# Clinic Results of Intraductal Meibomian Gland Probing Combined Intense Pulsed Light in Treating Patients With Refractory Obstructive Meibomian Gland Dysfunction: A Randomized Controlled Trial

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**Research article**

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# Abstract

Background: To optimize therapeutic regimen for refractory obstructive meibomian gland dysfunction (o-MGD) patients by combining intraductal meibomian gland probing (MGP) and intense pulsed light (IPL) to enhance their effect and reduce their limitations. Methods: This randomized, assessor blind study include 45 patients (90 eyes) with refractory o-MGD. They were divided into 3 groups by allocation concealment: IPL (group I, received an IPL treatment course: 3 times at 3-week intervals), MGP (group II, received MGP one time) and MGP combined IPL (group III, MGP at first then an IPL treatment course). Standard Patient Evaluation of Eye Dryness score (SPEED), tear break-up time (TBUT), corneal fluorescein staining (CFS), meibum grade and lid margin finding results were assessed at baseline, 3 weeks after final treatment in group I and III, 3 and 12 weeks after MGP in group II. Six months after final treatment, the SPEED and willingness to receive any treatment again were also collected in all groups. Paired Wilcoxon, Mann-Whitney U with Bonferroni correction and Kruskal-Wallis tests were used for data analysis. Results: In 3 groups, all above indexes improved significantly after treatment (all P□0.01). MGP-IPL was better than IPL and MPG in posttreatment SPEED, TBUT, meibum grade, lid telangiectasia (all P□0.05/3). Besides, the MGP-IPL was better than IPL in lid tenderness and better than MGP in orifices abnormality (all P□0.05/3 ). Six months later, the SPEED in MGP-IPL was also significantly lower than other groups (all P□0.05/3). And no patients in MGP-IPL group revealed the need to be treated again, while 35.7% or 20% of patients with IPL or MGP need retreatment. Conclusions: Compared with single IPL or MGP, the combination of MGP and IPL demonstrated the most efficient results in relieving all signs and symptoms and can help patients attain the most lasting symptom relief. Trial registration: http://clinicaltrials.gov, ChiCTR1900021273 (retrospectively registered 09 February 2019). Funding: This work was supported by the National Natural Science Foundation of China: [grant numbers: 81870624; 81700802]; Major Science and Technology Projects of Zhejiang Province [grant numbers: 2017C03046].


# Background

Dry eye is always being considered as a significant health concern that threatens individuals' life quality as well as personal and economic well-being[1,2]. Among various types of dry eye diseases, obstructive meibomian gland dysfunction (o-MGD) caused evaporative dry eye attracts broad attention of clinicians and scientists for its chronic course, recurrent potential and high incidence[3,4]. The obstruction of terminal tract of meibomian gland (MG) leads to hyposecretion and quality change of meibum from the orifices[5]. And these changes of meibum in ocular surface can result in instability of tear film and irritation of symptoms such as dryness and foreign body sensation[3]. Besides, unusually elevated intraglandular pressure and aggravated local inflammation that caused by meibum stasis further exacerbate the disease course, creating a vicious circle.

Traditional treatments for o-MGD include warm compress, massage, artificial tears, etc. However, studies have showed that these treatments are not sufficient for symptom relief[6,7]. And it is difficult for patients to comply with continuous medical therapies. Chinese o-MGD patients, in particular, always meet serious initial symptoms with MG orifices obstruction and no meibum secretion, making the treatment processes even more difficult. In recent years, great strides have been made in new treatment options for refractory o-MGD patients, one of which is intense pulsed light (IPL). IPL, which has long been used in medical cosmetology, can also be effective in dry eye mainly for its inhibition of telangiectasias along the eyelid that block the way of inflammatory cytokine and its heating effect[8,9]. Another relatively new method is intraductal meibomian gland probing (MGP), which was first described by Maskin in 2010. MGP uses a special meibomian cannula to probe the plugged meibomian gland, releasing the abnormal elevated intraductal pressure and reestablishing a healthy microenvironment favoring the growth of MG tissues[10].

Although the safety and effectiveness of IPL and MGP have been proved by previous studies[8,9,11–13], the deficiency of IPL and MGP could also be observed in our day-to-day clinical observation. The effect of IPL to open stubborn intraductal congestion or intraductal scar is comparatively limited. And for patients with severe intraductal inflammation or apparent blepharitis, only MGP is not enough to hamper the excessive inflammation. Besides, probing is an invasive method for patients. Sik Sarman et al reported that 20% of the patients need to be treated with probing again after an average of 4.6 months[12]. Repeated Probing may bring psychological burden to patients and would possibly cause scar proliferation. It is urgent to find an optimal therapeutic regimen, which can reduce the number of invasive treatments, open the MG obstruction, promote the discharge of meibum and at the same time, control inflammation.

Here, we devised a new treatment method that combined MGP with IPL course, and we compared it with MGP, IPL alone, hoping to find a way that could strength the advantages of MGP and IPL, and at the same time offset their side-effects. All participated patients were serious refractory o-MGD patients with more than half of the evaluated meibomian gland orifices obstructed and no lipid secretion, while Meibo-Scan showed no extensive atrophy area.

# Methods

45 patients that were clinically diagnosed with refractory o-MGD enrolled in this study. The inclusion criteria included: (1) Older than 18 years. (2) Standard patient evaluation of eye dryness (SPEED) questionnaire≥6. (3) More than half of the 15 evaluated meibomian gland orifices in each eyelid were obstructed and had no lipid secretion with extrusion. (4) Meibum grade≤24. (5) Breakup time of tear film (TBUT) ≤5s. (6) Schirmer test□5s. (7) Meibo-Scan (OCULUS) showed the atrophy area of meibomian gland in both upper and lower eyelids less than 1/3 of the total area. (8) Did not have symptom relief with conservative treatment (eyelid warming, massage and artificial tears) for at least 1 year before study treatment. (9) All patients had been informed of possible treatment-related complications and the possibility to be assigned to invasive treatment group. All agreed to receive the possible therapeutic regimen and signed informed consent. Patients with history of corneal contact lens, mite blepharitis, acute eye inflammation or infection and apparent eyelid margin scar as well as patients using lacrimal plug or receiving LASIK were excluded from our study.

Patients participated were randomly divided into 3 groups (15 patients per group) by block randomization, and allocation concealment was done with closed envelop method. Patients in group I received an IPL treatment course (treated with IPL 3 times at 3-week intervals). Patients in group II received an MGP treatment course (treated with MGP one time). In group III, 3 weeks after the initial MGP, patients also received an IPL treatment course. The clinical effects were assessed at baseline, 3 weeks and 12 weeks after MGP in group II, and 3 weeks after final treatment in group I and III. Besides□six months after the final treatment in 3 groups□all patients completed SPEED and answered the question if they have the requirement to receive any treatment again. Patients enrollment, random allocation sequence generation and intervention assignment were performed by first author (HXD).

### 2.2 Treatment Procedure

#### 2.2.1 Intraductal meibomian canal probing

With the help of SuZhou LiuLiu Medical Equipment co. LTD, we designed a private probe based on original Maskin probe and a rinse hollow tube. The probe was 4.5mm in length with a blunt end, having a diameter of 0.12 mm. The hollow tube was 2.0 mm in length and 0.16 mm in diameter. The process of intraductal MGP were as follows: (1) To ease the pain of probing, 4% lidocaine was injected into upper and lower eyelids paralleled to the palpebral margin, creating local bulgy of skin. (2) The eyelids were flipped outward using a cotton swab. Operating microscope was positioned over the target eyelid to show orifices clearly. Then, the operator inserted the probe to glands vertically with orifices. An impact force was necessitated when encounter any resistances from orifices or intraductal. After probing, chalazion forceps were used to squeeze remnant meibum out. Self-limited hemorrhage was the most common complication, during which a blood point and blood trickle could be observed and no particular treatment was needed. (3) Then, a hollow tube was used to swash the meibomian gland by injecting 0.1% Dexamethasone (Guangzhou Baiyun Mountain Pharmaceutical co. LTD, China) and 0.25% Amikacin (Qilu Pharmaceutical co. LTD, China) repeatedly. (4) Eventually, Tobradex eye ointment (Alcon, Belgium) was applied to conjunctival sac. All MGP procedures were performed by the first author (HXD).

### 2.2.2 Intense pulsed light

The M22 Multi-pulse therapeutic apparatus was used. Prior to treatment, ultrasound gel was applied to patient's face covering the area from tragus to tragus beneath the eyelid margin, temple and forehead with 1-2 mm thick. Then, the Pre-set Toyos parameters were administered to 1 or 2 test points of treatment area to test patient tolerance and/or comfort. The intensity of the IPL treatment was adjusted to 14J/$cm^2$-15J/$cm^2$, which was determined by Fitzpatrick Skin Type Grading. Placement of IPL eye shield over the eyes was necessary as it can protect eyes from stimulus of bright light. After that, 1 back-and-forth flash that emitted by IPL hand piece was placed on each skin area without pressure. Finally, chalazion forceps were used to squeeze MG tissues. Care should be taken to ensure that treatment areas of each participant were identical and all the procedures were done by the same doctor (LL).

All participated patients were required to use only artificial tears (Hailu, German) four times a day during the whole follow-up period.

## 2.3 Clinical Evaluation

The eye examiners involved were blind in which groups were the participants allocated

### 2.3.1 SPEED, CFS and TBUT

Standard Patient Evaluation of Eye Dryness (SPEED) validated questionnaire (0–28) was used to assess the symptoms, as previously described[14]. The corneal fluorescein staining (CFS) was evaluated by equally dividing the cornea into four parts. And the staining of each section was recorded on a 0-3 scale: 0=no punctate staining; 1=less than half staining; 2=more than half staining; 3=whole staining; and composite score for each quadrant (0–12 score). Tear break-up time (TBUT) was evaluated by 3 times and the average value was recorded.

### 2.3.2 Meibum grade

The lower and upper eyelid were divided into 3 parts respectively: nasal, bitamporal and middle, with a total of 15 glands in each eyelid. The scores of meibum characteristics secreted by each gland were as follows: 0=no secretion drainage;

1= inspissated toothpaste-like lipid; 2= viscous opaque or yellow lipid; and 3=liquid clear lipid. The scores of each expressed orifice within 3 parts of eyelids were added together to give the final score (0-90 score) of right or left eye.

### 2.3.3 Lid margin finding results

Lid margin finding results we evaluated included the abnormality of meibomian glands orifices, lid tenderness and telangiectasia, and were noted as 0-4 scale, with 0 being absent and 4 being the most severe.

### 2.4 Statistical Analysis

Statistical significance was set at $p<0.05$ and data analysis was performed using SPSS version 23. Continuous data were presented as means ± SD. A paired Wilcoxon test was employed to compare the parameters before and after treatment. Comparison was done between different groups using non-parametric Mann-Whitney U tests with Bonferroni correction or Kruskal-Wallis tests.

## Results

A total of 45 patients were enrolled in our research at first, while one patient in IPL group and one patient in MGP-IPL group were lost to follow-up. The age of 43 enrolled patients (86 eyes) ranged from 24 to 56 years (mean age 37.56±9.82), with a female to male ratio of 1.39. There were no differences in gender (P =0.409) and age (P =0.376) among 3 groups.

During the follow-up period, several MGP treated patients had subcutaneous ecchymosis of eyelid skin caused by injection of anesthetics, which can improve after cold compress. Besides, one patient occurred blepharokeratoconjunctivtis (BKC) during IPL treatment and was relieved after two-week administration of Tobradex.

The evaluation time in group II was 3 weeks and 12 weeks after MGP, but we found no differences of all indexes exist between 3 weeks and 12 weeks after MGP (SPEED: 11.87±3.44 vs. 11.93±3.26; TBUT: 4.74±1.28 vs. 4.81±2.03; CFS: 0.87±1.48 vs. 0.80±1.35; meibum grade: 24.73±10.66 vs. 26.57±11.63; lid telangiectasia: 1.73±0.58 vs. 1.73±0.64; orifices abnormality: 1.87±0.82 vs. 1.80±0.85; lid tenderness: 0.60±0.67 vs. 0.57±0.63; P was determined by Kruskal-Wallis test; all P□0.1). And in order to increase comparability of group II and III (both assessed at 12 weeks after initial MGP treatment), we decided to use the data of 12 weeks after MGP in group II as posttreatment data to analysis.

Before initial treatment, no differences exited in all parameters we studied among 3 groups (all P□0.05). After the finish of whole treatment course, all subjective symptoms and objective signs, including SPEED, TBUT, CFS, meibum grade, lid telangiectasia, orifices abnormality and lid tenderness, were significantly improved in all groups (all P□0.01; Table.1).

The improvement of ocular symptoms (SPEED) and TBUT was more obvious in MGP-IPL group compared with group of IPL and MGP (P=0.003 or P=0.012; Fig.1). But there was no difference in posttreatment CFS among all 3 groups (all P□

0.05; Fig.1). Between group IPL and group MGP, no differences existed in SPEED, TBUT, CFS after treatment (all P 0.05/3; Fig.1).

As for lid margin related indexes, the posttreatment meibum grade and lid telangiectasia improved more in group MGP-IPL than group IPL or group MGP (P=0.002 or P 0.001, respectively; Table.1, Fig.2). The orifices abnormality after treatment in MGP-IPL group was also significantly better than MGP group (P=0.016; Table.1, Fig.2). And for lid tenderness, group MGP-IPL had more significant improvement than group IPL (P 0.001; Table.1, Fig.2). No differences in meibum grade, lid telangiectasia and orifices abnormality were found between group IPL and group MGP (all P 0.05/3; Fig.2) except for lid tenderness, in which better results were seen in group MGP (P 0.001; Table.1, Fig.2).

As shown in figure 3, no patients got a SPEED score≤9 before treatment in all groups, while after treatment, 14.29%, 26.67% and 64.29% of patents in group I, II and III obtained a score of 0-9. Besides, we can see that all eyes in 3 groups had a TBUT≤5s before treatment, but 17.86%, 36.67% and 92.9% of eyes in group I, II and III showed a TBUT more than 5s after treatment (Fig.4).

Six months after final treatment the SPEED were still significantly lower in patients received MGP-IPL than MGP or IPL alone (14.50±3.76 vs. 14.60±3.11 vs. 11.36±2.10, P=0.01 or P=0.004). And 35.7% or 20% of patients treated with IPL or MGP alone said they need to receive treatment again to release recurrent dry-eye related symptoms, while for patients received MGP combined IPL course, no patients revealed the need to be treated again.

# Discussion

Previous researches have proved that both intraductal meibomian gland probing and intense pulsed light had significant efficacy in helping o-MGD patients achieve relief of symptoms and signs; yet, they also showed this improvement was just for the vast majority and recurrence may appear during the follow up period[12]. Up to now, no research has offered in-depth discussion for these exceptions. It seems researchers all focused on the pleasantly impressive results of these new treatments, but seldom noticed their inadequacies. Although MGP can re-open the MG orifices, it is limited in controlling inflammation. And it is an invasive treatment, so the repeated MGP should be restricted for patients. IPL treatment is minimally invasive and can promote the discharge of eyelid lipids, reducing the inflammation of the eyelid margin. However, the effect of IPL on the MG obstruction and scar is limited. So, we need a fire new treatment combination that could give full play to the best therapeutic effect of the two treatments, and reduce the complications and times of invasive probing.

Reiko Arita et al recently observed 81% of IPL treated refractory o-MGD eyes showed amelioration of ocular symptoms and 70% showed an improvement in TBUT[15]. Zeba A et al reported that 91.4% of their patients received MGP described subjective symptomatic improvement during follow up[16]. Similar results were also obtained in our study, with 85.7% and 100% of treated eyes in IPL and MGP group revealing relief of symptoms and 96.4% and 93.3% showing increase in TBUT respectively. However, in MGP-IPL group, all patients (100%) showed alleviation of dry eye related symptoms and extension of TBUT.

As the meibomian gland of o-MGD patient is usually ill-conditioned, in which abnormal meibum stasis accumulates rather than flows to the ocular surface, increased intraglandular pressure and duct expansion is evitable[13]. And with recurrent attacks of o-MGD, atrophy of meibomian glands can be usually noticed[17]. It has long been considered that this atrophy was irreversible until Maskin proposed intraductal meibomian gland probing and proved this treatment can increase MG tissue area and growth of atrophied MGs[10,17]. Meibomian gland probing opened the obstructed orifices and ducts mechanically. With the pop up of constrained meibum, keratinized epithelium and debris, vicious cycle of o-MGD progression was broken and the majority of patients received immediate relief of symptoms[11,16]. However, the quantity of meibum in ocular surface is not a decisive factor in retarding the evaporation of aqueous and stabilizing the tear film. The meibum lipid quality was found to play an even more important role in maintaining the ocular surface equilibrium[13,18]. Nakayama et al showed all cases had improvements in meibum viscosity (grade 3–0, 3–1, and 3–2) after MGP, as the abnormal meibum was released promptly with the sudden open of orifices and then gradually eliminated by blinking[13]. But there was just only one case returning to normal level. And growing evidence has suggested the inflammation reaction played an essential role in the formation of abnormal meibum. The enzymes produced by bacterial flora could result in altered lipid composition with increased melting point and viscosity[3,19]. We assumed that the single mechanical function of MGP to improve the meibum lipid quality is limited. Xiao Ma et al recommended the use of 0.1% fluorometholone after MGP to diminish inflammation, as MGP predispose the lid margin to a topical corticosteroid effect[11]. But we think, although MGP increased the accessibility of gland to anti-inflammatory drugs, traditional application of eyedrops or eye ointment after MGP can hardly deliver drugs to the deepest gland lumens. Since the inflammation of o-MGD has been proved to exist not only in eyelid margin and ocular surface but also within the glands[20], the unthorough evacuation of inflammation after MGP may be an essential reason for the re-obstruction and may also explain that why not all the patients attained the improvement after MGP and why a considerable number of patients need to receive repeated probing.

In 2002, Dr. Rolando Toyos noticed one of his patients with rosacea had obvious improvement of dry eye related symptoms after IPL therapy[21]. From then on, IPL has drawn more and more attention of ophthalmologists and has been proved to be effective and safe to treat patients with moderate or severe MGD. The surprising efficacy of IPL to ease symptoms of MGD patients can be mainly attributed to its effect of vasculature destruction and meibum melting[21,22]. Lid telangiectasia is a common characteristic of o-MGD and these tiny vessels along the eyelid margin also increase the access of inflammatory mediators, resulting in aggravated chronic inflammation above the palpebral edge or within the glands[23–25]. The 580 nm wavelength released by intense pulsed light can be absorbed by intravascular hemoglobin and then activate selective photothermolysis, leading to the development of blood clotting. And thus abnormal vessels gradually shut down and bacterial loading reduces[21]. Apart from that, the heat from either photothermolysis or light energy itself can enhance the liquidity of meibum. And compared with the traditional eyelid warming, the heat effect delivered by intense pulsed light is far more lasting and permeable[26]. Surprisingly, instead of showing reduction in symptoms, 2 patients (14.8%) in our study had even more serious symptoms at the end of single IPL treatment course. We speculate that this deterioration may relate to obstruction sites within the glands. Maskin has proposed 6 types of o-MGD according to the depths of fixed obstruction and function of MG[17]. In meibomian gland with a deep-seated intratubal obstruction or partial distal obstruction, IPL may work well as the vast melting meibum ahead the fixed area can easily move out under the extrusion force caused by forceps or daily blinking. While for gland that was completely fixed in distal part, it's actually the opposite, as the stagnant meibum was confined between the terminal of glands and the obstruction site, analogous to staying in a blind alley. The heat released by IPL and pressure caused by forceps may paradoxically increase the intraductal pressure and exacerbate the inflammatory response, thus IPL alone may not alleviate disease but irritate the condition. This effect can also be indirectly seen from our data that

posttreatment lid tenderness of IPL, albeit showed alleviation compared with baseline, was still significantly higher than MGP and MGP-IPL group.

It seems like neither IPL nor MGP is absolutely perfect method to treat all refractory o-MGD patients, while their unique advantages can effectively make up their inherent deficiency. This assumption was also confirmed by our research, as patients received MGP-IPL showed the best improvement results. With the opening of blocked glands by probing at first, meibum within glands can flow without any restriction. And the followed 3 times IPL treatments further attenuate inflammation and eliminate the abnormal meibum, leading to optimal therapeutic effect. Compared with single IPL or MGP, MGP combined IPL gained significant superiority in improving SPEED, TBUT, meibum grade and lid telangiectasia.

Once MGP cannot help all patients obtain continued symptom relief in our 6 months observation. 20% of patients still need repeated invasive probing, but these treatments would aggravate patients' misery. The combination of MGP with noninvasive IPL helped 100% of patients attain the most enduring symptom relief in our study. This combination treatment may achieve the maximum therapeutic effect of MGP and IPL, reducing the possibility of trauma and scarring caused by repeated probing.

Despite positive outcomes, there are still some limitations of our research: First, the participated patients in our study were comparatively small and the duration of follow-up was not long enough. Further investigation is warranted to evaluate the long-term results of these treatments with a large number of cases. Second, MGP is an invasive method that is more suitable for MGD patients with severe gland obstruction or gland scar, while IPL treatment is better in relieving intraductal inflammation. In this study, we found the combination of these two treatments could attain the best results, but we can't deny that this treatment mode would bring patients more financial, time and psychological burdens at the same time. Based on our results, we recommend patients that have at least half of orifices obstructed in each eyelid but with no apparent meibomian gland atrophy, and at the same time, have higher inflammatory index like lid telangiectasia scores receive MGP combined IPL therapy to exert the best curative effect of probing and anti-inflammation simultaneously.

## Conclusions

All of IPL, MGP and MGP combined IPL are effective methods for refractory o-MGD patients. But the combination of MGP and IPL could maximize the therapeutic benefits, which is especially suitable for patients who have severe meibomian gland obstruction and meanwhile obvious intraductal or eyelid margin inflammation, who want to gain the greatest amelioration in all clinical signs and subjective symptoms or still remain frustrated to either MGP or IPL.

## Abbreviations

Obstructive meibomian gland dysfunction (o-MGD); Intraductal meibomian gland probing (MGP); Intense pulsed light (IPL); Standard Patient Evaluation of Eye Dryness score (SPEED); Tear break-up time (TBUT); Corneal fluorescein staining (CFS); Meibomian gland (MG); Blepharon- keratoconjunctivtis (BKC)

## Declarations

- Ethics approval and consent to participate

This study was approved by Ethics Committee at the Affiliated Second Hospital, School of Medicine, Zhejiang University in Hangzhou, China. All the procedures adhered to the tenets of the Declaration of Helsinki. A written informed consent was obtained from each participated subject.

- Consent for publication

Not applicable.

- Availability of data and material

The datasets obtained and/or analyzed during the current study are available from the corresponding author on reasonable request.

- Competing interests

The authors declare that they have no competing interests.

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- Authors' contributions

XH: research design, manuscript preparation and treatment operation; QQ: data analysis and manuscript preparation; LW: data acquisition; JZ: data acquisition; LL: treatment operation; XJ: research design, manuscript preparation. All authors read and approved the final version of this manuscript.

- Acknowledgements

Not applicable.

- Additional statement

Our randomized controlled trial study adheres to CONSORT guidelines.

# References

1. Waduthantri S, Yong SS, Tan CH et al. Cost of dry eye treatment in an Asian clinic setting. PLoS One. 2012;7:e37711. doi:10.1371/journal.pone.0037711.
2. Miljanovic B, Dana R, Sullivan DA, Schaumberg DA. Impact of dry eye syndrome on vision related quality of life. Am J Ophthalmol. 2007;143:409–415. doi:10.1016/j.ajo.2006.11.060.
3. Nelson JD, Shimazaki J, Benitez-del-Castillo JM et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930–1937. doi:10.1167/iovs.10-6997b.

4. Rabensteiner DF, Aminfar H, Boldin I, Schwantzer G, Horwath-Winter J. The prevalence of meibomian gland dysfunction, tear film and ocular surface parameters in an Austrian dry eye clinic population. Acta Ophthalmol. 2018. doi:10.1111/aos.13732.
5. Foulks GN, Bron AJ. Meibomian gland dysfunction: a clinical scheme for description, diagnosis,classification, and grading. Ocul Surf. 2003;1:107–126.
6. Gayton JL. Etiology, prevalence, and treatment of dry eye disease. Clin Ophthalmol. 2009;3:405–412.
7. Goto E, Monden Y, Takano Y et al.Treatment of non-inflamed obstructive meibomian gland dysfunction by an infrared warm compression device. Br J Ophthalmol. 2002;86:1403–1407.
8. Gupta PK, Vora GK, Matossian C, Kim M, Stinnett S. Outcomes of intense pulsed light therapy for treatment of evaporative dry eye disease. Can J Ophthalmol. 2016;51:249–253. doi:10.1016/j.jcjo.2016.01.005.
9. Jiang X, Lv H, Song H et al. Evaluation of the Safety and Effectiveness of Intense Pulsed Light in the Treatment of Meibomian Gland Dysfunction. J Ophthalmol. 2016;2016:1910694. doi:10.1155/2016/1910694.
10. Maskin SL. Intraductal meibomian gland probing relieves symptoms of obstructive meibomian gland dysfunction. Cornea. 2010;29:1145–1152. doi:10.1097/ICO.0b013e3181d836f3.
11. Ma X, Lu Y. Efficacy of Intraductal Meibomian Gland Probing on Tear Function in Patients With Obstructive Meibomian Gland Dysfunction. Cornea. 2016;35:725–730. doi:10.1097/ico.0000000000000777.
12. Sik Sarman Z, Cucen B, Yuksel N, Cengiz A, Caglar Y. Effectiveness of Intraductal Meibomian Gland Probing for Obstructive Meibomian Gland Dysfunction. Cornea. 2016;35:721–724. doi:10.1097/ico.0000000000000820.
13. Nakayama N, Kawashima M, Kaido M, Arita R, Tsubota K. Analysis of Meibum Before and After Intraductal Meibomian Gland Probing in Eyes With Obstructive Meibomian Gland Dysfunction. Cornea. 2015;34:1206–1208. doi:10.1097/ico.0000000000000558.
14. Asiedu K, Kyei S, Mensah SN, Ocansey S, Abu LS, Kyere EA. Ocular Surface Disease Index (OSDI) Versus the Standard Patient Evaluation of Eye Dryness (SPEED): A Study of a Nonclinical Sample. Cornea. 2016;35:175–180. doi:10.1097/ico.0000000000000712.
15. Arita R, Mizoguchi T, Fukuoka S, Morishige N. Multicenter Study of Intense Pulsed Light Therapy for Patients With Refractory Meibomian Gland Dysfunction. Cornea. 2018. doi:10.1097/ico.0000000000001687.
16. Syed ZA, Sutula FC. Dynamic Intraductal Meibomian Probing: A Modified Approach to the Treatment of Obstructive Meibomian Gland Dysfunction. Ophthal Plast Reconstr Surg. 2017;33:307–309. doi:10.1097/IOP.0000000000000876.
17. Maskin SL, Testa WR. Growth of meibomian gland tissue after intraductal meibomian gland probing in patients with obstructive meibomian gland dysfunction. Br J Ophthalmol. 2018;102:59–68. doi:10.1136/bjophthalmol-2016-310097.
18. Ashraf Z, Pasha U, Greenstone V, Akbar J, Apenbrinck E, Foulks GN. Quantification of human sebum on skin and human meibum on the eye lid margin using Sebutape(R), spectroscopy and chemical analysis. Curr Eye Res. 2011;36:553–562. doi:10.3109/02713683.2011.574331.
19. Lee H, Chung B, Kim KS, Seo KY, Choi BJ, Kim TI. Effects of topical loteprednol etabonate on tear cytokines and clinical outcomes in moderate and severe meibomian gland dysfunction: randomized clinical trial. Am J Ophthalmol. 2014;158:1172–1183.e1. doi:10.1016/j.ajo.2014.08.015.
20. Liu S, Richards SM, Lo K, Hatton M, Fay A. Sullivan DA. Changes in gene expression in human meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011;52:2727–2740. doi:10.1167/iovs.10-6482.
21. Toyos R, McGill W, Briscoe D. Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study. Photomed Laser Surg. 2015;33:41–46. doi:10.1089/pho.2014.3819.

22. Dell SJ, Gaster RN, Barbarino SC, Cunningham DN. Prospective evaluation of intense pulsed light and meibomian gland expression efficacy on relieving signs and symptoms of dry eye disease due to meibomian gland dysfunction. Clin Ophthalmol. 2017;11:817–827. doi:10.2147/opth.s130706.
23. Bron AJ, Benjamin L, Snibson GR. Meibomian gland disease. Classification and grading of lid changes. Eye. 1991;5 ( Pt 4):395–411. doi:10.1038/eye.1991.65.
24. Geerling G, Tauber J, Baudouin C et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011;52:2050–2064. doi:10.1167/iovs.10-6997g.
25. Shine WE, McCulley JP. Polar lipids in human meibomian gland secretions. Curr Eye Res. 2003;26:89–94.
26. Arita R, Morishige N, Shirakawa R, Sato Y, Amano S. Effects of Eyelid Warming Devices on Tear Film Parameters in Normal Subjects and Patients with Meibomian Gland Dysfunction. Ocul Surf. 2015;13:321–330. doi:10.1016/j.jtos.2015.04.005.

# Tables

**Table1. Clinical Parameters Before and After Treatment in O-MGD**

| | Group (IPL) | | P | Group (MGP) | | P | Group (MGP-IPL) | | P |
|---|---|---|---|---|---|---|---|---|---|
| Scores | before | after | | before | after | | before | after | |
| SPEED | 16.14±3.53 | 12.43±3.84 | 0.001 | 17.13±3.23 | 11.93±3.26 | 0.001 | 18.00±3.51 | 9.00±1.80 | 0.001 |
| TBUT | 2.66±0.88 | 4.35±0.88 | 0.001 | 3.21±0.98 | 4.81±2.03 | 0.001 | 2.78±1.00 | 6.61±1.57 | 0.001 |
| CFS | 2.29±2.71 | 0.96±2.10 | 0.001 | 2.13±2.34 | 0.80±1.35 | 0.001 | 2.79±2.51 | 0.29±0.71 | 0.001 |
| Meibum grade | 7.11±4.57 | 20.82±11.83 | 0.003 | 8.23±3.15 | 26.57±11.63 | 0.001 | 6.64±3.41 | 41.11±10.26 | 0.001 |
| Lid telangiectasia | 2.36±0.49 | 1.43±0.50 | 0.006 | 2.27±0.45 | 1.73±0.64 | 0.001 | 2.54±0.51 | 1.07±0.26 | 0.001 |
| Orifices abnormality | 2.14±0.52 | 1.54±0.51 | 0.001 | 2.30±0.60 | 1.80±0.85 | 0.001 | 2.00±0.67 | 1.29±0.46 | 0.001 |
| Lid tenderness | 1.79±0.79 | 1.36±0.49 | 0.003 | 2.13±0.57 | 0.57±0.63 | 0.001 | 1.93±0.81 | 0.36±0.49 | 0.001 |

P values were determined with the paired Wilcoxon test

# Figures

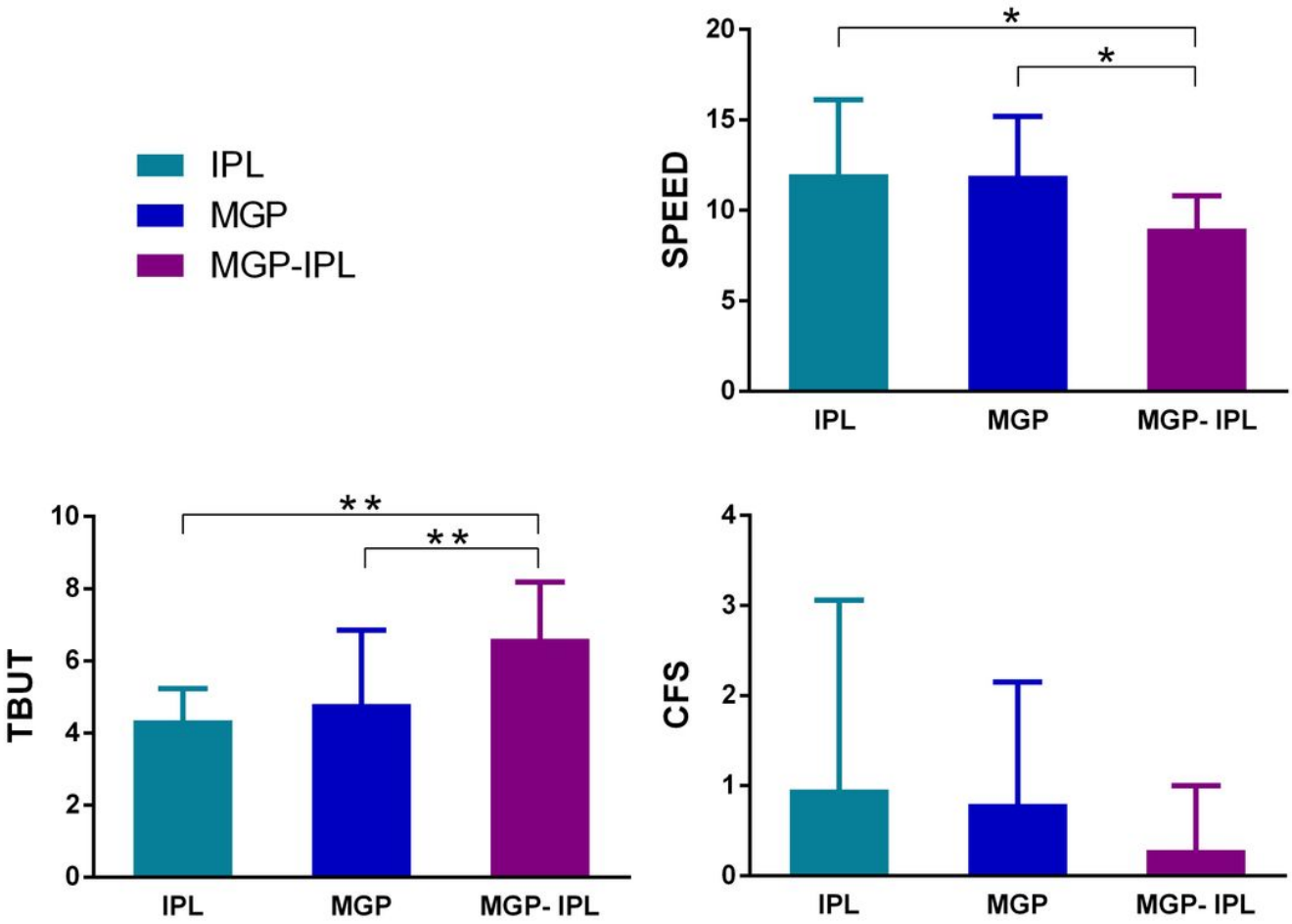
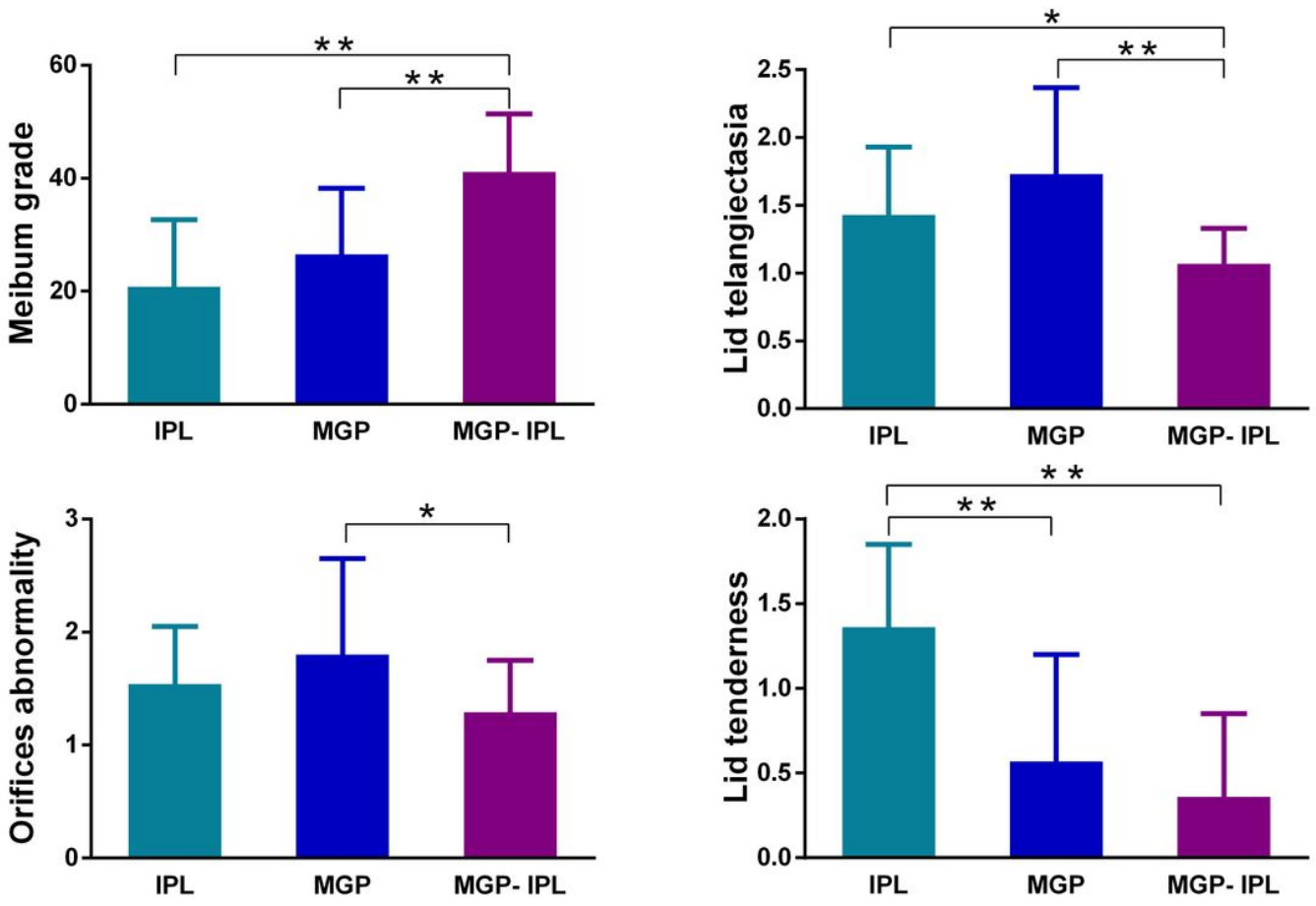



**Figure 1**

Comparation of SPEED score, TBUT and CFS after treatment in 3 groups (IPL, MGP, MGP-IPL). Notes: all parameters prior treatment had no statistical differences among 3 groups. *P≤0.05/3, **P0.001.




## Figure 2

Comparation of meibum grade and lid margin finding results after treatment in 3 groups. Notes: all parameters prior treatment had no statistical differences among 3 groups. *P≤0.05/3, **P0.001.

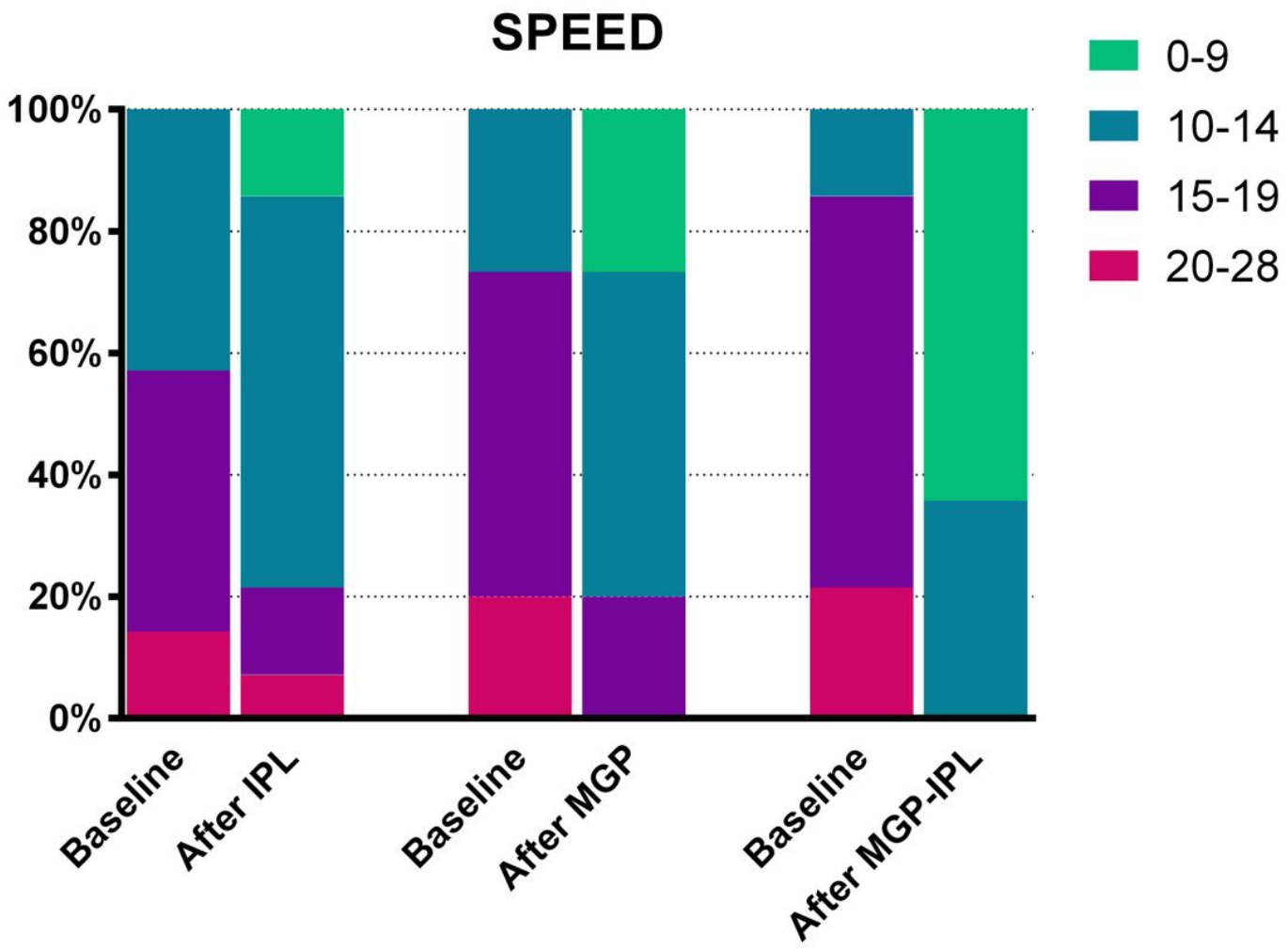



**Figure 3**

Change in the SPEED questionnaire score between baseline and after treatment in three groups.

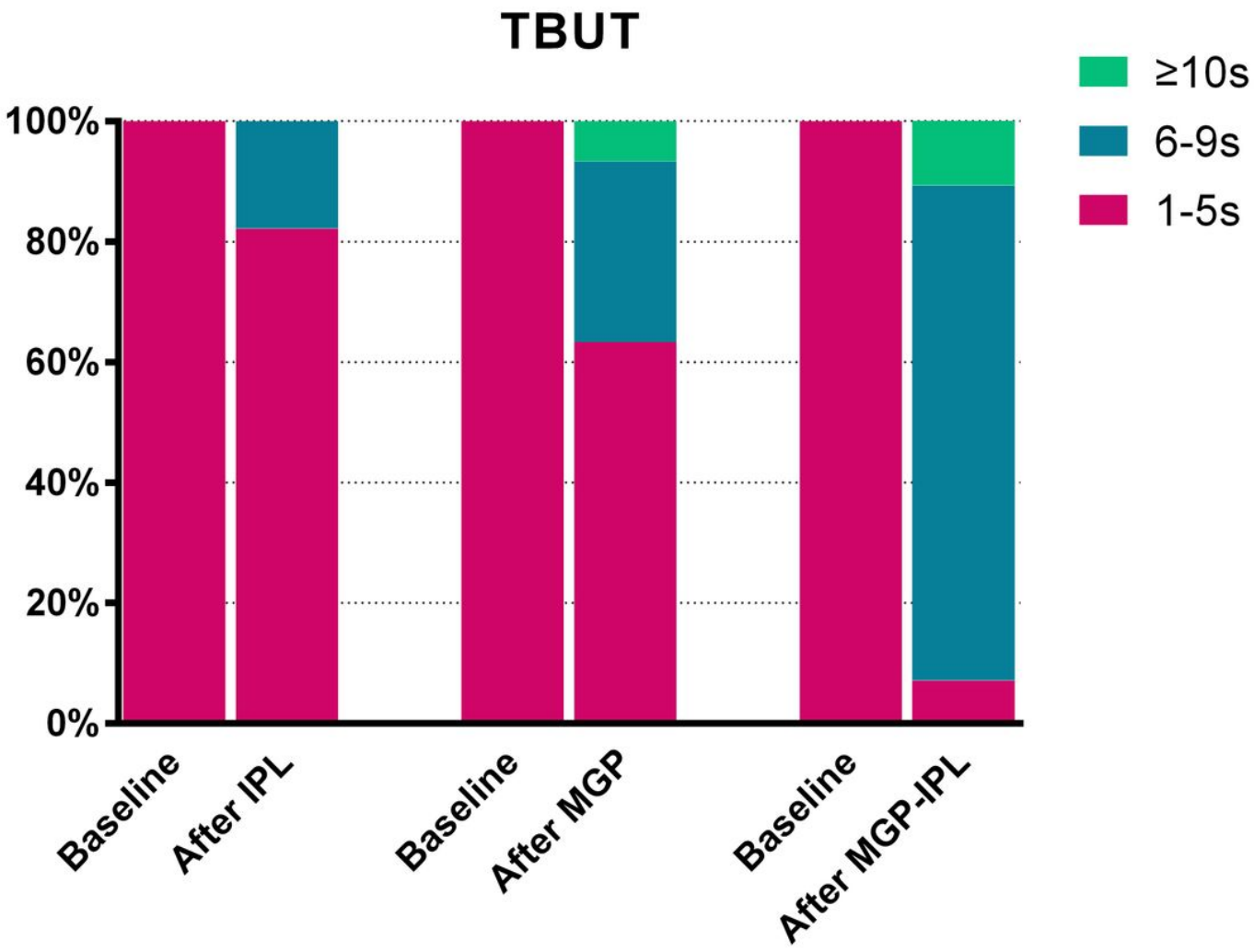



**Figure 4**

Change in TBUT between baseline and after treatment in three groups.

## Supplementary Files

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- supplement1.doc