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MODERN METHODS FOR THE TREATMENT OF MEIBOMIAN GLAND DYSFUNCTION

ABSTRACT

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The dissertation contains 174 pages and is illustrated with 25 tables, 14 figures and 1 appendix.

The bibliography contains 372 sources, of which 3 are in Cyrillic, 369 are in Latin, and 5 are Internet sources.

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CONTENTS

INTRODUCTION 3
I. PURPOSE, OBJECTIVES AND RESEARCH METHODOLOGY 5
1. Purpose, objectives 5
2. Materials and methodology of the study 5
2.1. Location of the study. 5
2.2. Subject of the study. 5
2.3. Selection criteria. 7
2.3.1. Inclusion criteria 7
2.3.2. Exclusion criteria 7
3. Research methodology 7
3.1. Taking a medical history, determining eye status 7
3.2. OSDI questionnaires 8
3.3. Biomicroscopic examination 11
3.4. Ophthalmoscopy 11
3.5. Tonometry 11
3.6. Measurement of non-invasive tear film break-up time (NIBUT1, s; NIBUTAV, s) 11
3.7. Meibography and determination of the percentage of meibomian gland deficiency (MGL) 13
3.8. Schirmer test (ST, mm) 14
3.9. Intense pulsed light (IPL) 15
4. Statistical methods 18
II. RESULTS AND DISCUSSION 19
1. Results and discussion of task 1. 19
1.1. General data on patients included in the study. 19
1.2. Investigation of the relationship between age group and degree of Meibomian dysfunction 20
1.3. Investigation of the relationship between gender and the degree of Meibomian dysfunction. 22
1.4. Study of tear film break-up time. 23
1.5. Investigation of the Schirmer test. 27
2. Results and discussion of task 2. 32
2.1. Study of tear film break-up time in cataract surgery patients. 33
2.2. Investigation of the Schirmer test in patients who have undergone cataract surgery. 35
3. Results and discussion of task 3. 3
3.1. TBUT 39
3.1.1. TBUT before IPL 39
3.1.2. TBUT after first IPL procedure 39
3.1.3. TBUT after second IPL procedure 39
3.2. Schirmer test 39
3.2.1. Schirmer test before IPL 39
3.2.2. Schirmer test after the first IPL procedure 40
3.2.3. Schirmer test after second IPL procedure 40
4. Results and discussion of task 4. 42
5. Results and discussion of task 5 5
Conclusion 6
Conclusions 65
Contributions 66
Scientific publications and communications 67

LIST OF ABBREVIATIONS USED

MGD	**Meibomian Gland Dysfunction**
MG	**Meibomian glands**
IPL	**Intense Pulsed Light**
VEGF	**Vascular Endothelial Growth Factor**
ATP	**Adenosine triphosphate**
PPARg	**Peroxisome Proliferator-Activated Receptor Gamma**
OSDI	**Ocular surface disease index**
STI	**Schirmer I**
STII	**Schirmer II**
TFI	**Tear film integrity, functional tear index**
TMH	**Tear meniscus height**
TBUT	**Tear Break-Up Time**
NIBUT	**Non Invasive Break-Up Time**
OCT	**Optical coherence tomography**
MGL	**Meibomian Gland Loss**
MMP	**Matrix Metalloproteinases**
LIPCOF	**Lid Parallel Conjunctival Folds**
NF-AT	**Nuclear factor of activated T-cells**
IL	**Interleukin**
MGX	**Meibomian Gland Expression**
DED	**Dry eye disease, dry eye syndrome**
SS	**Saugren syndrome**
CL	**Contact lenses**
LLLT	**Low-Level Laser Therapy**
QOV	**Quality of Vision questionnaire**
SPEED	**Standardized Patient Evaluation of Eye Dryness**
AZM	**Azithromycin**

INTRODUCTION

Dry eye syndrome is a common eye condition affecting approximately 350 million people worldwide. This syndrome occurs when the eye does not produce enough tears (water-deficient form) or when the tears it produces evaporate too quickly (evaporative form) or both. The most common cause of the evaporative form of dry eye syndrome is meibomian gland dysfunction (MGD). The aqueous deficiency form occurs in only about 10-15% of patients, while the evaporative component is observed in over 85% of them [Sheppard et al., 2023].

The meibomian glands (MG) secrete meibum, which forms the lipid layer of the tear film [Nichols et al., 2011]. MGD involves reduced meibum secretion or altered meibum composition, leading to disruption of the lipid layer of the tear film and accelerated tear evaporation [Mishra et al., 2023].

Patients with meibomian gland dysfunction experience symptoms such as burning, itching, and a gritty feeling in the eyes that interfere with daily activities, and visual problems such as blurred vision impede tasks requiring clear vision [Lemp et al., 2012]. These persistent symptoms often lead to anxiety and depression, with affected individuals reporting higher emotional distress [Messmer et al., 2015]. Current treatment of this condition prioritises treating symptoms on the surface of the eye, usually with eye lubricants. However, in the presence of lipid layer dysfunction, it is necessary to strive to improve the quantity and quality of the meibum, increase the stability of the tear film and reduce inflammation. Therapies used for this purpose include topical steroids, omega-3 fatty acid supplements, topical immunomodulators, autologous serum, topical azithromycin, oral doxycycline, warm compresses, manual expression of the meibomian glands, and others. Despite the numerous options available, there are often dissatisfied patients who feel that treatment has failed and are frustrated [Blackie et al., 2015].

Intense pulsed light (IPL) therapy is offered as a safe and effective therapeutic option for patients with evaporative dry eye associated with MGD, although it was originally developed for cosmetic dermatology [Rong et al., 2018]. IPL treatment involves the use of a high-powered pulsed lamp emitting a broad spectrum of incoherent light, typically in the range of 500 nm to 1200 nm. The therapy is usually performed in a series of sessions spread out over several months [Cote et al., 2020]. Objective tests show its effect on the structure and function of the MG, but there is little evidence regarding symptomatic changes. Despite the lack of absolute clarity regarding the mechanism of action, IPL therapy is establishing itself as an effective treatment for this pathology, whose main characteristic is its symptomatology.

The aim of this study is to determine the effectiveness of IPL therapy in patients with MGD by monitoring tear film break-up time (TBUT) and the Schirmer test, as well as through hypotheses for improvement of ocular surface symptoms, proposing it as a key treatment for MGD-related dry eye in refractory scenarios and even as a first-line option, thus suggesting a change in therapeutic regimens.

I. RESEARCH OBJECTIVES, TASKS AND METHODOLOGY

1. OBJECTIVES

Objective

The aim of this thesis is to investigate the efficacy and safety of intense pulsed light (IPL) for the treatment of dry eye syndrome due to meibomian dysfunction.

Tasks

The following **tasks** have been formulated to achieve the objective**:**

1. To investigate the efficacy of IPL in patients with first, second and third degree meibomian dysfunction by examining the non-invasive tear break-up time and Schirmer test, measured before IPL treatment and their change after two IPL procedures.

2. To investigate the effectiveness of IPL in patients with varying degrees of meibomian dysfunction one month after cataract surgery with multifocal intraocular lens implantation by examining the non-invasive tear break-up time and Schirmer test, measured before IPL treatment and their change after two IPL procedures.

3. To compare the effectiveness of IPL in patients with different degrees of meibomian dysfunction who have undergone cataract surgery and in patients without surgical intervention by analysing changes in non-invasive tear break-up time and Schirmer test results before and after two IPL procedures.

4. To analyse the subjective perception of patients with dry eye syndrome due to meibomian dysfunction based on responses to the standardised OSDI questionnaire before starting IPL therapy and their change after four procedures.

5. To develop an algorithm for the treatment of meibomian dysfunction in patients with a pronounced clinical picture.

2. MATERIALS AND METHODS OF THE STUDY

2.1. Location of the study

This is a prospective study conducted over a period of 5 years (2019–2024). The study was conducted at the Zora Eye Hospital in Sofia, Bulgaria. Subject of the study

2.2. Subject of the study

A total of 120 people with first, second and third degree meibomian dysfunction were examined, with almost equal representation of males and females (Table 1).

Table 1: Distribution by gender.

Gender	N	%
Men	58	48,3
Women	62	51,7
Total	120	100,0

Patients are divided into two age groups: under and over 45 years of age. Forty-nine (40.8%) patients are aged under 45 years, while 71 (59.2%) are aged over 45 years. The summary information is presented in Table 2.

Table 2: Distribution by age.

Age	N	%
up to 45	49	40,8
over 45	71	59,2
Total	120	100,0

Table 3: Distribution by average age and gender.

Gender	N	Mean	SD	Min	Max
Men	58	45,5	14,8	21,0	73,0
Women	62	54,8	16,1	20,0	85,0
Total	120	50,3	16,1	20,0	85,0

As presented in Table 3, the average age for men is 45.5 years, with an age range from 21.0 to 73.0 years. For women, the average age is 54.8 years, with an age range from 20.0 to 85.0 years.

Table 4. Distribution of patients who have not undergone cataract surgery and those who have undergone cataract surgery

Cataract	N	%
Unoperated	96	80,0
Operated	24	20,0
Total	120	100,0

Of the total 120 patients examined (240 eyes), 96, or 80.0% of all patients, did not undergo surgery. The remaining 24 patients, representing 20% of those examined, underwent cataract surgery, as summarised in Table 4.

2.3. SELECTION CRITERIA:

For the purposes of the study, the following inclusion and exclusion criteria were developed:

2.3.1. Inclusion criteria:

- Age over 18 and under 85
- Best corrected visual acuity.
- Diagnosed varying degrees of meibomian dysfunction, including ocular symptoms, blocked gland openings, reduced quality and quantity of meibum.
- Toyos skin type 1 to 4 according to sun sensitivity and skin type.
- No active lesions, skin cancer or specific skin pathology that would exclude IPL treatment.

2.3.2. Exclusion criteria:

- Age under 18 and over 85
- Visual acuity< 0.1
- Active eye infection.
- Active eye allergy.
- Other eye disease requiring the use of eye drops.
- Systemic use of antihistamines, antidepressants, corticosteroids and immunomodulators within 30 days prior to the examination.
- Chronic systemic diseases such as allergy, atopy, rheumatoid arthritis, diabetes, active herpes.

3. TEST METHODOLOGY

All tests were performed by the same investigator in the following sequence:

1. Detailed medical history, complete ophthalmological status, non-invasive tear film break-up time, meibography and determination of the percentage of meibomian gland deficiency, Schirmer test. A minimum interval of 5 minutes was observed between individual tests to avoid compromising any of the tests.
2. Standardised questionnaires (OSDI) were distributed to measure the severity of the disease.

3.1. Taking a medical history, determining eye e status

A detailed medical history of existing eye and general diseases was taken from all patients. During the interview with the patients, additional questions were asked about the health of the ocular surface

their subjective sensations and complaints. The examinations began with an assessment of visual function.

Refraction was measured using an auto keratorefractometer (Topcon-Japan, KR-800S, 2022). The best-corrected visual acuity was determined for each eye separately using the Visionix visual chart (L29i Chart Projector, China) at a distance of 6 metres. A darkened room with well-regulated lighting was used to ensure optimal visibility of the projected image. First, the left eye was covered, then the right. It was desirable to follow this order to create an algorithm and avoid confusion. Patients were asked to read all optotypes in sequence, starting with the largest and moving to the smallest. The smallest row that the subjects were able to read reflected the visual acuity of the corresponding eye. The same procedure was performed with the other eye.

3.2. OSDI questionnaires

All patients were given standardised questionnaires (OSDI) to measure the severity of the disease before the first IPL and after each subsequent procedure (Figure 1). The OSDI consists of 12 questions to assess the symptoms experienced by patients during the last week. It is divided into 3 parts, including the frequency of symptoms experienced, their impact on vision-related quality of life, and the presence of any environmental influences.

For each question, participants had to choose from 5 options. Each was rated on a scale ranging from 0 to 4:

- Never (0),
- Some of the time (1),
- Half the time (2),
- Most of the time (3) and
- All the time (4).

The final result was calculated on a scale from 0 to 100, with higher results representing a greater degree of dryness.

A score between 0 and 12 is considered normal, while a score between 13 and 22 represents a mild form, between 23 and 32 is moderate, and any number between 33 and 100 indicates a severe form of dryness.

Ocular Surface Disease Index© (OSDI©)[2]

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

Have you experienced any of the following *during the last week*?	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light? . .	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

Have problems with your eyes limited you in performing any of the following *during the last week*?	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

Have your eyes felt uncomfortable in any of the following situations *during the last week*?	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned? . . .	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

Add subtotals A, B, and C to obtain D
(D = sum of scores for all questions answered) (D)

Total number of questions answered
(do not include questions answered N/A) (E)

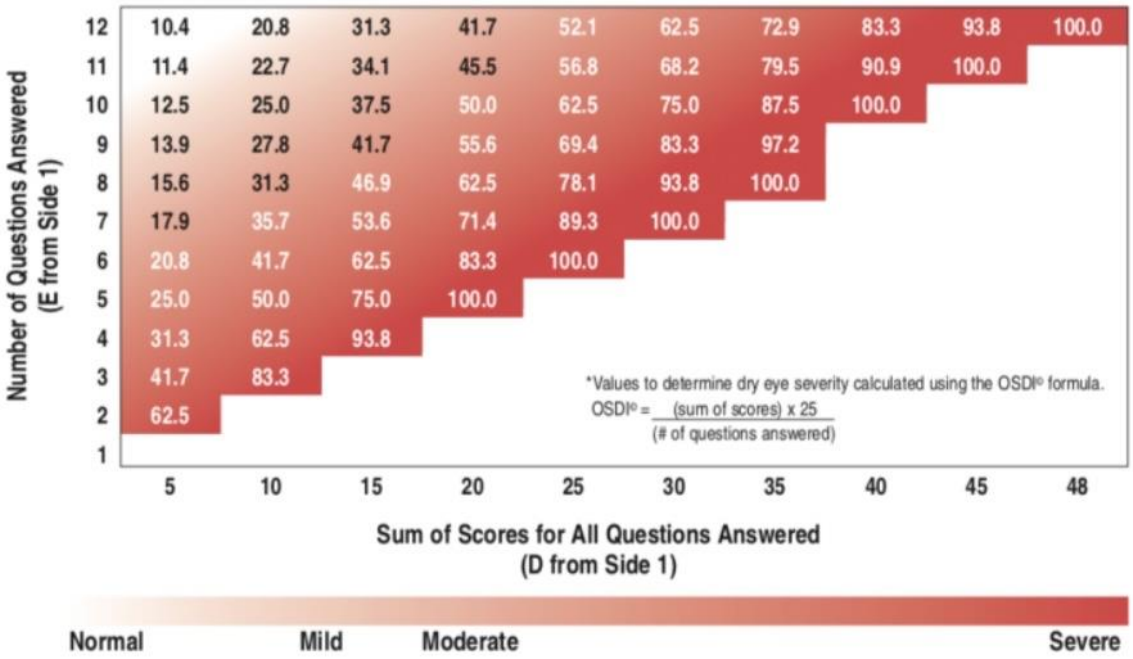
Please turn over the questionnaire to calculate the patient's final OSDI© score.

Evaluating the OSDI© Score[1]

The OSDI© is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI© is a valid and reliable instrument for measuring dry eye disease (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient's Dry Eye Disease[1, 2]

Use your answers D and E from side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.* Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.



Patient's Name: _____ Date: _____

How long has the patient experienced dry eye disease? _____

Eye Care Professional's Comments: _____

1. Data on file, Allergan, Inc.
2. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000;118:615-621

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Figure 1. OSDI questionnaire [Source: Internet].

3.3. Biomicroscopic examination

A biomicroscopic examination (Carl Zeiss Meditec AG, SL 115, 2017) was performed on all patients before the first procedure and after each subsequent procedure to assess the anterior segment, quality and expressivity of the meibum. A 0–3 scale was used to assess the quality of the meibum and the expressivity of the meibomian glands in accordance with the recommendations of TFOS DEWS II (Craig et al., 2017).

The quality of the meibum was assessed in each of the 8 glands of the central third of the lower eyelid on a scale of 0–3 for each gland:

- 0= clear meibum;
- 1= slightly cloudy;
- 2= cloudy and granular;
- 3= thick, like toothpaste.

The expression of meibum was assessed by 5 glands:

- 0= all glands are expressed;
- 1 = 3–4 glands expressible;
- 2= 1–2 glands expressible;
- 3= , no glandular expression.

This can be assessed in the lower or upper eyelid.

3.4. Ophthalmoscopy

The examination includes ophthalmoscopy with an indirect ophthalmoscopic lens (Ocular STD 90D) for a comprehensive assessment of the fundus, retina and optic nerve. This examination was necessary to rule out concomitant retinal or neuro-ophthalmological pathologies that could affect vision or prevent the IPL procedure from being performed.

3.5. Tonometry

In the present study, tonometry was performed with a non-contact tonometer (Canon TX-20P, Japan, 2018), which uses an air pulse to flatten the cornea and measure its resistance. The method is non-invasive, quick, comfortable for the patient and suitable for screening in outpatient settings. Intraocular pressure was measured for each eye immediately before inclusion in the IPL therapy protocol. Values outside the normal range (<10 mmHg or >21 mmHg) were grounds for further clarification or exclusion from the study.

3.6. Measurement of non-invasive tear break-up time (NIBUT1, s; NIBUTAV, s)

Non-invasive tear break-up time (NIBUT) is a test that was performed three times for each eye, according to the methodology proposed by Wiedemann and his colleagues [Wiedemann et al., 2010]. The Antares device (CSO, ANTARES – 2017, Italy) (Fig. 2) uses infrared interferometry to create an image of the tear film and monitor its stability. With the head fixed in position on the device, the

patient fixes a red dot with the eye being examined. While the patient's head remains fixed and positioned on the device, they must focus the eye being examined on the red dot. The examiner instructs the patient to look at the fixation point, blink twice in succession, and then open the examined eye wide and keep it open for as long as possible.

In infrared light mode, concentric circles are projected onto the cornea. The device automatically records the time and location of the first tear in the tear film in different sectors, expressed in seconds (NIBUT1, s). The device software calculates the average break time, taking into account the values from all sectors and the percentage of the examined area not covered by the tear film (NIBUTAV, s).

According to the device software parameters, values above 14 seconds for NIBUTAV are considered normal.

Physiological values for NIBUTAV are above 14 seconds and for NIBUT1 above 10 seconds [Wiedemann et al., 2010].

This indicator is key in diagnosing the evaporative form of dry eye, as it is comparable to the tear film break-up time after fluorescein application [Erb et al., 2012].



Figure 2. NIBUT examination of Antares (CSO, 2017, Italy) [Source: Skopemedical.no, 2025].

3.7. Meibography and determination of the percentage of meibomian gland (MGL) deficiency

The presence of meibomian glands was assessed using non-invasive infrared meibography with the ANTARES device (CSO, ANTARES – 2017, Italy) (Figure 3). The patient is comfortably seated in front of the device, placing their head in a stable position on a special support so that the eyelids can be properly visualised. After application of a local anaesthetic (proxymethacaine hydrochloride, Alcaine®), the upper and lower eyelids are everted. When the procedure starts, the device uses infrared light to illuminate the meibomian glands while taking pictures of the lower and upper eyelids. The device's camera captures detailed images that clearly show the condition of the meibomian glands. Using infrared light, the device can visualise both healthy and damaged or missing areas of the glands. The Antares device generates accurate numerical data on the coverage of the meibomian glands using specialised image analysis software. In addition to visualising healthy areas, the software also shows damaged areas, providing a clear picture of the degree of dysfunction. The results are presented not only as a percentage loss of glands, but also as the geographical location of the damaged areas on the eyelids. The software processes the captured infrared images and identifies areas of damage to the meibomian glands.

The degree of meibomian dysfunction is automatically reported by the device, which divides it into four categories:

- zero degree – 0% loss of glands,
- first degree -< 25% loss of glands,
- second degree - 25-50% loss of glands,
- third degree – 51% - 75% loss of glands and
- over 75% - fourth degree.



Figure 3. Determination of the degree of Meibomian dysfunction with the Antares device (CSO, ANTARES – 2017, Italy) [Crespo et al., 2021].

3.8. SCHIRMER TEST (ST, mm)

The Schirmer test (ST) is used to assess basal tear production. It is performed after the application of a local anaesthetic, proxymetacaine hydrochloride (Alcaine®, Alcon). The procedure involves placing two sterile paper strips measuring 5 x 35 mm (I-DEW tear strips, Ophthalmic Experts Ltd., Essex, UK) (Figure 4), which are folded and placed in the temporal 1/3 of the patient's lower eyelids. The patient is asked to keep their eyes closed for 5 minutes during the measurement, as this ensures more reproducible and accurate results [Didem et al., 2007]. The results are measured in millimetres, taking into account the wetted part of the strip after folding. Although there are different opinions regarding the physiological values of the Schirmer test, the most common norm is ST ≥ 10 mm for 5 minutes, which is also accepted in the present study [Jones, 1966].



Figure 4. Schirmer test (I-DEW tear strips, Ophthalmic Experts Ltd., Essex, UK) [photo: personal archive].

3.9. IPL

Over the past few decades, intense pulsed light (IPL) has been used primarily in dermatology to treat conditions such as rosacea and facial erythema, acne and seborrheic keratosis [Piccolo et al., 2014]. In 2015, Toyos et al. [Toyos et al., 2015] reported the use of IPL to improve the signs and symptoms of dry eye syndrome due to meibomian dysfunction. Based on this, numerous studies have investigated the potential use of IPL as a treatment for the signs and symptoms of primary and secondary forms of dry eye syndrome. Current manufacturers of IPL for ocular surface therapy are shown in Figure 5. The Lumenis M22 (M22; Yokneam, Israel/USA) combines optimal pulse technology with a modular laser multifunctional platform and is the most studied and published device for dry eye disorders [Xu et al., 2022].

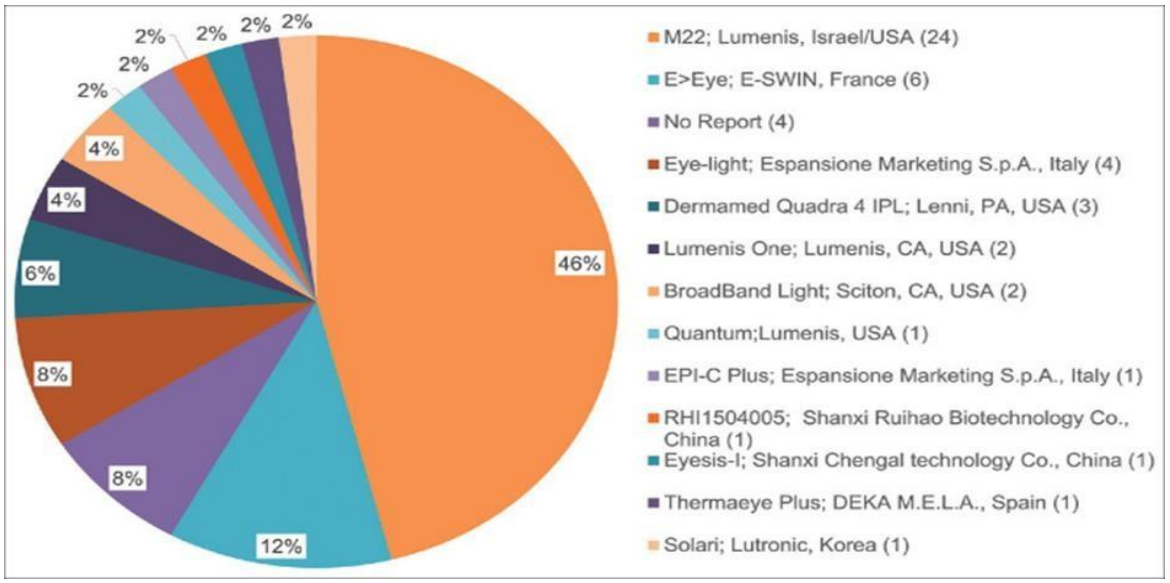


Figure 5. Devices for the treatment of dry eye studied in the literature (PubMed).

In the present study, an innovative intense pulsed light device, Lumenis M22 (Lumenis Ltd., Israel) (Figure 6)**,** was used to treat meibomian dysfunction**.** This platform is a multimodal system that allows the use of different light technologies, including IPL (Intense Pulsed Light), ResurFX and Nd:YAG. In ophthalmic practice, Lumenis M22 is mainly used through its IPL module, which is specially adapted for the treatment of evaporative dry eye syndrome associated with meibomian gland dysfunction (MGD) [Arita et al., 2018].



Figure 6. IPL Lumenis M22 (Lumenis Ltd., Israel) [source: https://lasertech.com.co/).

The IPL module of the Lumenis M22 uses Optimised Pulse Technology (OPT™), which ensures uniform distribution of light energy with controlled sub-pulses and cooling, ensuring safety and comfort during the procedure (Lumenis Ltd., 2023). The light spectrum is adjusted by interchangeable filters in the range 515–1200 nm, allowing precise targeting of blood vessels, Demodex mites and inflammatory mediators in the periorbital area [Toyos et al. 2020].

The device has two applicators – 35×15 mm and 15×8 mm, as well as a SapphireCool™ cooling tip, which maintains a constant low temperature on contact with the skin and protects against thermal damage. The energy parameters can be adjusted within the range of 10–35 J/cm², with a pulse duration of 4 to 20 ms and a repetition rate of up to 1 Hz, which provides flexibility for different skin types and symptom severity [Yin et al., 2020].

IPL therapy with Lumenis M22 is administered in a series of 3 to 4 procedures at intervals of 2 to 4 weeks [Dell, 2017]. When assessing the indications for IPL therapy, the skin of patients is classified according to Toyos' criteria (Type I – III: light to moderately dark skin – usually suitable for IPL with minimal risk; Type IV–VI: darker skin – increased risk of burns and pigmentation changes, IPL should be used with caution or is not recommended, taking into account the risks of side effects and the effectiveness of treatment). In order to minimise the risk of side effects and achieve maximum effectiveness of light therapy, only patients with skin phototype I–III according to Toyos classification, who are considered suitable candidates for IPL, were included in the study. The patient is positioned in a semi-recumbent position with special protective shields placed over the eyes. The area under the lower eyelids is covered with contact gel, after which 4 to 6 light pulses are applied to each side, covering the area from one tragus to the other, including the cheeks [Craig et al., 2017]. If necessary, the upper eyelid is also treated using an additional smaller cylindrical applicator.

After completion of light therapy, mechanical expression of the meibomian glands (MGX) is usually performed to facilitate the drainage of secretions and restore the lipid layer of the tear film [Arita et al., 2018].

The procedure is non-invasive, well tolerated and safe, with minimal risk of side effects. Thanks to the cooling system and individual adjustment of parameters according to skin phototype, the risk of erythema, pain or hyperpigmentation is extremely low.

4. STATISTICAL METHODS

The data obtained were processed using the specialised statistical package SPSS (Statistical Package for the Social Sciences) version
20.0. When interpreting the data, a critical level of significance $\alpha = 0.05$ was selected. Statistical significance is accepted when the p-value is less than α (p<0.05). Descriptive statistics were performed for the distribution of the entire sample by gender and age, as well as for the assessment of the central tendency (mean and median) and dispersion (standard deviation). A Friedman test was also performed. This is a non-parametric statistical method used to compare three or more related (dependent) samples. It is used as an alternative to one-way ANOVA for dependent (repeated) measurements when the data: do not follow a normal distribution or are at a rank level or are a small sample for which normality cannot be assumed. It is appropriate when there are repeated measurements on the same objects over time. The Friedman test assesses whether there are statistically significant differences between the medians of the related groups.

The Chi-Square test for independence was used to assess the possible dependence between categorical variables. It is a non-parametric statistical method used to test dependencies between categorical variables. It assesses whether the observed frequencies in certain categories differ significantly from the expected frequencies if there is no relationship between them.

In the present study, for statistical evaluation of the differences in the values of non-invasive tear break-up time (NIBUT) and the results of the Schirmer test between two independent groups – patients who had undergone cataract surgery and patients who had not undergone surgery – the non-parametric Mann–Whitney test was used. This test was chosen because the data in the groups did not meet the criteria for normal distribution. In addition, the sizes of the two groups were significantly different (operated – 24 eyes; non-operated – 210 eyes), which further justified the use of a non-parametric approach. The Mann–Whitney test allows comparison of the distribution and ranks of the measured values between two independent groups without requiring the data to be normally distributed or have equal variance. Statistical significance was assessed at a significance level of $\alpha = 0.05$.

2. RESULTS AND DISCUSSION

1. Results and discussion for task 1:

To investigate the efficacy of intense pulsed light (IPL) in patients with first, second and third degree meibomian dysfunction by examining the non-invasive tear break-up time and Schirmer test, measured before IPL treatment and their change after two IPL procedures.

1.1. General data on patients included in the study

Table 5 presents the distribution of eyes according to the degree of meibomian dysfunction in the study population, including a total of 192 eyes without cataract surgery. The categorisation was performed in three groups corresponding to the different degrees of severity of meibomian dysfunction:

- Group 1 (grade I) – mild dysfunction
- Group 2 (grade II) – moderate dysfunction
- Group 3 (grade III) – severe dysfunction

The relative share of eyes with moderate meibomian dysfunction (Group 2) is the highest – 134 eyes, representing 69.8% of all examined eyes. This shows that almost two-thirds of the eyes demonstrate moderate damage to the meibomian glands, which can be interpreted as the main clinical manifestation of meibomian dysfunction in the study group.

Mild meibomian dysfunction (Group 1) was found in 19 eyes (9.9%), which is a relatively low percentage. This may be due to both late diagnosis of the condition and the fact that patients more often seek medical help when they have more pronounced symptoms.

Severe meibomian dysfunction (Group 3) was observed in 39 eyes (20.3%), representing approximately one-fifth of those examined. Although less common than the moderate form, this group of patients is at increased risk of significantly impaired tear film quality and ocular surface stability, requiring more intensive and targeted treatment.

The distribution by severity highlights the need for early diagnosis and intervention in patients with meibomian dysfunction to prevent progression to more severe forms of the disease. The data also suggest that the moderate form is the most common stage at which patients reach ophthalmological evaluation.

Table 5: Comparative analysis according to the number of eyes with first, second and third degree meibomian dysfunction.

Group	*N*	*%*
Group 1	19	9,9
Group 2	134	69,8
Group 3	39	20,3
Total	192	100,0

1.2. Study of the relationship between age group and the degree of meibomian dysfunction

Table 6 presents the distribution of 96 patients with established meibomian dysfunction, classified into three severity grades: mild (Group 1), moderate (Group 2) and severe (Group 3). The patients were further divided into two age groups: up to 45 years and over 45 years, with the aim of assessing a possible relationship between age and the severity of meibomian dysfunction.

A total of 24 patients were included in Group 1 (mild meibomian dysfunction), of whom 15 (31.3%) were aged up to 45 years and 9 (18.8%) were over 45 years. This indicates that mild meibomian dysfunction is more common in the younger population in the study. A possible explanation for this is that in younger patients, the manifestations of dysfunction are still minimal and are identified at an early stage, possibly due to preventive examinations or increased sensitivity to symptoms of dryness.

Group 2 (moderate meibomian dysfunction) included the largest number of patients (57), with a relatively balanced distribution across age groups: 27 (56.3%) are aged up to 45 years and 30 (62.5%) are over 45 years. This suggests that the moderate form of meibomian dysfunction is the most common in the entire sample and does not show a clear predominance of one of the two age categories. It is possible that this degree represents a transitional stage between the mild and severe forms, which occurs in a wide age group.

Group 3 (severe form of meibomian dysfunction) includes 15 patients, of whom 6 (12.5%) are under 45 years of age and 9 (18.8%) are over 45 years of age. Although the number is relatively small, there is a tendency for severe forms to occur more frequently in older patients, which is consistent with the hypothesis that prolonged exposure to predisposing factors (e.g.hormonal changes, chronic inflammation, accumulation of morphological damage in the glands) may lead to more pronounced changes with age.

The Chi-Square Test performed shows a p-value of 0.323, which exceeds the threshold of statistical significance ($p < 0.05$). Therefore, it cannot be assumed that there is a statistically significant relationship between the age of the patient

and the degree of meibomian dysfunction in this sample. Despite the lack of statistical significance, the trend towards a higher frequency of severe forms in patients over 45 years of age is present and may become significant in a larger sample. This pattern is consistent with a number of literature sources that recognise age as a potential risk factor for meibomian dysfunction, although the effect is often not clearly established in all populations.

Experimental and clinical data show that ageing leads to structural changes in the meibomian glands, including atrophy, fibrosis and reduced glandular cell function [Nien et al., 2011]. These changes contribute to a reduction in the lipid layer of the tear film, increasing tear evaporation and causing symptoms of dryness. With advancing age, patients are not only more prone to developing meibomian dysfunction, but also more likely to present with more severe forms of the disease [Bron et al., 2017]. This is due to both the cumulative effect of age-related changes and age-related changes in hormonal balance and metabolism. On the other hand, age-related changes can also affect the ability of the glands to regenerate and recover, further exacerbating the clinical picture.

Advancing age also requires an adapted approach to the treatment of meibomian dysfunction. Older patients often show a weaker response to standard therapies due to more pronounced structural changes and reduced gland function [Stapleton et al., 2017]. This requires complex treatment, which may include both medication and various methods such as warm compresses, massage of the meibomian glands, and IPL.

The data from the present study show a tendency for the severity of meibomian dysfunction to increase with age, although statistical significance cannot always be achieved, probably due to the limited sample size. This is consistent with the published literature, where age is one of the most stable and significant predictors of the presence and progression of meibomian dysfunction.

Table 6. Chi-Square Test to examine the relationship between age and the severity of meibomian dysfunction.

Chi-Square Tests

			Age		Total	p
			up to 45 years	over 45 years		
Group	Group 1	N	15	9	24	0,323
		%	31,3%	18,8%	25,0%	
	Group 2	N	27	30	57	
		%	56,3%	62,5%	59,4%	
	Group 3	N	6	9	15	
		%	12,5%	18,8%	15,6%	

1.3. Study of the relationship between gender and the degree of meibomian dysfunction.

Table 7 presents the results of a study of patients with meibomian dysfunction, divided into three clinical groups according to the severity of the disease (Group 1 – mild, Group 2 – moderate, Group 3 – severe) and gender. A Chi-Square Test was performed to establish a relationship between gender and the degree of meibomian dysfunction.

The largest percentage of patients are in group 2 – moderate meibomian dysfunction (59.4%), followed by group 1 (25.0%) and group 3 (15.6%). The moderate form predominates in men (69.4%), while in women the proportion of the mild form is higher (31.9% compared to 18.4% in men).

The obtained p-value was 0.124, which does not reach statistical significance ($p > 0.05$), but may indicate a trend that would be more clearly expressed in a larger sample would be more clearly expressed.

There are conflicting data in the literature regarding gender as a risk factor for meibomian dysfunction. Some authors report that men are more commonly affected, probably due to poorer hygiene habits, greater exposure to external irritants and less attention to symptoms [Yeh et al., 2018].

However, other studies emphasise that postmenopausal women are more prone to meibomian dysfunction due to reduced androgen levels, which have a direct effect on the meibomian glands. Androgens stimulate lipid secretion and suppress inflammatory processes in the glandular epithelium [Sullivan et al., 2002].

Another study shows that men have a lower frequency of spontaneous blinking and longer intervals between blinks, which leads to increased tear evaporation and contributes to symptoms of dry eye and meibomian dysfunction. This behavioural difference may explain the higher incidence of moderate to severe forms in men [Ong, 1996].

According to the international consensus of the TFOS MGD Workshop, gender is recognised as a risk factor for the development of meibomian dysfunction, especially in the context of hormonal balance. Postmenopausal women and men over 50 years of age fall into risk categories, albeit through different mechanisms [Lemp et al., 2012].

Although in the current sample women more often fall into the group with mild meibomian dysfunction and men into the moderate group, this does not lead to a statistically significant dependence ($p = 0.124$). This is consistent with some epidemiological studies showing earlier detection of symptoms in women (who seek medical help more often), while men may reach moderate or severe forms before diagnosis.

Table 7. Chi-Square Test to examine the relationship between gender and the degree of meibomian dysfunction.

Chi-Square Tests

			Gender		Total	P
			Men	Women		
Group	Group 1	N	9	15	24	0,124
		%	18,4%	31,9%	25,0%	
	Group 2	N	34	23	57	
		%	69,4%	48,9%	59,4%	
	Group 3	N	6	9	15	
		%	12,2%	19,1%	15,6%	

1.4. Tear film break-up time study

One of the goals of our study is to check out how well IPL works for people with different levels of meibomian dysfunction by looking at tear film break-up time (TBUT). Non-invasive tear break-up times (NIBUT1 and NIBUTAV) are indicative of normal film stability [Wiedemann et al., 2010, Rico-del-Viejo et al., 2018]. The first tear in healthy individuals is considered to occur at values above 10 s [Wiedemann et al., 2010, Tian et al., 2016]. These threshold values are also adopted in this thesis as reference values for assessing tear film stability. In this context, intense pulsed light (IPL) therapy is gaining increasing clinical importance as an innovative method for improving the function of the meibomian glands and stabilising the tear film.

A total of 192 eyes were initially included in the study. For various reasons – including dropout, incomplete completion of all procedures or lack of data for follow-up measurements – not all eyes were followed up after the first or second IPL session.

As summarised in Table 8, the study included three groups of eyes with varying degrees of meibomian dysfunction: group 1 (or first degree of meibomian dysfunction) (11 eyes), group 2 (second degree of meibomian dysfunction) (77 eyes) and group 3 (third degree of meibomian dysfunction) (22 eyes). For each eye, the TBUT was measured at three time points: before the first session, after the first IPL and after the second IPL. Statistical analysis was performed using the Friedman test, a non-parametric test for comparing three or more related measurements. In addition to the p-value, the mean, median, standard deviation (SD), and minimum and maximum values were calculated for each time point.

In the first group, the initial TBUT value was 10.84 seconds on average, with a median of 10.00 seconds. After the first IPL, an increase to 13.24 seconds (median 17.00 seconds) was observed, suggesting improvement in some of the eyes. After the second session, the value decreased slightly to 11.94 seconds (median 11.80 seconds). The standard deviation was relatively high in all three measurements (between 3.71 and 5.52 seconds), indicating significant interocular variability. Despite the positive trend, the differences are not statistically significant ($p = 0.105$).

In the second and largest group of eyes, the baseline TBUT value was 9.33 seconds on average (median 7.90 seconds), indicating marked instability of the tear film before therapy. After the first session, an increase to 12.46 sec. (median 12.50 sec.) was reported, and after the second session – 12.44 sec. (median 12.00 sec.). The improvement is lasting and consistent. The Friedman test shows clear statistical significance ($p < 0.001$), confirming the effectiveness of IPL therapy in this group.

The initial value of the TBUT in the third group is 9.58 seconds (median 8.65 seconds). After the first IPL, a significant increase to 12.99 seconds (median 14.95 seconds) was observed, and after the second IPL, 13.60 seconds (median 15.05 seconds). This is the only group in which not only preservation but also an additional increase in TBUT was observed after the second IPL. The values are more concentrated (SD = 3.69–4.58 sec.), which indicates a more uniform response to therapy. The Friedman test again shows a statistically significant difference ($p < 0.001$).

The results obtained show that IPL therapy leads to a significant improvement in tear film stability, as measured by TBUT, especially in groups with a larger number of eyes. In groups 2 and 3, the improvement is clearly pronounced and statistically significant, with group 3 also showing accumulation of the therapeutic effect after the second procedure. A positive trend was observed in group 1, but it did not reach statistical significance, probably due to the limited sample size and individual differences between the

eyes. The presence of a lasting positive effect in most cases indicates the high clinical potential of IPL therapy as a means of influencing meibomian dysfunction and dry eye syndrome.

Table 8. Follow-up of TBUT dynamics before IPL, after the first and after the second IPL.

Friedman Test

Group	TBUT	N	Mean	Median	SD	Min	Max	p
Group 1	TBUT before IPL	11	10,84	10,00	4,25	4,50	16,90	0,105
	TBUT after 1st IPL	11	13,24	17,00	5,52	4,90	17,80	
	TBUT after 2nd IPL	11	11,94	11,80	3,71	4,00	17,00	
Group 2	TBUT before IPL	77	9,33	7,90	4,76	2,40	20,00	<0,001
	TBUT after 1st IPL	77	12,46	12,50	4,15	4,00	17,00	
	TBUT after 2nd IPL	77	12,44	12,00	4,20	2,50	17,00	
Group 3	TBUT before IPL	22	9,58	8,65	4,58	3,10	17,00	<0,001
	TBUT after 1st IPL	22	12,99	14,95	4,56	4,30	17,00	
	TBUT after 2nd IPL	22	13,60	15,05	3,69	6,90	17,00	

The results of the present study demonstrate a clear improvement in tear break-up time (TBUT) in eyes treated with intense pulsed light (IPL) therapy, especially after the first and second sessions (Figure 7). These observations are consistent with a growing body of published data confirming the efficacy of IPL in the treatment of meibomian dysfunction (MGD) and the associated dry eye syndrome.

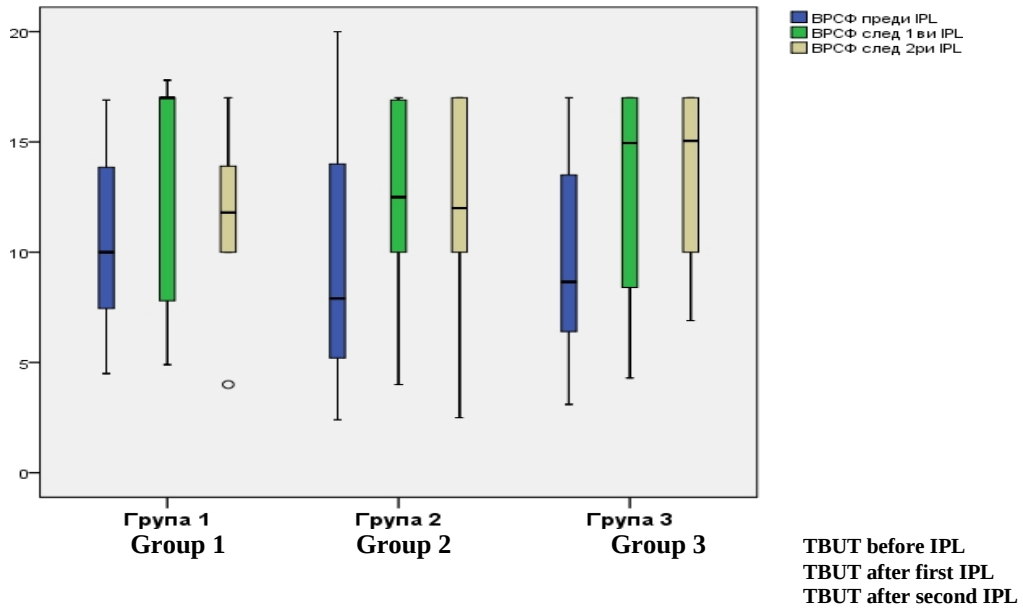


Figure 7. Change in TBUT dynamics in the three groups

The relatively high TBUT values after IPL, especially in the second and third groups of the present study, suggest an improved lipid component of the tear film associated with functional restoration of the meibomian glands. This is consistent with the hypothesis that IPL therapy acts through selective photothermolysis, reducing telangiectasia and alleviating obstruction of the gland ducts.

Some studies report an increase in TBUT of 2–5 seconds on average after 2 to 4 IPL procedures, with the therapeutic response being particularly pronounced in patients with lower baseline values [Toyos, 2015]. In our study, the most significant increase in TBUT was also found in eyes with initial values below 10 seconds, highlighting the potential of IPL as a personalised therapy for moderate to severe MGD.

According to Craig et al. [Craig et al., 2015], IPL leads to improved meibomian secretion, reduced inflammatory markers and improved tear stability. Similar to our results, they report a significant increase in TBUT after the first procedures. Publications such as Gupta et al. [Gupta et al., 2021] also describe a stable and cumulative effect of IPL therapy that persists even weeks after the end of treatment.

An interesting aspect is that in the small sample in group 1, the results did not reach statistical significance. A similar discrepancy between clinically and statistically significant effects was also described in the study by Vegunta et al. [Vegunta et al., 2016], who note that the response to IPL may be more variable in a limited number of cases and depends on factors such as age, chronicity of symptoms, and the presence of accompanying inflammatory diseases.

1.5. Schirmer test

The Schirmer test is one of the most commonly used tests to assess tear production. In the cohort studied, a significant difference was found between the Schirmer test values observed. This may be related to the way the study was conducted. According to the literature, the test was performed after anaesthesia with the subjects' eyes open, whereas in the present study, the subjects were asked to keep their eyes closed. A significant difference was found between the results obtained with open and closed eyes [Serruya et al., 2009].

Reduced tear secretion is a characteristic finding in dry eye syndrome, especially in the course of meibomian dysfunction (MGD). The present study analysed the dynamics of Schirmer test results in patients undergoing intense pulsed light (IPL) therapy at three time points: before treatment, after the first session, and after the second session.

The analysis was performed on three groups of eyes with first, second and third degree meibomian dysfunction, using again the Friedman test – a non-parametric method for analysing repeated measurements on dependent samples. The values presented include the mean, median, standard deviation (SD), minimum and maximum values.

As summarised in Table 9, in group 1, or eyes with first-degree meibomian dysfunction, the mean Schirmer test value before IPL was 13.45 mm, with a median of 13.00 mm, which is considered borderline normal. After the first IPL session, an increase to 15.27 mm (median 16.00 mm) was observed, and after the second session, an increase to 17.64 mm (median 19.00 mm) was observed. Despite the trend towards improvement, the result did not reach statistical significance ($p = 0.148$), probably due to the small size of the group.

In eyes with grade II meibomian dysfunction or group 2, the initial Schirmer test value is 10.27 mm (median 10.00 mm), which corresponds to a mild to moderate deficiency of the aqueous component of the tear film. After the first IPL, the results increased significantly to 15.38 mm, and after the second to 16.68 mm. The increase is clearly pronounced and statistically significant ($p < 0.001$). The standard deviation also increased after therapy, suggesting a variable response, but the overall trend is clearly positive.

In group 3 (eyes with third-degree meibomian dysfunction), the baseline Schirmer test value was 11.68 mm (median 11.00 mm), with slightly improved baseline values compared to group 2. After the first IPL, an increase to 17.32 mm was observed, and after the second – to 19.23 mm (median 20.50 mm). The values indicate significantly increased secretion, with high clinical significance (p 0.001). Friedman The test confirms statistical significance ($p< 0.001$). Here again, a cumulative effect of the second procedure is observed.

Table 9. Tracking the dynamics of the Schirmer test before the first and after two IPL procedures

Friedman Test

Group	Schirmer	N	Mean	Median	SD	Min	Max	p
Group 1	Schirmer before IPL	11	13,45	13,00	7,81	3,00	25,00	0,148
	Schirmer after 1st IPL	11	15,27	16,00	3,64	8,00	20,00	
	Schirmer after 2nd IPL	11	17,64	19,00	4,78	10,00	26,00	
Group 2	Schirmer before IPL	77	10,27	10,00	4,42	3,00	20,00	<0,001
	Schirmer after 1st IPL	77	15,38	15,00	5,71	5,00	30,00	
	Schirmer after 2nd IPL	77	16,68	16,00	6,54	2,00	30,00	
Group 3	Schirmer before IPL	22	11,68	11,00	4,39	5,00	22,00	<0,001
	Schirmer after 1st IPL	22	17,32	17,00	7,66	5,00	30,00	
	Schirmer after 2nd IPL	22	19,23	20,50	7,10	5,00	30,00	

The dynamics observed in the Schirmer test results support the hypothesis that IPL not only improves the lipid component of the tear film, but may also modulate neurovascular and inflammatory mechanisms leading to increased water secretion. This observation is consistent with the results of studies such as those by Rong et al. [Rong et al., 2018] and Arita et al. [Arita et al., 2018], which describe an increase in tear production after IPL, especially when combined with meibomian gland expression (MGX).

The most significant improvement was observed in group 3, where after two sessions the mean values reached almost hypersecretion limits (>20 mm), suggesting marked individual sensitivity to the therapy (Figure 8). In the literature, this effect is explained by a reduction in chronic inflammation and regulation of nerve endings, leading to a normalised tear reflex arc.

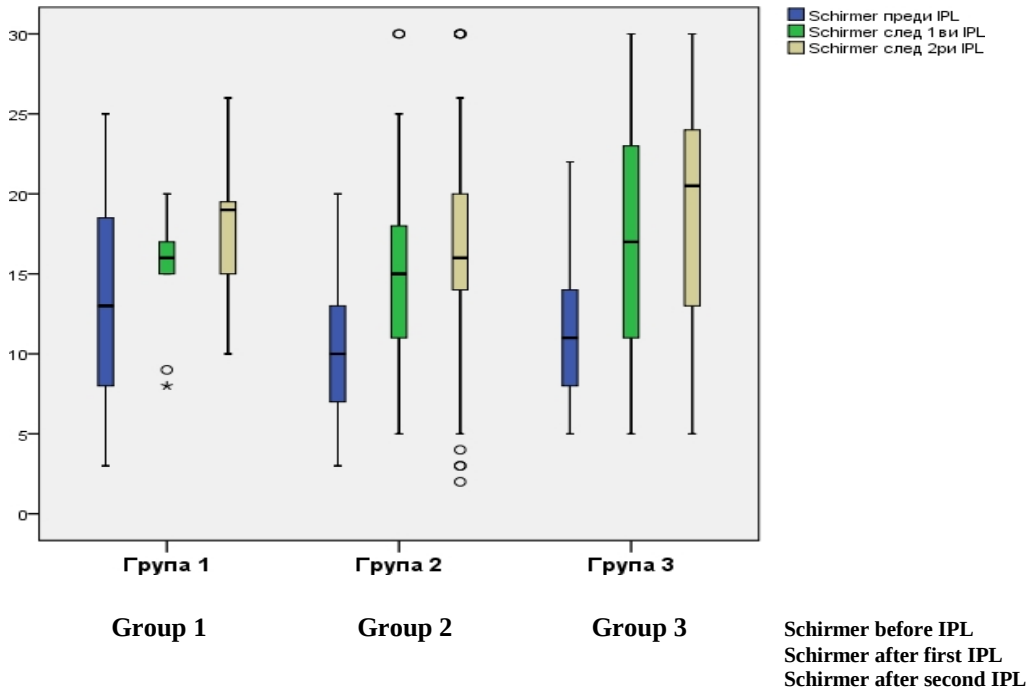


Figure 8. Change in Schirmer test dynamics in the three groups

In the context of group 1, the lack of statistical significance is consistent with clinical observations that small samples and borderline baseline values may mask a potential therapeutic effect. Similar results have been observed in studies with a limited number of participants [Toyos, 2015], in which it is recommended to continue therapy with more than two sessions to achieve maximum effect.

The data show that IPL therapy leads to a significant improvement in Schirmer test results in patients with MGD, especially in larger samples and when treatment is continued for more than one session. These results support the role of IPL as an effective and multifactorial therapeutic approach that not only improves tear film quality but also supports aqueous secretion in patients with dry eye.

IPL has traditionally been viewed primarily as a therapy aimed at improving the lipid layer of the tear film by alleviating obstruction of the meibomian glands. However, more and more data (including our study) show that IPL has a broader effect, including on water secretion as measured by the Schirmer test.

Supporting our results is a study by Dell et al. in 2017, which evaluated the efficacy of IPL in combination with meibomian gland expression in 40 patients with moderate to severe meibomian dysfunction [Dell et al., 2017]. With the exception of lipid layer thickness, all studied markers such as BAC and standard patient assessment of eye dryness (SPEED) were significantly improved after 15 weeks. The results show that IPL in combination with glandular expression reduces symptom severity in patients with moderate to severe dysfunction. The limitation of this study is that the therapeutic effect of gland expression and IPL cannot be distinguished due to the lack of a control group. In contrast, the

control in the study by Rong et al. was more rigorous, using IPL plus meibomian gland expression to treat 44 patients with meibomian dysfunction in a double-blind, randomised, controlled study. After three procedures, dry eye symptoms, BVCF, meibomian gland secretion function, and ocular surface condition improved. This study concluded that IPL in combination with gland expression is safe and effective in the treatment of meibomian dysfunction [Rong et al., 2018].

In 2018, the first prospective, multicentre study by Arita et al. was conducted, which observed improvement in subjective symptoms and objective signs of refractory severe meibomian dysfunction after a series of three IPL treatments combined with meibomian gland expression [Arita et al., 2018]. After the procedures, the patients observed improved tear film stability, lipid layer dynamics, and meibomian gland function. This study, conducted in 3 centres, included patients with refractory severe meibomian dysfunction and did not exclude those with a history of contact lens wear or eye surgery. TBUT was typically reduced in patients with meibomian dysfunction. A previous study demonstrated a significant improvement in TBUT from 5.28 to 14.11 seconds after IPL treatment [Craig et al., 2015]. In this study, TBUT increased from 3.3 to 7.8 seconds, representing a significant clinical improvement comparable to our results.

The efficacy of IPL treatment is also discussed in a study by Lee et al. involving 63 patients, in which Schirmer test results improved by approximately 40% after 3 IPL procedures [Lee et al., 2024]. In addition, improvements in the ocular surface were also significant compared to the results before IPL treatment. In a previous study, Schirmer test results after IPL procedures also demonstrated significant improvement compared to pre-treatment results [Mejía et al., 2019], while another study did not report effective Schirmer test results after IPL treatment [Ocak et al., 2020].

Recently, Wu et al. [Wu et al., 2022] investigated the efficacy of IPL combined with eye drops containing deproteinised calf blood extract (DCBE) in the treatment of dry eye syndrome with allodynia (a sensation of pain that arises or intensifies from stimuli that do not normally cause pain). This study included 23 patients with four treatments every 4 weeks. The results showed that the visual analogue scale (VAS), OSDI, ocular pain assessment scale (OPAS), insomnia scale, generalised anxiety disorder (GAD-7), meibum quality and expression scores were significantly reduced. The Schirmer I test and TBUT significantly improved after treatment. The study concluded that IPL combined with DCBE eye drops for four treatments is an effective treatment for relieving eye pain in patients with dry eye syndrome, in addition to restoring corneal nerve density. Although not proven, these findings suggest that there may be a link between IPL treatment and corneal nerve recovery.

To further investigate the factors influencing the clinical outcomes of IPL, Chen et al. [Chen et al., 2021] followed 48 patients with meibomian gland dysfunction (MGD) for 120 days. The characteristics of effective and ineffective

outcomes of IPL therapy were evaluated in this study. The analysis found that the effective treatment rate with IPL was higher in patients who were younger, had higher baseline OSDI, higher baseline Schirmer I test, and moderate meibomian dysfunction. The effective IPL rate decreases with increasing age [Knop et al., 2011]. Surprisingly, there is no noticeable association between mild meibomian dysfunction and effective IPL, and the authors explain that individuals with mild MGD have a greater capacity for MG expression for improvement than those with severe MGD, leading to less improvement in OSDI after IPL in patients with mild MGD. These results should be further verified through large-scale multicentre experiments.

Contact lens (CL) wearers often suffer from dryness, discomfort, and pain [Kojima et al., 2018]. Dry eye disease (DED) is emerging as the most common reason for discontinuing contact lens wear. The onset of an inflammatory cascade on the ocular surface, leading to hyperosmolarity of the tear film in contact lens wearers, is considered one of the main mechanisms of contact lens-related dry eye (CL-DE). The use of IPL in the treatment of CL-DE was first reported by Yang et al. [Yang et al., 2022]. The results of this randomised controlled study revealed that two cycles of IPL treatment improved meibomian gland function, as demonstrated by improved NIBUT along with clinical symptoms of DED. No adverse effects were reported in this trial.

LASIK is the most commonly performed laser vision correction procedure. Post-operative dry eye syndrome occurs due to damage to the corneal nerves during surgery [Toda, 2018]. Patients may experience eye discomfort along with visual quality disturbances after LASIK [Pietilä et al., 2018]. Some patients do not improve after traditional treatment with medication and suffer from long-term problems. Pazo et al. [Pazo et al., 2021] conducted a prospective study of IPL in the treatment of refractive dry eye syndrome after Lasik and found that IPL treatment improved dryness symptoms and reduced dependence on artificial tears. One year later, their team used IPL combined with 0.1% sodium hyaluronate and an eye mask after Lasik [Wu et al., 2022]. The combined therapy was significantly-effective than IPL alone in improving meibomian gland function and reducing dry eye symptoms and scores in this prospective randomised controlled study, which demonstrated an increase in the lipid layer of the tear film in 100 patients after two sessions.

2. Results and discussion for task 2:

To investigate the efficacy of intense pulsed light (IPL) in patients with varying degrees of meibomian dysfunction one month after cataract surgery with multifocal intraocular lens implantation by examining the non-invasive tear break-up time and Schirmer test, measured before IPL treatment and their change after two IPL procedures.

Patients with multifocal intraocular lenses often report for: blurred vision, halos around light sources, reduced contrast sensitivity, visual fatigue or discomfort. Many of these complaints are not due to surgical error or the lens, but to problems with the quality of the tear film – even with normal preoperative status. After cataract surgery, temporary or prolonged meibomian gland dysfunction (MGD) may occur, tear secretion and film stability may be impaired, and in some cases, postoperative antibiotic drops sometimes worsen the condition of glands. Numerous studies report that over 50% of patients after cataract surgery experience symptoms of dry eye, even without a history of such problems. Unlike monofocal lenses, multifocal models divide light between several focal points, making them more sensitive to any aberrations or instabilities. Even slight disturbances in the tear film can impair visual quality and create subjective dissatisfaction, especially in patients with high expectations.

Why did we choose to investigate the effect of IPL in patients after cataract surgery with multifocal intraocular lens implantation?

1. They are **more sensitive to problems with the tear film.**
2. Cataract surgery can impair **the function of the meibomian glands.**
3. IPL has **a proven effect** on tear film stabilisation.
4. This treatment has the potential to **improve visual comfort and postoperative results** without the need for additional surgical interventions.

This study included 24 eyes diagnosed with varying degrees of meibomian dysfunction, operated on for cataracts with implantation of a multifocal intraocular lens. The following drops were applied to all operated eyes after surgery: Ofloxacin 3 mg/ml eye drops (Floxal) 5 times daily, Dexamethasone 1 mg/ml (Maxidex) 5 times daily, Hypromellose 3.2 mg/ml (Artelac) 5 times daily for the first 2 weeks, after which all three types of drops were reduced to 3 times daily for another 2 weeks. All patients underwent BRSF and Schirmer tests and their changes were monitored after two IPL procedures.

2.1. Examination of tear film break-up time in patients who had undergone cataract surgery

Table 10 shows the tear film breakup time (TBUT) values in 24 patients who underwent cataract surgery with multifocal intraocular lens implantation at three consecutive time points: before the start of intense pulsed light (IPL) therapy, after the first IPL procedure, and after the second IPL procedure. The aim is to monitor the effect of IPL therapy on tear film stability in this specific group of patients.

Table 10. Examination of TBUT in operated patients before IPL and its change after 2 IPL procedures.

Friedman Test

TBUT	N	Mean	Median	SD	Min	Max	p
TBUT before IPL	24	7,04	6,00	4,20	2,00	15,00	<0,001
TBUT after 1st IPL	24	7,90	7,00	3,48	3,00	17,00	
TBUT after 2nd IPL	24	9,38	9,00	4,61	0,80	17,00	

As can be seen in Table 10, before the start of therapy, the mean TBUT value was 7.04 seconds, with a standard deviation (SD) of 4.20 seconds. The median was 6.00 seconds, which means that at least half of the patients had values below this threshold. The minimum measured value is 2.00 seconds and the maximum is 15.00 seconds. These values indicate a mild to moderate tear film stability disorder, typical of early forms of dry eye, often seen after cataract surgery. In the context of multifocal lenses, even a slight deviation from normal TBUT (>10 s) can lead to significant visual dissatisfaction.

After the first IPL procedure, a moderate increase in TBUT was observed, to a mean value of 7.90 seconds (S D = 3.48), and the median rises to 7.00 seconds. The minimum value in this phase is 3.00 seconds, and the maximum reaches 17.00 seconds. This shows the first signs of improvement in tear stability in most patients, although the values are still below the optimal levels for a healthy tear film.

After the second IPL procedure, a significant increase in TBUT was observed, reaching a mean value of 9.38 seconds (SD = 4.61). The median increased to 9.00 seconds, indicating that more than half of the patients now had TBUT close to or within the physiological normal range (>10 s). The minimum TBUT value in this phase was 0.80 seconds, suggesting the presence of isolated cases of severe dysfunction, while the maximum value remained 17.00 seconds.

The value of $p < 0.001$ (calculated using the Friedman test – when comparing more than 2 related groups, where the distribution of the studied variable is different from the normal distribution) shows that the differences between the three measurements are statistically significant. This confirms the effect of IPL therapy on improving tear film stability in patients after cataract surgery.

In summary, it can be said that TBUT before therapy shows an unstable tear film, which may be the cause of subjective visual discomfort in patients with multifocal intraocular lenses. After the first IPL procedure, a slight improvement is observed. After the second IPL session, the TBUT approaches the physiological norm in most patients, which may indicate a clinically relevant improvement in visual quality (Figure 9).

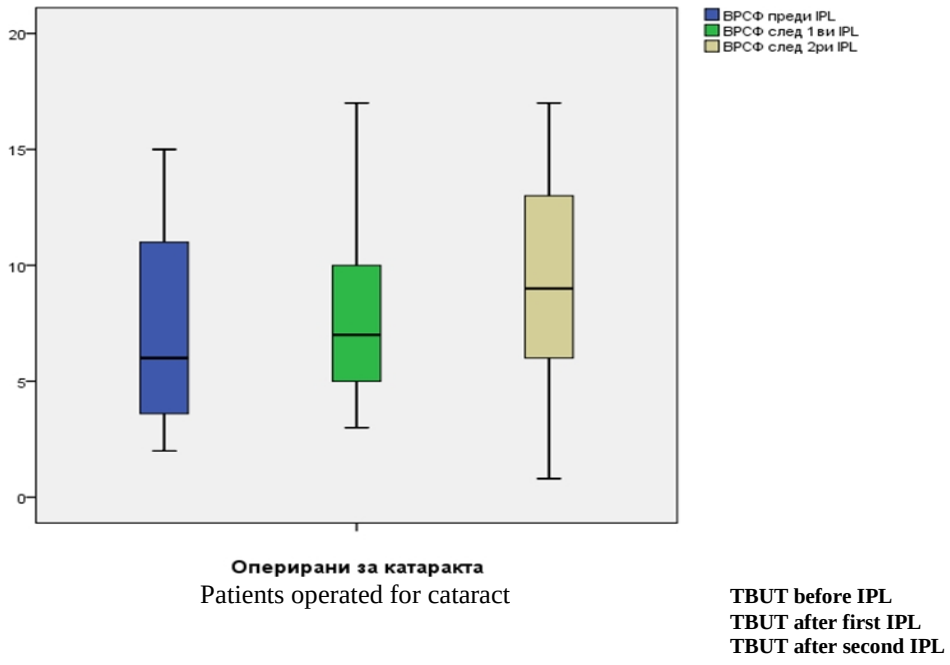


Figure 9. Change in TBUT dynamics in operated patients before and after IPL.

2.2. Schirmer test in patients operated for cataract

Table 11 presents the results of the Schirmer test in 24 patients who underwent cataract surgery with multifocal intraocular lens implantation. The aim of the study is to evaluate the effect of intense pulsed light (IPL) therapy on quantitative tear secretion. The Schirmer test was performed at three time points: before the start of therapy, after the first IPL procedure and after the second IPL procedure.

Table 11. Follow-up of the Schirmer test in operated patients before and after IPL. Friedman test

Schirmer	N	Mean	Median	SD	Min	Max	p
Schirmer before IPL	24	9,76	10,00	4,11	4,00	20,00	<0,001
Schirmer after 1st IPL	24	10,80	11,00	4,23	5,00	22,00	
Schirmer after 2nd IPL	24	11,88	13,00	4,59	4,00	22,00	

As can be seen from Table 11, before the start of IPL therapy, the mean Schirmer test value was 9.76 mm with a standard deviation (SD) of 4.11 mm, and the median was 10.00 mm. The minimum measured value was 4.00 mm and the maximum was 20.00 mm. The data show that some patients have values bordering on or falling within the hyposecretory dry eye zone (values below 10 mm), which may be the cause of visual discomfort in patients with multifocal intraocular lenses, despite the good surgical outcome.

After the first IPL procedure, a slight increase in tear production was observed – the mean value increased to 10.80 mm, while the median remained at 11.00 mm. The standard deviation was 4.23 mm, and the values ranged from 5.00 mm to 22.00 mm. This indicates an initial improvement in the amount of tear secretion, probably due to reduced inflammation, activation of the meibomian glands and improved capillary blood flow in the eyelid margin area.

After the second IPL procedure, a more pronounced improvement was observed. The mean Schirmer test value reached 11.88 mm, and the median increased to 13.00 mm, indicating that more than half of the patients now had values significantly above the diagnostic threshold of 10 mm, which is considered normal tear secretion. The standard deviation is 4.59 mm, and the values again vary widely (4.00–22.00 mm), but with a clear trend towards improvement.

The Friedman test was used again to assess the differences between the three time points. The p-value obtained (<0.001) indicates that the differences between the stages are statistically significant. This means that IPL therapy has a real effect on the amount of tear secretion measured by the Schirmer test.

So far, we can summarise the following:

Before IPL, some of the patients had subnormal tear secretion (4–10 mm), which may be the cause of visual discomfort.

After the first IPL, we observe a moderate increase in values, with a tendency towards normalisation.

After the second IPL, there was a significant increase in Schirmer values in most patients. Last but not least, the differences are statistically significant according to the Friedman test ($p < 0.001$) (Figure 10).

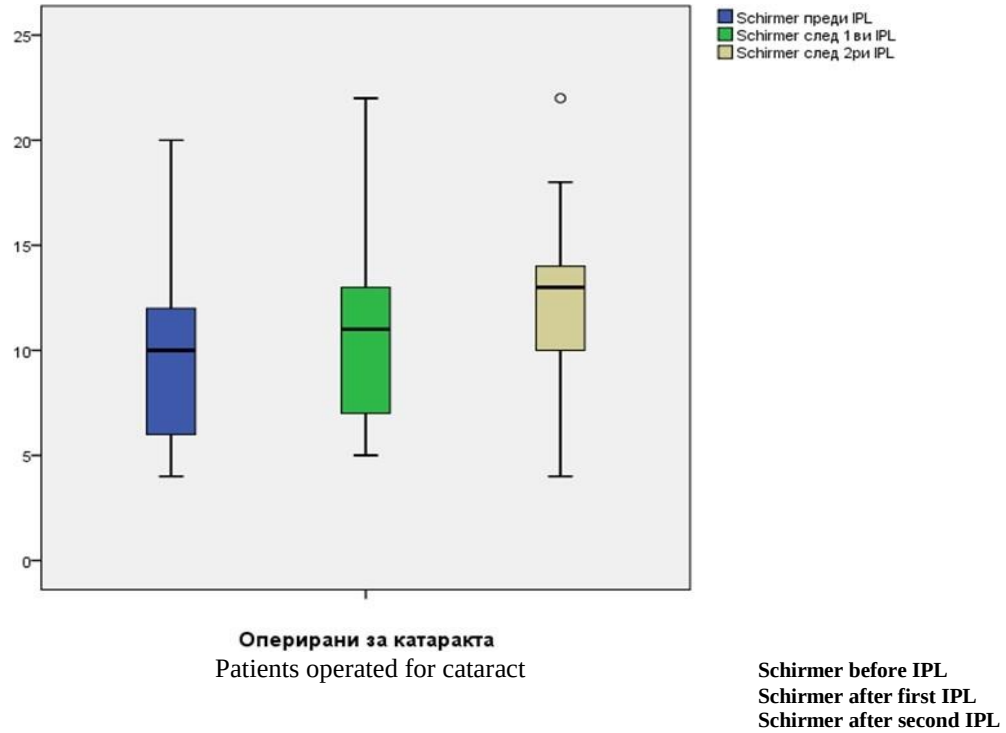


Figure 10. Schirmer test in dynamics in operated patients before and after IPL treatment.

The results of the Schirmer test show that IPL therapy leads to a significant improvement in quantitative tear secretion in patients with multifocal intraocular lenses after cataract surgery. This improvement may contribute to better visual quality, fewer visual complaints and higher subjective satisfaction with the outcome of surgery.

The Prospective Health Assessment of Cataract Patient Ocular Surface study showed that more than 60% of patients scheduled for cataract surgery had reduced tear film break-up time [Trattler et al., 2017]. In addition, dry eye syndrome, including meibomian dysfunction, may worsen after cataract surgery [Li et al., 2007, Ram et al., 2002, Han et al., 2014]. Thus, patients with dry eyes associated with meibomian dysfunction are more susceptible to impaired vision after cataract surgery, especially those with trifocal intraocular lens implantation. Therefore, the combination of trifocal intraocular lenses and meibomian dysfunction may worsen postoperative visual quality and, as a result, reduce postoperative patient satisfaction [Puell et al., 2006, Teshigawara et al., 2022, De Vries et al., 2011].

Evidence on the effect of postoperative treatment of meibomian dysfunction with IPL on TBUT, ocular surface status, and tear secretion in patients undergoing cataract surgery with trifocal intraocular lenses is limited.

Lane et al., Toyos et al., and Safir et al. were the first to report successful treatment of meibomian dysfunction with LipiFlow thermal pulsation, IPL, and the thermomechanical device Tixel, respectively [Lane et al., 2012, Toyos et al., 2015, Safir et al., 2022]. Park et al. reported the efficacy of preoperative treatment of dry eye associated with meibomian dysfunction with LipiFlow on postoperative tear film stability and ocular surface status [Park et al., 2021]. Similarly, Ge et al. describe the benefits of IPL treatment on postoperative tear film stability and ocular surface status [Ge et al., 2020]. Their study aims to evaluate the effect of IPL therapy on 60 patients who underwent cataract surgery with mild to moderate meibomian dysfunction. The results of the OSDI questionnaire, tear meniscus height, and tear film break-up time were evaluated. These indicators were examined to assess the effects of IPL therapy on postoperative functional symptoms in patients with meibomian dysfunction. Patients received IPL therapy before and 1 and 2 months after surgery. The results of the OSDI questionnaire show that after IPL treatment, postoperative dry eye symptoms not only improve but also exceed preoperative levels. A significant difference between TBUT0 and TBUT3 ($p = 0.026$) was demonstrated, indicating that TBUT improved after IPL treatment. No complications such as iris depigmentation and dilated pupils were observed during the procedures, which demonstrates the efficacy and safety of IPL treatment and supports our data. The difference with our study is that Ge et al. did not perform gland expression after IPL treatment [Ge et al., 2020]. Cataract surgery is not only for improving visual acuity but also for significantly improving the quality of life of patients. Therefore, ophthalmologists are required to carefully assess the condition of the patient's ocular surface before surgery, especially in those with meibomian dysfunction, so that patients can feel satisfied with the postoperative results [Ge et al., 2020].

Dry eye associated with meibomian dysfunction worsens after cataract surgery [Han et al., 2014, Park et al., 2021]. However, the mechanisms underlying postoperative worsening of meibomian dysfunction remain unclear. The study by Teshigawara T. et al. included 134 eyes that were diagnosed with dry eye and meibomian dysfunction and underwent cataract surgery with implantation of a diffractive multifocal lens. Their study presents the mean values of TBUT, central surface point keratopathy and high-order aberrations approximately 1 week after IPL treatment but before cataract surgery. Significant differences were observed in the mean values of tear film stability and ocular surface condition (all $p < 0.01$). Unlike ours, it aims to demonstrate the efficacy of preoperative IPL treatment of dry eye associated with meibomian dysfunction to improve postoperative visual outcomes in patients with diffractive trifocal intraocular lens implants [Teshigawara et al., 2024].

However, both studies conclude that postoperative tear film stability and ocular surface status improve after IPL treatment. Their study is the first to demonstrate that preoperative treatment with IPL can significantly improve postoperative visual quality and increase patient satisfaction, especially in patients with a combination of dry eyes and diffractive trifocal intraocular lens implantation [Teshigawara et al., 2024].

IPL therapy is a promising intervention for improving postoperative visual outcomes and comfort in patients with trifocal intraocular lenses and concomitant MGD. However, the present study has some limitations. The sample size is limited and the follow-up period is short. Future studies should include larger and more diverse patient groups and longer follow-up after surgery. This will provide a more in-depth assessment of the place of IPL in modern cataract surgery, especially in an era of increasingly high expectations for visual quality and functional outcomes after surgery.

3. Results and discussion for task 3:

Compare the effectiveness of IPL in patients with different degrees of meibomian dysfunction who underwent cataract surgery and in patients without surgical intervention by analysing changes in non-invasive tear break-up time and Schirmer test before and after two IPL procedures.

Initially, 240 eyes were included in the study. During the analysis, some of them were excluded due to missing or poor-quality data, resulting in a variable number of eyes used in the final analyses. In this task, the study was conducted on a total of 234 eyes with varying degrees of meibomian dysfunction, divided into two groups – 210 unoperated eyes and 24 eyes operated for cataracts. The Mann–Whitney nonparametric test was used for statistical evaluation of the differences between the two independent groups, with a significance level of $p < 0.05$. All results are presented as mean, median, standard deviation, minimum and maximum values. The parameters evaluated include non-invasive tear break-up time and Schirmer test results measured before treatment, after the first and after the second IPL procedure.

3.1. TBUT

3.1.1. TBUT before IPL

As summarised in Table 12, the mean TBUT value in unoperated patients is 10.61 seconds (median 10.20; SD 4.76), while in operated patients it was significantly lower – 7.05 seconds (median 5.85; SD 4.03). The minimum value in both groups was around 2 seconds, and the maximum reached 20 seconds in unoperated patients and 15 seconds in operated patients. The statistical test shows a significant difference with $p< 0.001$, which indicates poorer tear film stability in the operated patients even before the start of IPL therapy.

3.1.2. TBUT after the first IPL procedure:

In the group of unoperated patients, the mean TBUT value increased to 12.89 seconds (median 13.95; SD 4.36), while in the operated group it reached 7.98 seconds (median 7.00; SD 3.32). The minimum and maximum values also remained higher in the non-operated group (0.80–17.80 seconds) compared to the operated group (3.00–17.00 seconds). The difference between the groups continued to be highly statistically significant ($p < 0.001$).

3.1.3. TBUT after the second IPL procedure:

The mean value in the non-operated group decreased slightly to 12.08 seconds (median 12.00; SD 4.36), while in the operated group it increased to 9.38 seconds (median 9.00; SD 4.61). The maximum values remained similar (around 17 seconds), and the minimum values were 0.80 seconds in both groups. The statistical significance of the difference between the groups decreased but remained significant ($p = 0.005$).

3.2. Schirmer test

3.2.1. Schirmer test before IPL:

The mean tear secretion in unoperated patients is 11.15 mm (median 10.00; SD 5.12), and in operated patients – 9.64 mm (median 10.00; SD 3.98). The difference is not statistically significant ($p = 0.161$), which suggests that before IPL therapy, basal tear secretion did not differ significantly between the two groups.

3.2.2. Schirmer test after the first IPL procedure:

After the first procedure, the mean value in the non-operated group increased to 15.20 mm (median 15.00; SD 6.15), while in the operated group it reached 11.11 mm (median 11.50; SD 4.14). Here, the difference is statistically significant ($p = 0.001$), indicating a better response to IPL therapy in non-operated patients.

3.2.3. Schirmer test after the second IPL procedure:

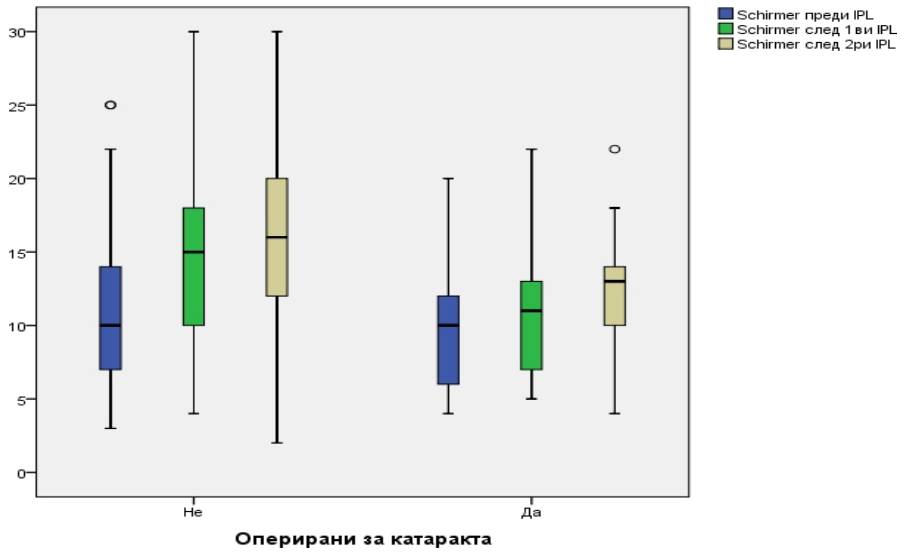
After the second procedure, the mean value reached 16.32 mm (median 16.00; SD 6.70) in the non-operated patients and 11.88 mm (median 13.00; SD 4.59) in the operated patients. The difference remained significant ($p = 0.002$), with a continuing trend towards stronger recovery of tear secretion in patients who had not undergone cataract surgery.

Table 12. Follow-up of TBUT and Schirmer test before and after IPL in patients who did not undergo cataract surgery and those who did.

Mann-Whitney test

Indicator	Eye status	N	Mean	Median	SD	Min	Max	p
TBUT before IPL	Unoperated	210	10,61	10,20	4,76	2,40	20,00	<0,001
	Operated	24	7,05	5,85	4,03	2,00	15,00	
TBUT after 1st IPL	Unoperated	200	12,89	13,95	4,36	0,80	17,80	<0,001
	Operated	24	7,98	7,00	3,32	3,00	17,00	
TBUT after 2nd IPL	Unoperated	127	12,08	12,00	4,36	0,80	17,00	0,005
	Operated	24	9,38	9,00	4,61	0,80	17,00	
Schirmer before IPL	Unoperated	210	11,15	10,00	5,12	3,00	29,00	0,161
	Operated	24	9,64	10,00	3,98	4,00	20,00	
Schirmer after 1st IPL	Unoperated	200	15,20	15,00	6,15	4,00	30,00	0,001
	Operated	24	11,11	11,50	4,14	5,00	22,00	
Schirmer after 2nd IPL	Unoperated	127	16,32	16,00	6,70	2,00	30,00	0,002
	Operated	24	11,88	13,00	4,59	4,00	22,00	

To summarise Table 12, it can be confirmed that both groups showed improvement after IPL therapy, both in tear film stability and in the results of the Schirmer test. However, patients who underwent cataract surgery demonstrated lower baseline values and a weaker therapeutic response compared to those who did not undergo surgery, with all differences after treatment being statistically significant (except for the baseline Schirmer test). The lower baseline TBUT values in operated patients suggest that cataract surgery may lead to apoptosis of conjunctival cells, impair meibomian gland function, or have a negative effect on the tear film, probably due to intraoperative stress, the use of preservative-containing eye drops preservatives, postoperative inflammatory response, or use of a femtosecond laser (in some cases) [Yeh et al., 2019]. However, the improvement observed after IPL in both groups indicates that the procedure is clinically effective even in patients with an additional risk factor such as cataract surgery. This highlights the role of IPL as a promising therapeutic approach for improving symptoms in meibomian dysfunction, regardless of the patient's previous condition (Figure 11).



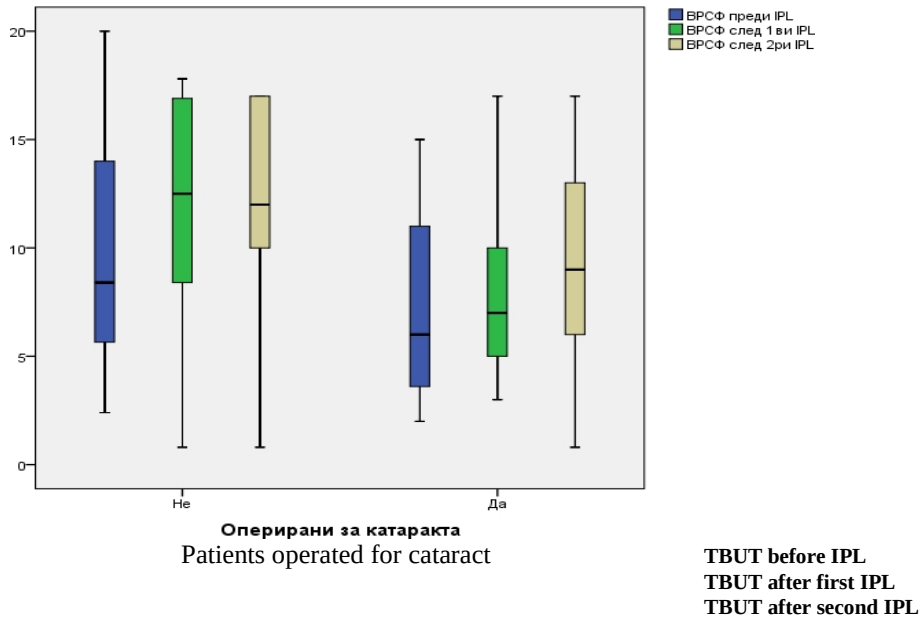


Figure 11. Graphical representation of the change in TBUT and Schirmer test in both groups before and after IPL.

The current data confirm that cataract surgery has an adverse effect on the ocular surface, leading to reduced tear film stability (reduced TBUT) and partially impaired tear secretion, even before the start of IPL therapy. This is consistent with the results of studies such as that by El Ameen A et al., which describe temporary damage to the meibomian glands and impaired ocular comfort in the postoperative period [El Ameen et al., 2018]. Their study on the effect of cataract surgery shows

that after surgery, there is a deterioration in TBUT and meibomian gland function, which can persist for up to 3 months postoperatively.

However, in patients who have undergone cataract surgery, the improvement is weaker and slower, which may be due to structural changes in the lacrimal system and a more pronounced inflammatory response after surgical intervention [Tsubota et al., 2020]. In this context, it is important to note that IPL therapy may have a limited effect in the early postoperative period, but the benefit is expected to increase with time and additional procedures.

Our results suggest that intense pulsed light is an effective therapy in both patients with meibomian dysfunction without surgery and in those who have undergone surgery, but the latter require longer follow-up and possibly an individualised therapeutic approach.

4. Results and discussion for task 4:

To analyse the subjective perception of patients with dry eye syndrome due to meibomian dysfunction based on responses to standardised OSDI questionnaires before IPL and their change after four IPL procedures.

The Ocular Surface Disease Index (OSDI) is perhaps the most commonly used tool for assessing disease severity in dry eye syndrome. It has been used in various studies to assess the severity of dry eye associated with specific conditions [Gurdal et al., 2011, Adatia et al., 2004] and to evaluate the efficacy of dry eye treatments [Monaco et al., 2011, Gurdal et al., 2010]. The tool, introduced in 1997 by the Outcomes Research Group (Allergan Inc., Irvine, CA), consists of 12 items that assess symptoms, functional limitations and environmental factors associated with dry eye syndrome. Each item has the same response option from five Likert-type categories, and each of the three subscales has its own question type [Walt et al., 1997].

Our questionnaire study on the Ocular Surface Disease Index (OSDI) included 120 patients, both unoperated and operated for cataracts. Their responses were tracked before treatment with IPL and their change after four procedures.

FIRST QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced discomfort in your eyes in any of the following situations during the past week? - Irritation from light*

As summarised in Table 13, before the first IPL, when asked whether they had experienced discomfort in their eyes due to light sensitivity in the last week, 20% (24) of patients reported no such complaints. 21.7% (26) reported that the irritation occurred occasionally. 10% (12) of those who participated in the survey reported experiencing such discomfort for half of the week, and 15 % (18) This problem occurs most of the time. 6.7% (8) of those surveyed experience constant light sensitivity, while 26.7% (32) are unable to give a specific answer. To summarise the results obtained from the first question before and after the fourth IPL, it can be noted that after the first procedure, there was an increase in the number of patients who had no complaints of light sensitivity, as well as those who responded that it occurred occasionally. There was a decrease in the number of patients who reported feeling discomfort during half of the week, as well as in those who reported feeling discomfort most of the time or all the time. The results show that after the second, third and fourth IPL, there was a progressive decrease in the number of patients who reported no such complaints, occasional discomfort, discomfort during half of the week, and discomfort all the time.

Table 13: First question from the OSDI questionnaire

Have you experienced discomfort in your eyes in any of the following situations during the last week? - Irritation from light	**OSDI - BEFORE**		**OSDI - AFTER I**		**OSDI - AFTER II**		**OSDI - AFTER III**		**OSDI - AFTER IV**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
I have not had such complaints	24	20,0	30	25,0	22	18,3	13	10,8	2	1,7
Occurs occasionally	26	21,7	37	30,8	19	15,8	11	9,2	7	5,8
Half of the week	12	10,0	7	5,8	5	4,2	0	0,0	0	0,0
Most of the time	18	15,0	8	6,7	5	4,2	0	0,0	0	0,0
All the time	8	6,7	5	4,2	1	0,8	0	0,0	0	0,0
I cannot answer	32	26,7	33	27,5	68	56,7	96	80,0	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

SECOND QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced discomfort in your eyes in any of the following situations during the past week? - Feeling that you have "sand in your eyes"*

Table 14 shows that to the second question, whether the respondents had experienced a feeling of "sand in the eyes" during the last week before IPL treatment, 14.2% (17) of them answered that they had not had such complaints. 18.3% (22) indicated that this sensation occurred occasionally. 15% (18) of those who participated in the survey said that they experienced a feeling of "sand in the eyes" for half of the week, and 20% (24) said that this problem occurred most of the time. 7.5% (9) of patients have a feeling of "sand in the eyes" all the time, and 25% (30) reported that they could not answer the question. The results of the answers to the second question can be summarised as follows: there was an increase in the number of patients compared to before the first IPL who reported that they did not have a feeling of "sand in the eyes" after the first procedure. After the second, third and fourth IPL, a decrease in the number of patients who reported a feeling of "sand in the eyes" during half of the week, most of the week and all of the time can be observed.

Table 14: Second question from the OSDI questionnaire

Did you experience discomfort in your eyes in any of the following situations during the past week? - Feeling that you have "sand in your eyes"	OSDI - BEFORE		OSDI - AFTER I		OSDI - AFTER II		OSDI - AFTER III		OSDI - AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	17	14,2	24	20,0	16	13,3	7	5,8	2	1,7
Occurs occasionally	22	18,3	41	34,2	22	18,3	10	8,3	4	3,3
Half of the week	18	15,0	7	5,8	7	5,8	2	1,7	1	0,8
Most of the time	24	20,0	13	10,8	5	4,2	2	1,7	2	1,7
All the time	9	7,5	2	1,7	2	1,7	0	0,0	0	0,0
I cannot answer	30	25,0	33	27,5	68	56,7	99	82,5	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

THIRD QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced discomfort in your eyes in any of the following situations during the last week? - Painful or inflamed eyes*

This question from the survey seeks to determine whether patients experienced painful or inflamed eyes during the week prior to the IPL procedure.

As summarised in Table 15, 10% (12) of respondents reported no such complaints. 21.7% (26) reported experiencing pain and inflammation in their eyes from time to time. 15% (18) of the participants in the survey said that they experience such discomfort half of the week, with 19.2% (23) experience this problem most of the time, and 9.2% (11) of those surveyed feel that their eyes are painful and inflamed all the time. 25% (30) say they cannot answer.

Again, as with the previous two questions, there is an increase in the number of patients who, after the first IPL, respond that they have no such complaints or that they occur occasionally.

After the second, third and fourth IPL, again, as with the first two questions in the questionnaire, there is a decrease in the number of patients who answered "half of the week", "most of the time" and "all the time".

Table 15: Third question from the OSDI questionnaire

Have you experienced discomfort in your eyes in any of the following situations during the last week? - Painful or inflamed eyes	OSDI - BEFORE		OSDI - AFTER I		OSDI - AFTER II		OSDI - AFTER III		OSDI - AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	12	10,0	30	25,0	19	15,8	9	7,5	3	2,5
Occurs occasionally	26	21,7	32	26,7	19	15,8	7	5,8	5	4,2
Half of the week	18	15,0	15	12,5	9	7,5	5	4,2	0	0,0
Most of the time	23	19,2	6	5,0	5	4,2	1	0,8	1	0,8
All the time	11	9,2	4	3,3	1	0,8	0	0,0	0	0,0
I cannot answer	30	25,0	33	27,5	67	55,8	98	81,7	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

FOURTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced any discomfort in your eyes in any of the following situations during the past week? - Blurred vision?*

Table 16 shows that when asked whether they had experienced blurred vision during the week prior to IPL treatment, 20.8% (25) of them reported no such complaints, while 28.3% (34) responded that blurred vision occurred occasionally. 10.8% (13) of the participants in the survey indicated that they experienced this type of discomfort for half of the week, while for 10.8% (13) this problem occurred most of the time during the last seven days. 4.2% (5) of respondents experience blurred vision continuously, while 25% (30) are unable to answer.

There has been an increase in the number of patients who responded "I have not had such complaints" after the first IPL, which is a trend that has been maintained from the previous three questions. It can be seen that, unlike the results of the first three questions, where after the first IPL there is an increase and then after the second a decrease in the number of patients who answered "occurs from time to time", in the question "Have you experienced blurred vision in the last week?", there is a decrease in the number of patients who answered "yes", which continues after the other three procedures.

The trend from the previous three questions is maintained in the remaining answers, where there is a decrease in the number of patients who answered "half of the week", "most of the time" and "all the time" after each subsequent IPL.

Table 16: Fourth question from the OSDI questionnaire

Have you experienced discomfort in your eyes in any of the following situations during the last week? - Blurred vision?	OSDI - BEFORE		OSDI - AFTER I		OSDI - AFTER II		OSDI - AFTER III		OSDI - AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	25	20,8	40	33,3	29	24,2	13	10,8	6	5,0
Occurs occasionally	34	28,3	33	27,5	17	14,2	7	5,8	2	1,7
Half of the week	13	10,8	7	5,8	5	4,2	2	1,7	1	0,8
Most of the time	13	10,8	6	5,0	1	0,8	0	0,0	0	0,0
All the time	5	4,2	0	0,0	1	0,8	0	0,0	0	0,0
I cannot answer	30	25,0	34	28,3	67	55,8	98	81,7	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

FIFTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced discomfort in your eyes in any of the following situations during the past week? - Poor vision*

When asked in Table 17 whether they had experienced blurred vision during the week prior to IPL treatment, 32.5% (39) of respondents reported no such complaints. 17.5% (21) reported experiencing this sensation from time to time. 8.3% (10) said they had poor vision for half of the week, and 8.3% (10) had the problem most of the time. 5% (6) of the survey participants had blurred vision all the time. The percentage of patients who cannot answer the question specifically is 28.3% (34). The trend from the first questions continues here, with an increase in the number of respondents who, after the first IPL, answer that they have not had such complaints and that they occur from time to time. The trend of a decrease in the number of patients after each subsequent IPL who give answers s u c h a s "half of the week", "most of the time" and "all the time" also continues.

Table 17: Fifth question from the OSDI questionnaire

Have you experienced discomfort in your eyes in any of the following situations during the last week? - Poor vision	**OSDI - BEFORE**		**OSDI - AFTER I**		**OSDI - AFTER II**		**OSDI - AFTER III**		**OSDI - AFTER IV**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
I have not had such complaints	39	32,5	45	37,5	30	25,0	15	12,5	7	5,8
Occurs occasionally	21	17,5	29	24,2	16	13,3	5	4,2	2	1,7
Half of the week	10	8,3	6	5,0	5	4,2	1	0,8	0	0,0
Most of the time	10	8,3	4	3,3	1	0,8	1	0,8	0	0,0
All the time	6	5,0	1	0,8	0	0,0	0	0,0	0	0,0
I cannot answer	34	28,3	35	29,2	68	56,7	98	81,7	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

SIXTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you had any problems with your eyes that prevented you from performing the following activities - Reading*

The question about reading in Table 18 shows that before IPL, 27.5 %, 16.7% (20) reported that they experienced visual disturbances from time to time. 14.2% (17) felt discomfort when reading on half of the days of the week, while for 7.5% (9) these complaints intensify and spread over most of the week, and for 9.2% (11) they occur constantly. 25% (30) of patients say they cannot answer. The trend is the same here, with an increase in the number of patients who, after the first IPL, say they have no complaints when reading. Again, there is a decrease in the number of patients who, after four IPLs, respond "half of the week", "most of the time" and "all the time".

Table 18: Sixth question from the OSDI questionnaire

Have you ever had eye problems that prevent you from doing the activities listed below - Reading	**BEFORE**		**AFTER I**		**AFTER II**		**AFTER III**		**AFTER IV**	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	33	27,5	44	36,7	28	23,3	10	8,3	2	1,7
Occurs occasionally	20	16,7	24	20,0	13	10,8	9	7,5	4	3,3
Half of the week	17	14,2	8	6,7	5	4,2	2	1,7	2	1,7
Most of the time	9	7,5	6	5,0	5	4,2	2	1,7	0	0,0
All the time	11	9,2	4	3,3	2	1,7	0	0,0	1	0,8
I cannot answer	30	25,0	34	28,3	67	55,8	97	80,8	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

SEVENTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you had any problems with your eyes that prevented you from performing the activities listed below?*
- Driving at night

When driving at night, 26.7% or 32 of the patients said they had no such complaints before IPL treatment. 13.3% or 16 of those asked said the discomfort happens sometimes.

For 5% or a total of 6 respondents, complaints when driving in the dark occur half of the week, and for 9.2% or 11 of the patients, such disturbances are noticeable most of the time. 10.8% (13 people) responded that they experience such problems all the time, while 35% or 42 of those surveyed could not specify any of the answers given, as shown in Table 19.

We can note an absolutely identical pattern to the answers given so far – an increase in the number of patients who answered "I have not had such complaints" and "occurs from time to time" after the first IPL and a decrease after each subsequent procedure.

Again, there is a progressive decrease in the number of patients after each IPL treatment in terms of eye problems while driving at night, who feel this discomfort half the week, most of the time, and all the time.

Table 19: Question 7 from the OSDI questionnaire

Have you had eye problems that prevent you from performing the activities listed below - Driving at night	BEFORE		AFTER I		AFTER II		AFTER III		AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	32	26,7	49	40,8	25	20,8	10	8,3	3	2,5
Occurs occasionally	16	13,3	17	14,2	16	13,3	4	3,3	3	2,5
Half of the week	6	5,0	4	3,3	3	2,5	0	0,0	0	0,0
Most of the time	11	9,2	6	5,0	1	0,8	4	3,3	0	0,0
All the time	13	10,8	4	3,3	1	0,8	0	0,0	1	0,8
I cannot answer	42	35,0	40	33,3	74	61,7	102	85,0	113	94,2
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

EIGHTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you had any problems with your eyes that have prevented you from performing the activities listed below - Working with a computer*

When working with a computer, 19.2% (23) of the participants in the survey said they had no such complaints before the first IPL procedure. Table 20 shows that 14.2% (17) of patients reported occasional eye discomfort when using computer devices. 11.7% (14) of those who completed the questionnaire reported discomfort during half of the week, and for 17.5 % (21) experience this problem most of the time. 8.3% (10) of patients have eye problems when working with a computer all the time, and 29.2% (35) report that they cannot answer the question. Here, too, there is an increase in the number of patients who did not have eye problems when working with a computer and who experience them occasionally after the first IPL. Again, there is a progressive decrease in the number of patients who answered "half of the week", "most of the time" and "all the time". After the third IPL, one patient still reports having problems with computer work all the time.

Table 20: Eighth question from the OSDI questionnaire

Have you had eye problems that prevent you from performing the activities listed below - Working with a computer	BEFORE		AFTER I		AFTER II		AFTER III		AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	23	19,2	35	29,2	19	15,8	9	7,5	1	0,8
Occurs occasionally	17	14,2	26	21,7	21	17,5	6	5,0	4	3,3
Half of the week	14	11,7	13	10,8	5	4,2	2	1,7	2	1,7
Most of the time	21	17,5	7	5,8	7	5,8	4	3,3	0	0,0
All the time	10	8,3	4	3,3	0	0,0	1	0,8	0	0,0
I cannot answer	35	29,2	35	29,2	68	56,7	98	81,7	113	94,2
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

NINTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you had any problems with your eyes that have prevented you from performing the activities listed below* - Watching TV

Table 21 shows that before the IPL procedure, 23.3% (28) of respondents reported no such complaints when watching television. Twenty percent (24) of respondents reported feeling discomfort in their eyes from time to time, 14.2% (17) reported feeling discomfort half of the week, and 10.8% (13) reported experiencing this problem most of the time while watching television. 5.8% (7) of patients feel pain all the time, and 25.8% (31) cannot answer the question. The results are identical to the previous ones in terms of the increase in patients after the first IPL who respond that they have not had such complaints or that they occur occasionally, and after the second to fourth IPL, a decrease in the number of patients is already observed. There is a progressive increase in the number of patients who cannot answer the question after each subsequent IPL.

Table 21: Ninth question from the OSDI questionnaire

Have you had eye problems that prevented you from performing the activities listed below: Watching TV	**BEFORE**		**AFTER I**		**AFTER II**		**AFTER III**		**AFTER IV**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
I have not had such complaints	28	23,3	38	31,7	25	20,8	11	9,2	3	2,5
Occurs occasionally	24	20,0	30	25,0	18	15,0	6	5,0	5	4,2
Half of the week	17	14,2	7	5,8	4	3,3	1	0,8	1	0,8
Most of the time	13	10,8	8	6,7	4	3,3	1	0,8	0	0,0
All the time	7	5,8	2	1,7	1	0,8	2	1,7	0	0,0
I cannot answer	31	25,8	35	29,2	68	56,7	99	82,5	111	92,5
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

TENTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced eye discomfort in the last week in any of the following situations - windy weather*

In windy weather, 22.5% (27) of patients reported that they had no such complaints, while 15% (18) reported experiencing visual disturbances in windy conditions from time to time, as shown in Table 22. 6.7% (8) feel discomfort in windy weather on half of the days of the week, for 16.7% (20) these complaints extend over most of the week, while for 11.7% (14) the discomfort is constant. 27.5% (33) of respondents say they cannot answer.

Table 22: Tenth question from the OSDI questionnaire

Have you had eye discomfort in the last week in any of the following situations? situations - windy weather	BEFORE		BEFORE I		AFTER II		AFTER III		AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	27	22,5	38	31,7	24	20,0	11	9,2	0	0,0
Occurs occasionally	18	15,0	27	22,5	19	15,8	9	7,5	5	4,2
Half of the week	8	6,7	6	5,0	4	3,3	1	0,8	2	1,7
Most of the time	20	16,7	8	6,7	2	1,7	3	2,5	1	0,8
All the time	14	11,7	5	4,2	2	1,7	0	0,0	0	0,0
I cannot answer	33	27,5	36	30,0	69	57,5	96	80,0	112	93,3
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

ELEVENTH QUESTION OF THE OSDI QUESTIONNAIRE - *Have you experienced eye discomfort in the past week in any of the following situations - Places/seasons with low humidity*

In rooms or during seasons with low atmospheric humidity 30.8% or 37 of those surveyed said they had no such complaints. 17.5% or 21 patients reported that discomfort in low humidity occurs occasionally. For 9.2% or 11 people, complaints in rooms with dry air occur half of the week, and for 8.3% or 7 of those surveyed, visual problems are noticeable most of the time. 5.8 % (7 people) respond that they experience similar discomfort all the time. 28.3% or 34 of the respondents cannot give a specific answer to the question, as clearly documented in Table 23.

Table 23: Eleventh question from the OSDI questionnaire

Have you experienced eye discomfort in the last week in any of the following situations - Places/season with low humidity	BEFORE		AFTER I		AFTER II		AFTER III		AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	37	30,8	50	41,7	27	22,5	14	11,7	1	0,8
Occurs occasionally	21	17,5	20	16,7	17	14,2	4	3,3	4	3,3
Half of the week	11	9,2	6	5,0	2	1,7	2	1,7	2	1,7
Most of the time	10	8,3	7	5,8	4	3,3	2	1,7	0	0,0
All the time	7	5,8	1	0,8	1	0,8	0	0,0	1	0,8
I cannot answer	34	28,3	36	30,0	69	57,5	98	81,7	112	93,3
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

TWELFTH QUESTION OF THE OSDI QUESTIONNAIRE - ***Have you experienced eye discomfort in the last week in any of the following situations - in rooms heated/cooled by air conditioning***

In rooms heated or cooled by air conditioning, 26.7% (32) of respondents said they had no eye discomfort. 25% (18) of patients reported occasional eye discomfort, 8.3% (10) reported experiencing this problem half of the week, and 13.3% (16) reported discomfort caused by air conditioners most of the time. 8.3% (10) of respondents experience visual disturbances all the time, and 28.3% (34) are unable to answer the question, as documented in Table 24.

Table 24: Twelfth question from the OSDI questionnaire

Have you had eye discomfort in the last week in any of the following situations - in rooms heated/cooled by air-condition	BEFORE		AFTER I		AFTER II		AFTER III		AFTER IV	
	N	%	N	%	N	%	N	%	N	%
I have not had such complaints	32	26,7	44	36,7	25	20,8	11	9,2	1	0,8
Occurs occasionally	18	15,0	25	20,8	19	15,8	7	5,8	4	3,3
Half of the week	10	8,3	6	5,0	3	2,5	1	0,8	2	1,7
Most of the time	16	13,3	8	6,7	4	3,3	2	1,7	1	0,8
All the time	10	8,3	2	1,7	0	0,0	0	0,0	0	0,0
I cannot answer	34	28,3	35	29,2	69	57,5	99	82,5	112	93,3
Total	120	100,0	120	100,0	120	100,0	120	100,0	120	100,0

To summarise the results of the last three questions, it can be said that the trend remains the same as in all previous questions. There is an increase in the number of patients who, after the first IPL, report that they have not had such complaints or that they occur occasionally. For the rest, the status quo is maintained in terms of a decrease in the number of patients after the second and each subsequent IPL who report such complaints during half of the week, during most of the week, or all the time. The same trend is observed with regard to the progressive increase in patients after each IPL who are unable to answer the question.

Similar results to ours were observed in a prospective interventional study by Wei et al. [Wei et al., 2020]. Their study included 53 people who received a series of 3 IPL treatments at intervals of 3-4 weeks. The results of the OSDI questionnaire, the height of the lacrimal meniscus, and the non-invasive tear break-up time were studied. In addition, an automated software programme with artificial intelligence was used in their study to analyse the corneal nerves. They concluded that the OSDI score was significantly reduced after IPL treatment compared to baseline ($P < 0.001$). OSDI was reported to be a reliable and valid parameter for distinguishing the severity of dry eye disease. Wei et al. found that the value was significantly reduced after IPL treatment compared to baseline, which is consistent with studies by other researchers [Choi et al., 2019, Albietz et al., 2018]. Based on these results, they conclude that IPL can alleviate symptoms to a certain extent.

Seo et al. evaluated 17 people who underwent 4 IPL treatments (M22, Lumenis, Tokneam, Israel, 11 J/cm2) at 3-week intervals. These patients were followed up for 1 year. Fifteen of them (88.2%) were satisfied with the

treatment. The results of the OSDI questionnaire and the quality of the meibum (assessed using a scale from 0 to 3) improved in a statistically significant manner over the duration of the study, while the results of the BRSF improved only during the first 12 weeks [Seo et al., 2018].

Similar results to ours were observed in a prospective, longitudinal study of patients with moderate to severe meibomian dysfunction by Verges et al. [Vergés et al., 2021]. Treatment consisted of 4 consecutive IPL sessions, with all subjects assessed before each IPL session and 1 and 4 months after the last procedure. The study included 44 patients (88 eyes), 20 men (40 eyes) and 24 women (48 eyes), with a mean age 52.5± 13.6, ranging from 22 to 78 years. Comparing the percentage of subjects with improvement of more than 10 points on the OSDI questionnaire between baseline and the last visit, the results show a high level of significance, $p < 0.005$. Compared to baseline, all symptoms showed improvement 4 months after the last IPL session. The most significant changes were observed in the sensation of dryness and pain ($p <0.005$) and foreign body sensation ($p <0.001$). Veges et al. conclude that improvement in most symptoms begins between 14 and 28 days after the start of IPL treatment [Vergés et al., 2021]. No significant difference was observed between visits – on the first and fourth month after the last IPL session. Although no improvement was observed during this period, the results remained stable four months after the last IPL session ($p < 0.003$).

Similarly, Li et al. [Li et al., 2020] applied IPL to the upper eyelid of some patients with severe upper eyelid symptoms. Thirty patients were divided into a traditional IPL group and an additional upper eyelid group. After therapy, dry eye symptoms improved in both groups; however, OSDI, outcome, and patient satisfaction in the upper eyelid group were better than those of traditional IPL therapy. These findings suggest that adding IPL therapy to the upper eyelid may be a possible option for patients with refractory upper eyelid symptoms.

Low-intensity light therapy (LLLT), which relies on photobiomodulation, is used in combination with IPL. Stonecipher et al. studied 230 patients treated with LLLT in combination with IPL [Stonecipher et al., 2019]. According to their findings, both meibomian gland function and OSDI scores improved significantly after therapy.

However, there are some limitations to the study. The lack of a control group cannot determine the therapeutic effect of a given therapy.

A study by Yin et al. [Yin et al., 2018] aimed to clarify the specific effects of IPL on the meibomian glands. Comparisons were made with a control group treated with eyelid hygiene, and it was observed that OSDI scores, conjunctival staining, BRSF, and gland function improved after IPL treatment. It is worth noting that the study looked at the microstructure indices of the meibomian glands and found that changes in OSDI were associated with the acinar unit of the glands. There is a positive correlation between changes in OSDI and changes in the density of the acinar units of the meibomian glands. The researchers believe that IPL manages meibomian gland dysfunction by improving the microstructure of the glands, which may be one of the therapeutic mechanisms of IPL.

IPL can significantly improve visual quality in addition to relieving dry eye symptoms according to Fan et al. [Fan et al., 2020]. The Quality of Vision Questionnaire (QOV) was used to evaluate 64 participants who underwent two IPL sessions separated by 3 weeks. It was observed that the subjective OSDI and QOV scores of patients improved significantly after therapy, mainly manifesting as glare, halos, and blurred vision.

5. Results and discussion for task 5:

Develop an algorithm for the treatment of meibomian dysfunction in patients with a pronounced clinical picture.

Meibomian dysfunction (MGD) is a chronic disease in which there is impaired function of the meibomian glands and a change in the quality of the lipid layer of the tear film. This results in tear film instability, leading to symptoms such as dryness, irritation, burning, blurred vision and impaired visual comfort. Treatment of this condition requires an integrated, individually tailored approach involving both conservative and device-based methods, among which intense pulsed light (IPL) plays a leading role.

The following treatment algorithm has been developed at our clinic:

During the initial assessment, the specialist collects a detailed medical history, focusing on the frequency and severity of symptoms. The ophthalmological examination looks for obstruction of the meibomian glands along the eyelid margin, hyperemia, and the presence of telangiectasia. Next, the non-invasive tear film break-up time (NIBUT) is measured, which in patients with MGD is often reduced to less than 7 seconds, and a Schirmer test is performed to assess the amount of tear secretion.

If possible, meibomography is performed to visualise morphological changes in the meibomian glands. Inflammatory markers such as interleukin-6 are sometimes also tested.

After diagnosis, the ophthalmologist classifies the disease according to severity – mild, moderate or severe. The mild form is characterised by minimal complaints and a slightly shortened TBUT, while severe cases show pronounced symptoms, stable structural degeneration of the glands and severe inflammation. Treatment usually begins with conservative measures. Prescription artificial tears without preservatives are used to improve the stability of the tear film. The patient applies warm compresses and massages the eyelids to stimulate the secretion of lipids. In the presence of inflammatory or infectious elements, the ophthalmologist prescribes local or systemic antibiotics and, in some cases, anti-inflammatory drops. It is recommended to avoid aggravating factors such as excessive screen work or exposure to irritants.

In patients who do not respond adequately to conservative therapy after 4 to 6 weeks, the specialist proceeds to IPL treatment. This decision is made based on the presence of visible vascular changes, chronic inflammation, worsened TBUT, and inadequate response to conventional therapy. IPL therapy is performed with a Lumenis M22 device, which emits light in the 515–590 nm spectrum. The session includes cooling the skin, putting on protective glasses, and treating the areas around the eyelids, treating both the upper and lower eyelids with the appropriate tip. The standard protocol includes 3–4 sessions, spaced 2 to 4 weeks apart. During treatment, the patient should avoid sun exposure and use photoprotection.

After completion of therapy, treatment continues with supportive care – artificial tears, warm compresses and eyelid hygiene. Follow-up includes repeat TBUT measurement, Schirmer test and symptom assessment. If necessary, maintenance IPL sessions are scheduled every 3–6 months. Clinical findings and the patient's response guide the specialist in tailoring future therapy.

This approach, based on consistent diagnosis, targeted treatment and objective follow-up, demonstrates high efficacy in restoring meibomian gland function and improving the quality of life of patients with dry eye due to MGD (Table 25).

Table 25. Algorithm for the diagnosis and treatment of MGD

Stage	Action	Description / Details
1. Initial assessment	Collect medical history	Focus on frequency and severity of symptoms
	Ophthalmological examination	Gland obstruction, hyperemia, telangiectasia
	NIBUT measurement	Tear film break-up time (often < 7 seconds in MGD)
	Schirmer test	Assessment of tear secretion
	Meibomian gland imaging (if possible)	Visualisation of morphological changes in the glands
	Examination of inflammatory markers	For example, interleukin-6 (at discretion)
2. Diagnosis and classification	Diagnosis of MGD	Confirmation of the presence of the disease
	Classification by severity	Mild, moderate, severe form according to symptoms and findings
3. Initial treatment	Conservative measures	Artificial tears without preservatives, warm compresses, eyelid massage
	Local/systemic medications	Antibiotics, anti-inflammatory drops in case of inflammation or infection
	Change in habits	Avoid screen time and distractions
4. Assessment after 4-6 weeks	Response assessment	Assessment of symptoms and indicators
	If response is insufficient	Switch to IPL therapy
5. IPL therapy	Perform IPL with Lumenis M22	Light spectrum 515–590 nm, cooling, protective eyewear
	Treatment of the eyelids	Upper and lower eyelids with appropriate tip
	Protocol	3-4 sessions over 2-4 weeks
	Precautions	Avoid sun exposure and use sunscreen
6. Maintenance therapy and follow-up	Supportive treatment	Artificial tears, warm compresses, eyelid hygiene
	Follow-up	Repeat TBUT measurement, Schirmer test, symptom assessment
	IPL maintenance plan	Sessions every 3-6 months as needed
7. Individualisation of treatment	Therapy adjustments	Based on clinical response and patient preferences

Meibomian gland dysfunction is the leading cause of dry eye syndrome, with its prevalence ranging widely from 3.5% to 70% depending on age, gender, and ethnicity [Schaumberg et al., 2017].

There are no existing guidelines for the treatment of meibomian dysfunction in the literature. In Japan, guidelines for the treatment of

dry eye syndrome [Dry Eye Research Society Clinical Practice Guidelines Preparation Committee, 2019]. Some of its content may be useful in the treatment of dry eye that develops simultaneously with meibomian dysfunction. Across the Atlantic, however, the TFOS MGD International Workshop published a report stating that this is more of a review article than evidence-based practical guidelines [Nichols et al., 2011].

Meibomian dysfunction is diagnosed based on subjective symptoms, eyelid margin abnormalities, gland opening status, and degree of meibum. Approaches such as conventional meibography and confocal microscopy for observing the morphology of the meibomian glands, as well as tear interferometry for assessing gland function, are also available [Tomlinson et al., 2011], but they are not widely accepted in clinical practice. Non-contact meibography is a developed non-invasive method that allows relatively rapid imaging of the meibomian glands with high reproducibility and provides images that are convincing to patients of the need for treatment [Fineide et al., 2020]. It is now widely accepted in clinical practice for the assessment of meibomian gland disorders.

Treatment options for meibomian dysfunction have increased significantly, particularly with the recent introduction of non-pharmaceutical methods [Arita et al., 2020], following the International Workshop on Meibomian Gland Dysfunction in 2011. The choice of treatment is currently based on the classification of stages proposed at the 2011 workshop [Geerling et al., 2011]. This classification is based on a comprehensive assessment of subjective symptoms, eyelid margin abnormalities (obstruction, vascularisation), meibum grade and degree of staining of the ocular surface. However, it is often difficult to select a treatment method according to this complex classification in clinical practice. Furthermore, it is unclear at what stage non-pharmaceutical treatment options such as intraductal probing [Maskin, 2010], thermal pulse therapy [Greiner, 2012] and intense pulsed light [Toyos et al., 2015] should be performed.

That is why Arita et al. propose a treatment algorithm based on a retrospective study of the characteristics of patients with meibomian dysfunction who visited the Itoh Clinic between April 2014 and September 2020 and received one of five types of treatment. The efficacy of each treatment was reassessed in terms of non-invasive meibography (meiboscore) at baseline [Atita et al., 2020]. The inclusion criteria were as follows: (1) age at least 20 years; (2) diagnosis of meibomian dysfunction according to Japanese diagnostic criteria [Amano et al., 2010], including ocular symptoms, blocked gland openings, vascularisation and uneven eyelid margins, and reduced meibum quality and quantity (Shimazaki grade) [Shimazaki et al., 1995]. The exclusion criteria include: active eye infection, inflammatory eye disease, and Schirmer test value ≤5 mm. All included patients perform eyelid warming and practise eyelid hygiene twice daily. During the study period, five types of therapy were performed: (1) eyelid hygiene alone for 3 months (years 2014– 2016), (2) four

sessions of meibum expression with an Arita (Katena) meibum gland compressor at 3-week intervals together with eyelid hygiene for 3 months (years 2015–2016), (3) application of azithromycin (AZM) eye drops for 2 weeks together with eyelid hygiene (years 2019–2020), (4) one session of treatment with the LipiFlow thermal pulsation system (Johnson & Johnson) together with eyelid hygiene for 1 month (years 2015–2017) and (5) four sessions of treatment with intense pulsed light (IPL) together with eyelid hygiene for 3 months (years 2016–2017). Johnson) together with eyelid hygiene for 1 month (years 2015–2017) and (5) four treatment sessions with intense pulsed light (M22, Lumenis) at 3-week intervals, again with eyelid hygiene for 3 months (years 2016–2019). All patients were allowed to use artificial tears four times a day. All patients were examined before and 1 month after the end of the treatment period. Eye symptoms were assessed using the Standardised Patient Evaluation of Dry Eye (SPEED) questionnaire. The thickness of the lipid layer of the tear film was measured with a LipiView interferometer (Johnson & Johnson). Eyelid margin abnormalities — including obstruction (scale of 0–3) and vascularisation (scale of 0–3), as well as fluorescein-based tear film break- up time (scale of 0–9) and meibum grade (scale of 0–3) are assessed by microscopic examination. The Meiboscore (0–3 for each eyelid), which reflects the degree of loss of the meibomian gland, is determined using a non-contact meibograph system (Topcon) and the Meiboscore for both eyelids is summed (total 0–6). The volume of tear fluid is measured using the Schirmer test, performed without the use of anaesthetic. Eyes are categorised as showing improvement (i.e. treatment was effective) if the SPEED score decreases by ≥4 points and the meibum score decreases by ≥1 point after treatment compared to before treatment. Data for this study are obtained from the right eye of each subject, unless the right eye is excluded, in which case data from the left eye are used.

It was observed that the SPEED test result decreased significantly in the first month after the end of the treatment period for all groups. The thickness of the lipid layer increased significantly in the glandular expression group and the LipiFlow group. Obstruction improved significantly in all groups except for the eyelid hygiene group. Improved vascularisation was also observed in the AZM, LipiFlow and IPL groups. The TBUT significantly lengthened in all groups except for the AZM and LipiFlow groups.

The eyes in each treatment group were classified based on the meiboscore (1 or 2, mild glandular loss; 3 or 4, moderate glandular loss; 5 or 6, severe glandular loss). The eyes are also categorised as showing improvement (treatment is effective) if the SPEED score decreases by ≥4 points and the meibum score decreases by ≥1 point compared to pre-treatment values. In the eyelid hygiene group, 100% of patients with mild glandular loss showed improvement. However, none of those with moderate or severe glandular loss showed improvement. In the glandular expression group, 88% of patients with mild glandular loss improved, compared to 55% of those with moderate glandular loss and none of those with severe glandular loss. In the AZM group,

92% of patients with mild glandular loss and 100% of those with moderate glandular loss improved, while none of those with severe glandular loss did. In the LipiFlow group, 75%, 10% and 0% of patients with mild, moderate or severe glandular loss, respectively, showed improvement. Finally, in the IPL group, all patients with mild to severe glandular loss improved.

The diagnosis of meibomian dysfunction is largely based on a combination of subjective symptoms and biomicroscopic findings [Tomlinson et al., 2011], but guidelines for selecting treatment according to disease severity are unclear. Given that more than half of patients with meibomian dysfunction are asymptomatic [Arita et al., 2016] and that the duration of the disease is difficult to assess, existing guidelines are insufficient for accurately determining the severity of meibomian dysfunction. According to the study by Arita et al., their findings suggest that some treatment options may be selected according to the degree of destruction of the meibomian gland morphology visible in images obtained by non-contact meibography [Arita et al., 2020]. The specificity and sensitivity for diagnosing meibomian dysfunction based on the morphology of the meibomian glands are high, at 85% and 96.7%, respectively [Adil et al., 2019]. Meibography images convince patients of the need for treatment. However, it is difficult to quantify the area of the meibomian glands in such images, and they are not suitable for follow-up, as the gland area does not easily recover with treatment. Tests of meibomian gland function, such as meibum classification, are relatively subjective. Tear interferometry is quantitative, but findings are easily influenced by conditions such as humidity, room and body temperature, and eye makeup. On the other hand, meibography is objective and highly reproducible and can accurately diagnose meibomian dysfunction [Xiao et al., 2019] and assess disease status [Xiao et al., 2019, Xiao et al., 2020]. Assessment of gland morphology and function would be the ideal way to evaluate the efficacy of meibomian dysfunction treatment in the future. Tear film break-up time was measured with fluorescein in the study by Arita et al. [Arita et al., 2020], which began before the publication of the TFOS DEWS II report [Wolffsohn et al., 2017], which recommends the use of non-invasive measures to assess tear film stability. In general, if the technology is available, it is preferable to use the average result of several measurements of non-invasive tear break-up time (NIBUT) based on the Placido disc [Hong et al., 2013]. The invasiveness of the procedure in the study by Arita et al. [Arita et al., 2020] is minimised by carefully applying fluorescein- stained paper to the conjunctival sac and asking the patient to blink twice.

The study by Arita et al. concluded that all five types of treatment significantly improved subjective symptoms and objective tear film parameters compared to baseline [Arita et al., 2020]. They demonstrate that eyelid hygiene tends to be an effective method only in patients with mild meibomian dysfunction and that intense pulsed light is effective for all degrees and is the only effective treatment in patients with severe disease characterised by the loss of many glands. The efficacy of meibomian gland expression and the LipiFlow

device are similar, consistent with the results of a previous study suggesting that LipiFlow is not effective in patients with very advanced meibomian dysfunction [Greiner, 2016]. However, their results do not suggest that intense pulsed light causes regeneration of the meibomian glands. The efficacy of IPL may depend on its anti-inflammatory effect as well as the liquefaction of the meibum, and therefore may be more effective in severe meibomian dysfunction associated with a very high percentage of blocked glands than the LipiFlow device, whose efficacy is thought to rely on liquefaction of the meibum and massage of the glands. In addition, the standard protocol for intense pulsed light therapy consists of four sessions at 3-week intervals, while the LipiFlow protocol is a single application.

In conclusion, their results suggest that the most appropriate treatment can be selected for each patient with meibomian dysfunction based on the meiboscore. When it comes to mild or moderate meibomian dysfunction, there are several treatment options. When gland loss is severe, treatment with intense pulsed light is recommended. In this way, meibography can predict the effectiveness of future treatment and inform the patient about the best treatment option, especially in individuals with a high percentage of lost glands. Future prospective studies are needed to confirm the results of their study.

CONCLUSION

Dry eye syndrome is a widespread, chronic and often underestimated condition that can lead to serious visual impairment, irritation, pain and a significantly reduced quality of life. Despite advances in diagnosis and treatment, a large proportion of patients continue to experience symptoms despite standard therapies, particularly in cases associated with meibomian dysfunction, the most common cause of dry eye.

In this context, intense pulsed light (IPL) is emerging as an innovative and pathogenetically targeted therapy. It works by warming and unblocking the meibomian glands, reducing inflammation and improving the quality of the lipid layer of the tear film. Despite international interest in this technology, there has been no systematic clinical study investigating the effect of IPL in patients with dry eye in Bulgaria to date.

This thesis presents an in-depth clinical evaluation of the efficacy and safety of IPL therapy in patients with dry eye syndrome and proven meibomian dysfunction, based on real observations from ophthalmological practice in Bulgaria.

The study included 120 patients (a total of 240 eyes), each of whom received an individualized therapeutic approach with IPL. Diagnostic and follow-up assessment included subjective indicators (symptom questionnaires) as well as objective parameters such as non-invasive tear break-up time (NIBUT), meibomian expression and morphology, as well as visual assessment of skin phototype according to Toyos, in order to adapt the treatment parameters to the individual characteristics of the patient.

The results of the study show a statistically significant improvement in both subjective complaints and objective clinical parameters after the course of IPL procedures. Patients report a reduction in irritation, burning, visual instability and foreign body sensation, while instrumental indicators confirm improved stability and quality of the tear film.

The innovation of this dissertation lies both in the application of a modern, device-based therapeutic method, previously unknown in Bulgarian ophthalmological practice, and in the comprehensive diagnostic and therapeutic approach based on personalised medicine. In addition, Toyos' classification based on skin phototype has been integrated into the therapeutic protocol in order to adapt the light energy to the individual sensitivity of the skin and ensure maximum safety. The study contributes both scientifically and in terms of applied clinical contribution, as offers a realistic, working model for integrate IPL into the therapeutic arsenal of eye disease specialists. The collected data can serve as a basis for the development of national therapeutic protocols and good practices in the treatment of dry eye in Bulgaria.

Given the positive results, safety and good tolerability of the procedure, IPL therapy deserves wider clinical application and inclusion in long-term strategies for the management of chronic dry keratoconjunctivitis. Additional multicentre

and randomised studies with longer follow-up periods are needed to optimise the therapeutic protocol and confirm the long-term efficacy of the method.

In conclusion, this thesis highlights the role of IPL as an innovative, non-invasive and promising method in the treatment of dry eye, with real potential for application in Bulgarian clinical practice and a significant contribution to the development of modern ophthalmology in our country.

CONCLUSIONS

1. Based on the analysis, there is no statistically significant relationship between age and the degree of meibomian dysfunction in the patients studied ($p = 0.323$), suggesting that age is not a determining factor for the severity of the disease in the present sample.

2. No statistically significant correlation was found between gender and the degree of meibomian dysfunction in the studied patients ($p= 0.124$). However, in the present sample, women were more likely to fall into the group with mild meibomian dysfunction, while men were more likely to fall into the group with moderate meibomian dysfunction.

3. IPL therapy leads to a significant improvement in tear film break-up time (TBUT) in patients with more severe meibomian dysfunction (Groups 2 and 3; $p < 0.001$), while in patients with a milder form (Group 1) no statistically significant improvement was found ($p = 0.105$).

4. The Schirmer test showed a significant increase in tear secretion after IPL therapy in groups 2 and 3 ($p< 0.001$), while in group 1 the improvement did not reach statistical significance ($p = 0.148$).

5. In patients who had undergone cataract surgery, a statistically significant improvement was observed both in tear break-up time (TBUT) and in the results of the Schirmer test after IPL therapy ($p< 0.001$). This confirms the effectiveness of IPL in patients with dry eye induced or worsened after cataract surgery.

6. The tear break-up time (TBUT) and Schirmer test values are significantly lower in cataract-operated patients compared to non-operated patients, both before and after IPL therapy. The differences are statistically significant for all TBT measurements ($p < 0.001$ and $p = 0.005$) and for Schirmer test values after the first and second procedures ($p = 0.001$ and $p = 0.002$), while the difference before therapy is not significant ($p = 0.161$). This indicates a weaker response to therapy in postoperative patients and highlights the need for an individualised approach to the treatment of dry eye in this group.

7. The OSDI questionnaire shows a significant reduction in subjective complaints in patients after IPL therapy, confirming the beneficial effect of the treatment not only on objective but also on subjective symptoms of dry eye.

CONTRIBUTIONS OF THE DISSERTATION

I. Contributions of a scientific and theoretical nature

1. For the first time in a dissertation in Bulgaria, a systematic clinical study was conducted on the effectiveness of IPL in patients with dry eye syndrome associated with meibomian dysfunction.
2. A comprehensive analysis of objective indicators (tear film break-up time, Schirmer test) and subjective symptoms (OSDI questionnaire) was performed, providing a comprehensive assessment of the therapeutic effect of IPL.
3. A significant correlation was found between the degree of meibomian dysfunction and the response to IPL therapy, which contributes to a better understanding of the pathogenesis and treatment of the disease.
4. The role of age and gender as factors influencing the severity of meibomian dysfunction and the effectiveness of IPL therapy was analysed, which supports a personalised approach to treatment.
5. A comparative analysis between cataract patients who underwent surgery and those who did not is presented, revealing differences in clinical course and therapeutic response, contributing to a more targeted approach to different patient subgroups.

II. Contributions of a scientific and applied nature

1. An algorithm for the assessment, treatment and follow-up of patients with dry eye, applicable in clinical ophthalmological practice, has been developed and proposed.
2. The data from the study confirm IPL therapy as an effective and safe method for the treatment of meibomian dysfunction, which creates a basis for its widespread application in Bulgaria.
3. A scientific basis for the inclusion of IPL therapy in clinical pathways and standards for the treatment of patients with dry eye has been presented, which may improve the quality of healthcare services and patient satisfaction.

III. Contributions of a confirming nature

1. The effectiveness of IPL therapy in improving both subjective symptoms and objective indicators in patients with dry eye is confirmed, which is consistent with the results of international studies.
2. The significant role of age and gender as factors influencing the severity and clinical course of meibomian dysfunction is confirmed, in line with data from the existing literature.
3. The correlation between subjective symptoms assessed with OSDI and objective indicators (BRSF and Schirmer test) is confirmed, supporting a multidisciplinary approach to the diagnosis and treatment of dry eye.

SCIENTIFIC PUBLICATIONS AND COMMUNICATIONS RELATED TO THE DISSERTATION

I. Scientific publications related to the dissertation

1. **Dimitrova, M.,** Irinkova, B., Gatseva, A., Petkova, I., Kuneva, I., Intense Pulsed Light (IPL) – an innovative method for the treatment of meibomian dysfunction in patients with dry eye syndrome, Bulgarian Ophthalmological Review, 2023; 67(1);30-36

2. **Dimitrova, M.,** Modern treatment of dry eye syndrome associated with meibomian dysfunction, (2021), MEDINFO, issue 4624, 24-26

3. **Dimitrova, M.,** Kuneva I., Intense Pulsed Light (IPL) – Treatment strategy for Meibomian gland dysfunction, Journal of IMAB, 2025 Jan-Mar; 31 (1)

II. Participation in scientific forums

1. "Intense Pulsed Light (IPL) – an innovative method for treating meibomian dysfunction in patients with dry eye syndrome" – News in Ophthalmology and XV Vitreoretinal Symposium, 14-17 October 2021, Borovets, (oral presentation)

2. "Persistent subretinal fluid due to central serous chorioretinopathy in the presence of silicone tamponade," XIV Congress, News in Ophthalmology and XV Vitreoretinal Symposium, 14-17 October 2021, Borovets, (poster)

3. "Intense pulsed light and glaucoma", XV Congress, Bulgarian Ophthalmological Society, 28 September-1 October 2023, Albena, (oral presentation)