

# Intense pulsed light treatment in meibomian gland dysfunction

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## ABSTRACT

Dry eye disease (DED) associated with meibomian gland dysfunction (MGD) is a chronic and progressive disease that can cause numerous eye symptoms, such as discomfort, irritation, stabbing, and vision disturbances. Previously used treatment methods are insufficient for some patients. The article describes the indications, method of performing, mechanisms of action, and effectiveness of intense pulsed light (IPL) regarding available literature. The technique involves using a series of impulses of non-coherent, polychromatic broad-bandwidth wavelengths in the periorbital area to the skin around the eyes and eyelids. Numerous studies have shown the effectiveness of IPL for MGD, a decrease in symptoms connected with DED assessed by Ocular Surface Disease Index (OSDI) questionnaire, an increased tear break-up time (TBUT), and improvement of meibomian glands function indicators.

**KEY WORDS:** intense pulsed light therapy; meibomian gland dysfunction; dry eye disease; treatment

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## INTRODUCTION

Dry eye disease (DED) is a chronic and progressive disease that can cause symptoms such as discomfort, irritation, stinging, dryness, eye fatigue, fluctuating visual disturbances, and an unstable tear film, with possible damage to the eye surface. In 2017, Tear Film & Ocular Surface Society (TFOS) in the Dry Eye Workshop II (DEWS II) defined DED as a multifactorial eye surface disease characterized by a loss of tear film homeostasis, which is associated with hyperosmolar tear film instability and inflammation causing neurosensory irregularities [1]. The sequence of changes underlying the pathomechanism of DED is compared to a vicious circle, where the starting point is: meibomian gland dysfunction, eyelid margin inflammation, allergies, ocular surgeries, contact lens use and other external factors that contribute to hyperosmolarity and tear film instability, apoptosis and inflamma-

tion, which interact with each other in a positive feedback loop. The “vicious circle” concept may explain why, after removing the primary triggering factor, for example, discontinuing contact lens use, DED symptoms persist.

The frequency of occurrence of DED is estimated between 5–35%, depending on age, race, and the definition of the disease. The American studies estimate that 3.2 million women and 1.6 million men aged 50 or older suffer from moderate to severe dry eye [2].

Meibomian glands located in the tarsal plates in the upper and lower eyelids secrete lipids and proteins (meibum) on the eye surface, forming the outer layer of the tear film. It provides stability to the tear film and protects against evaporation. Dysfunction of the meibomian glands (MGD) is defined by the International Workshop on MGD as a chronic, diffuse abnormality of the Meibomian glands, usu-

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ally characterized by blockage of the terminal ducts and/or qualitative and quantitative changes in gland secretion. It may cause changes in the tear film, eye irritation, inflammation, and eye surface disease.

The frequency of MGD ranges from 46% to 70% in Asian countries, while in Caucasian populations, it ranges from 3.5% to 20%. Differences may be due to inconsistent diagnostic criteria between countries [3]. The development of tear film changes associated with MGD may be due to many causes, including eye surgery or hormonal treatments, such as hormone replacement therapy in women and antiandrogen therapy in men [4]. In addition, ocular factors such as aniridia, proliferation of *Demodex* spp., eyelid tattooing, floppy eyelid syndrome, giant papillary conjunctivitis, and trachoma are believed to be associated with MGD [5].

So far, the treatment of MGD contains moisturizing eye drops, eyelid margin massage, improvement of eyelid hygiene by removing blocked meibum, warm compresses, local anti-inflammatory agents, antibiotics, and supplements with omega-3 fatty acids [6]. However, these traditional treatment options for MGD do not bring long-lasting satisfactory results for the patients, so new potential therapeutic interventions are needed.

Intense pulsed light (IPL) therapy has been developed and is widely used in the treatment of dermatological diseases. Accidental observations of its impact on meibomian glands and DED symptoms suggest that it may also be effective in that disease. This technique involves a series of impulses of non-coherent, polychromatic light in the periocular area, with a wavelength range of 500–1200 nm on the skin around the eyes and eyelids. The selection of fluence during IPL therapy in  $\text{J}/\text{cm}^2$  is determined by the Fitzpatrick scale to assess patient skin types to minimize the risk of melanin damage and subsequent hypopigmentation. It is usually in the range of 8 to 14  $\text{J}/\text{cm}^2$ . In addition to selecting the correct wavelength, the effectiveness of treatment depends on the duration, intervals, and smoothness of impulses applied to the target surface. Delivery of the impulse may be repeated once, twice, or three times over a time, typically ranging from 0.5 to > 20 ms [7].

A review of current guidelines and scientific research on IPL treatment associated with MGD was conducted. The literature search included the PubMed database and used the keywords “Intense pulsed light, meibomian gland dysfunction, dry eye disease, treatment, DED, IPL, MGD.”

## IPL — MECHANISMS OF ACTION

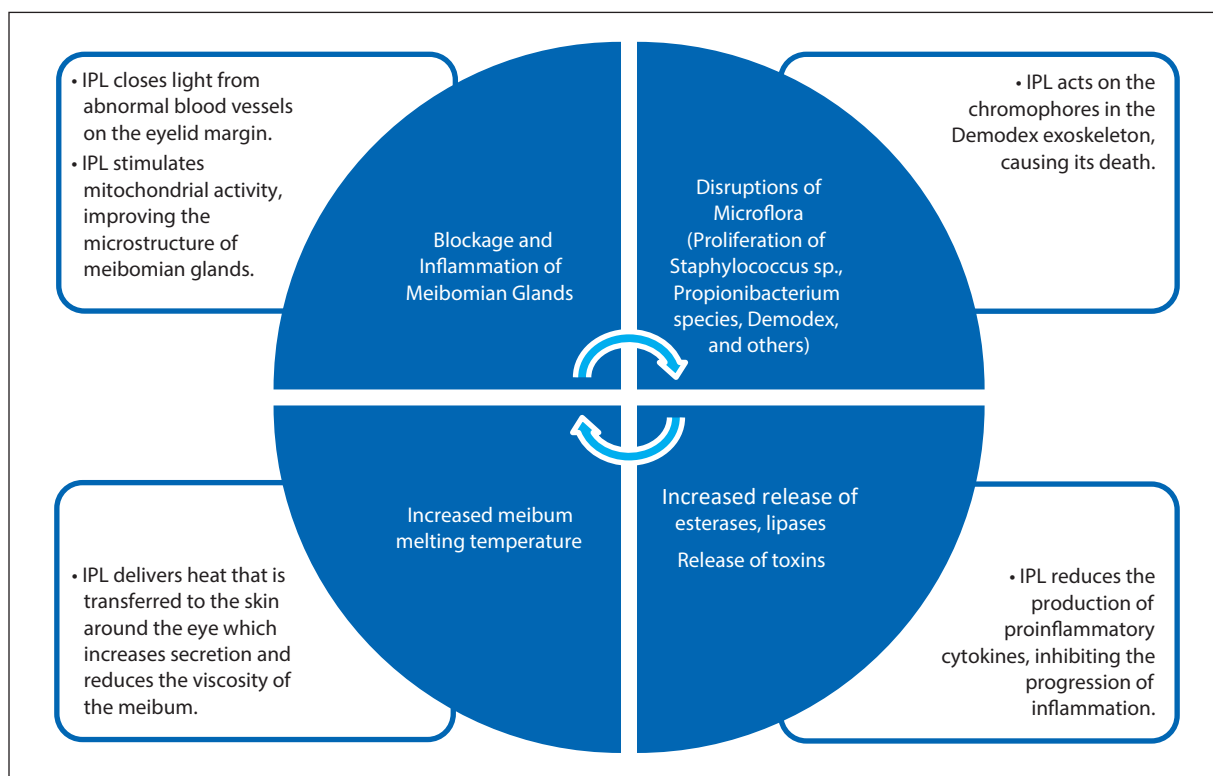
Several mechanisms are described in which IPL can affect the symptoms related to MGD. The European Dry Eye Society (EuDES) presents the concept of MGD vicious circle, where improper gland function exacerbates the proliferation of abnormal bacterial flora and *Demodex* spp. Enzymes secreted by bacteria, lipase, and esterase, raise the melting temperature of meibum, leading to its accumulation in the gland ducts. It conducts inflammation and creates favorable conditions for the proliferation of abnormal bacterial flora. Figure 1 shows the modified scheme of MGD vicious circle with mechanisms of action of the IPL treatment.

The laser produces heat, which is transmitted to the skin around the eye. This widens the openings of the glands and facilitates the dissolution and release of pathological secretion [9]. Improved secretion and decreased viscosity of meibum contribute to increased stability of the tear film and reduce dry eye symptoms due to excessive evaporation [10].

Additionally, the device emits energy, which is absorbed by chromophores in hemoglobin. That closes abnormally forming vessels on the edge of the eyelid and the attached conjunctiva [11]. Furthermore, IPL reduces the production of pro-inflammatory cytokines, inhibiting the progression of the inflammatory state. A randomized, double-blind trial by Ruixing Liu et al. analyzed the effect of IPL therapy on the level of interleukin 17A, interleukin 6, and prostaglandin E2 in the tear film. It showed decreased levels of interleukins and prostaglandins in patients with MGD without a significant difference in the level of these factors in the control group [12].

The photostimulatory effect of IPL has been proven to promote cell activity, such as photorejuvenation and wound healing [13]. Studies show that it stimulates the activity of cell mitochondria, improves the microstructure of the meibomian glands, and reduce the number of inflammatory cells around the glands [14]. There are also reports of reducing neuropathic pain and inflammation-related pain through the described therapy [15].

Extracellular matrix fibers loosen with age, which worsens the natural stiffness and elasticity of the tissues. At the level of eyelid skin, it can lead to poor adhesion of the eyelid margins and incomplete blinking. This process can reduce the pumping of meibum from the meibomian glands and leads to increased evaporation of tears. Studies show that photomodulation can stimulate fibroblast proliferation and increase collagen fiber synthesis in vitro [16].



**FIGURE 1.** The vicious circle of meibomian gland dysfunction (MGD) and possible mechanisms of action of intense pulsed light (IPL) therapy. Adapted from [8]

One of the factors causing MGD is microflora changes. *Demodex* spp. is a type of external parasite that feeds on gland secretions. Its colorful exoskeleton contains a chromophore that absorbs IPL energy, causing its death. According to available data, IPL therapy can impact reducing the number of bacteria on eyelid margins, limiting the inflammatory process in those tissues [17, 18].

### INDICATIONS TO IPL TREATMENT

According to the latest TFOS guidelines, IPL treatments are recommended for patients with MGD as a second-line treatment after patient education, eyelid hygiene recommendations, eyelid warming, massage, and lubricating eye drops. IPL therapy may be effective for individuals with MGD and proliferation of *Demodex folliculorum*, with floppy eyelid syndrome, aniridia, giant papillary conjunctivitis, trachoma, and during hormonal therapy.

### CONTRAINDICATIONS TO IPL TREATMENT

The procedure should not be performed on patients with active inflammatory conditions in

the orbital region, uncontrolled glaucoma, while using photosensitizing agents and with skin changes in the IPL treatment area like active infection, dysplastic lesion, neoplastic or premalignant changes, or tattoos. Wearing contact lenses is not recommended during the procedure [19].

### PERFORMING IPL

Before the procedure, it is necessary to apply eye covers and glasses with a filter for the person performing the procedure. Eye covers that do not allow light to pass through or corneal inserts and lash covers placed under the eyelids after local anesthesia are applied to the eyelid surface.

Existing skin marks should be covered, and gel should be applied to the eye socket area.

Depending on the manufacturer's recommendations and the patient's complexion, the strength of a single pulse is adjusted (most commonly 9–16 J/cm<sup>2</sup>).

Recommended place of application of the head and the number of pulses by most manufacturers are 4 impulses in the cheek area around the orbit with a vertical head setting and 1 impulse around

the eye socket from the temple. If corneal inserts are used, and the lashes are covered, 1 impulse can be delivered directly to the upper eyelid.

For the first 48 hours after the procedure, the use of UV filter creams is recommended.

The procedure should be repeated 3 to 5 times in a previously established schedule, depending on the manufacturer's recommendations, it may be day 0, 15, 45, 75 [20, 21].

### THE EFFICIENCY OF IPL TREATMENT

Numerous data assessing the effectiveness of IPL therapy in treating symptoms related to DED have emerged. Based on current literature, it can be concluded that IPL therapy is a safe procedure which reduces symptoms connected with dry eye and improves some eye surface parameters. The therapy does not lead to changes in tear production (based on Schirmer's test) and tear osmolarity.

Available meta-analyses of studies on the effectiveness of IPL therapy in treating MGD indicated a small number of qualitative studies. The American Academy of Ophthalmology report reviewed literature from 2019 considered 12 studies, of which 4 were rated level II and 8 were rated level III, based on a scale developed by the British Centre for Evidence-Based Medicine. All studies documented improvement in clinically significant parameters, including tear break-up time (TBUT), meibum quality measurements, meibomian gland patency, and results of the Ocular Surface Disease Index (OSDI) and Standard Patient Evaluation of Eye Dryness Questionnaire (SPEED). Adverse effects of the therapy were rare and included discomfort, skin redness, lash loss, and floaters of a self-limiting nature [22].

The meta-analysis and systematic review by Shuang Liu et al. from 2020 were based on the non-invasive tear break-up time (NIBUT) indicator and the SPEED questionnaire. Data was collected from four randomized controlled trials involving 122 people with MGD treated with IPL and 120 people in the control group. The collective analysis showed no statistically significant difference in the results of SPEED questionnaire between the two groups [95% confidence interval (CI): -0.16, (-0.41, 1.10)], but a statistically significant increase in NIBUT [95% CI: -0.90, (-0.41, 1.40)]. The results of the study did not provide conclusive evidence of the efficacy of IPL therapy in treating MGD [23].

A review of evidence-based therapies for MGD by Pun Yuet Lam et al. summarized data from 35 scientific articles. The authors considered the following treatment options: eyelid warming, thermal pulsation (Lipiflow), IPL therapy, meibomian gland probing, locally and orally administered antibiotics, and eye drops containing lipids or perfluorohexyloctane. The study showed that all mentioned methods are effective in treating MGD [24]. Ten articles on IPL therapy were considered, where authors observed improvement in lipid layer quality, meibum quality and meibomian gland expression measurements, TBUT and Visual Analogue Score (VAS). Moreover, eyelid margin abnormalities such as an increased number of blood vessels and meibomian gland blockages enhanced in individuals with advanced stage of MGD [25]. In patients undergoing phacoemulsification and photorefractive keratectomy (PRK), there were significantly fewer symptoms connected with dry eye, when IPL therapy was administered beforehand [26]. IPL was also compared with conventional eyelid warming and manual massage. The OSDI, TBUT, meibomian gland expression, and meibum quality improved after treatment in both treatment groups ( $p < 0.05$ ). Changes in the macrostructure of glands, for example, maintaining the largest diameter and the densification of meibomian gland lobules three months after treatment, were in both groups, but the IPL-treated group got better results [27].

In a randomized, double-blind study from 2022 by R. Toyos et al., 88 patients with moderate to severe stage of MGD were randomly assigned to 4 sessions of IPL therapy with meibomian gland massage at 2-week intervals or to a control group with simulated IPL therapy and meibomian gland massage. TBUT measurements increased in both groups. In the IPL therapy group it was 4.0 (95% CI: 3.6, 4.4) to 6.0 seconds (95% CI: 5.4, 6.6); in the control group, it was 3.8 (95% CI: 3.4, 4.1) to 4.6 seconds (95% CI: 4.0, 5.1), this difference was statistically significant ( $p = 0.5253$ ). Other symptoms that improved in both groups but were more pronounced in the treatment group included the qualitative and quantitative assessment of meibomian glands —  $\Delta$ MGS increased by  $5.2 \pm 0.7$  points ( $\mu \pm$  SEM) (95% CI: 3.8, 6.6) in the control group it was  $18.5 \pm 1.3$  points (95% CI: 15.8, 21.2) ( $p < 0.0001$ ). These results suggest that for patients with moderate to severe symptoms, combined IPL therapy and meibomian gland expression may be a safe and valuable method for relieving symptoms connected with MGD [28].

There is a large variability in available studies, such as the number of sessions, duration of IPL therapy, and the usage of additional procedures, for example, meibomian gland massage, eyelid hygiene, warm compresses, and artificial tears. The lack of guidelines for the IPL treatment of MGD can explain this. So far, the optimal number of IPL therapy sessions and the intervals between sessions have not been established, so further research is needed to determine the optimal settings [29].

## CONCLUSIONS

DED is a multifactorial disease. Patients often perceive multiple daily eye drops as tedious, time-consuming, and uneconomical, which can worsen both: quality of life and compliance with ophthalmologists. Therefore, IPL therapy can represent a real therapeutic option for these patients. Although the mechanism of action is not entirely understood yet, many studies indicate that this treatment can reduce both causes and symptoms of DED.

Numerous studies have shown the efficacy of IPL therapy for MGD, with a reduction in symptoms associated with DED, assessed by OSDI questionnaire, TBUT, and improvement in meibomian gland function parameters. There are known numerous potential mechanisms by which IPL therapy can reduce the inflammation of eyelid margins. The possibility of a synergistic effect of IPL therapy with meibomian gland massage has been demonstrated.

In the TFOS DEWS II stepwise management algorithm, IPL technology is recommended as a second-stage treatment for dry eye syndrome after eyelid hygiene and various types of eye lubricants [30]. In February 2021, The United States Food and Drug Administration (FDA) issued approval for the Lumenis device for IPL treatment of DED connected with MGD. Further research is needed to determine the optimal number and duration of sessions and the possibility of using individualized protocols based on patient response.

## Conflict of interests

The authors report no competing interests.

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