex sp. cause OSD?
- One study found the prevalence of Demodex blepharitis to be 57.7% among all patients visiting eye care clinics, using the presence of collarettes as diagnostic criteria.² In a study of eyelashes with and without collarettes, 100% of the lashes with collarettes were found to have Demodex mites.

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Ocular Surface Disease Patients have an "Infection".

Confirmed

Plausible

Busted

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Myth;

- Conjunctivochalasis (CCH) is redundant tissue and therefore requires procedural removal of the excess tissue to treat the condition.

Conjunctivochalasis

- Conjunctivochalasis (CCH) is a common OSD co-insider.



Conjunctivochalasis



- CCH is defined as loose, redundant conjunctival tissue most commonly found in the inferior bulbar conjunctiva.
- It is frequently identified based on conjunctival folding, staining, and prolapse.
- The prevalence of CCH has been shown to increase with age; the incidence ranges between 44% and 98% of individuals 60 years of age and older.
- Investigators theorize that the cause of CCH lies in processes such as mechanical friction, inflammation, and delayed tear clearance.

Conjunctivochalasis



- Some patients with CCH will remain asymptomatic,
- Most present with similar symptoms to patients with other forms of OSD, such as dry eye disease,
- including irritation, dryness, fatigue, burning, and fluctuating vision.
- CCH can act as a dam or inhibitor of tear flow, sometimes even plugging the punctal openings, which leads to symptoms of tear overflow, including epiphora and watery eyes.

Conjunctivochalasis



- Treatment strategies for CCH start with removing mechanical irritation and inflammation with medical therapies, such as topical steroids and frequent lubrication.
- Some clinicians theorize that low dose brimonidine may also be a treatment option for CCH, but this strategy remains controversial.

Conjunctivochalasis



- For significant or recalcitrant CCH, procedures such as excision and ligation tend to be the go-to treatment
- Cauterization or radio wave electrosurgery techniques may have the added benefits of increased safety profile and decreased recovery time.

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CCH Requires Procedural Intervention

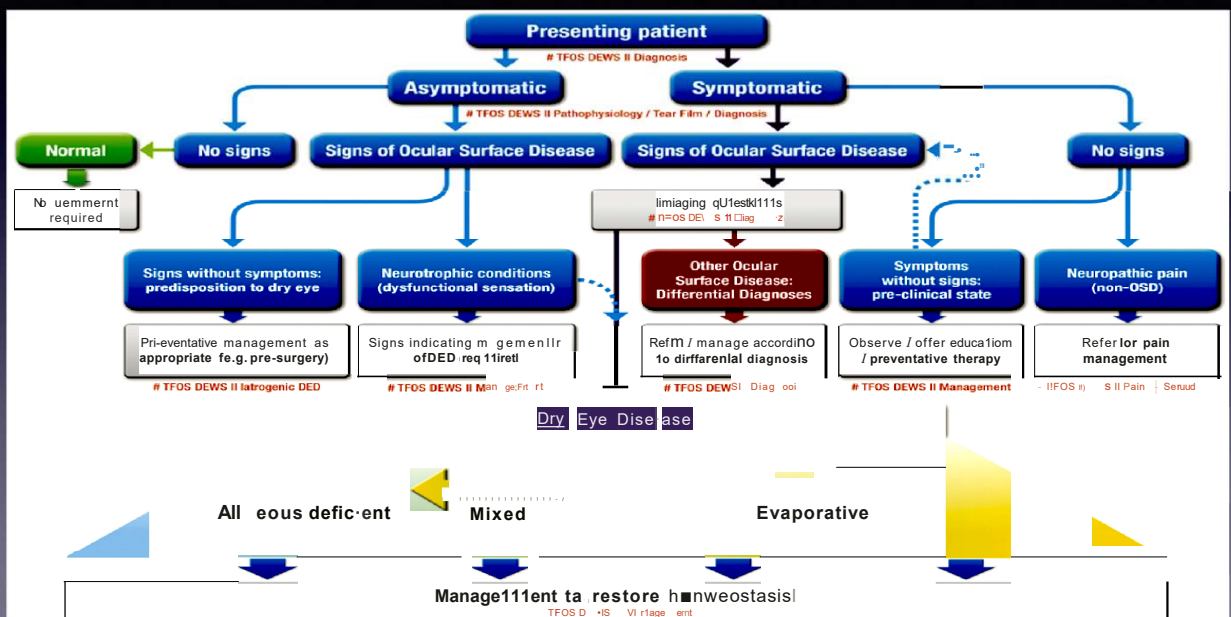
Confirmed

Plausible

Busted

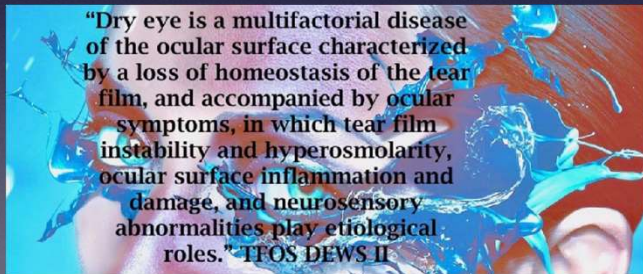
Myth;

- All Dry Eye is Evaporative in Nature



Defining Dry Eye

- The Lacrimal Functional Unit consists of the cornea, conjunctiva, lacrimal and meibomian glands and the lacrimal drainage system, connected reflexly by a neural network. Its failure to respond adequately to desiccating stress is a key initiator of DED.



Defining Dry Eye

- “It is evident that many hybrid forms of DED exist in which lacrimal deficiency and increased evaporative loss collaborate to cause enhanced ocular surface hyperosmolarity. These are summarised in Table 13. Such hybrid states should be recognised in the inclusion criteria of clinical trials and in subgroup analyses of outcomes. Once a dry eye is of sufficient severity to cause **tear breakup** within the interblink interval, an additional **evaporative component** will be **added** to any form of DED, so that any **ADDE will acquire an evaporative component** and the evaporative basis of an existing EDE will be amplified. Studies which test this prediction by comparing the ocular protection index with evaporation rate and tear osmolarity would be of value.”

Defining Dry Eye

- Two forms of DED are recognized, ADDE and EDE. In ADDE, tear hyperosmolarity results when lacrimal secretion is reduced, in conditions of normal evaporation from the eye. In EDE, tear hyperosmolarity is caused by excessive evaporation from the exposed tear film in the presence of a normally functioning lacrimal gland. Since tear osmolarity is a function of tear evaporation in either ADDE or EDE, tear **hyperosmolarity arises due to evaporation** from the ocular surface and, in that sense, **all forms of DED are evaporative**. In other words, EDE is more accurately considered a hyper-evaporative state.

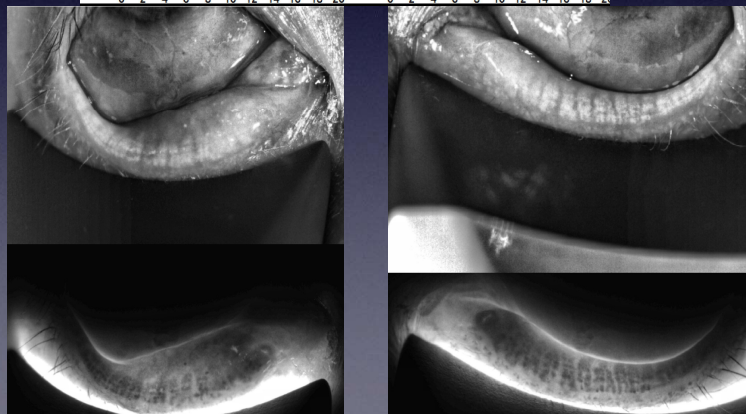
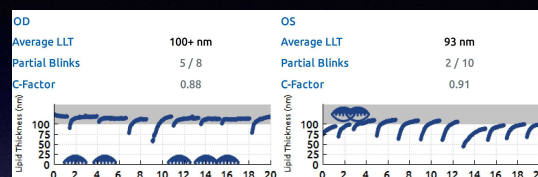
Case Presentation

- 67yo WF referred by outside eyecare provider for MGD Consult and Lipiflow treatment.
- CC; Very painful eyes (Stabbing, FB sens.), burn, all day long. Using PF ATs hourly, ung. qhs, Takes Fish Oil, Hot Compress 2x day

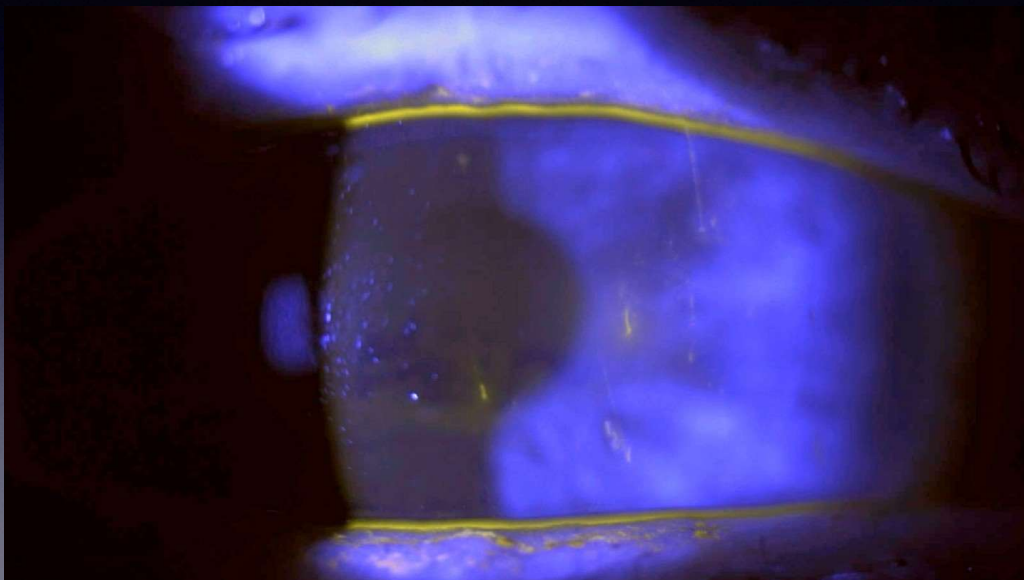
Case Presentation

- SPEED 20/28
- Inflammadry- Very Faint Positive OU
- TearLab- OD 354, OS 341

Case Presentation



Slit Lamp Exam



AqDef > MGD

- 85% of DED has MGD
 - 15% Doesn't
 - Spectrum of Disease
- Have we as educators done too good of a job with MGD?

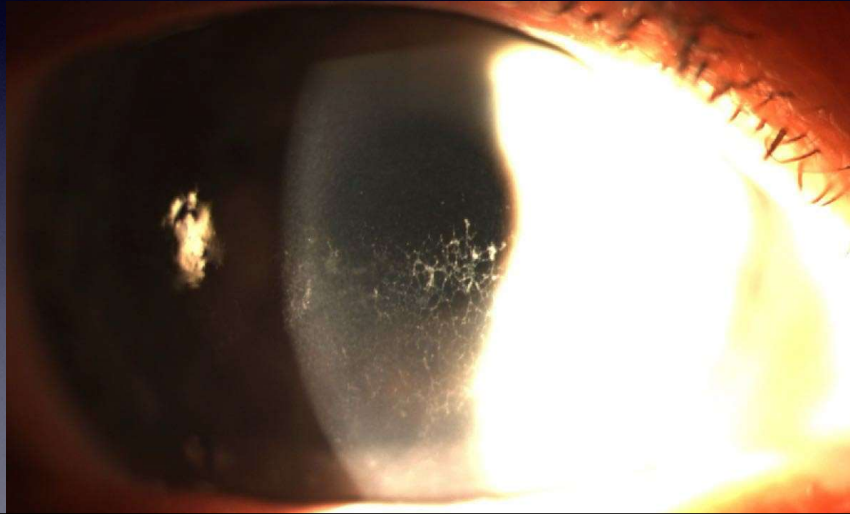
JRL Tips for AqD

- number of tears per day/hour
 - Question #4 on SPEED
- "Stuck shut at night"
- Vision vs Pain?
 - Is Pain a valid question?
- Tear Meniscus Height
- Osmolarity >> MMP-9
- Filaments
- Coalesced SPK
- Reticular Epitheliopathy

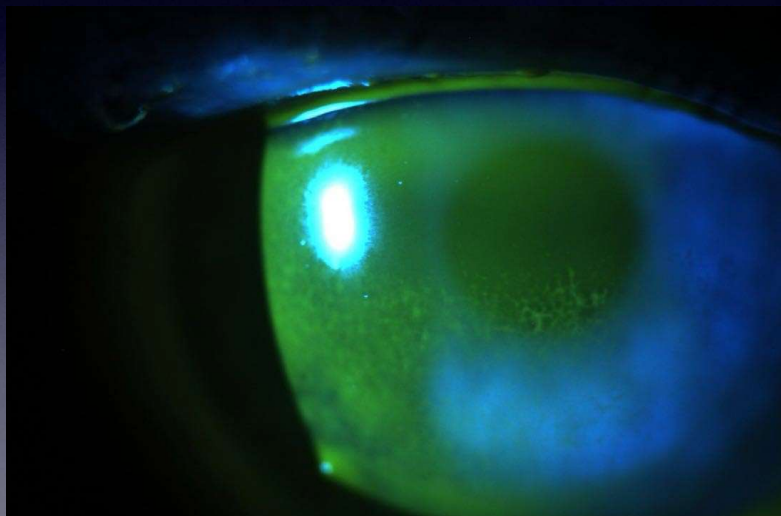
Reticular Epitheliopathy?

- Cracked glass like opacities in epithelium with mild/moderate FL uptake
- Severe autoimmune related OSD and Neurotrophic OSD

Reticular Epitheliopathy?



Reticular Epitheliopathy?



ASCRS Pre-Op Algorithm

- Look
- Lift
- Pull
- Push

LOOK

- Blink Quality and Quantity
- Malposition, lagophthalmos, Proptosis, Exposure, and Trichiasis
- Tear Meniscus Height
- Anterior and Posterior Blepharitis, Demodex, Chalazia
- Follicles and Papillae, Discharge, Concretions, Conjunctivochalasis, Pingueculae, Pterygia, and Conjunctival Scarring and Symblepharon
- Scarring, Salzmann Nodules, Filaments, and Anterior Dystrophies

LIFT

- “Lifting up and then pulling out of the upper eyelid is an often overlooked portion of the ocular surface examination”.
- Superior limbic keratitis
- Superior EBMD
- Superior Scars (VKC, Shield Ulcers)

PULL

- Eyelid laxity
- Floppy Eyelid Syndrome

PUSH

- MGD Expression
 - Quality,
 - Quantity
 - Flow
- Non-obvious MGD, a form of obstructive MGD in which classic inflammatory signs are absent.

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All Dry Eye is Evaporative in Nature

Confirmed

Plausible

Busted

Myth;

- IPL Treats Rosacea but not Dry Eye Disease

HOW IPL?

- ▶ The mechanism of action (MOA) of IPL, with respect to DED due to MGD, is **not yet fully understood**.
- ▶ One possibility is that IPL closes abnormal telangiectasia and blocks the inflammatory mediators they secrete. As a result, a major source of inflammation of the peri-orbital area is removed.
- ▶ Support for this mechanism is the finding that IPL **significantly reduces** the levels of key **cytokines** in tear samples.

- ▶ Liu R, Rong B, Tu P, Tang Y, Song W, Toyos R, et al. Analysis of cytokine levels in tears and clinical correlations after intense pulsed light treating meibomian gland dysfunction. Am J Ophthalmol. 2017 Nov 1; 183:81–90. <https://doi.org/10.1016/j.ajo.2017.08.021> PMID: 28887117

HOWPL?

- ▶ Another possibility is that IPL activates cells by **photobiomodulation** (PBM).
 - ▶ In PBM, light (especially in the red and near infra-red range) (590nm-Amber) is absorbed within cytochrome C oxidase of mitochondria resulting in a boost in ATP production and modulation of intracellular calcium levels.
 - ▶ Previous studies have shown that PBM can;
 - ▶ Upregulate **anti-oxidant** defenses
 - ▶ Reduce **reactive oxygen species** in oxidative stressed cells
 - ▶ Reduce the levels of pro-inflammatory **cytokines** in activated inflammatory cells
 - ▶ Change the phenotype of macrophages (from a form specialized in killing bacteria and pathogens, to a form involved in removal of protein debris and stimulation of healing)

▶ Calderhead RG. The photobiological basics behind light-emitting diode (LED) phototherapy. *Laser Therapy*. 2007; 16(2):97–108.

▶ Hamblin MR. Mechanisms and applications of the anti-inflammatory effects of photobiomodulation. *AIMS Biophys*. 2017; 4(3):337–361. <https://doi.org/10.3934/biophy.2017.3.337> PMID: 28748217

HOWPL?

- ▶ In addition, IPL may also attenuate melanogenic gene overexpression, and suppress UVB-induced cytokine expression .
 - ▶ All of these could contribute to **reduce inflammation** and trigger healing mechanisms at the ocular surface and meibomian gland levels.
- ▶ Another possibility is that IPL could induce heat-shock production, as was demonstrated in skin cells.

▶ Kim J, Lee J, Choi H. Intense pulsed light attenuates UV-induced hyperimmune response and pigmentation in human skin cells. *Int J Mol Sci*. 2021 Mar 20; 22(6):3173. <https://doi.org/10.3390/ijms22063173> PMID: 33804685

▶ Prieto VG, Diwan AH, Shea CR, Zhang P, Sadick NS. Effects of intense pulsed light and the 1,064 nm Nd: YAG laser on sun-damaged human skin: histologic and immunohistochemical analysis. *Dermatol Surg*. 2005 May; 31(5):522–525. <https://doi.org/10.1111/j.1524-4725.2005.31154> PMID: 15962734

▶ Wang ML, Liu DL, Yuan Q. Effect of intense pulsed light on heat shock protein 70 expression in skin. *Di Yi Jun Yi Da Xue Xue Bao* 2005 Jan 1; 25(1):109–110. Chinese PMID: 15684014

HOW IPL?

- ▶ It is also possible that IPL reduces the population of **Demodex mites**, another significant risk factor in DED due to MGD

- ▶ Prieto VG, Sadick NS, Lloreta J, Nicholson J, Shea CR. Effects of intense pulsed light on sun-damaged human skin, routine, and ultrastructural analysis. *Lasers Surg Med.* 2002; 30(2):82–85. <https://doi.org/10.1002/lsm.10042> PMID: 11870785
- ▶ Zhang X, Song N, Gong L. Therapeutic effect of intense pulsed light on ocular demodicosis. *Curr Eye Res.* 2019 Mar 4; 44(3):250–256. <https://doi.org/10.1080/02713683.2018.1536217> PMID: 30321061

HOW IPL?

- ▶ Other researchers proposed that meibomian gland health depends on relative hypoxia.

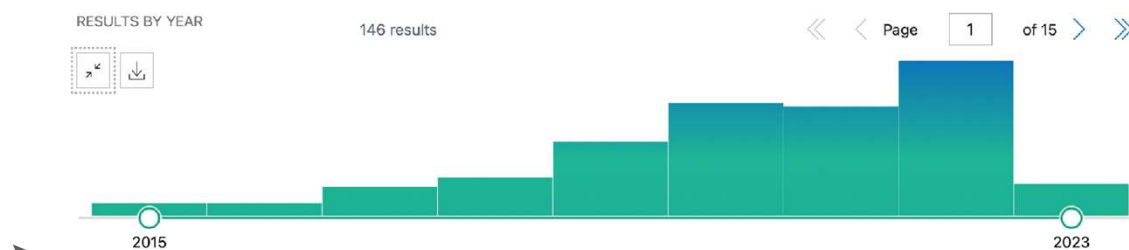
- ▶ Loss of hypoxic conditions could lead to MGD
- ▶ The thrombotic effects of IPL are useful for closing excessive blood vessels
 - ▶ **Restoring the hypoxic conditions** necessary for normal function of the meibomian glands.

- ▶ Liu Y, Chen D, Chen X, Kam WR, Hatton MP, Sullivan DA. Hypoxia: a breath of fresh air for the meibomian gland. *Ocul Surf.* 2019 Apr 1; 17(2):310–317. <https://doi.org/10.1016/j.jtos.2018.12.001> PMID: 30528291

HOW IPL?

- ▶ Finally, there is the possibility that IPL **generates heat** which softens abnormally inspissated secretions of dysfunctional meibomian glands. This last explanation is, however, controversial.
 - ▶ Some researchers proposed that even brief pulses of IPL are sufficient to transfer heat to the eyelids, melt an abnormally inspissated meibum within the meibomian glands, and thus facilitate their expression.
 - ▶ Other researchers argued that IPL can induce only short term thermal effects, with minimal changes in skin surface temperature. According to this line of reasoning, IPL pulses are too brief to induce sustained changes of the meibum.
 - ▶ Toyos R, Toyos M, Willcox J, Mulliniks H, Hoover J. Evaluation of the safety and efficacy of intense pulsed light treatment with meibomian gland expression of the upper eyelids for dry eye disease. *Photobiomodul Photomed Laser Surg*. 2019 Sep 1; 37(9):527–531. <https://doi.org/10.1089/photob.2018.4599> PMID: 31335299
 - ▶ Craig JP, Chen YH, Turnbull PR. Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction. *Invest Ophthalmol Vis Sci*. 2015 Feb 12; 56(3):1965–1970. <https://doi.org/10.1167/iov.14-15764> PMID: 25678687

IPL AND ‘THE LITERATURE’



IPL AND 'THE LITERATURE'

- ▶ Lei Y, Peng J, Liu J, Zhong J. Intense pulsed light (IPL) therapy for meibomian gland dysfunction (MGD)-related dry eye disease (DED): a systematic review and meta-analysis. *Lasers Med Sci.* 2022 Dec 19;38(1):1. doi: 10.1007/s10103-022-03690-1. PMID: 36534219.

ORIGINAL ARTICLE

Intense pulsed light (IPL) therapy for meibomian gland dysfunction (MGD)-related dry eye disease (DED): a systematic review and meta-analysis

Yahui Lei¹ · Jing Peng² · Jiayan Liu¹ · Jingxiang Zhong^{1,3}

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A SYSTEMATIC REVIEW AND META-ANALYSIS.

- ▶ Jan 2023
- ▶ **Conflict of Interest;** The authors declare no competing interests.
- ▶ This systematic review was conducted and reported in accordance with the **Cochrane handbook** and the **Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)**. The registration number in PROSPERO is CRD42022309060 (www.crd.york.ac.uk/prosp/ero).
- ▶ **Exclusion Criteria;**
 - ▶ Animal studies, case reports, case-series reports, and literature reviews.
 - ▶ Conference abstracts and published clinical trial protocols whose authors could not successfully be contacted for the data.
 - ▶ Lack of a control group or self-controlled study design.
 - ▶ DED arising from causes other than MGD.

ASYSTEMATIC REVIEW AND META-ANALYSIS.

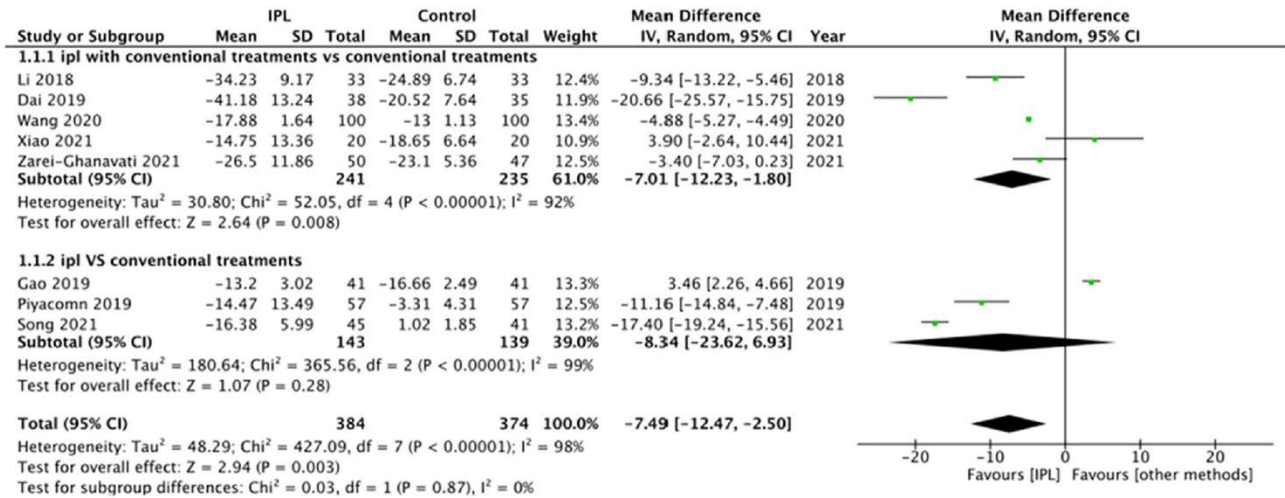
- ▶ Databases Searched;
 - ▶ Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), VIP, Wanfang Database, and China Biology Medicine (CBM)
- ▶ 1068 articles were evaluated by titles and abstracts
- ▶ 950 were excluded due to an inappropriate study type
- ▶ Subsequently, we excluded 107 papers due to a lack of important outcomes or a suitable control group.
- ▶ 11 articles met the eligibility criteria.

ASYSTEMATIC REVIEW AND META-ANALYSIS.

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- ▶ Subsequently, we excluded 107 papers due to a lack of important outcomes or a suitable control group.
- ▶ 11 articles met the eligibility criteria.
- ▶ “Our study excluded self-controlled (Monocular) studies owing to the possibility of correlation between subjects’ eyes, and we believe eyes of the same subject cannot be treated alone”.
 - ▶ Therefore, our conclusion of the meta-analyses would be more convincing than those of previous studies.

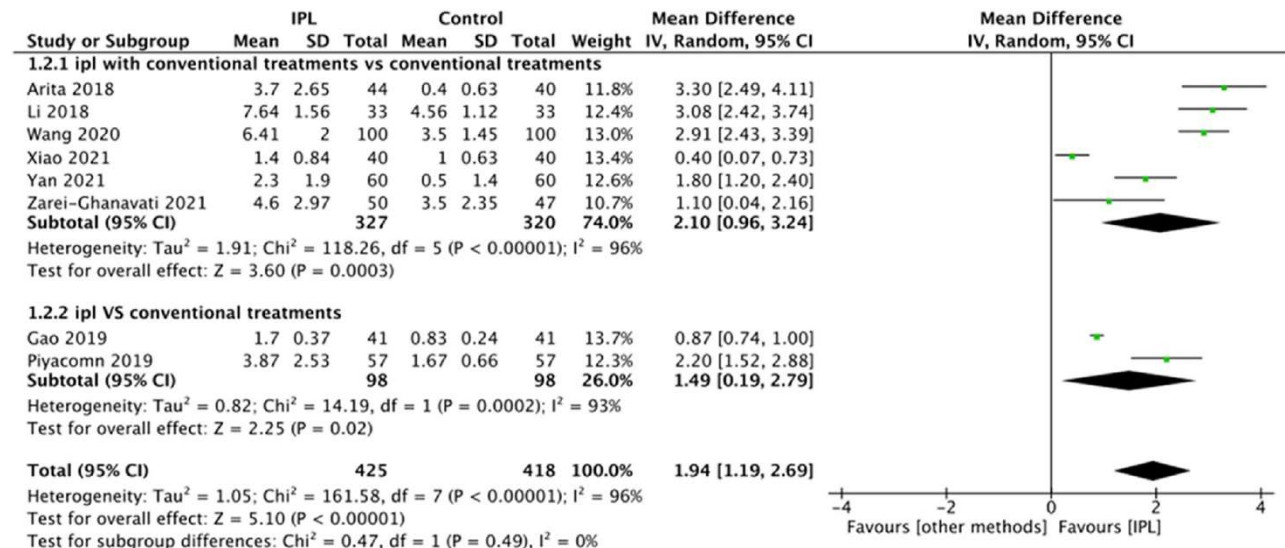
A SYSTEMATIC REVIEW AND META-ANALYSIS.

► Forest plots of changes in Primary outcome measures **OSDI**



A SYSTEMATIC REVIEW AND META-ANALYSIS.

► Forest plots of changes in Primary outcome measures **TBUT**

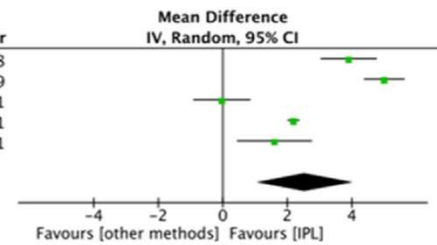


A SYSTEMATIC REVIEW AND META-ANALYSIS.

- Forest plots of changes in secondary outcome measures **NIBUT**

Study or Subgroup	IPL			Control			Weight	Mean Difference		Year
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI		
Arita 2018	4.5	2.65	44	0.6	1.26	40	19.8%	3.90	[3.03, 4.77]	2018
Dai 2019	6.2	2.38	76	1.2	1.44	70	20.5%	5.00	[4.37, 5.63]	2019
Ren 2021	0.13	2.86	130	0.16	4.28	130	19.8%	-0.03	[-0.91, 0.85]	2021
Song 2021	2.69	0.7	90	0.5	0.55	82	21.2%	2.19	[2.00, 2.38]	2021
Zarei-Ghanavati 2021	5.7	3.14	50	4.1	2.71	47	18.8%	1.60	[0.43, 2.77]	2021
Total (95% CI)			390			369	100.0%	2.55	[1.07, 4.04]	

Heterogeneity: Tau² = 2.71; Chi² = 111.64, df = 4 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.37 (P = 0.0008)



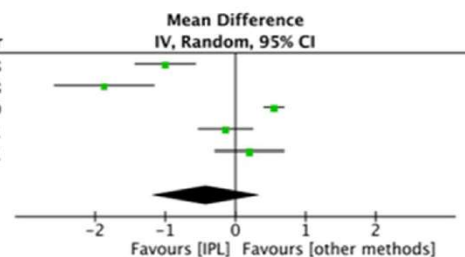
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A SYSTEMATIC REVIEW AND META-ANALYSIS.

- Forest plots of changes in secondary outcome measures **CFS (FL Staining)**

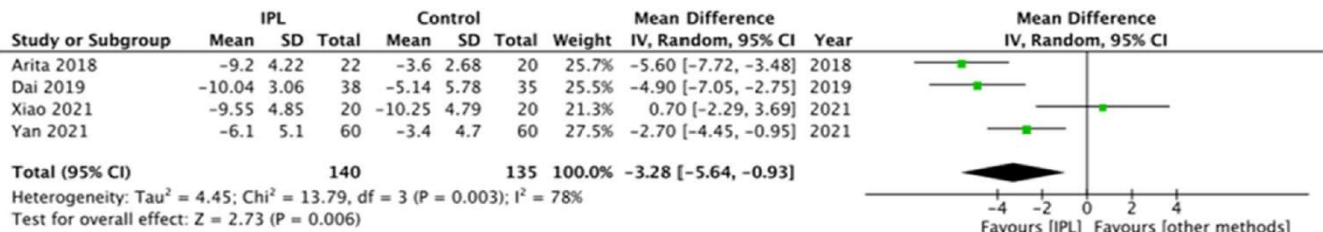
Study or Subgroup	IPL			Control			Weight	Mean Difference		Year
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI		
Arita 2018	-1	1.33	44	0	0.63	40	20.2%	-1.00	[-1.44, -0.56]	2018
Li 2018	-3.83	2.66	66	-1.96	1.32	66	18.2%	-1.87	[-2.59, -1.15]	2018
Gao 2019	-1.06	0.25	41	-1.61	0.42	41	21.4%	0.55	[0.40, 0.70]	2019
Xiao 2021	-0.47	0.78	40	-0.33	1	40	20.4%	-0.14	[-0.53, 0.25]	2021
Yan 2021	-0.6	1	60	-0.8	1.7	60	19.8%	0.20	[-0.30, 0.70]	2021
Total (95% CI)			251			247	100.0%	-0.41	[-1.19, 0.36]	

Heterogeneity: Tau² = 0.72; Chi² = 84.08, df = 4 (P < 0.00001); I² = 95%
Test for overall effect: Z = 1.05 (P = 0.29)



A SYSTEMATIC REVIEW AND META-ANALYSIS.

- Forest plots of changes in secondary outcome measures **SPEED Scores**



C

A SYSTEMATIC REVIEW AND META-ANALYSIS.

- **Safety Data**

- Eight studies reported safety data, and none of these studies reported adverse events caused by IPL therapy.
- The rest of the included studies did not specify whether any adverse events occurred.

ASYSTEMATIC REVIEW AND META-ANALYSIS.

- ▶ Discussion- Primary Outcomes (OSDI & TBUT)
 - ▶ According to the quantitative analysis, the application of IPL could ameliorate the BUT of DED patients, even in a relatively short follow-up time.
 - ▶ A significant difference in the reduction in the OSDI score between the two groups may require a relatively long follow-up time to emerge.
 - ▶ Unsurprisingly, it takes time to improve tear film stability to ameliorate DED symptoms.
 - ▶ In brief, the results of our analysis showed that both IPL treatment and traditional treatments could improve the stability of tear film and subjective symptoms of patients.
 - ▶ Moreover, the effect of IPL application in improving the stability of tear film was markedly better than that of traditional treatments.

ASYSTEMATIC REVIEW AND META-ANALYSIS.

- ▶ Discussion- Secondary Outcomes (CFS, NITBUT & SPEED)
 - ▶ The application of IPL **outdoes** conventional treatments in increasing **NITBUT** and reducing the **SPEED** scores.
 - ▶ The observed increases indicated the improvement of tear film stability.
 - ▶ Further confirmed the therapeutic potential of IPL treatment in MGD-related dry eye diseases.
 - ▶ While the CFS showed a downward trend, there was no statistical significance between the two groups.
 - ▶ In 3 studies, a decrease in CFS was found in **both** the IPL application and conventional treatment groups.

IPL AND 'THE LITERATURE'

- ▶ Toyos R, Desai NR, Toyos M, Dell SJ. Intense pulsed light improves signs and symptoms of dry eye disease due to meibomian gland dysfunction: A randomized controlled study. PLoS One. 2022 Jun 23;17(6):e0270268. doi: 10.1371/journal.pone.0270268. PMID: 35737696; PMCID: PMC9223330.

RESEARCH ARTICLE

Intense pulsed light improves signs and symptoms of dry eye disease due to meibomian gland dysfunction: A randomized controlled study

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- ▶ **This data lead to the FDA approval of Lumenis IPL device for DED**
- ▶ **Funding:** The funders of this study (Lumenis) designed the study in conjunction with the authors and analyzed portions of the data. Clinreg, a vendor of Lumenis, performed the majority of the analysis for the primary, secondary and exploratory endpoints and was responsible for the randomization sequence. The funders had no role in data collection or decision to publish.
- ▶ **Competing Interests:** Dr. Rolando Toyos - speaks, consult, research for Lumenis Dr. Steven Dell - speaks, consult, research for Lumenis Dr. Neel Desai - speaks, consult, research for Lumenis Dr. Melissa Toyos - research for Lumenis These competing interests do not alter our adherence to PLOS ONE policies on sharing data and materials.
- ▶ This research was approved by an Institutional Review Board (Sterling IRB, # 6051), and registered in ClinicalTrials.gov (NTC03396913).

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► Purpose;

- To compare the safety and efficacy of intense pulsed light (IPL) followed by meibomian gland expression (MGX), against monotherapy of MGX.
- This was a prospective, interventional, multi-site (3), parallel-group, two-arms, randomized, active-controlled with a 1:1 allocation ratio.
- The trial is set to assess the superiority of the study arm versus the control arm.
- The study was conducted in the Unites States.

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► Inclusion Criteria;

- Adults aged 22 to 85 years of age with signs and symptoms of dry eye disease due to MGD
- Tear break-up time (TBUT) less than or equal to 7 seconds in the study eye
- Patients with a meibomian gland secretion (MGS) less than or equal to 12 in the study eye
 - Where MGS is a score evaluating the quality of meibum along the lower eyelid, as described by Lane and colleagues (0,1,2,3 scale, 5 glands-3 regions)
 - Patients with at least 5 non-atrophied meibomian glands in the lower eyelid of the study eye; and patients with an OSDI questionnaire score greater than or equal to 23 (moderate to severe symptoms of dry eye)

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► Exclusion Criteria;

- Fitzpatrick skin type V or VI
- Use of prescription eye drops within 7 days (excluding artificial tears or glaucoma drops) of recruitment
- Facial IPL treatment within the past 12 months
- Any thermal treatment of the eyelids or meibomian gland expression within the past 6 months
- Ocular surface and eyelid abnormalities
- Any systemic condition that may cause dry eye
- Use of photosensitive drugs within the past 3 months
- pre-cancerous lesions
- Skin cancer or pigmented lesions within the treatment area
- Over exposure to sun within the past 1 month
- Ocular infections within the past 6 months
- Uncontrolled infections or immunosuppressive diseases
- Unwillingness or inability to abstain from the use of medications known to cause dryness

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► Methods

- Patients were randomly assigned to receive IPL treatment followed by meibomian gland expression (the study arm) or sham IPL followed by meibomian gland expression (the control arm).
- Each patient underwent a series of 4 treatment sessions, 2 weeks apart.
- In each session, the eyes of the patient were occluded with eye protection (adhesive eye patches + Lumenis opaque goggles).
- In the study arm, IPL was generated by a Lumenis M22 system, with a 560 nm or 590 nm cut-off filter
- In the control arm, IPL was generated by the same system, but all light signals were blocked with an aluminum plate instead of the 560/590 cut-off filter
- In all patients, a single follow-up (FU) session was scheduled 4 weeks after the fourth treatment session.
- Participants were allowed to **continue using artificial tears or warm compresses during the study.**

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► Primary Outcome (TBUT)

► A-Absolute vs B-Change in TBUT

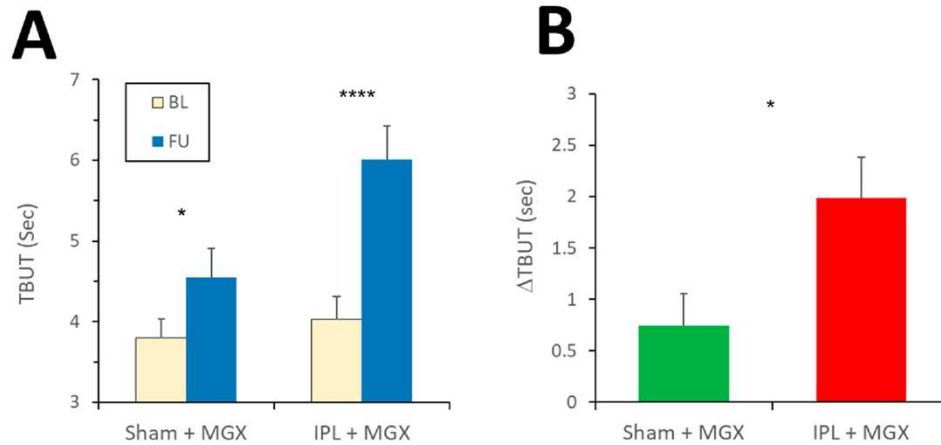


Fig 2. Change of primary outcome (TBUT). A. Absolute values of TBUT. Statistical tests within arms: paired two-sided t-test; **: $p < 0.01$; ****: $p < 0.0001$. B. Δ TBUT (the change of TBUT from BL to FU). Statistical test between arms: least squares fit of Δ TBUT. **: $P < 0.01$.

<https://doi.org/10.1371/journal.pone.0270268.g002>

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

► Symptom Change (OSDI)

► A-Absolute vs B-Change in OSDI

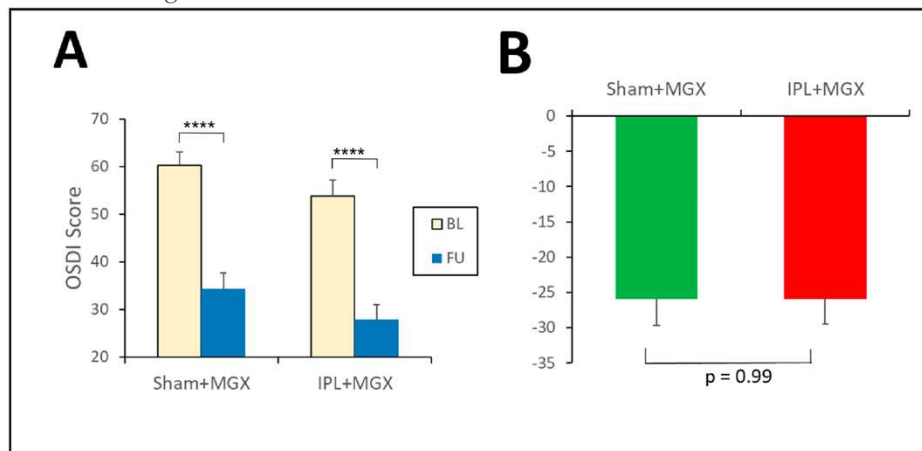


Fig 3. Change of symptoms (OSDI). A. Absolute values of OSDI; Statistical tests: 2-sided paired t-test of FU versus BL (within each arm); ****: $p < 0.0001$. B. Δ TBUT; Statistical test: 2 sided least squares fit of Δ OSDI (between arms).

<https://doi.org/10.1371/journal.pone.0270268.g003>

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► MG Function Change (MGS)

► A-Absolute vs B-Change in MG Scores

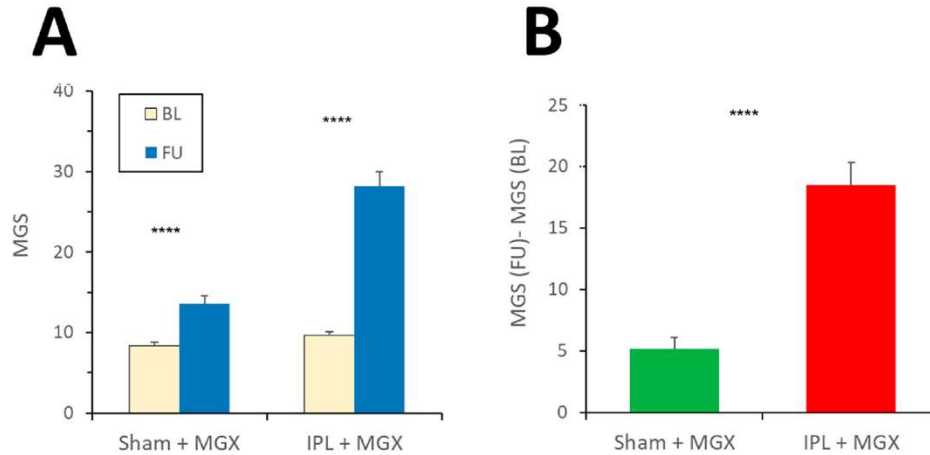


Fig 4. Change of MGS. A. Absolute values of MGS at BL and FU; ****: p (within arms) <0.0001 . **B.** Change of MGS from BL to FU (AMGS); ****: P (between arms) <0.0001 .

<https://doi.org/10.1371/journal.pone.0270268.g004>

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► **Skin Rosacea** (Post-hoc outcome measure).

- The severity of skin rosacea was defined as normal, mild, moderate, or severe.
- Within arms, there were no significant changes in the severity of skin rosacea (Control arm: $p = 0.9397$; Study arm: $p = 0.3327$).
- Between the two arms there was a tendency for more improvement in study patients compared to control patients, but the difference was not statistically significant ($P = 0.0506$).

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

- ▶ **Daily use of Artificial Tears** (Post-hoc outcome measure)
 - ▶ In both arms, there was a statistically significant decrease the number of artificial tear drops used per day (Control arm: $p = 0.0176$; Study arm: $p = 0.005$).
 - ▶ The difference between the two arms was not statistically significant ($P = 0.8216$).

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

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 - ▶ The difference between the two arms was not statistically significant ($P = 0.8216$).

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

- ▶ **Daily use of Warm Compresses** (Post-hoc outcome measure)
 - ▶ Neither arm showed a significant decrease in the number of warm compresses used (Control arm: $p = 0.0566$; Study arm: $p = 0.1267$).
 - ▶ There was no difference between the two arms ($P = 0.3525$).

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

- ▶ **Biomicroscopy** (Post-hoc outcome measures)
 - ▶ For each of the examined features (lid margin thickening, conjunctival injection, and loss of eye lashes), an improvement is defined as an increase in the number of eyes which switched from abnormal to normal

Biomicroscopy	Lid Margin thickening	Control	Abnormal: 62 (72%) Normal: 24 (28%)	-1 (Deteriorated): 0 0 (Did not change): 79 (92%) +1 (Improved): 7 (8%)	0.2103	0.0605
		Study	Abnormal: 41 (52%) Normal: 37 (46%)	-1 (Deteriorated): 0 0 (Did not change): 64 (82%) +1 (Improved): 14 (18%)	0.0212*	
Conjunctival injection	Control	Abnormal: 70 (81%) Normal: 16 (19%)	-1 (Deteriorated): 9 (11%) 0 (Did not change): 75 (87%) +1 (Improved): 2 (2%)	0.2024	0.0002***	
	Study	Abnormal: 38 (49%) Normal: 40 (51%)	-1 (Deteriorated): 5 (6%) 0 (Did not change): 61 (77%) +1 (Improved): 17 (22%)	0.0055**		
Loss of eyelashes	Control	Abnormal: 25 (29%) Normal: 61 (71%)	-1 (Deteriorated): 5 (6%) 0 (Did not change): 75 (86%) +1 (Improved): 6 (7%)	0.8674	0.3594	
	Study	Abnormal: 14 (18%) Normal: 64 (82%)	-1 (Deteriorated): 3 (4%) 0 (Did not change): 67 (86%) +1 (Improved): 8 (10%)	0.3267		

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

- ▶ **Number of Expressible Glands** (Post-hoc outcome measure)
- ▶ **Pain due to MGX** (post-hoc outcome measure)
- ▶ **Pain due to IPL** (post-hoc outcome measure)
- ▶ **Predominant Quality of Meibum** (post-hoc outcome measure)
 - ▶

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

- ▶ **Adverse Events**
- ▶ There were no serious adverse events reported.
- ▶ The incidence of adverse events was 8.9% in the study arm (mild: n = 1; moderate: n = 3), and 20.9% in the control arm (mild: n = 5; moderate: n = 3; severe: n = 1).
- ▶ Although there was a tendency for more adverse events in the control arm, the difference between the two arms was not statistically significant ($P = 0.06$).
- ▶ In the study arm, 1 subject experienced 2 ocular-related adverse events (moderate allergic conjunctivitis and moderate bacterial conjunctivitis).
- ▶ The treating physician determined that the seasonal allergic conjunctivitis (detected first) was not related to the procedure nor the device, but the bacterial allergic conjunctivitis (detected two weeks later) was possibly related to the procedure (i.e., the meibomian gland expression).
- ▶ As a result of this adverse event, this subject was discontinued from the study.

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

► Adverse Events

- Another subject experienced mild skin pain (possibly related to the procedure).
- A third subject experienced moderate blepharitis (unrelated to both procedure and device).
- No subjects experienced **systemic** adverse events.
- In the control arm, one subject experienced a severe conjunctival telangiectasia (unrelated to both procedure and device); one subject experienced a mild chalazion (unrelated) skin related adverse events (mild chalazion, mild stye), and 6 subjects experienced systemic adverse events (mild bronchitis, mild sinus infection, moderate sinus infection, mild hyperlipidemia, and 2 cases of seasonal allergy worsening).
- Except for the mild pain and the moderate bacterial conjunctivitis which were both possibly related to the procedure, none of the other reported adverse events were related to either the procedure or the device.

IPL IMPROVES SIGNS AND SYMPTOMS OF DRY EYE DISEASE DUE TO MGD

► Study Limitations

- It was not possible to completely ensure participant blinding since IPL is normally felt as a sensation ranging from mild discomfort to moderate pain, some patients could have correctly guessed their group assignment, based on their preliminary expectations and their sensations during the IPL treatment.
- Since study patients were treated with both MGX and IPL, it is difficult to isolate the contribution of IPL.
- In the design of the control arm, who were treated with MGX alone, we implicitly assumed that the two components are compounded, and therefore simple subtraction of the changes in the two arms should have given us a good estimation of the effect size.
 - It is possible that the two components combine in a more complex way than simple linear addition.
- Another limitation of the study was that the follow-up period was relatively short.
 - Further studies are necessary to elaborate on the durability of IPL's long-term effectiveness.
- Next, this study was not designed to determine the efficacy of IPL in groups with different severity levels of MGD.
 - Depending on complex interactions involving several such outcome measures. In such a case, between-group differences in the baseline severity of MGD could have biased the results.
- Future studies are required to determine the efficacy of IPL as function of MGD severity, so that clinicians may be better informed who of their patients are more likely to benefit from this technology.
- Finally, findings from this study is based on a specific population, namely patients with mild to moderate MGD, predominantly Caucasian, age 22–85, and with Fitzpatrick skin types I-IV (predominantly II to III).
- Future studies are warranted to justify the group differences in the more general population.

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► **Conclusion**

- The current study suggests that IPL, when combined with MGX, may be useful to improve signs and symptoms of MGD in a North American population.
- With respect to at least some of the signs, patients treated with IPL and MGX could benefit more than patients treated with MGX alone.

@ When poU is active, respond at pollev.com/jacoblant676

— Text **JACOBLANT676** to **22333** once to join

IP Treats Rosacea but not Dry Eye Disease

Confirmed

Plausible

Busted

Questions???

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 @SeeOneTeachOne