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Research Progress of M22 Intense Pulsed Light in the Field of Ophthalmology

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Abstract: This study reviews the application of M22 Intense Pulsed Light (IPL) technology in the field of ophthalmology. It elaborates on the evolutionary history and theoretical basis of this technology, and conducts an in-depth analysis of its latest research progress in the treatment of ophthalmic diseases (such as dry eye disease and retinal vascular diseases) as well as periorbital skin disorders. Meanwhile, this paper also evaluates the safety of this therapeutic method and its potential adverse reactions. Looking ahead, through continuous technological improvement, expansion of therapeutic indications and exploration of combined treatment regimens, M22 IPL technology is expected to significantly promote the advancement of ophthalmic medicine and provide innovative perspectives and methods for the treatment strategies of ophthalmic diseases.

Keywords: M22 Intense Pulsed Light; Ophthalmic Diseases; Periorbital Skin Treatment; Research Progress.

1. Introduction

With the in-depth application of optical technology in the medical field, M22 Intense Pulsed Light (IPL) has pioneered a brand-new approach for the treatment of ophthalmic diseases and the cosmetology of periorbital skin, relying on its unique photothermal and photochemical effects. By emitting high-energy broadband intense light, this technology can precisely target ocular tissues, thereby achieving the dual effects of disease treatment and ocular appearance improvement. This paper aims to systematically sort out the research progress of M22 IPL in the field of ophthalmology, providing valuable references for clinical application and technological optimization.

2. Development Origin of M22 Intense Pulsed Light

Intense Pulsed Light (IPL) is a type of non-laser visible and near-infrared light composed of single-pulse or multi-pulse incoherent high-energy composite light. Since Dr. Bitter proposed and first applied it to the treatment of cutaneous photodamage and photoaging in 1988, IPL has become one of the core technologies and essential equipment in most laser cosmetic clinics and medical centers. The Broad Bandwidth Intense Pulse Light (BBL) developed by him has also been widely acclaimed for its outstanding performance and curative effect. Optimal Pulse Technology (OPT), Equally Distributed Fluence (EDF) technology, and optimized spectral technology have enhanced the ability to control photon energy, altered the emission mode of photon pulses, not only expanding clinical indications but also improving safety, making treatment more flexible and precise. Initially, IPL technology was mainly used to treat skin problems such as hyperpigmentation and vascular lesions. With the continuous maturity of technology and the gradual expansion of clinical applications, researchers have begun to explore its potential value in the field of ophthalmology. As a representative device of IPL technology, M22 has undergone multiple technological iterations. By optimizing light source performance, spectral adjustment systems, and pulse control technology, it has greatly improved the accuracy and safety of treatment. Since its introduction into the field of ophthalmology, M22 IPL has provided new solutions for the treatment of various ophthalmic diseases, effectively promoting the innovation of ophthalmic treatment technologies.

3. Application Basis of M22 Intense Pulsed Light

The spectral range of M22 IPL is 400–1200 nm. Its photothermal effect can precisely regulate temperature, enabling target tissues to absorb light energy and convert it into thermal energy, triggering a series of biological reactions while minimizing damage to surrounding normal tissues. The photochemical effect stimulates cells to produce biochemical reactions, promoting tissue repair and regeneration. IPL has a wavelength range of 400–1200 nm and exhibits the wave-particle duality of electromagnetic radiation, i.e., it has a specific wavelength and frequency, and energy is transmitted in the form of photons. Specific wavelengths can be selected with the help of filters to achieve selective effects on different target tissues of the eye. The broadband spectrum and adjustable output mode of IPL determine that its output energy can be absorbed by different target components in skin tissues (including melanin, hemoglobin, water, etc.) in different proportions, achieving various therapeutic purposes.

4. Mechanism of Action of M22 Intense Pulsed Light

4.1. Meibomian Gland Function Activation

Meibomian gland dysfunction (MGD) is one of the main causes of dry eye. The thermal effect of M22 IPL can penetrate into the meibomian glands, lower the melting point of the blocked lipids in the glands, make them melt and restore fluidity, thereby promoting lipid excretion and improving the secretory function of meibomian glands. At the cellular level, the photothermal effect can stimulate the proliferation and differentiation of meibomian gland epithelial cells, maintaining the normal physiological

structure and function of meibomian glands. Relevant studies have shown that IPL may affect the synthesis and secretion of meibomian gland lipids by regulating the expression of lipid synthesis-related genes (such as fatty acid synthase, FAS)[1].

4.2. Collagen Changes

A study [2] irradiated the dorsal skin of BALB/c mice with IPL and collected skin samples for detection before treatment and at 1 day, 3 days, 5 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 6 weeks, and 8 weeks after treatment. Histological analysis showed that the dermis was thickened, accompanied by an increase in collagen and improvement in tissue structure. Under the condition of IPL irradiation dose ranging from 2 W to 8 W, the staining intensity of type I and type III collagen in the IPL-treated group was significantly higher than that in the sham-operated group. It can be concluded that IPL irradiation can not only promote the synthesis of new collagen but also inhibit collagen degradation in the skin, thereby achieving the effect of photorejuvenation.

4.3. Anti-inflammatory Effect

M22 IPL can seal abnormally dilated capillaries on the ocular surface, reduce the exudation of inflammatory mediators (such as interleukin-6 and tumor necrosis factor-α), inhibit the chemotaxis and activation of inflammatory cells, thereby alleviating the ocular surface inflammatory response. Its photochemical effect can also regulate immune cell function, inhibit the differentiation of Th17 cells, reduce the secretion of Th17-related cytokines, and promote the proliferation and activation of regulatory T cells, enhancing immunosuppressive function, and effectively reducing chronic ocular surface inflammation. In addition, the photothermal effect can reduce the activity of matrix metalloproteinases, decrease the degradation of extracellular matrix, and protect ocular surface tissues from inflammatory damage.

4.4. Inhibition of Demodex Growth

Demodex infection is an important factor causing dry eye. The energy generated by M22 IPL can destroy the living microenvironment of Demodex. Its thermal effect may directly damage the cellular structure of Demodex, affect its metabolism and reproductive capacity, thereby inhibiting its growth and reproduction and alleviating dry eye symptoms caused by Demodex infection.

The optimized M22 IPL therapy exerts a selective photothermal effect that effectively induces the coagulation and occlusion of abnormal palpebral marginal capillaries, consequently attenuating inflammatory factor release. In addition, the thermal radiation effect of this therapy can soften meibum and increase its fluidity, effectively solving the problem of meibomian gland obstruction, and reducing the load of Demodex, bacteria, and other microorganisms at the eyelid margin. This therapy can also promote the synthesis of adenosine triphosphate (ATP) in the mitochondria of meibomian gland cells, stimulate the proliferation of fibroblasts, and thus improve the microstructure of meibomian glands[3-4]. Through multi-dimensional mechanisms of action, optimized M22 IPL therapy improves the meibomian gland and ocular surface microenvironment, reduces the level of inflammatory factors in ocular surface tissues, thereby enhancing tear film stability and alleviating dry eye symptoms in patients.

5. Research Progress of M22 Intense Pulsed Light in the Treatment of Ophthalmic Diseases

5.1. Dry Eye Treatment

A large number of clinical studies have shown that most patients with MGD-related dry eye experience significant relief from dry eye symptoms (such as dryness, foreign body sensation, and asthenopia) after receiving 2–4 sessions of M22 IPL treatment. The tear secretion volume increases significantly, the tear film breakup time is prolonged, and the ocular surface inflammation indicators are decreased. Some patients can maintain good therapeutic effects for several months after treatment, with high treatment safety and few adverse reactions.

Some studies have attempted to apply M22 IPL to retinal vascular diseases, such as retinal vein occlusion and diabetic retinopathy. Theoretically, its specific wavelengths can be absorbed by hemoglobin in retinal blood vessels, sealing abnormal neovascularization, reducing vascular leakage, and improving retinal blood circulation. From the perspective of molecular mechanisms, IPL may inhibit the expression and activity of vascular endothelial growth factor (VEGF), reduce its stimulation of vascular endothelial cells, thereby inhibiting neovascularization. In addition, its photothermal effect can coagulate proteins in blood vessels, leading to vascular occlusion. However, this application is still in the exploratory stage with limited clinical cases, and further large-sample, multi-center studies are needed to clarify its therapeutic effect and safety.

Gontijo LC et al.[5] treated 76 dry eye patients with Intense Regulated Pulsed Light (IRPL) therapy, with patients receiving sequential light pulses on the bilateral periorbital area at 1 day, 15 days, 45 days, and 75 days after the initial evaluation. In addition to basic ophthalmic examinations, the tear osmolarity of both eyes was carefully measured. It was found that after 4 sessions of IRPL treatment, both subjective (OSDI) and objective (osmolarity) parameters of dry eye evaluation were improved in the clinically intervened patients.

Whang WJ et al.[6] found that when evaluating the changes in objective optical quality of patients with meibomian gland (MG) dysfunction after IPL treatment combined with meibomian gland expression (MGX), compared with baseline, not only all clinical symptoms and signs of patients were significantly improved, but also the optical quality parameters were significantly increased after IPL treatment combined with MGX.

Efficacy: A 2023 Meta-analysis (n=1200) showed that M22 IPL combined with meibomian gland massage can increase the tear film breakup time (TBUT) by 2.5 times and reduce the OSDI score by 47%.

Parameter Optimization: The recommended energy density is 10–14 J/cm[2] and the pulse interval is 30–40 ms (to avoid epidermal burns). JJ Kudrna[7] summarized the history, indications, safety, and effectiveness of IPL in the treatment of MGD, as well as its mechanism of action. IPL has been used in dermatology since the 1980s and is now also used in ophthalmology for MGD treatment, including reducing meibum viscosity and photocoagulation. Literature supports IPL as a safe and effective method for the management of MGD. MGD is a common ophthalmic disease, and IPL provides a new treatment method for refractory MGD.

Dr. Toyos R is a pioneer in the use of IPL technology to

treat MGD patients. In his published literature, he described that rosacea patients with various ocular diseases experienced significant improvement in telangiectasia and facial flushing symptoms after receiving IPL treatment. Notably, these patients reported improved skin conditions, accompanied by enhanced ocular comfort and visual acuity after treatment. Through clinical examinations, they observed positive changes in the patients' eyelid margins, meibomian gland function, and tear film breakup time. Based on these findings[8], he and his research team began to explore the potential link between IPL treatment and ocular health. They confirmed that this phototherapy technology is not only suitable for rosacea patients but also effective for most individuals with MGD who are eligible for IPL treatment. From 2003 to 2009, Dr. Toyos R successfully treated hundreds of patients with IPL technology. He also formulated a non-proprietary standardized treatment protocol to ensure that any properly trained ophthalmologist can achieve the best therapeutic effect.

Toyos R also conducted a study[9] on the effect of using Lumenis M22 (micropulsed IPL, 590 nm filter) on the Visual Analogue Scale for Pain, evaluating the severity, frequency, and characteristics of ocular pain. Results: After treatment, all evaluation indicators were improved, the tear film breakup time was statistically significantly increased, and the frequency of dry eye symptoms and ocular pain episodes was significantly reduced. No serious or non-serious adverse events occurred. Conclusion: Preliminary studies have shown that the 6 mm cylindrical handpiece using the Lumenis M22 IPL machine can safely and effectively increase the tear film breakup time and improve dry eye symptoms.

5.2. Demodectic Blepharitis

Zhang Xiaogang et al.[10] evaluated the clinical efficacy of Lumenis M22™ IPL in reducing Demodex infection in eyelashes. The study included 40 patients, with one group receiving IPL treatment and the other group using 5% tea tree oil as a control. Multiple indicators were evaluated before and after treatment, including Demodex count and Ocular Surface Disease Index (OSDI) score. The results showed that there were significant differences in OSDI score, tear film breakup time (TBUT), meibum quality, and other indicators between the IPL group and the control group at 30 days and 90 days after treatment. The Demodex eradication rate in the IPL group was also higher than that in the control group.

Currently, the treatment strategies for ocular surface diseases have gradually shifted to comprehensive treatment regimens aimed at maintaining the overall ocular surface homeostasis. Eyelid lesions such as meibomian gland dysfunction (MGD), Demodex infection, and blepharitis interact with each other, causing varying degrees of damage to ocular surface health. These lesions disrupt the balance of ocular surface homeostasis, thereby inducing dry eye and keratitis. Due to the anatomical structure of the eyelid, the efficacy of traditional treatment methods such as manual physical hot compress massage is limited. However, IPL technology can effectively eliminate capillary inflammation or kill Demodex through the thermal effect generated by penetrating light energy. In addition, LipiFlow technology eliminates other major causes of ocular surface inflammation through thermal effect and physical compression, providing a more crucial and long-lasting therapeutic effect for MGD[11]. Therefore, personalized treatment technologies based on photothermal effect show potential effectiveness. Looking ahead, IPL and LipiFlow technologies are expected to eliminate immune inflammatory factors causing ocular surface diseases or block the transmission pathways related to systemic immune-related diseases.

Chen Jingling[12] adopted developed and optimized IPL technology to treat blepharitis-related dry eye and evaluated its biomedical effects on meibomian gland function and corneal epithelial repair. The study concluded that the optimized IPL technology showed significant improvement in the treatment of blepharitis-related dry eye and could effectively improve meibomian gland function. However, this technology did not show a significant promoting effect on corneal epithelial repair, so it is recommended to consider other alternative treatment options.

5.3. Periorbital Skin Treatment

Shergill M et al.[13] stated that IPL is a promising treatment method for ocular rosacea, and its ability to alleviate dry eye symptoms with limited adverse events proves its value. Further research on this new treatment method is necessary to determine its role in the management of ocular rosacea.

The periorbital skin is thin and rich in blood vessels, prone to the appearance of red blood streaks and flushing. M22 IPL can precisely target abnormally dilated capillaries. Its photothermal effect enables hemoglobin in blood vessels to absorb light energy and convert it into thermal energy, causing damage and coagulation of vascular endothelial cells, contraction and atrophy of vascular walls, which are then absorbed by the body, thereby improving the color of periorbital skin and restoring its normal appearance. At the cellular and molecular levels, the photothermal effect may also regulate the expression of angiogenesis-related factors, such as inhibiting the expression of angiopoietin-2 and promoting the restoration of vascular stability. Clinical practice has shown that after 3–5 sessions of treatment, the area of red blood streaks and flushing around the eyes of patients is significantly reduced, the color fades, and there are no obvious adverse reactions.

For periorbital solar lentigines, freckles, and other pigmented spots, the selective photothermal effect of M22 IPL can make pigment granules absorb light energy, then break down and be phagocytized and cleared by macrophages. In this process, the photothermal effect may activate the mitogen-activated protein kinase signaling pathway in cells, promote the apoptosis of melanocytes, and reduce melanin synthesis. Clinical observations have found that combined treatment with external whitening drugs can further improve the effect of pigment spot lightening, and the skin recovers quickly after treatment, with a low incidence of adverse reactions such as hyperpigmentation.

With aging, the periorbital skin will experience problems such as sagging and increased wrinkles. The photothermal and photochemical effects of M22 IPL can stimulate fibroblasts in the periorbital skin, making them synthesize and secrete more collagen and elastic fibers. From the perspective of molecular mechanisms, the photothermal effect can activate the transforming growth factor-β signaling pathway, promote the transcription and translation of collagen genes, and inhibit the degradation of collagen by matrix metalloproteinases. After multiple treatments, the elasticity of the patients' periorbital skin is enhanced, wrinkles are reduced, and the overall appearance of the eyes is younger.

5.4. Other Indications

Sella[14] evaluated the efficacy of IPL therapy using OPT technology as an adjuvant therapy for preventing the recurrence of moderate to severe blepharokeratoconjunctivitis (BKC). The study involved 33 BKC patients, of whom 21 received OPT treatment and 11 received only MGX treatment. Evaluation indicators included meibum quality, MG secretory function, eyelid margin signs, Corneal Fluorescein Staining (CFS) score, Non-Invasive Tear Film Breakup Time (NITBUT), OSDI score, Schirmer's I Test (SIT), Tear Film Lipid Layer Thickness (TFLL), and Meibomian Gland Dropout Rate (MGDR). Safety indicators included visual acuity, intraocular pressure, ocular structural damage, and facial skin appearance. Results: The treatment group showed greater improvements in meibum quality, MG expression, eyelid margin signs, and OSDI score. NITBUT and MGDRs were significantly improved in the treatment group. No adverse events occurred in either group, and no BKC recurrence was observed in the treatment group. Conclusion: IPL is a safe and effective adjuvant therapy for BKC, which may be more effective than MGX alone in reducing eyelid margin inflammation and preventing recurrence.

6. Safety and Adverse Reactions of M22 Intense Pulsed Light Treatment

M22 IPL has high overall safety in ophthalmic applications, but some adverse reactions may still occur. After dry eye treatment, some patients may experience transient ocular symptoms such as tingling, photophobia, and lacrimation, which can generally be relieved within a few hours. After periorbital skin treatment, local erythema, edema, pain, etc., may occur, usually subsiding within 1–2 days. To reduce the risk of adverse reactions, doctors need to strictly control treatment indications, accurately set treatment parameters, and guide patients to perform proper postoperative care.

A relevant study[15] observed and evaluated the efficacy and safety of IPL directly applied to the eyelids of MGD patients without corneal shield protectors. It was found that during 3 sessions of IPL treatment, the non-invasive tear film breakup time, redness degree, and OSDI questionnaire scores of patients were improved, and a significant improvement in the percentage of meibomian gland loss was also observed ($p=0.024$). No serious adverse reactions were reported during treatment and follow-up.

Lee et al.[16] conducted a retrospective analysis of 2 cases of ocular injury after IPL in the Palmer Eye Institute and found that one patient developed ocular pain, pupil defect, ocular inflammation, and other symptoms after treatment. Within 10 months, the injury progressed to posterior iris transillumination defect, eventually evolving into permanent iris photophobia lasting for many years. The other patient developed ocular pain, visual impairment, pupil defect, and endophthalmitis 3 days after surgery. Two months later, the patient still had photophobia and pain, and the pupil defect remained permanent.

7. Future Development Directions of M22 Intense Pulsed Light in the Field of Ophthalmology

7.1. Technological Optimization and Equipment Innovation

In the future, M22 IPL equipment is expected to achieve further optimization in terms of light source stability, spectral regulation accuracy, and pulse energy uniformity. The development of new filters and intelligent control systems can accurately adjust treatment parameters according to individual differences and lesion characteristics of patients, improve treatment effects, and reduce the incidence of adverse reactions. At the same time, combined with artificial intelligence technology, it can realize intelligent diagnosis of ocular lesions and personalized formulation of treatment plans, improving the intelligent level of treatment.

Shami ME et al.[17] conducted a retrospective chart review to evaluate the effect of "EyeLight", a new device combining IPL and Low-Level Light Therapy (LLLT), on patients with refractory dry eye who were unresponsive to conventional drug therapy. Each patient received 2 to 5 sessions of treatment, and clinical measurements were performed before and after each session, including tear film breakup time (TBUT), ME-CHECK-meiboscale, and ME-CHECK questionnaire. The same clinical evaluations were conducted 3 to 5 weeks after the final treatment. Significant improvements in objective clinical signs were found: TBUT increased from 6.98±1.41 s to 9.27±1.25 s, and the ME-CHECK-meiboscale decreased. A reduction in the severity classification of ME-CHECK-meiboscale was observed in 90% of the studies, and subjective clinical symptoms on the ME-CHECK questionnaire were improved simultaneously. No ocular or facial adverse events were found during treatment. They proposed that "EyeLight" is an effective treatment method for refractory MGD-related dry eye syndrome (DES) that is unresponsive to conventional treatment.

7.2. Expansion of Therapeutic Indications

With the deepening of research, M22 IPL is expected to play a role in the treatment of more ophthalmic diseases.

Glaucoma: It is theoretically speculated that M22 IPL may improve ocular aqueous humor circulation through its photothermal effect. On the one hand, it can regulate aqueous humor production by acting on the ciliary body; on the other hand, it can promote the metabolism and repair of trabecular meshwork tissue, enhance aqueous humor outflow, and thereby reduce intraocular pressure. However, this hypothesis still requires rigorous experimental research and clinical verification to clarify its feasibility and safety.

JM et al. [18] first proposed the use of IPL to treat glaucoma patients with ocular surface diseases caused by long-term use of intraocular pressure-lowering eye drops. This study included 30 glaucoma patients with dry eye induced by intraocular pressure-lowering eye drops, all of whom received four sessions of treatment with the Optima IPL system. Analysis showed that after treatment, symptom scores were significantly reduced, corneal staining scores were decreased, tear meniscus height and osmolarity were improved, and meibomian gland expression was enhanced. The conclusion indicates that IPL treatment is an effective method to improve the symptoms of ocular surface diseases in glaucoma patients.

Macular Diseases: Some researchers have attempted to use M22 IPL to stimulate the metabolism and repair of cells in the macular area. Specific wavelengths of light may promote the functional recovery of retinal pigment epithelial cells in the macular area and inhibit the abnormal growth of choroidal neovascularization. However, due to the particularity of the structure and function of the macular area, how to accurately control treatment parameters to avoid damage to the macular area remains an urgent problem to be solved.

Corneal Dystrophy: The photochemical effect of M22 IPL may promote corneal cells to secrete more extracellular matrix, repair damaged corneal tissue, and improve corneal transparency and function. At present, research in this field is still in the initial stage, and further animal experiments and clinical trials are needed to explore its therapeutic effect and application prospects.

Scleritis: In view of the anti-inflammatory properties of M22 IPL, it is expected to reduce the inflammatory response of scleral tissue, inhibit the excessive activation of immune cells, and alleviate the pain and discomfort symptoms of scleritis patients. However, relevant research needs to be further carried out to determine the optimal treatment parameters and course of treatment.

7.3. Exploration of Combined Treatment Regimens

To improve treatment effects, more attention will be paid to the combined application of M22 IPL and other treatment methods in the future. For example, combining with drug therapy, laser therapy, surgical treatment, etc., to give play to the advantages of different treatment methods and achieve synergistic effects. In the treatment of dry eye, combined with artificial tears, anti-inflammatory drugs, etc., for comprehensive treatment; in the treatment of retinal vascular diseases, combined with anti-VEGF drugs to improve treatment effects and delay disease progression.

8. Conclusion

The application of M22 IPL in ophthalmology has achieved significant progress, showing good efficacy and safety in dry eye treatment, periorbital skin cosmetology, and other aspects. From its initial application in dermatology to the current extensive exploration in ophthalmology, M22 IPL has become one of the important means of ophthalmic treatment. In the future, with continuous technological optimization and in-depth clinical research, it is expected to make breakthroughs in the field of retinal vascular diseases and other areas, providing better options for the treatment of ophthalmic diseases and ocular cosmetology, and promoting the sustainable development of ophthalmic medicine.

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