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CASE STUDY REPORT – CLINICAL FINDINGS AND MANAGEMENT OF THE PATIENT WITH EVAPORATIVE DRY EYE DUE TO MEIBOMIAN GLAND DYSFUNCTION

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Master's thesis
Fall term 2022
Master of Health Care, Clinical Optometry
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ABSTRACT

Oulu University of Applied Sciences
Master of Health Care, Clinical Optometry

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Title of the thesis: Case Study Report – Clinical Findings and Management on the Patient with Evaporative Dry Eye due to the Meibomian Gland Dysfunction
Supervisors: Dr. Robert Andersson and Tuomas Juustila
Term and year of thesis completion: Fall term 2022
Pages: 52 + 5 appendices

PURPOSE

This case study report aims to describe the assessment and symptom-based management of an evaporative dry eye patient and to discuss this using evidence-based literature. Two measurements and different managements were used for the case study patient with evaporative dry eye.

METHODS

This case study report included the clinical assessment and management of a 62-year-old Caucasian female who came to a private clinic for a dry eye examination on the 11th of February 2022. The dry eye examination included a comprehensive eye examination and measurements using Oculus Keratograph 5M with Jenvis Pro Dry Eye Report. Topcon Myah measurements were made before IPL therapy, and EyeLight IPL was given according to the private clinic's protocol. After IPL measurements, the Rexon Eye dry eye therapy was given according to the manufacturer's protocol. The IRB approval was not needed in this case study. Descriptive statistical analysis was performed for the case study.

RESULTS

The following clinical differences were achieved in seven months: redness values improvement, topography values and tear meniscus height values showed no major change, and meibography showed a slight improvement on both lids. Slit lamp examination with fluorescein staining showed slight improvement objectively on the FBUT; similar results showed the K5M values.

CONCLUSION

Dry eye disease patients feel their symptoms differently. It is essential to perform the adequate assessment of the problem and treat the correct cause. The imaging tools are good assistants for evaluations and follow-ups. However, according to DEWS II, the three necessary tests in the dry eye assessment are the osmolarity test, NIBUT test, and staining test with the slit lamp examination. Artificial tear drops are a handy tool to treat dry eye symptoms. However, the proper treatment can have extended-lasting benefits for dry eye patients.

Keywords: dry eye disease, meibomian gland dysfunction, DEWS II, quality of life, DED treatment.

CONTENTS

1 INTRODUCTION

This thesis introduces a case study on a patient with Meibomian Gland Dysfunction (MGD) (Chhadva P. & al. 2017), and it reviews the literature on Dry Eye Disease (DED) (Messmer EM. 2015). Dry eye is a multifactorial disease with the loss of tear film homeostasis. It is accompanied by different ocular symptoms, in which hyperosmolarity, tear film instability, ocular inflammation, and neurological abnormalities are present. The main risks for dry eye disease are age, female sex, medications, low humidity environment, smoking, and computer use. Insufficient time outdoors and eye surgeries—proper assessment and management based on the pathophysiology play a vital role in DED. The most important key to resolving the problematic dry eye is to find the etiological cause, break the vicious circle and restore homeostasis. The case study patient assessment used Oculus Keratograph 5M (K5M) and Topcon Myah. Oculus K5M is a topographer with the Jervis Pro Dry Eye Report software to evaluate dry eye severity. The JENVIS Pro Dry Eye Report has a fail-safe test sequence covering all the assessment criteria required for a comprehensive analysis of dry eye syndrome. The Oculus K5M is a corneal topographer with a built-in real keratometer and a color camera optimized for external imaging. The other features include the meibomian glands examination, non-invasive Keratograph break-up time (NIKBUT), the tear meniscus height measurement, and lipid layer evaluation. The test protocol was planned in the matter to avoid any unnecessary manipulation of the eye. Topcon Myah measurements included corneal topography, 5% TBT non-invasive break-up time, which means the first time at which the percentage of breakup sectors reached the level of 5%, and meibomian glands imaging, only on the lower lids. The tear meniscus height was not evaluated.

The management used Intense Pulsed Light (IPL) therapy and continued with the new Quantum Molecular Resonance (QMR) therapy called Rexon Eye. The Eye-Light Intense Pulsed Light (IPL) therapy used a laser probe in 5 different locations on the lid area of the patient, and after this, the thermal mask was placed on the patient's face for 15 minutes. This treatment stimulates the meibomian glands. Rexon-Eye is a non-invasive device based on QMR technology providing long-lasting treatment for all forms of dry eye syndromes. It works by applying low-power high-frequency electric fields capable of stimulating the metabolism and natural regeneration of cells. The correct assessment gives good guidelines for successful management.

2 THEORETICAL BACKGROUND

In the past 30 years, the definition of dry eye has variated (Craig, J. P & al. 2017). In 1995, National Eye Institute and Clinical Trials published the first definition of dry eye in the Dry Eye working group. It was categorized as a tear film disorder with associated ocular symptoms—the consensus on the meaning of the tear film quality and the tear quantity to the Dry Eye. In 2007, TFOS DEWS (Tear Film Ocular Surface Dry Eye Work Shop) was published, and there was the first time mentioned that dry eye is a disease, but the mechanism of DED was not present in the statement. In 2015, a preliminary subcommittee discussed that the subject of the original DEWS definition should remain. 77% of responders voted for the change of the definition. TFOS DEWS II members noted the vital role of inflammation and hyperosmolarity, including the DED pathway, but the challenge was to include precise terms in the definition. The group of representatives from the Definition and Classification Committee had a meeting in December 2016 and went through all the proposed reports. Several issues were discussed, like a loss of tear film homeostasis can be due to multiple factors such as eyelid and blink abnormalities and ocular surface or tear component deficiencies. These modifications can cause tear film instability and hyperosmolarity, leading to increased evaporation from the tear film and Vicious Circle in DED (Baudouin, C. & al. 2016). It is essential to understand the etiology elements when defining dry eye to distinguish it from other ocular surface diseases. The homeostatic imbalance is a comprehensive definition and needs to have a broad enough interpretation of the possibility to allow researchers of dry eye to have flexible and growing chances in the meaning of the Dry Eye. There has been much evidence of the role of neurosensory abnormalities in managing and understanding DED. Neuropathic pain is caused by damage in the somatosensory nervous system, which departs it from DED. Nociceptive pain is due to local tissue damage. Nociceptors in the cornea transmit somatosensory "pain" information to the central nervous system and can be sensitized if physiological or noxious stimulation, such as hyperosmolarity or inflammation, occurs (Mehra D. & al. 2020).

Classification of dry eye disease (DED) shows first the assessment of symptoms and then moves to signs of ocular disease. DED has both signs and symptoms, so the triaging questions and additional testing differentiate DED from other ocular surface diseases. When the patient has no symptoms or signs of DED, that can be considered non-DED, and no treatment is required. When Dry Eye disease is diagnosed, depending on whether it is EDE (evaporative dry eye), ADDE (aqueous deficient dry eye), or a mixed version, the primary management is to restore the homeostasis of

the tear film. Differentiation of these forms is prescribed in the TFOS DEWS II Pathology-physiology report (Bron, A. J. & al. 2017), and Tear Film report (Willcox, M. D. P. & al. 2017a), and management and diagnoses of DED are described in the TFOS DEWS II report (Jones, L. & al. 2017a).

2.1 Dry Eye Disease

Over two decades of patient examinations and research have helped to understand the DED better. Symptomatic involvement and existing DED-associated ocular surface signs are necessary for diagnosing DED. Using the TFOS DEWS II classification scheme, it is possible to differentiate DED from other ocular surface diseases utilizing existing signs or symptoms of DED.

2.2 Other Ocular Surface Diseases

Different ocular surface conditions, like giant papillary conjunctivitis and allergic conjunctivitis (Villani E. & al. 2018), remind or happen simultaneously with DED. Because of this, excluding diagnosis is needed in dry eye treatment. TFOS DEWS II Diagnostic Methodology report (Wolffsohn, J. S. & al. 2017) suggests using "triaging questions" together with the clinical findings to differentiate DED from the other ocular surface conditions that can be needed for specific management. As mentioned, other ocular surface diseases can happen simultaneously with DED or remind it, so it is essential to arrange management with systematic monitoring of symptoms and signs. Lagophthalmos is one of the conditions where dry eye signs and symptoms can be found, but managing DED alone will not be successful as the lid closure is most likely the reason for ocular surface dryness. Instead, surgically managing lagophthalmos can resolve the symptoms and signs of dry eye (Zeev MS. & al. 2014).

2.3 Symptoms Without Signs: Neuropathic Pain

In the Pain and Sensation Subcommittee report (Belmonte, C. & al. 2017), there is a scenario where a somatosensory system lesion or disease causes neuropathic pain, and symptoms of the ocular pain do not match the clinical signs. In this case, DED therapy is not ideal for needed pain management.

2.4 Symptoms Without Signs: Preclinical State of the Dry Eye

When symptoms of DED exist but no clinical signs, especially if the symptoms are not regular, it can be considered preclinical dry or episodic Dry Eye. Continuous estimation of the signs and symptoms is considered beneficial via education and prevention (McMonnies CW. 2021).

2.5 Signs Without Symptoms: Reduction of the Corneal Sensitivity

When patients have clear signs of DED without symptoms, dry eye management can e considered. Prolonged DED can damage corneal nerves, and reduced cornea sensitivity can hide the discomfort. Other corneal diseases accompany corneal sensation reduction, and the correct management should be done (Zhou T. & al. 2022).

2.6 Signs Without Symptoms: Tendency to Dry Eye

In ocular surgery, preliminary examination, like refractive surgery or cataract, may reveal ocular surface alterations without the symptoms and could be the risk factor for the patient to develop postoperative DED. The asymptomatic MGD (Meibomian Gland Dysfunction) has been reported as double the prevalence of symptomatic MGD in the Caucasian population (Vieira GCF. & al. 2021).

2.7 Classification of Dry Eye Disease Based on Predominant Etiology

TFOS DEWS II classification of dry eye etiologically divides dry eye into aqueous deficient (ADDE) and evaporative (EDE) forms, but they are often present simultaneously. According to the common understanding, EDE is more common than ADDE. MGD causes most dry eye based on studies (Allansmith MR. & al. 1978; Chan TCY. & al. 2019).

2.8 Pathophysiology

Several clinical studies (Perez VL. & al. 2020; Ng D. & al. 2022; Asbell PA. & al. 2018) have revealed that dry eye is an inflammatory disease. Several internal and external factors cause tear

film instability and hyperosmolarity. These tear composition changes may be related to systemic factors and can cause a cycle of inflammation, causing epithelial disease to the ocular surface and stimulating the neural pathways. The acute ocular surface dryness activates the ocular surface epithelial and immune cells stress pathways and trigger the inflammatory mediator's production, which contributes to matrix metalloprotease (MMP) production, dendritic cell maturation, and inflammatory cell requirement. It may lead to the T cell-mediated response. The lysis of the tight epithelial junctions creates corneal barrier interference and leads to cell death, corneal surface irregularity, lubrication problems, and activation of nociceptors in the epithelium. These changes further cause tear film destabilization, increasing inflammation, and a vicious circle ready (Baudouin C. & al. 2016).

Dry eye is a multifunctional inflammatory disease.

Increased tear osmolarity causes tear instability, leading to the activation of stress-signaling pathways in the ocular surface epithelium. External factors like dry environment, contact lens wear, LASIK surgery, and internal factors like aging, medications, female sex, and systemic autoimmunity can all increase the risk of inflammation in the ocular surface, which is unique mucosa. The goblet cell-rich epithelium is structurally organized, hindering microbes, inflammation, and the environment. The ocular surface also has many macrophages, dendritic cells, natural killers, and T cells that offer mainly antimicrobial defense (Periman LM. & al. 2020). However, it may also be part of the dry eye pathogenesis (Allansmith, M. R. & al. 1978). The cornea epithelium has to maintain comfort and clarity in the different environmental challenges. The ocular surface epithelium and lacrimal glands provide several antimicrobial factors such as IgA, alpha and beta-defensins, and lysozyme in the tear film function and maintenance. In the dry eye, many of these homeostasis mechanisms are being disturbed. The inflammatory mediators like IL-1beta, TNF-alpha, IL-6, chemokines, and MMP-9 interact with each other in a complex way, increasing inflammation (Luo, L. & al. 2004). Other dry eye patients have also noted increased MMP-9 values in tears (Sambursky, R. & al. 2014). The epithelial cells on the ocular surface also secrete chemokines attracting the inflammatory cells. The other effect of dry eye is the innate inflammatory pathways regulation (Chi, W. & al. 2017). Atopic and vernal keratoconjunctivitis, recurrent corneal erosions, and ocular burns with corneal disruption also show increased levels of MMP-9 in tears (Smith, V. A. & al. 2001). The loss of goblet cells and metaplasia in the epithelium of the conjunctiva is a sign of aqueous tear deficiency. Very severe ocular surface diseases like mucous membrane pemphigoid (MMP), Stevens-Johnson syndrome, and severe alkali burns, where conjunctiva is involved, include often missing conjunctival goblet cells. T helper cytokines can differentiate the conjunctival

goblet cells. Th2 cytokine IL-13 plays a role in mucus production and proliferation stimulation, while Th1 cytokine IFN- γ induces goblet cell attachment and decreases mucus production and apoptosis (Tukler Henriksson J. & al. 2015). Immune tolerance maintenance in mucosal tissues between the dendritic cells and goblet cells is essential. Gobblet cell-associated passages (GAPs) delivering surface antigens to dendritic cells underneath and promoting tolerance have been found in both theconjunctiva and intestine (Barbosa FL. & al. 2017). The patients with dry eye show increased conjunctival dendritic cells and a larger quantity of cells expressing the dendritic cell maturation biomarker HLA-DR (Barbosa FL. & al. 2013). The dendritic cells are the base for Th1 and Th17 T cells in the lymph nodes of the conjunctiva. These T cells produce interferon-gamma (IFN-y) and IL-17, which affect cytokines in the Dry Eye (Pflugfelder SC. & al. 2015). IFN-y plays a role in the goblet cell loss in the conjunctiva and the acinar of the lacrimal gland, while IL-17 causes lymphangiogenesis and corneal barrier disorders. Dysfunction of the lacrimal gland is inflammation generated with aging, also in autoimmune disease, Sjögren's syndrome (SS) (Whitcher JP. & al. 2010). Keratoconjunctivitis sicca, dry mouth, serum autoantibodies, and lymphocytic infiltration of glands are the characteristic of SS. Several studies indicate that ocular surface inflammation and apoptosis lead to glandular dysfunction in age-related dry eyes and SS (Masli S. & al. 2020; Mizoguchi S. & al. 2017).

2.9 The Dry Eye Epidemiology

The subcommittee of TFOS DEWS II reviewed the epidemiological studies of dry eye disease (DED) based on reports of the incidence, prevalence, natural history, morbidity, risk factors, and questionnaires (Stapleton F. & al. 2017). The published prevalence data meta-analysis considered the effect of age and sex, and the range of the prevalence of dry eye disease was between 5 to 50% globally. The confirmation by meta-analysis was given that prevalence is age-related, but an increase in signs was more significant than symptoms in each decade. Women's prevalence was significantly higher than men's only with age. The risk factors were qualified, and Asian ethnicity was a continuous risk factor. The economic background and effects on the vision, work productivity, quality of life, and pain were remarkable, especially the burden caused by reduced work productivity. There were variations in the usefulness of the questionnaires used in the DED. Future studies should determine the prevalence among different age groups and possible risk factors like using digital devices. It is also essential to discover the environmental and socioeconomic factors and

impact of the climate using geospatial mapping and notify the limitations of the studies in treated and untreated DED to improve future research.

2.10 Sex, Gender, and Hormones in Dry Eye Disease

Females are more likely to have DED than men (Sullivan DA. & al. 2017). It is due mainly to sex steroids, glucocorticoids, insulin, hypothalamic-pituitary hormones, insulin-like growth factor 1, and thyroid hormones. Also, the complement of the sex chromosome, sex-specific autosomal factors, and epigenetics play a role. Sex, gender, and hormones play a vital role in the ocular surface and adnexal tissue regulation, as well as the differences between sexes. Over 2000 years, it has been notised that the influence of sex on the eye has increased. Several eye conditions (blepharospasm, conjunctivitis, eyelid edema, keratitis, corneal ulcers, iritis, cataract, glaucoma, amblyopia, herpetic reactivation, optic neuritis, scotoma, optic nerve atrophy, and blindness) have differences between sexes. Sex steroids seem to act on the meibomian gland, conjunctiva, lacrimal gland, cornea, iris, anterior chamber, ciliary body, vitreous, lens, and retina. These steroids have also been connected to the developing, progressing, and treating many ocular conditions, including dry eye disease, wound healing, meibomian gland dysfunction (MGD), corneal transplant rejection, keratoconjunctivitis, and corneal pathologies (Truong S. & al. 2014). Autoimmmune diseases like Sjögren's syndrome related to DED are a more significant risk for the female sex. There have been many studies and risk factor identification among the female sex worldwide.

2.10.1 Differences Between Sexes in the Quality of Life

The Women's Health and Physician's Health Study (Miljanović B. & al. 2006) showed that men were six years older than women at the time of DED diagnosis; the average age for men was 60 years compared to women's 66 years. Also, Ocular Surface Index Disease (OSDI) measured remarkably higher levels of DED symptoms for women. Additionally, the women had a more significant effect of DED on their visual quality, including poor vision, blurred vision, and unstable vision, as well as in general tasks like reading, driving at night, working on the computer, and watching television.

2.10.2 Differences Between Sexes in DED Treatment and Satisfaction for Them

The Canadian study also showed the differences between sexes in management and treatment satisfaction (Denton, M. & al. 2004). According to this study, traditional DED therapies, like moisturizing drops and omega-three supplements, were much more likely to be used by women. Also, women who used topical cyclosporine were more unsatisfied with their side effects which correlate well with the already recognized downsides of this treatment.

Differences between sexes have also been recognized in anatomy, physiology, and pathophysiology of the cornea, meibomian and lacrimal glands, conjunctiva, and tear film (Schaumberg DA. & al. 2013).

2.11 Tear Film

2.11.1 Overview

Tears are essential for ocular surface protection and lubrication (Willcox MDP. & al. 2017; Pflugfelder SC, Stern ME. 2020). The tear film production is mainly organized in the lacrimal units, which are prominent and accessory lacrimal glands, Meibomian glands, the cornea epithelium, the eyelids, the mucosal and glandular immune system, and the interconnection intervention. The tear film is formed from the aqueous-mucin layer, which contains soluble factors and fluid from the lacrimal glands and mucin produced in the goblet cells. The mucin layer is against the corneal epithelium. The outmost layer of the tear film is a lipid layer (Pflugfelder SC. & al. 2020). The combination of proteins, lipids, and glycoproteins in tears provides a smooth and lubricated optical surface. Tear functions also include assisting wound healing, decreasing inflammation, and defending against microbe infections. Any dysfunction or disease in the tear production factors causes tear film instability, inflammation, increased evaporation, and effects on the visual quality (García-Marqués JV. & al. 2022; Guo OD LW. & al. 2020).

2.11.2 Structure and Dynamics of the Tear Film

The tear film lipid layer is formed from meibum in the lid margins, and in each blink, it spreads over the tear film and plays a vital role in the tear film stabilization. The imaging technology gives opportunities to evaluate the lipid layer thickness based on the interference images. The lipid layer thickness is typically 42 nanometers. The total tear film thickness has been estimated with different techniques, and OCT finds it in the range of 2 to 5,5 micrometers. Other methods to clarify the tear film structure are to use fluorescein tear break up time (TBUT), Schirmer test, and Oculus Pentacam Scheimpflug camera together with fluorescein to record videos of the lipid layer. Most of the tear volume is secreted from the lacrimal glands and only a tiny amount by the conjunctiva. The sympathetic and parasympathetic nerves are activated in the main lacrimal glands. The lacrimal glands' stimulation and secretion happen via the cornea, trigeminal nerve-brainstem, facial nerve, and lacrimal gland two-neuron pathway. The ocular surface stimulation activates the afferent sensory nerves. The efferent nerves are activated to stimulate the secretion in the lacrimal gland cells (Dartt DA. 2009; Belmonte C & al. 2017).

Four major types of tears have been classified - basal, reflex, emotional, and closed eye. The basal tears coat the eye when it is open. The reflex tears activation occurs in the ocular surface or the afferent-efferent pathway stimulation, and the emotions like sadness stimulate emotional tears. The closed-eye tears are on the ocular surface after sleeping. In asleep, the lacrimal gland secretion decreases, so the composition of the closed-eye tears is quite different compared to the other three tear types (Nättinen J. & al. 2022; Perumal N. & al. 2016).

The blinking is the crucial element in establishing the tear film to the ocular surface. First, the upper lid goes up, making a tear film layer over the cornea. Then the lipid layer comes behind, taking aqueous tears with it. This phenomenon can be watched and recorded using interferometry imaging (Zhao Y. & al. 2015).

Different methods can value the tear volume and production, but the correlation between these methods is limited (Sullivan BD. & al. 2014). The most common method for tear volume measurement is the Schirmer test, where test trips with a millimeter scale are used, but due to its invasive nature, it is poorly repeatable and unreliable. The tear meniscus height (TMH) can be measured with a slit lamp, optical coherence tomography (OCT), and Oculus K5M, which are all noninvasive methods. These noninvasive devices are mostly operator related, which can lead to measurement mistakes (Wang Y. & al. 2022).

2.11.3 Tear Film Stability and Circular Wettability

The stability of the tear film has been considered one of the most distinctive signs of the health of the ocular surface. Usually, the tear film will break up in less than 30 seconds after the first blink, causing local drying areas of the tear film and giving the brain the signal to blink again. In the tear break-up time (TBUT) tests, the areas of break-up and thinning of the tear film mostly match the corresponding areas. However, in some cases, the same lipid area was not thinner than the lipids area surrounding, which is a sign of lipid not being an excellent barrier to evaporation. Therefore, other reasons can cause the unstable tear film than only the lipid layer (King-Smith PE. & al. 2013). In the comparison between Non-Invasive Keratograph Break-Up Time (NIKBUT) (Oculus Keratograph 4) and fluorescence break-up time (FBUT), there was a correlation between the first NIKBUT and FBUT. However, the average NIKBUT on three measurements showed more consistent values (Cox SM. & al. 2015). Despite the lack of information on all the devices measuring the NIBUT (non-invasive break-up time), their variance is around 10% compared to traditional TBUT measurement, which is around three times better. The BUT usually is half the time in dry eye patients compared to typical eye patients (Downie LE. 2015).

2.11.4 Quality of the Vision

The study of the visual acuity and contrast sensitivity in dry eye patients has shown that the visual symptoms are noticed more in worse visual acuity (VA) than in worse contrast sensitivity. The worse contrast sensitivity was related to more extensive instability of the tear film (Szczotka-Flynn LB. & al. 2019).

2.11.5 Tear Osmolarity

In the study on diagnosing and managing DED, tear osmolarity was shown to be the best single value for diagnosing and classifying dry eye disease (Lemp MA. & al. 2011). The tear osmolarity value in normal eyes has been considered 302 mOsm/L (Bron AJ. & Willshire C. 2021). The basal tear osmolarity is suggested to be the point-of-care test for screening preclinical and clinical dehydration. Many devices are available for osmolarity measurement, but the TearLab has been used

in most clinical trials. Also, laboratory tests using blood samples from the plasma have been used (Benelli U. & al. 2010; Bron AJ, Willshire C. 2021)

2.11.6 PH

Ph values vary individually from 5,2 to 8,6. Most tears were collected from the lower tear meniscus; they have a limited effect on the ocular surface, according to the studies made in the 1980s and 1990s. There is limited data on the pH value change with DED (Andrés S. & al. 1988).

2.11.7 Evaporation of the Tears and the Lipid Layer

The blinking of the eye is related to the evaporation of the tear film, and lipid layer stability is an excellent indicator to reveal a higher evaporation rate that causes thinning of the tear film, ocular discomfort, and dryness (Mathers WD. 1993). There is no commercially available device to measure tear evaporation. The lipid layer thickness does not seem to affect tear evaporation unless the lipid layer is less than 24nm thin or missing (King-Smith PE. & al. 2010). The study on the effect of the expression of the meibomian glands shows reduced tear film evaporation (Arciniega JC. & al. 2011). Three proposals on the evaporation suppressions have been suggested: (1) lipid layer organization based (McCulley JP. & Shine W. 1997), (2) not only lipid layer based, but also protein or mucin interactions play a role ([Iwata S. & al. 1969), and lipids do not control (3) evaporation of the water (Cerretani CF. & al. 2013). The latest study on meibum expression shows that meibum reduces around 30% of the evaporation rate (Blanco-Campoy DG. & al. 2022).

2.11.8 Total Lipids of the Tears

The lid rim expression in normal eyes causes clear oil production to the tear film. There are a minimum of 30 times the reservoir of meibum in the meibomian glands compared to the amount in the tear film (Chew CK. & al. 1993). The meibum comprises around 95% of non-polar lipids and 5% amphipathic lipids, which include wax and cholesterol esters, as well as a small number of triglycerides (Butovich IA. 2013). The biological science approach to human tears has offered remarkable information on the pathophysiology of multiple ocular and systemic disorders during the last twenty years. The lipidomics versus metabolomics approach has been used more widely. The

new analytical methods make it possible to use a minimal tears for the investigation (Khanna RK. & al. 2022).

2.11.9 Mucins

The mucins are glycoproteins that are produced mainly in the epithelial cells on the ocular surface. They create a barrier against pathogens to protect and lubricate the eye via glycocalyx (Ablamowicz AF. & Nichols JJ. 2016). There are at least 20 mucin genes identified, and there are two main types, transmembrane and secretory mucins. They have different subdivisions. The secretory mucins have large gel-forming and small soluble mucins. The gel-mucins origin is from the conjunctival goblet cells. These mucins are essential for the hydration of the ocular surface, preventing pathogens from binding to ocular cells, preventing debris, and helping to assist in undamaging the cells. The mucins play an essential role in the health of the ocular surface (Ablamowicz AF, Nichols JJ. 2016).

2.11.10 The Biomarkers of the Tears

The human eye's proteasome (the total amount of proteins) can provide crucial information on the disease's DED and pathways (Semba RD. & al. 2013). The latest knowledge has found almost 1800 proteins from human tears. The tear collection methods used are microcapillary tubes, Schirmer strips, and sponges, just to name a few. Also, topical anesthesia may be used to avoid reflex tearing, and tears can be collected from open or closed eyes. Because of the differences in the techniques, the results may also vary (Green-Church KB. & al. 2008). The tear biomarkers can estimate, diagnose and even work as therapists for ocular surface diseases. Nine different biomarkers were noted in the studies: epidermal growth factor (EGF), which was reduced in Sjögren's syndrome and ADDE, increased in EDE, interleukin 1α (IL-α) that increased in Sjögren's syndrome and MDG, interleukin 6 (IL-6), that increased in Sjögren's syndrome, lactoferrin (LTF), that reduced in Sjögren's syndrome, lipocalin 1 (LCN1) that degreased in MGD, matrix metalloproteinase 9 (MMP-9) that increased in Sjögren's syndrome, unchanged in MGD, MUC5AC, that reduced in Sjögren's syndrome, plasmin activation (PLG) that increased in Sjögren's syndrome and phospholipase A2 group that increased in dry eye. Several other proteins are due to Sjögren's syndrome (Stefanski AL. & al. 2017).

Biomarkers should include the diagnosis and prognosis by monitoring the patients. To date, only two commercial options for tear film assessment are available, TearScan and Inflammadry.

2.11.11 Other Factors Affecting the Tear Film

Wearing contact lenses is an increased risk factor for dry eye development (Yang WJ. & al. 2015). Also, low levels of androgen have been associated with dry eye (Mathers WD. & al. 1998). Thyroid disease can play a role in abnormalities in tear functions. Furthermore, as mentioned earlier, sex also affects the risk of dry eye disease. Different displays at a close distance have been reported to increase tear osmolarity (Yazici A. & al. 2015). The surrounding air humidity and temperature are related to the tear film homeostasis (Alves M. & al. 2014).

2.12 Pain and Sensation

Pain definition - unpleasant physical feeling caused by illness or damage (Raja SN. & al. 2020)

The word pain has been in quite limited use in eye care as many severe eye diseases, like open-angle glaucoma, retinal pathologies, or cataract, have no pain sensation (Belmonte, C & Tervo, T 2006). Slightly unpleasant discomfort is often related to common ocular surface diseases, like allergic conjunctivitis or DED. However, they have been prescribed the terms like itch, dryness, and discomfort without mentioning the pain sensation. Photorefractive surgery patients have reported pain sensations after surgery, and contact lens wearers have informed discomfort experiences. These complaints have directed eye care professionals toward the mechanisms and origin of these sensations from the ocular surface. The DED patients suffered from dryness sensation and severe ocular symptoms, but very few clinical signs could be seen on the examination of the slit lamp. The neurobiological mechanisms in the background causing these sensations seem to parallel with other ocular pathologies causing ocular pain. The dry eye sensations should be considered and examined as a specific form of ocular pain associated with this disease (Belmonte C. & al. 2017). Pain is an emotional and unpleasant experience by the International Association for the Study of Pain (IASP) (Raja SN. & al. 2020).

2.12.1 Nociceptive Pain

Nociceptive pain activates the nociceptors caused by the threatened or actual tissue damages.

Nociceptors are receptors for the sensation of the peripheral somatosensory nervous system. They have plenty of tissue-damaging harmful thermal, chemical, and mechanical stimuli, which signal the tissue injury's size, intensity, location, and duration (Dubin AE, Patapoutian A. 2010).

2.12.2 Neuropathic Pain

The IASP has defined neuropathic pain as pain due to a lesion or a disease of the somatosensory nervous system (Di Stefano G. & al. 2020). Neuropathic pain requires noticeable damage or somatosensory nervous system disease that fulfills the neurological diagnostic benchmarks and is usually referred to as pain without biological value or pathological pain. Neuropathic pain has been described based on the etiology (traumatic, degenerative, infectious, toxic, and metabolic) and the anatomy (peripheral or central) as a kind of pain due to disorders in the functionality of various parts of the nervous system. Peripheral sensory nerve injury's nature dictates the abnormalities of the nociceptive neurons of the sensory ganglia and the peripheral nerve terminals. The common feature of peripherical neuropathic pain is the changed gene expression due to cell body damage, peripheral axon defects, and local inflammation (von Hehn CA. & al. 2012). The peripheral nerve damage can cause abnormal activity in the pathways from peripherical nerves to the central nervous system. The excitability of central pain pathways is further increased by impairment of the descending inhibitory modulation and microglia's local activation and higher central nervous system areas (Tulleuda A. & al. 2011). A stroke, trauma, or genetic abnormality can cause malfunction of the CNS and can lead to central neuropathic pain.

2.12.3 Itch

The itch can be described as an unpleasant sensation with similar compartments with pain, present often in the eye. However, the need for scratching and sensory quality make it a separate perceptual entity. The evidence of the experiment on the skin shows that itch is activated by activating specific receptors on the sensory neuron's peripheral sensory fibers in the dorsal root ganglia and the trigeminal ganglia. Distinct from the nociceptors, these sensory neurons are usually separated

into mechanically sensitive and chemically sensitive itch neurons. They have typical molecular and cell signatures and different sensory pathways. The pathways from ítch and pain are segregated; they interact on several levels in the central nervous system to create the conscious itch or pain sensations (Robertson SD. & al. 2013). The ocular itch is usually the pathological sign of allergic conjunctivitis (Leonardi A. & al. 2015). The mechanisms mentioned above do not necessarily happen exclusively but can be concurrently present, and clinicians can struggle to distinguish them.

2.13 Iatrogenic Dry Eye

Many iatrogenic interactions (medical treatments causing the clinical condition) may cause dry eye. The TFOS DEWS II Iatrogenic report published significant causes of iatrogenic dry eye in 2017 (Gomes JAP. & al. 2017). Systemic medications may affect secondary DED by a variety of mechanisms and topical drugs can cause toxic, allergic, immunological, and inflammatory influences on the ocular surface. The preservatives like benzalkonium chloride may worsen the DED. The contact lens use influences or is accompanied by DED as well. An increasing number of various surgical operations like refractive surgery (LASIK) and keratoplasty can cause DED due to the intervention of the corneal nerve cutting and the use of drugs after the surgery. The other risk factors for iatrogenic DED are cataract and lid surgeries, botox, and other cosmetic operations mean of causing visual problems, poor surgical results, and unsatisfied patients.

2.14 Diagnostic Methodology

The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II Diagnostic Methodology Subcommittee suggested the protocol for DED diagnostics in their Diagnostic Methodology report from 2017 (Wolffsohn JS. & al. 2017).

2.14.1 Questionnaires

Before the diagnosis, it is necessary to rule out the conditions mimicking DED by using triaging questions. Questionnaires with OSDI (Ocular Surface Disease Index) or DEQ-5 (Dry Eye Questionaire - 5) reveal the possibility of DED and suggest further testing. Other questionnaires are available, but OSDI is mostly used in clinical trials (Wolffsohn JS. & al. 2017).

2.14.2 Break-up Time

The testing should also start from the least invasive and move to the most invasive. The break-up time (non-invasive recommended) measures the time between the blink and the first break in the tear film (Uchino M. & al. 2018). The break-up time can be tested with fluorescein or non-invasively by Oculus Keratograph 5M or other high-speed videokeratoscope devices.

2.14.3 Tear Meniscus

The tear meniscus is one indicator of a dry eye based on the volume of tears in millimeters in the lower eyelid. The most reliable measurement of the tear meniscus can be achieved using OCT, but primarily it is measured with the slit lamp (Niedernolte B. & al. 2021). The principle is to measure the length of the tear meniscus from the three different locations. The tear meniscus value under 0,25 mm is considered suspicious to DED.

2.14.4 Schirmer Test and Phenol Red Test

In the Schirmer test, a paper strip is placed on the patient's lower eyelid temporal corner between the lid and the conjunctiva. The measuring takes 5 minutes, and the result can be read on the paper strip on a millimeter scale. The phenol red thread (PRT) test uses thin cotton thread and is used in the lower eyelid for 15 seconds, and the results can also be read from the millimeter scale. There is no significant clinical difference between these two tests (Vashisht S. & Singh S. 2011).

2.14.5 Tear Osmolarity Test

The expression of osmolar compression in tears can be evaluated using devices like the Tear-scope, which gives good information on the tear film osmolarity (Benelli U. & al. 2010). The ocular surface hyperosmolarity is typical of DED (Baudouin C. & al. 2013).

2.14.6 Staining, LIPCOF, and Sensitivity

The most popular stains for evaluating ocular surface damage are fluorescein, lissamine green, and rose bengal. The fluorescein is suitable for evaluating epithelial loss in the cornea. The fluorescein reveals the staining in the conjunctiva better than the lissamine green (Eom Y. & al. 2015). The rose bengal stains the degenerated and dead cells well, but it is more irritating than lissamine green and increases reflex tearing. The lissamine green stains epithelial cells in the ocular surface that are unprotected by glycocalyx or mucin, as well as the damaged cells. Impression cytology is a method for placing filter paper on the ocular surface with anesthetics. Lid-parallel conjunctival folds (LIPCOF) are located parallel to the lower lid margin in the lower bulbar conjunctiva. The LIPCOF may appear similar to mild conjunctivochalasis stages, but there are slightly different clinical characteristics. The LIPCOF area is smaller than the conjunctivochalasis (Pult H. & al. 2015). The LIPCOF is graded as the number of folds, and one needs to distinguish the permanent folds from the disrupted micro folds. The in-vivo confocal microscopy (IVCM) allows non-invasively to evaluate the cellular level damage in the DED (Villani E. & al. 2013). Cochet-Bonnet or non-invasive esthesiometers can evaluate the sensitivity of the cornea. The palpebral conjunctiva's sensitivity seems more critical than the cornea's sensitivity in DED assessment (Cox SM. & Nichols JJ. 2015).

2.14.7 Redness

The most typical sign clinically of ocular surface inflammation is redness in the conjunctiva. The ocular redness can be evaluated using a slit lamp or digital imaging devices (Downie LE. & al. 2016).

2.14.8 Laboratory Tests

The levels of MMP-9 can be tested by a diagnostic device called InflammaDry. The cytokines and chemokines in tears reveal the epithelial disease level (Leonardi A. & al. 2009). These can be found in laboratory tests.

2.14.9 Interference, Meibography, and Blinking

The tear film spreads over the ocular surface of the upper and lower lid marginals conjunctiva. Staining with DED patients can be evaluated using fluorescein and lissamine green. This phenomenon is called lid wiper epitheliopathy (LWE) (Efron N. & al. 2016).

By spreading oil or lipids to the water surface like the tear film, an interference phenomenon will occur, where the refractive index of the front and back of the oily layer is different. The front is against the air, and the back is against the aqueous tear film. The meibomian glands usually deliver lipids to the ocular surface and help the tear film to be stabilized. The interferometer LipiView gives lipid layer thickness measurement automatically, but its diagnostic value is yet to be established (Finis D. & al. 2013)

Meibography optimizes the meibomian gland's silhouette observation using an infrared video camera. The new technologies use LEDs together with infrared cameras. Different scoring scales are available for the meibography evaluation (Ban Y. & al. 2013).

The meibum quality, quantity, and easiness of expressing them define the meibomian gland functionality. Typically meibomian glands are open and provide clear meibum expressed by the lids in each blink. In MGD, the meibomian glands can be obstructed, and the substance is cloudy, like toothpaste. The expression of the meibomian glands digitally improves the dry eye symptoms in patients with MGD (Kaiserman I. & al. 2021).

The blinking is vital for the homeostasis of the ocular surface. The blinking is also crucial for the activity of the meibomian glands and tear film lipid layer formation. A significant number of incomplete blinks has been reported in the healthy population. One study showed that the normal subjects spent 0,7% of a minute their eyes closed, whereas dry eye patients kept 4,5% of their eyes closed (Ousler GW 3rd. & al. 2014). The increased blink rate may be related to shorter break-up time.

2.15 Management and Therapy

The dry eye classification can be divided into tear deficient (hyposecretion) and evaporative (hyper evaporative) forms. Tear deficient DED can be divided into Sjögren's syndrome related to primary

or secondary or non-Sjögren's tear deficiency, where there is lacrimal disease or deficiency, lacrimal obstruction, or reflex block present. Evaporative form can be intrinsic with oil deficiency, lid related or with low blink rate, or extrinsic due the topical drug preservatives, vitamin A deficiency, contact lens, ocular surface change, or drug-related (Li J. & al. 2008).

2.15.1 Lifestyle

The main goal for DED management and treatment consists of improving the quality of life and visual acuity, symptom relief, ocular surface, and tear film homeostasis, and managing the underlying reasons for DED. A lifestyle change is the most efficient way to relieve dry eye symptoms. Patients with DED should avoid long periods of consistent working with computers, watching television, and using tablets or mobile phones. The prolonged use of different digital devices reduces the blink rate and increases evaporation (Al-Mohtaseb Z. & al. 2021).

2.15.2 Artificial Tears

It is recommended to use artificial tears and short breaks during these devices. Preservative-free artificial tears are recommended, but these products do not replace growth factors and cytokines in the lacrimal glands. They have little or no effect on inflammation (Labetoulle M. & al. 2022). Low humidity, the smoke, wind, and high altitudes should also be avoided (Yao W. & al. 2011).

2.15.3 Lid Hygiene, Warm Compresses, and Topical Antibiotics

When necessary, warm compresses, eyelid hygiene, and topical antibiotics are essential for meibomian gland dysfunction and chronic blepharitis treatment. These procedures reduce bacterial changes and tear film evaporation (Jones L. & al. 2017).

2.15.4 Supplements

The role of the supplements Omega 3 and Omega 6 in dry eye disease management exists, and there are multiple studies on this subject. However, the evidence is controversial, although the results show improvement in dry eye symptoms (Liu A, Ji J. 2014).

2.15.5 Anti-inflammatory Agents

The anti-inflammatory agent's therapy may be helpful for patients with corneal disease, and the artificial tears do not offer enough relief from the symptoms. The topical corticosteroids, cyclosporine A, and fatty acids are primarily used as anti-inflammatory drugs (Erdinest N, Solomon A. 2019). Before using these medications, possible side effect assessments should be considered (McCabe E & Narayanan S. 2009). The autologous serum tears can be used in patients with severe dry eyes. The tears are made from the patient's blood, and the results have been promising (Higuchi A. 2018).

2.15.6 Punctal Plugs and Eyewear

The punctal plugs can give relief to ADDE patients utilizing blocking the drainage from the eye and making the tear meniscus wider. Several types of punctal plugs are on the market and are considered relatively safe. However, their primary function is not to take care of the inflammation, only to reduce the outflow of the tears (Ervin AM. & Pucker AD. 2017). The moisture-release eyewear relieves evaporative dry eye patients by shielding the eyes from the environment's pollen, dust, and wind (Waduthantri S. & al. 2015).

2.15.7 Contact Lenses

The hydrophilic bandage contact lenses can protect the cornea, work as a barrier against the environment, give better wettability to the ocular surface, and may relieve pain. The hydrophilic bandage contact lens can also relieve dry eye symptoms after eye surgeries.

Some surgical procedures can be used in severe dry eye cases, like lower lid surgery, amniotic membrane transplant, stem cell replacement, and permanent punctal closure (Wu X. & al. 2021 and Chen X. & al. 2019).

2.15.8 Therapy Devices

Intense Pulsed Light (IPL) has been known in dermatology for years to treat acne and rosacea. IPL uses light in the 400 to 1200 nanometer (nm) area, and in the skin, the used area is around 500

nm. The light affects the blood cell's light absorption, coagulates, and closes the blood vessels. Abnormal growth of blood vessels (telangiectasia) grows between the meibomian glands and causes gland malfunctions. IPL treatment to the lids closes the blood vessels and helps the MGD improvement. (Toyos R. & al. 2015). One study showed IPL to be more effective in MGD than the warm eye mask with eyelid compression (Yan S. & Wu Y. 2021).

Quantum Molecular Resonance (QMR) therapy has been used for several years in wound healing therapy. This technology offers electrical stimulation with certain high-frequency and low intensity, the same frequency (resonance), with the molecular bonds in biological tissue with a minimum heat effect. This signal stimulates the metabolism and natural regeneration of biological tissue and cells. Recently, a device called Rexon Eye entered the market for treating dry eye patients (Fraccalvieri M. & al. 2017). The significant benefit is that it can relieve ADDE and EDE patients (Alexandra T. & al. 2022).

3 THE PURPOSE, OBJECTIVES, AND TASKS OF THE RESEARCH DEVELOPMENT WORK AND THE DIFFERENT STAGES

3.1 Purpose of the Study Statement

This case study report aimed to look into the latest publications on dry eye disease, describe the various elements of dry eye and its effects on patients living. Also, the purpose was to use two different measurements, Oculus K5M and Topcon Myah, and two different managements, IPL and QMR, given for the patient with evaporative dry eye due to the meibomian gland dysfunction.

3.2 Statement of the Research Question

Can IPL therapy and QMR therapy offer clinically measurable benefits for evaporative dry eye patients caused by Thyroid disease?

3.3 *Summary Des*cription of the Experimental Design

This case study describes the assessment and management of a 63-year-old caucasian female with MGD due to Thyroid disease. The assessment was made using Oculus Keratograph 5M Jenvis Pro dry eye analysis and Topcon Myah. The management was given the Eye-Light IPL therapy device and Rexon Eye QMR therapy. The slit lamp examination was made accordingly. Additionally, evidence-based literature was used for discussing the nature of the dry eye.

3.4 Study Objectives

The study objectives are the literature review and the case study.

3.5 Methodology

3.5.1 The Literature Search

The literature search was conducted on the 9th of June 2022 to find out the existing studies on dry eye management and assessment. The literature review was conducted using PubMed with subject terms DEWS II AND dry eye; dry Eye AND meibomian gland dysfunction; dry Eye AND management; meibomian gland dysfunction AND quality of life AND treatment.

Only studies between 2000 and 2022 were chosen, and filtered Free Full Text, Clinical Trial, Randomized Controlled Trial, Review, and Systematic Review. Out of those, the most relevant to the case study was selected for the literature review.

3.5.2 The Confidentiality and Data Storage

The confidentiality agreement was not made, but both private clinics are following GDPR regulations. The IRB approval was not needed in this case study.

3.6 Setting

3.6.1 Discription of the Study Environment

The study was conducted in two private clinics in Helsinki. The other clinic provided Oculus K5M measurements with slit lamp examination, Rexon Eye therapy, Topcon Myah measurements, and IPL treatment.

3.6.2 Dry Eye Assessment

A slit lamp examination was performed in a private clinic. It included the following procedures: general observation of the eyes, examination of lids and lashes, tear film, conjunctiva, cornea, anterior chamber, evaluation of the anterior chamber angle, and examination of the iris and the lens. The posterior part of the eye was examined without dilation, mainly observing the optic disc with Volk 90 D lens. The Oculus K5M Jenvis Pro analysis was performed using Individual mode, which includes all needed parameters for Dry Eye analysis. In the Topcon Myah examination, the

measured parameters included corneal topography, TBT[TJ1] (the first time the percentage of break-up sectors reached 5%), non-invasive break-up time, and meibomian glands imaging, only on the lower lids.

3.6.3 Dry Eye Management of Evaporative Dry Eye

IPL therapy with Eye-Light was done twice in a private clinic, and QMR therapy with Rexon Eye was performed four times in one-week intervals in a private clinic.

3.6.4 Rexon Eye Quantum Molecular Resonance (QMR) Therapy

Figure 90 Rexon Eye therapy on process

Rexon-Eye is a non-invasive device based on QMR technology, providing relief for dry eye syndromes. It applies low-power, high-frequency electric fields capable of stimulating cells' metabolism and natural regeneration.

4 IMPLEMENTATION OF THE RESEARCH DEVELOPMENT WORK

4.1 Case Study

This case study report included the clinical assessment and management of a 62-year-old white female in a private clinic dry eye examination on the 18th of February, 2022. It included comprehensive eye examination and measurements using Oculus Keratograph 5M with Jenvis PRO Dry Eye report. Topcon Myah measurements were made before IPL therapy, and EyeLight IPL was given according to the manufacturer's protocol. The QMR (Quantum Molecular Resonance) therapy was given according to the manufacturer's protocol three months after the last IPL treatment. The results of both treatments were measured before and after the treatment.

4.1.1 Clinical Case Report

The patient was a 62-year-old caucasian female, retired, who came to the comprehensive eye exam on the 18th of February 2022. The chief complaint was watering eyes and occasional headaches.

4.1.2 Ocular Patient History

The patient had an ophthalmologist consultation on January 2009, and the diagnosis was dry eye, which was treated with artificial tears. The ocular health was not resolved, and the patient visited another ophthalmologist clinic specializing in skin and eye diseases. The ophthalmologist diagnosed a chronic conjunctivitis, the dry eye and atopic skin and arranged the needed management.

The patient had cataract surgery on May 2019 in a private hospital in Spain for both eyes, and multifocal IOLs were installed. Before the surgery, she used eyewear daily and contact lenses twice a year. She has been using artificial tear drops daily.

4.1.3 Patient Systemic History

The patient's last medical exam was made in 2019. She has hypothyroidism, which is treated with Thyroxin 100 micrograms of half a tablet every other day, and one tablet every other day. She is treated with Femoston Conti 1/5 with one tablet daily for hormonal balance. She has increased cholesterol levels but has no medication for that yet. She also takes vitamin C 400 mg, and D 100 ym each one tablet daily, NivelActive 58g daily for joints, spirulina four tablets daily, and Omega-3 Forte (1000 mg fish oil, Omega-3 fat acids 620 mg, E-EPA fat acids 310 mg and E-EHA fat acids 205 mg) supplements one tablet daily. The patient was diagnosed with atopic skin and rosacea in the eyelids in 2020. Her blood pressure was normal, 130/65.

4.1.4 Family Ocular and Medical History

Her parents have both been diseased with cancer, but the patient does not remember any eye diseases in the family. She and her older sister are both myopic.

4.1.5 Visual Acuity and Eye Functions

Far distance vision monocularly was VA 0.9 in both eyes, binocularly 1.0, spherical trial lens -0,25 both eyes monocularly showed visual acuity 1.0, a binocularly aided vision acuity was 1.0, and near distance 0.67. The cover test showed slight exophoria, pupil reactions were Pupils Equal Round Reactive to Light PERRL, no afferent pupillary defect, Hirshberg was symmetric, and confrontation fields were regular. Near-point of convergence was 10 cm, and color vision with Ishihara 24 plates color test was standard. Contrast sensitivity was measured with the Unicos ACP-900 LCD chart in 2,5% contrast, and the result was 0.5 -1 in the right eye, 0.5 -2 in the left eye, and binocular contrast sensitivity was 0.6.

4.1.6 Slit Lamp Examination

In the anterior eye, biomicroscopy showed arcus senilis in both eyes, and lids and lashes had signs of blepharitis with blocked meibomian glands and telangiectasia in both eyes. On the left lower lid surface, there was a tiny brownish mold. The conjunctiva showed dryness in the fluorescein stain-

ing in both eyes, LIPCOF had two folds in both eyes, and the cornea was clear. The anterior chamber was deep and quiet, the angle fully open. The iris was grey and looked normal. Van Herrick performed 4 in both eyes. Some small spots were found on the IOL's back surface. The non-dilated examination of the retina with the Volk 90D lens showed that the C/D ratio was 1/3, the A/V ratio 2/3, and the optic disc, the macula, and the fovea looked typically related to age. The slit lamp examination was performed after the measurements with the Oculus Keratograph 5M.

4.1.7 Oculus Keratograph 5 M and Slit Lamp Measurements

Oculus Keratograph 5 M (K5M) is a topographer with the Jervis Pro Dry Eye Report software to evaluate dry eye severity.

The JERVIS Pro Dry Eye Report has a fail-safe test sequence covering all the assessment criteria required for a comprehensive analysis of dry eye syndrome. The OCULUS Keratograph 5M is a corneal topographer with a built-in real keratometer and a color camera optimized for external imaging. The other features include the meibomian glands examination, non-invasive Keratograph break-up time (NIKBUT), the tear meniscus height measurement, and lipid layer evaluation. The test protocol was planned in the matter to avoid any unnecessary manipulation of the eye.

4.1.8 Topography

The topography values were measured from the tear film of the cornea due to the technique of the topographer devices.

4.1.9 Tear Meniscus Heigh

The tear meniscus height was measured with an integrated ruler, and its development along the edge of the bottom lid can be assessed.

4.1.10 NIKBUT

The subsequent measurement was NIKBUT (Non-Invasive Keratograph Break Up Time), a fully automatic, non-invasive measurement using infrared illumination.

4.1.11 Lipid Layer

The third measurement was the Lipid Layer, where the interference colors of the lipid layer and their structure were made visible. The thickness of the lipid layer was assessed based on the structure and color.

4.1.12 TF Dynamics (Tear Film Dynamics)

The fourth measurement was the TF Dynamics by recording a video that enabled the observation of the tear film particle flow, from which conclusions regarding the viscosity of the tear film were drawn.

4.1.13 R-Scan

R-Scan (Redness Scan) was the automatic classification of the bulbar redness. The redness of the conjunctiva is commonly assessed by the examiner subjectively, but the R-Scan did the bulbar and limbal degree of redness classification automatically and objectively. The R-Scan detected the conjunctival blood vessels and evaluated the degree of redness.

4.1.14 Meibo Scan

The Meibo Scan measurement was done for superior and inferior eyelids. The superior eyelid needs to be turned for imaging. Therefore this was saved for the last.

Morphological changes in the gland tissue were made visible using the Meibo-Scan and were subjectively classified with the JENVIS Meibo Grading Scales.

4.1.15 OSDI

OSDI questionnaire was made every time after the measurements of Oculus K5M as it is implemented in the software. It includes 12 questions for evaluating the severity of potential dry eye disease. OSDI classification Oculus K5M gives numerical values on a scale starting from zero. The

normal score can be considered between values 0 and 10, values between 11 and 26 mild, values between 27 and 66 moderate, and values over 66 severe.

4.1.16 Differential Diagnosis

The differential diagnosis for keratoconjunctivitis sicca or DED is plenty. All conditions concerning the different forms of conjunctivitis (bacterial, allergic, giant papillary, viral, atopic, and vernal keratoconjunctivitis) showed no signs in the patient. There were no signs of infectious diseases like herpes simplex, no corneal abrasions or erosions, but there were signs of blepharitis related to the dry eye disease.

4.1.17 The measurements on the 18th of February, 2022 on Oculus K5M

The first measurements with the K5M were made on the 18th of February, 2022, and the results showed the following:

OSDI value was 13.

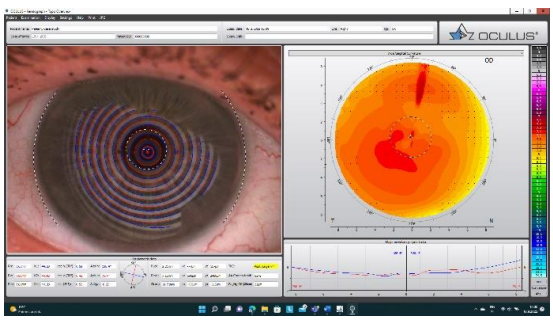


Figure 1 Topography Right Eye

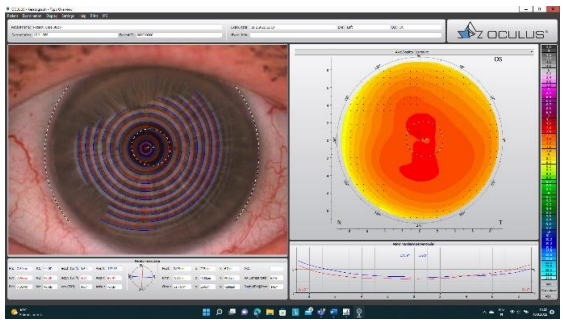


Figure 2 Topography Left Eye

Right Eye K1 7,63 mm 164 degrees, K2 7,60 mm 74 degrees

Left eye K1 7,54 mm 176 degrees, K2 7,46 mm, 86 degrees

The tear meniscus was measured from the three locations at 6 o'clock, 8 o'clock, and 4 o'clock.

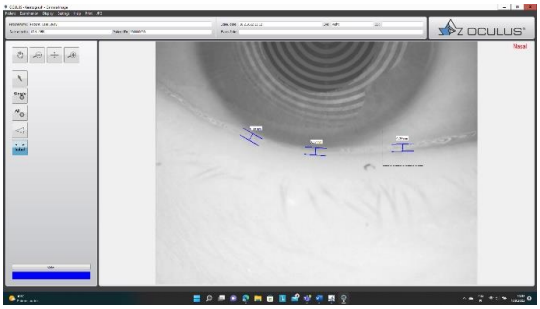


Figure 3 TMH Right Eye

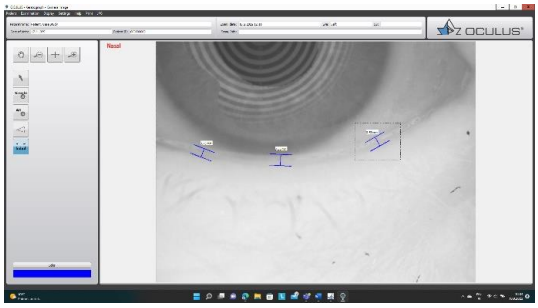


Figure 4 TMH Left Eye

Right eye 0,38 mm, 0,37 mm, and 0,35 mm

Left eye 0,45 mm, 0,55 mm, and 0,50 mm

NIKBUT Jenvis Scale classification:

The tear film stability is classified (level 0, level 1, level 2) with the average break-up value.

Level 2: break-up (average) <7s (unstable tear film/dry eye)

Level 1: break-up (average) >=7s bis <14s (critical tear film stability)

Level 0: break-up (average) >=14s (stable tear film)

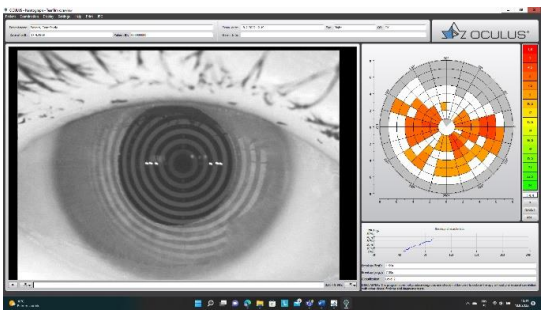


Figure 5 NIKBUT Right Eye

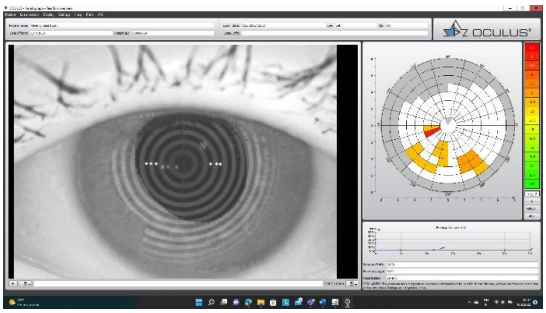


Figure 6 NIKBUT Left Eye

NIKBUT right Eye first break 4,59 seconds, break up 7,00 seconds, level 2 (Jenvis Scale)

NIKBUT left eye first break 3,63 seconds, break-up 9,40 seconds, level 2 (Jenvis Scale)

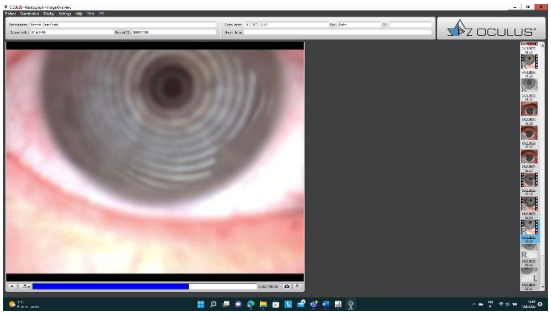


Figure 7 Lipid Layer Right Eye

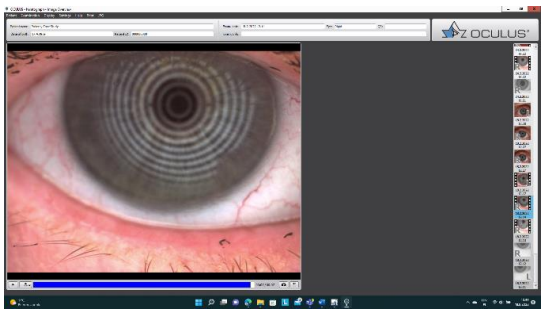


Figure 8 Lipid Layer Left Eye

LIPID LAYER very pale-whitish hue on both eyes, significant lipid deficit

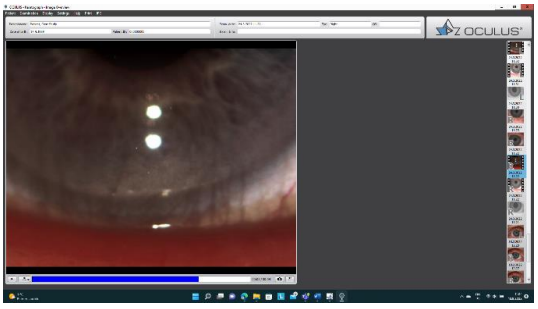


Figure 9 TF Dynamics Right Eye

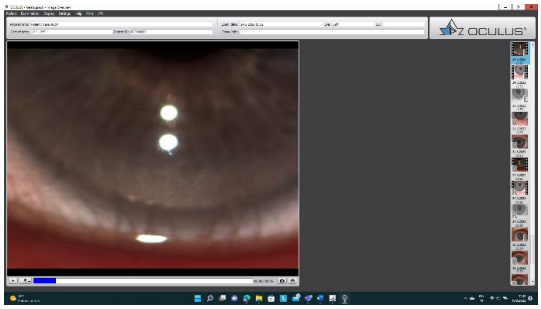


Figure 10 TF Dynamics Left Eye

TF DYNAMICS both eyes showed moderate flow, normal to viscous.

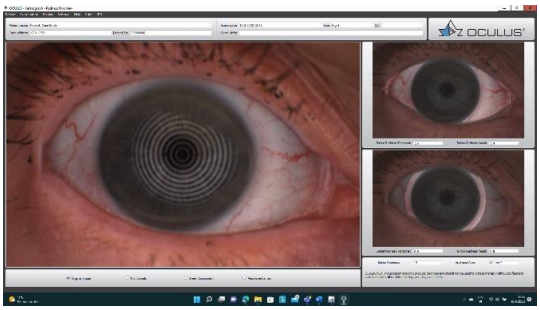


Figure 11 Redness Right Eye

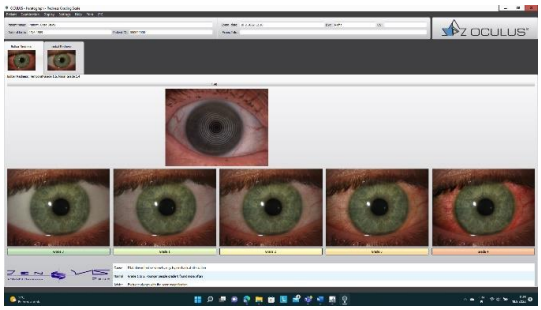


Figure 12 Redness Jenvis Scale Right Eye

Redness Right Eye

Bulbar redness temporal 1,6, nasal 1,4

Limbal redness temporal 0,6, nasal 0,5

Bulbar redness 1,5, analyzed area 16,1 mm2

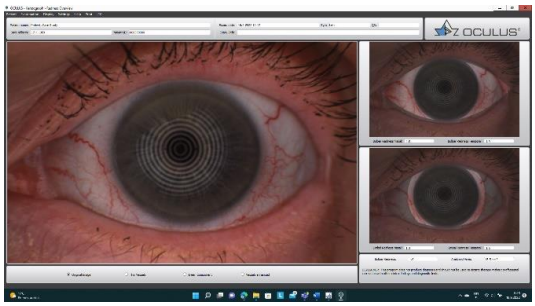


Figure 13 Redness Left Eye

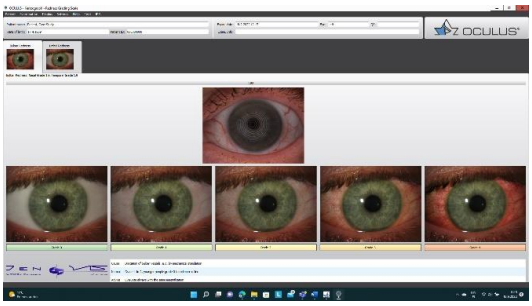


Figure 14 Redness Jenvis Scale Left Eye

Redness Left Eye

Bulbar redness temporal 1,9, nasal 1,9

Limbal redness temporal 1,0, nasal 1,5

Bulbar redness 1,9, analyzed area 15,5 mm2

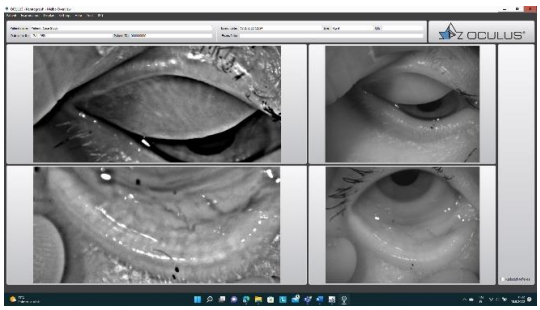


Figure 15 Meibo Scan Right Eye

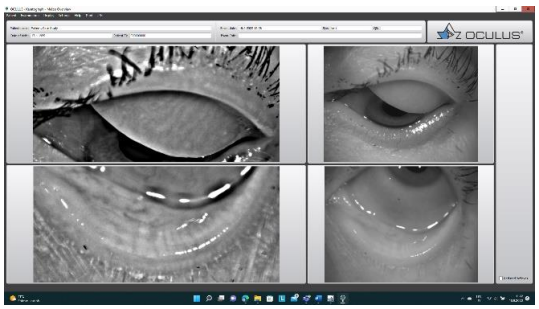


Figure 16 Meibo Scan Left Eye

Meibo Scan using Jenvis grading scale right eye, the estimated value is two on the upper lid, 1,5 on the lower lid, and left eye on the upper lid, the estimated value is two on both upper and lower lid.

The slit lamp examination was performed after the K5M measurement, including the fluorescein staining. There were clear signs of dry eye in conjunctiva on both eyes: cornea was clear, but the conjunctival staining grade 2 was detected, Jenvis Scaling from Oculus K5M was used as also other Jenvis Scalings during the studies, and fluorescein break-up time (FBUT) was 5 seconds on the right and 4 seconds on the left. There were no signs of viral or bacterial infections or other ocular surface diseases. The diagnosis suspect was evaporative dry eye due to MGD. The referral to the symptom-based management was offered to the patient, and she agreed on first-line relief to proceed with IPL therapy and QMR therapy due to successful clinical trials (Trivli A. & al. 2022).

4.1.18 The measurements on the 18th of February, 2022

4.1.19 Topcon Myah Measurements

On the exact dates that IPL therapy was given, the measurements with Topcon Myah proceeded before the therapy. They included corneal topography, TBT (the first time at which the percentage of break-up sectors reached the level of 5%), non-invasive break-up time, and meibomian glands imaging, only on the lower lids. The tear meniscus height was not evaluated.

5% Level TBT means the first time the percentage of breakup sectors reached the level of 5%. Average IBI means the average inter-blink interval, used for calculated OPI (Ocular Protection Index) index, and average OPI means OPI < 1 - Indicates that the tears break-up before the blink, highlighting the increased risk of ocular surface damage from dry eye. OPI >1 - Indicates that the blink occurs before the tears break-up.

On the 18th of February 2022 was the first Topcon Myah measurements before the IPL therapy.

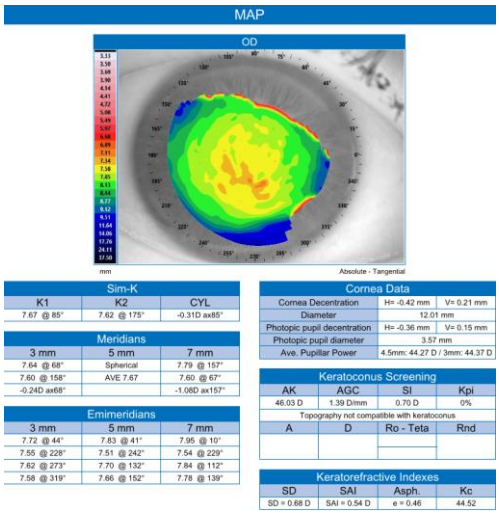


Figure 85 Topography Right Eye

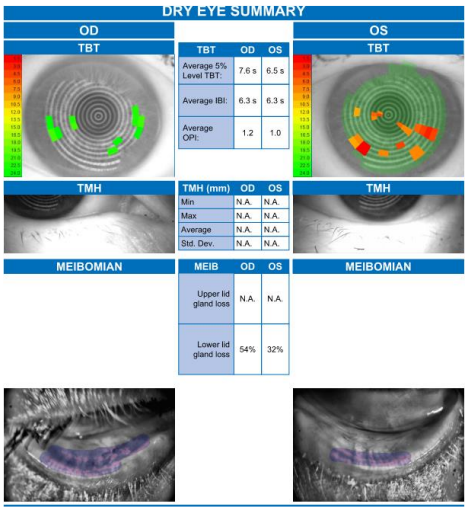


Figure 86 Dry Eye summary Right and Left Eye

The corneal topography SIM-K values in the right Eye were K1 7,67 mm 85 degrees and K2 7,62 mm 175 degrees, and in the left eye, values were not taken.

TBT values on the average 5% level in the right eye were 7,6 seconds and in the left Eye 6,5 seconds. The Average IBI was 6,3 seconds on both eyes. The Meibomian gland measurement

proceeded only for the lower lids, and the lower lid gland loss was 54% on the right eye and 32% on the left eye. The left lower lid was not fully seen in the image, which may influence the result.

4.1.20 IPL therapy

4.1.21 Intense Pulsed Light therapy

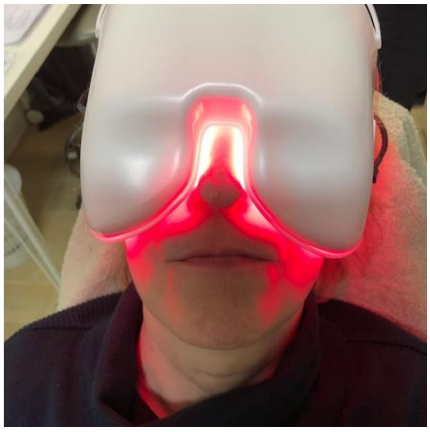


Figure 89 Thermal mask on the patient

The Eye-Light Intense Pulsed Light (IPL) therapy from Innova proceeded the same day after the slit lamp examination, K5M, and Myah measurements. The practitioner placed a laser probe in 5 different locations on the lid area of the patient, and after this, the thermal mask was placed on the patient's face for 15 minutes. This treatment stimulates the meibomian glands. According to the private clinic's protocol, the treatment was done twice in one-month intervals.

4.1.22 The measurements on the 24th of March, 2022

The second measurement and IPL treatment were made on the 24th of March, 2022, and the protocol followed the previous one except for the comprehensive eye exam. The slit lamp examination showed the same findings as the first time; FBUT was 6 seconds on the right eye and 5 seconds on the left eye.

Oculus K5M measurements showed the following results:

OSDI value was 6.

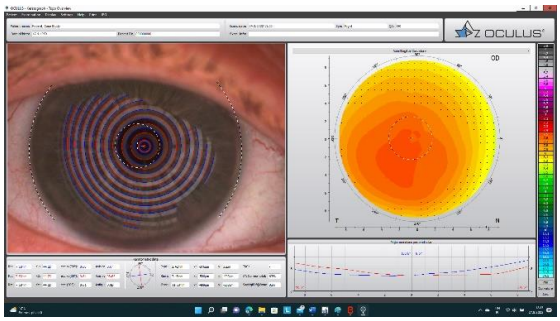


Figure 17 Topography Right Eye

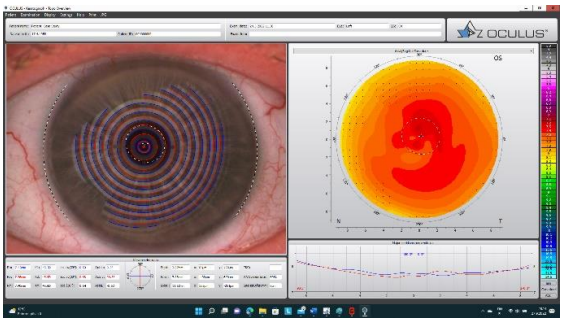


Figure 18 Topography Left Eye

Topography Right eye K1 7,63 mm 9 degrees, K2 7,63 mm 99 degrees

Topography Left eye K1 7,45 mm 0 degrees, K2 7,36 mm 90 degrees

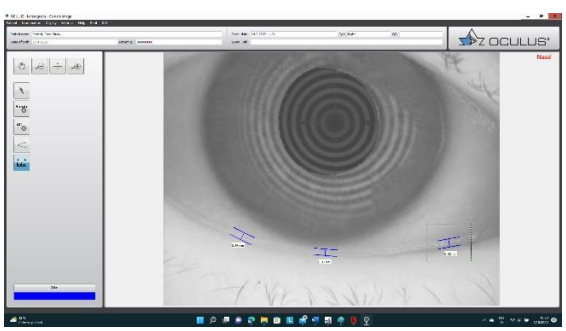


Figure 19 TMH Right Eye

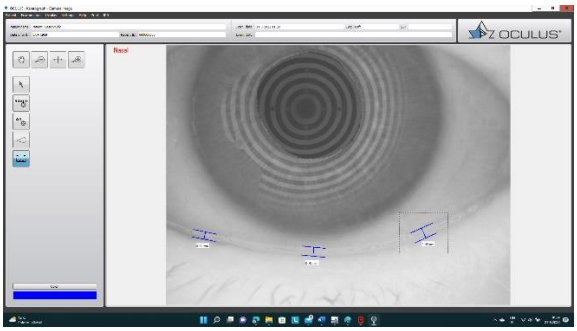


Figure 20 TMH Left Eye

The tear meniscus was measured from the three locations at 6 o'clock, 8 o'clock, and 4 o'clock.

Right eye 0,31 mm, 0,36 mm, and 0,38 mm

Left eye 0,41 mm, 0,34 mm, and 0,49 mm

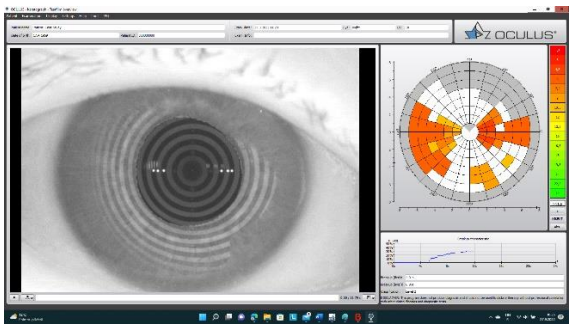


Figure 21 NIKBUT Right Eye

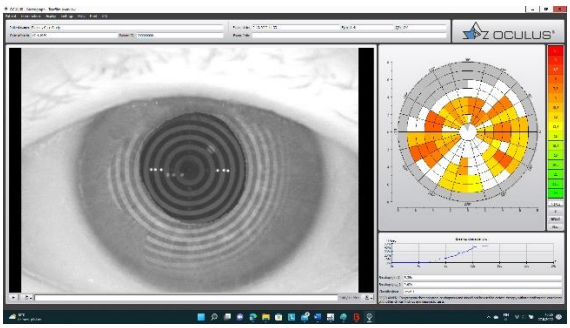


Figure 22 NIKBUT Left Eye

NIKBUT right Eye first break 4,01 seconds, break up medium 6,96 seconds, level 2 (Jenvis Scale)

NIKBUT left eye first break 5,36 seconds, break up medium 9,62 seconds, level 1 (Jenvis Scale)

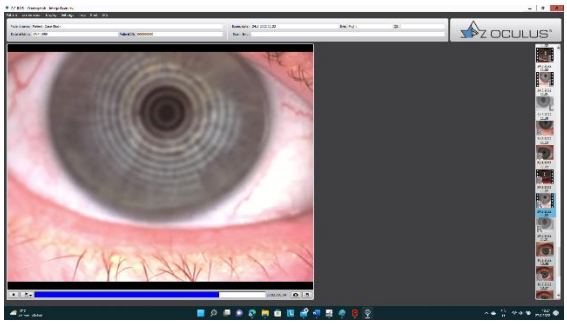


Figure 23 Lipid Layer Right Eye

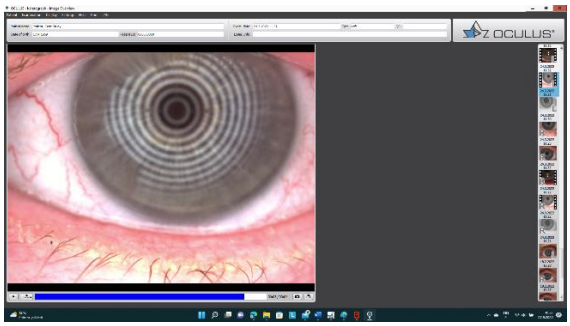


Figure 24 Lipid Layer Left Eye

LIPID LAYER very pale-whitish hue on both eyes, significant lipid deficit

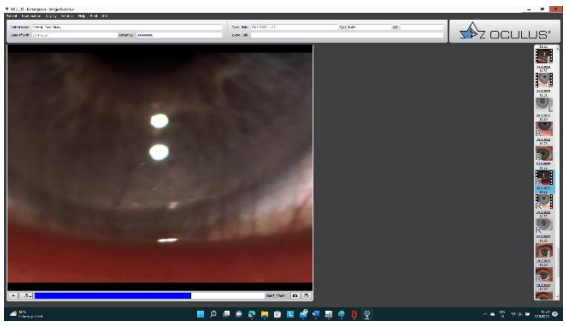


Figure 25 TF Dynamics Right Eye

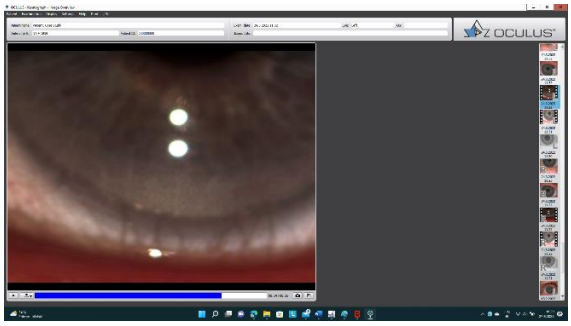


Figure 26 TF Dynamics Left Eye

TF DYNAMICS both eyes showed moderate flow, normal to viscous

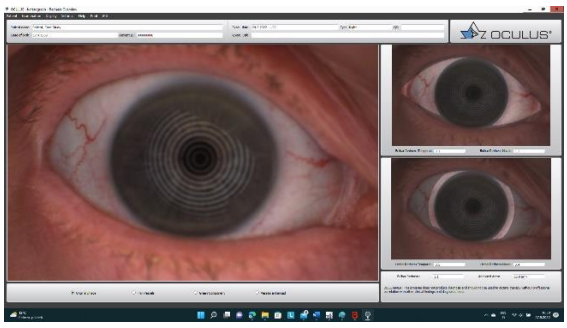


Figure 27 Redness Right Eye

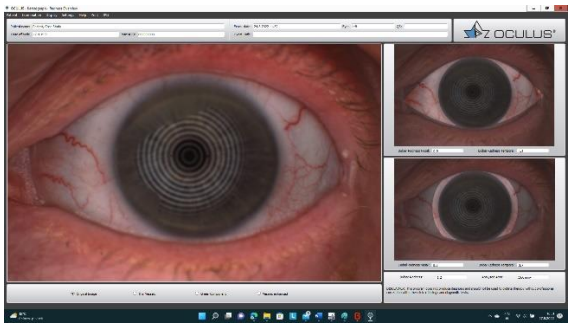


Figure 28 Redness Left Eye

Redness Right Eye

Bulbar redness temporal 1,1, nasal 1,2

Limbal redness temporal 0,5, nasal 0,4

Bulbar redness 1,1, analyzed area 16,9 mm2

Redness Left Eye

Bulbar redness temporal 1,5, nasal 0,9

Limbal redness temporal 0,7, nasal 0,5

Bulbar redness 1,2, analyzed area 16,6 mm2

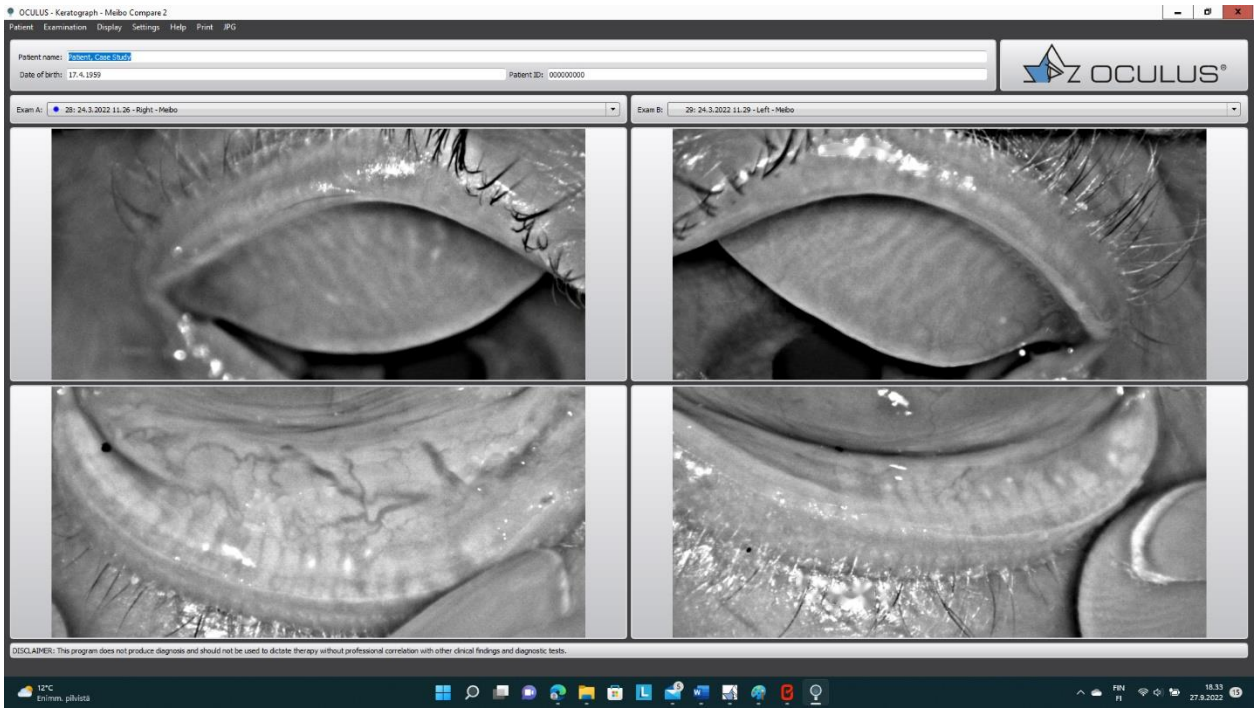


Figure 29 Meibo Scan Right Eye

Figure 30 Meibo Scan Left Eye

Meibo Scan using Jenvis grading scale right eye, the estimated value was two on the upper lid, 1,5 on the lower lid, and left eye, the estimated value was 1,5 on both the upper and lower lid.

The slit lamp examination was performed after the K5M measurement, including the fluorescein staining. There were slight improvements on the lids, lashes, conjunctiva, and cornea were the same as the last measurement, the fluorescein break-up time (FBUT) was 6 seconds on the right eye and 6 seconds on the left eye.

4.1.23 The measurements on the 29th of June, 2022 on Oculus K5M

The third measurement was made on the 29th of June, 2022, three months after the second IPL treatment, and the protocol followed the previous one except for the comprehensive eye exam. The slit lamp examination showed the same findings as the first time; FBUT was 6 seconds on the right eye and 5 seconds on the left eye.

Oculus K5M measurements showed the following results:

OSDI value was 8.

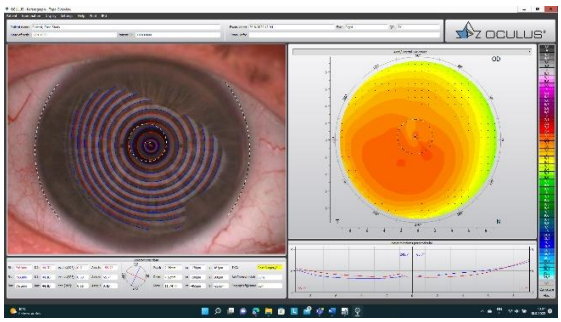


Figure 31 Topography Right Eye

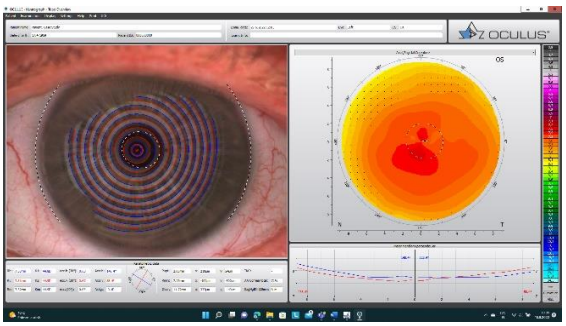


Figure 32 Topography Left Eye

Topography Right eye K1 7,64 mm 156 degrees, K2 7,66 mm 66 degrees

Topography Left eye K1 7,53 mm 148 degrees, K2 7,51 mm 58 degrees

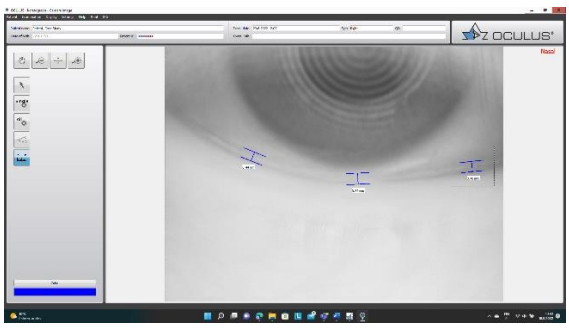


Figure 33 TMH Right Eye

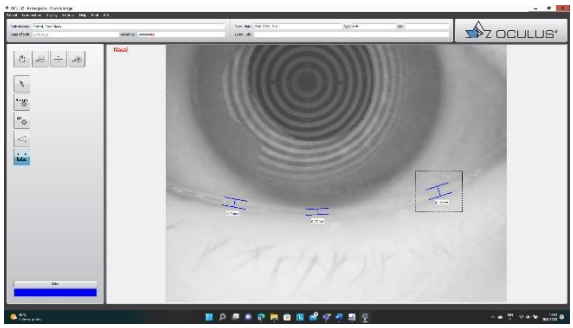


Figure 34 TMH Left Eye

The tear meniscus was measured from the three locations at 6 o'clock, 8 o'clock, and 4 o'clock.

Right eye 0,37 mm, 0,30 mm, and 0,37 mm

Left eye 0,27 mm, 0,37 mm, and 0,48 mm

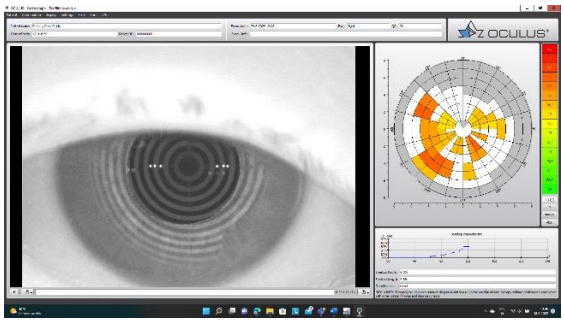


Figure 35 NIKBUT Right Eye

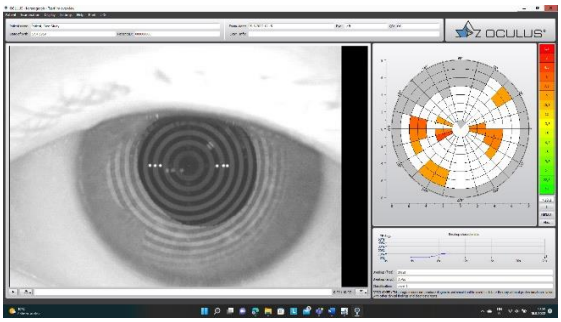


Figure 36 NIKBUT Left Eye

NIKBUT right Eye first break 6,37 seconds, break up medium 9,68 seconds, level 1 (Jenvis Scale)

NIKBUT left eye first break 3,82 seconds, break up medium 7,76 seconds, level 1 (Jenvis Scale)

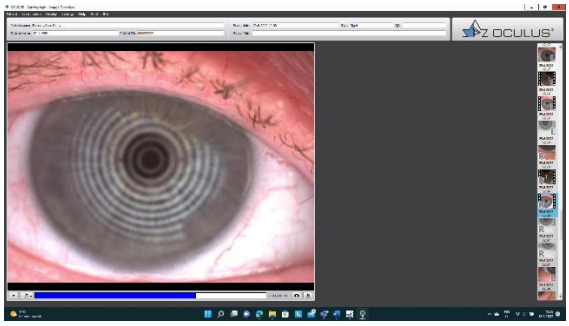


Figure 37 Lipid Layer Right Eye

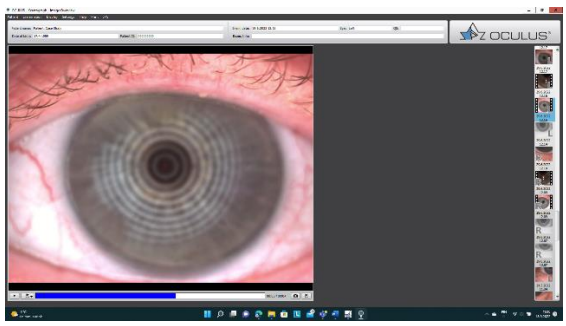


Figure 38 Lipid Layer Left Eye

LIPID LAYER very pale-whitish hue on both eyes, significant lipid deficit

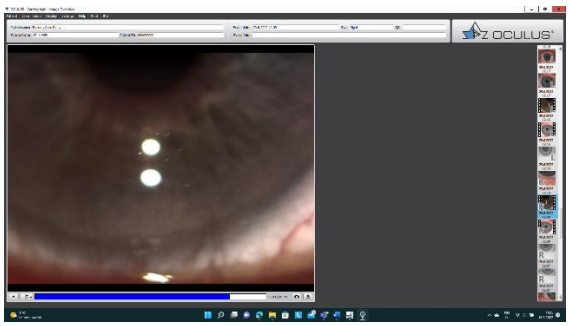


Figure 39 TF Dynamics Right Eye

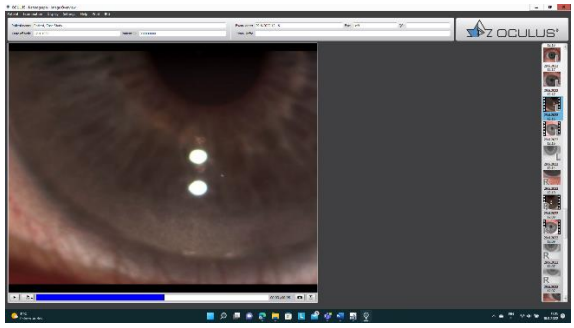


Figure 40 TF Dynamics Left Eye

TF DYNAMICS both eyes showed moderate flow, normal to viscous.

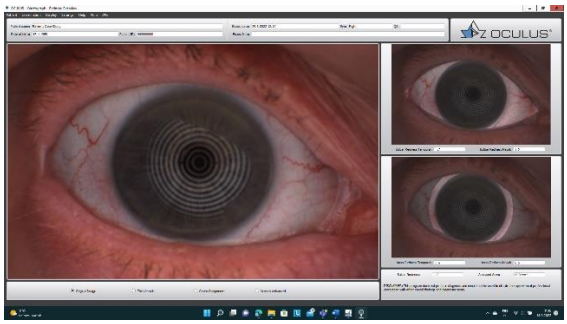


Figure 41 Redness Right Eye

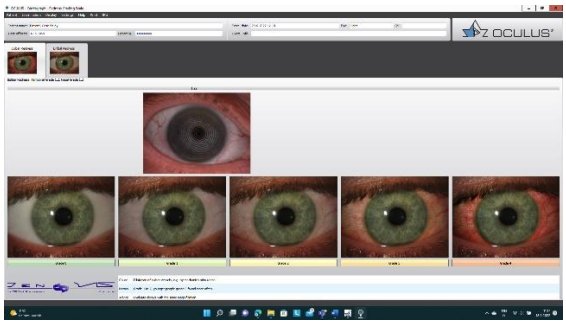


Figure 42 Redness Jenvis Scale Right Eye

Redness Right Eye

Bulbar redness temporal 1,2, nasal 1,2

Limbal redness temporal 0,6, nasal 0,5

Bulbar redness 1,2, analyzed area 15 mm2

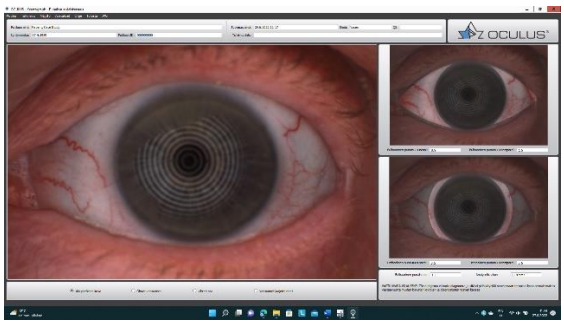


Figure 43 Redness Left Eye

Figure 44 Redness Jenvis Scale Left Eye

Redness Left Eye

Bulbar redness temporal 1,6, nasal 0,9

Limbal redness temporal 0,6, nasal 0,5

Bulbar redness 1,1, analyzed area 16,4 mm2

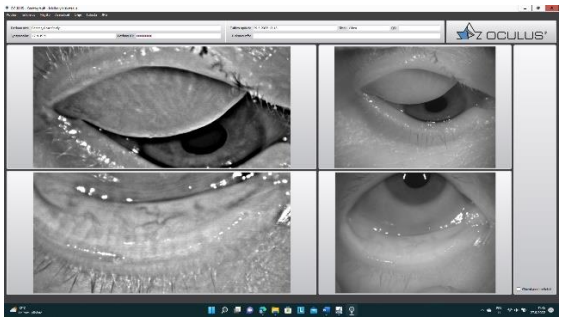


Figure 45 Meibo Scan Right Eye

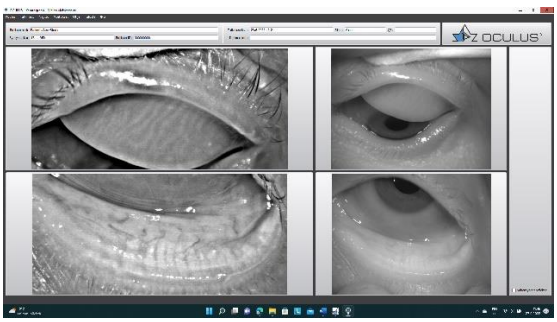
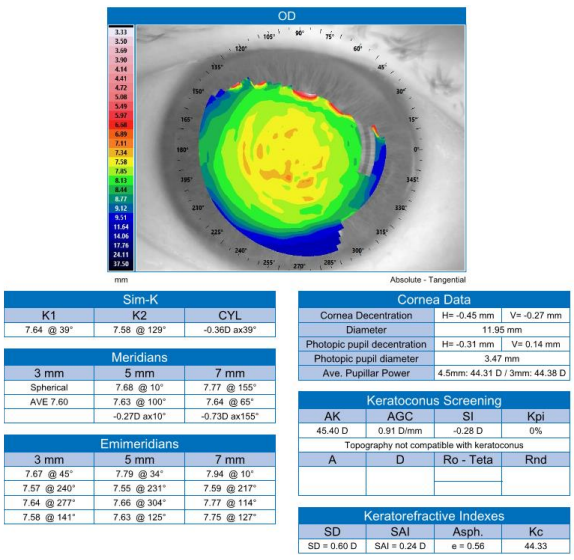


Figure 46 Meibo Scan Left Eye

Meibo Scan using Jenvis grading scale right eye, the estimated value is 1,5 on the upper lid, 1,5 on the lower lid, and left eye on the upper lid, the estimated value is 1,5 on both upper and lower lid.

The slit lamp examination was performed after the K5M measurement, including the fluorescein staining. There were slight improvements on the lids, lashes, conjunctiva, and cornea were the same as the last measurement, the fluorescein break-up time (FBUT) was 6 seconds on the right eye and 6 seconds on the left eye.

4.1.24 The measurements on 29th of June, 2022 on Topcon Myah



Sim-K		
K1	K2	CYL
7.64 @ 39°	7.58 @ 129°	-0.36D ax39°

Meridians		
3 mm	5 mm	7 mm
Spherical	7.68 @ 10°	7.77 @ 155°
AVE 7.60	7.63 @ 100°	7.64 @ 65°
	-0.27D ax10°	-0.73D ax155°

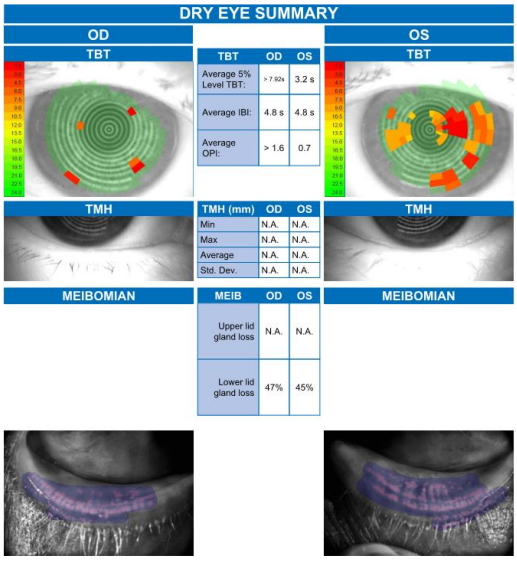
Emimeridians		
3 mm	5 mm	7 mm
7.67 @ 45°	7.79 @ 34°	7.94 @ 10°
7.57 @ 240°	7.55 @ 231°	7.59 @ 217°
7.64 @ 277°	7.66 @ 304°	7.77 @ 114°
7.58 @ 141°	7.63 @ 125°	7.75 @ 127°

Cornea Data		
Cornea Decentration	H= -0.45 mm	V= -0.27 mm
Diameter	11.95 mm	
Photopic pupil decentration	H= -0.31 mm	V= 0.14 mm
Photopic pupil diameter	3.47 mm	
Ave. Pupillar Power	4.5mm: 44.31 D / 3mm: 44.38 D	

Keratoconus Screening			
AK	AGC	SI	Kpi
45.40 D	0.91 D/mm	-0.28 D	0%
Topography not compatible with keratoconus			
A	D	Ro - Teta	Rnd

Keratorefractive Indexes			
SD	SAI	Asph.	Kc
SD = 0.60 D	SAI = 0.24 D	e = 0.56	44.33

Figure 87 Topography Right Eye



TBT	OD	OS
Average 5% Level TBT:	> 7.92s	3.2 s
Average IBI:	4.8 s	4.8 s
Average OPI:	> 1.6	0.7

TMH (mm)	OD	OS
Min	N.A.	N.A.
Max	N.A.	N.A.
Average	N.A.	N.A.
Std. Dev.	N.A.	N.A.

MEIB	OD	OS
Upper lid gland loss	N.A.	N.A.
Lower lid gland loss	47%	45%

Figure 88 Dry Eye summary Right and Left Eye

On the 29th of June, three months after the first measurements, the corneal topography SIM-K values in the right Eye were K1 7,67 mm 85 degrees and K2 7,62 mm 175 degrees, and in the left eye, values were not taken.

TBT values on the average 5% level in the right eye were 7,92 seconds and in the left eye 3,2 seconds. The average IBI was 4,8 seconds on both eyes. The meibomian gland measurement proceeded only for the lower lids, and the lower lid gland loss was 47% on the right eye and 45% on the left eye. The left lower lid was not fully seen in the image, which may influence the result.

4.1.25 The Rexon Eye therapy 20th of July, 2022

Rexon-Eye is a non-invasive device based on QMR technology that relieves dry eye syndromes. It applies low-power, high-frequency electric fields capable of stimulating cells' metabolism and natural regeneration. The Rexon Eye therapy was given the first time on the 20th of July, 2022, and the setup was the following: treatment time 20 minutes, swap time right and left eye 30 seconds, power three on both eyes. The treatment was given four times in one-week intervals.

4.1.26 The measurements on the 27th of July, 2022

The fourth measurements were made on the 27th of July, 2022, one week after the first Rexon Eye dry eye therapy. Between the third and fourth measurements, the Jenvis Pro software was installed, giving more opportunities for dry eye imaging. The slit lamp examination showed the same findings as the last time; FBUT was 6 seconds on the right eye and 6 seconds on the left eye.

Oculus K5M measurements showed the following results:

OSDI was 8.

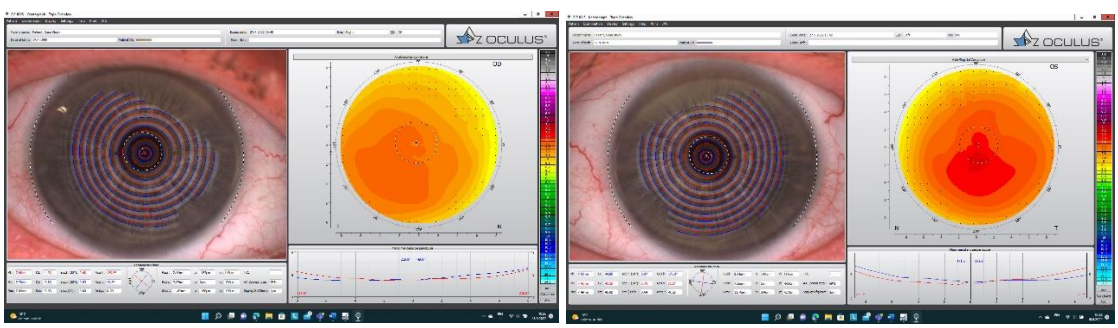


Figure 47 Topography Right Eye

Figure 48 Topography Left Eye

Topography Right Eye K1 7,68 mm 140 degrees, K2 7,70 mm 50 degrees

Topography Left eye K1 7,53 mm 171 degrees, K2 7,46 mm 81 degrees

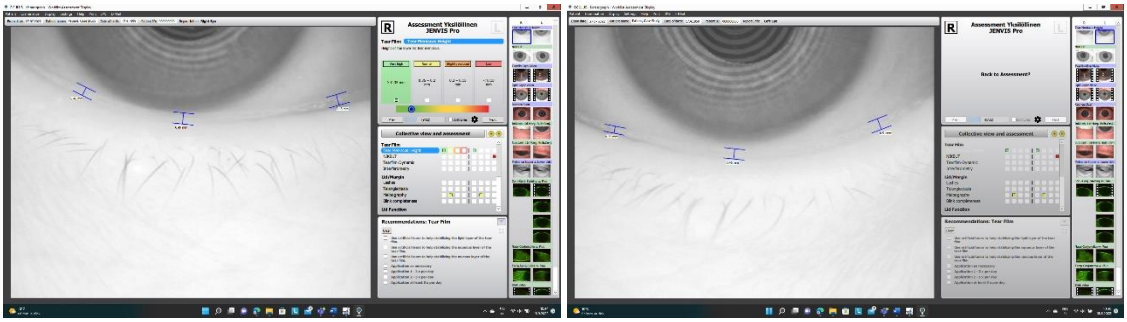


Figure 49 TMH Right Eye

Figure 50 TMH Left Eye

The tear meniscus was measured from the three locations at 6 o'clock, 8 o'clock, and 4 o'clock.

Right eye 0,29 mm, 0,34 mm, and 0,49 mm

Left eye 0,32 mm, 0,35 mm, and 0,49 mm

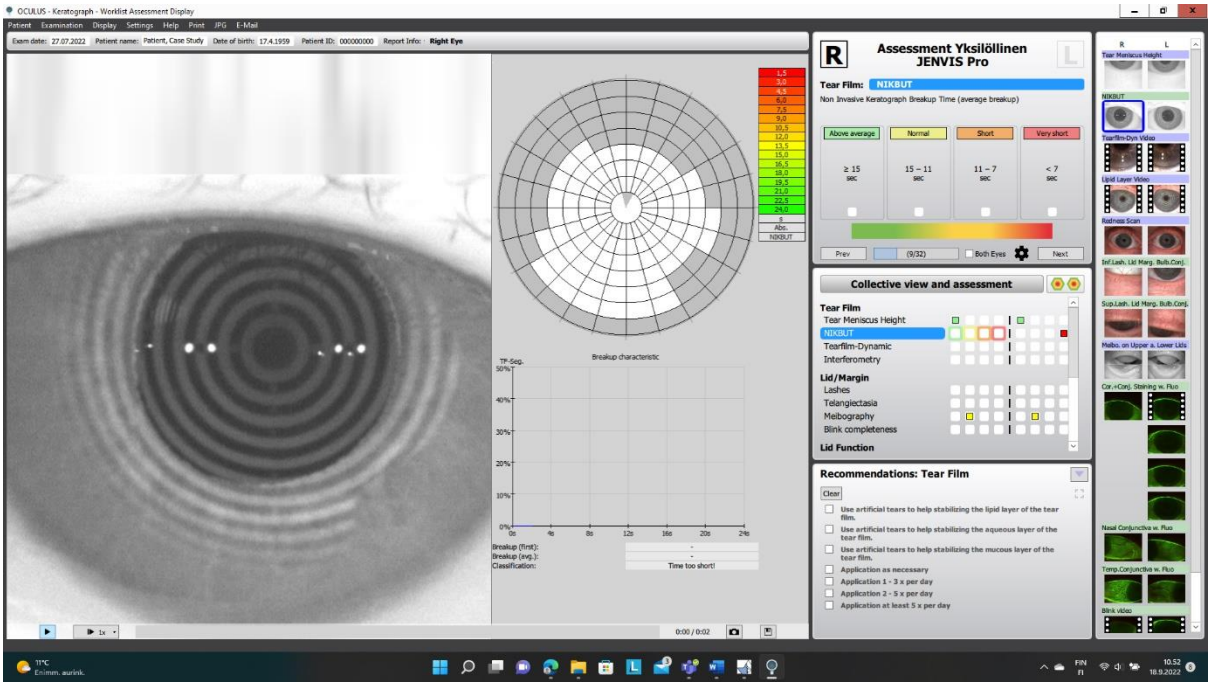


Figure 51 NIKBUT Right Eye

NIKBUT's right eye measuring time was less than 2 seconds, and the device did not give a break-up time due to the blink. The measurement was not repeated.

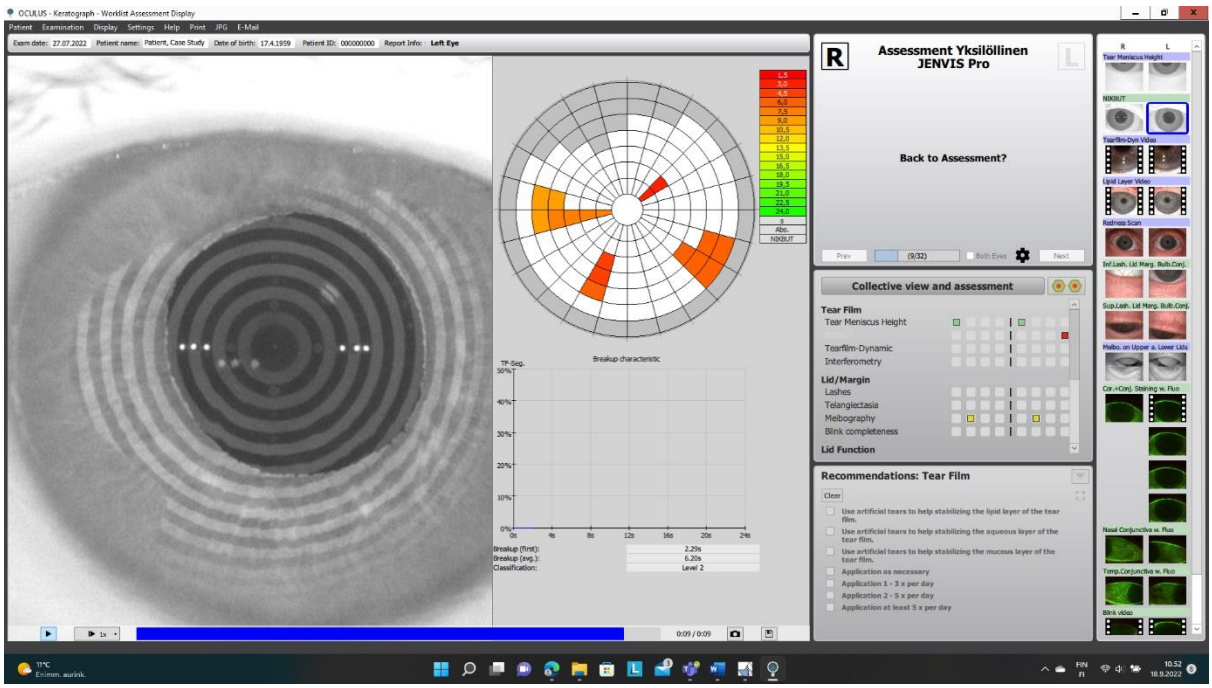


Figure 52 NIKBUT Left Eye

NIKBUT left eye first break 2,29 seconds, break up medium 6,20 seconds, level 2 (Jervis Scale), and first blink in 9,18 seconds. The distortions in the Placido rings can be seen at 4 o'clock.

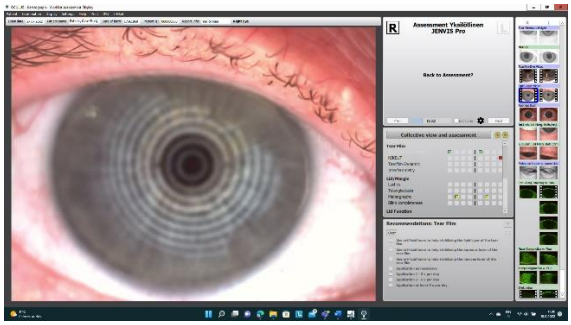


Figure 53 Lipid Layer Right Eye

Figure 51 Lipid Layer Left Eye

LIPID LAYER very pale-whitish hue on both eyes, significant lipid deficit

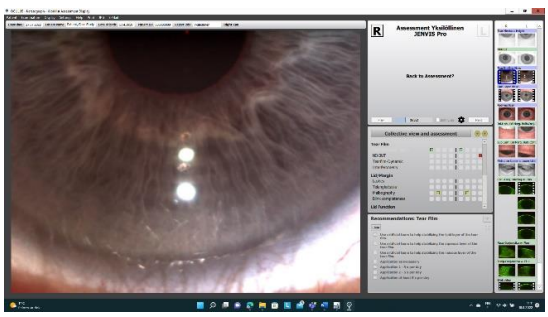


Figure 55 TF Dynamics Right Eye

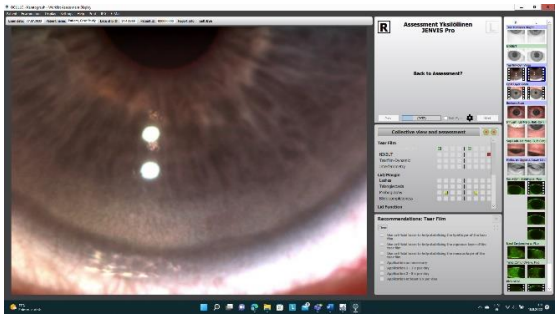


Figure 56 TF Dynamics Left Eye

TF DYNAMICS both eyes showed moderate flow, normal to viscous.

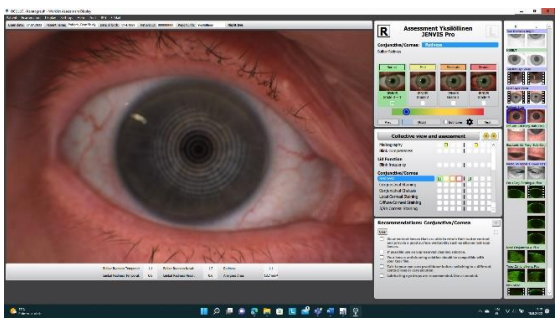


Figure 57 Redness Right Eye

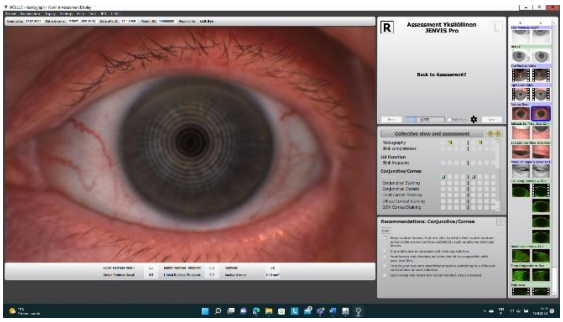


Figure 58 Redness Left Eye

Redness Right Eye

Bulbar redness temporal 1,1, nasal 1,2

Limbal redness temporal 0,6, nasal 0,6

Bulbar redness 1,1, analyzed area 13,7 mm2

Redness Left Eye

Bulbar redness temporal 1,1, nasal 0,9

Limbal redness temporal 0,7, nasal 0,5

Bulbar redness 1,0, analyzed area 14,0 mm2

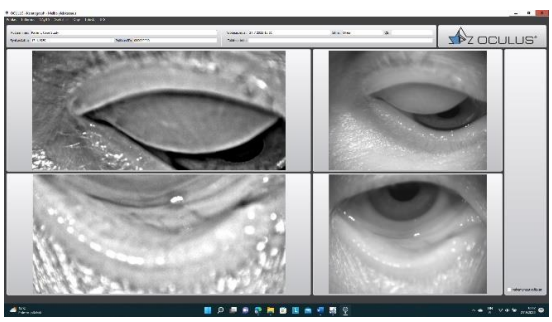


Figure 59 Meibo Scan Right Eye

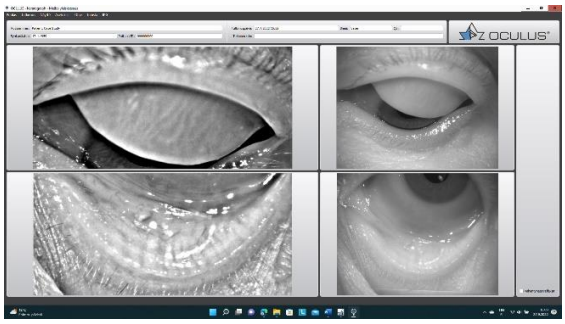


Figure 60 Meibo Scan Left Eye

Meibo Scan using the Jenvis grading scale right eye, the estimated value is 1,5 on the upper lid, 1,3 on the lower lid, and left eye on the upper lid, the estimated value is 1,0 on both upper and lower lid. Hence, there was a change after measurement made on the June 29, 2022.

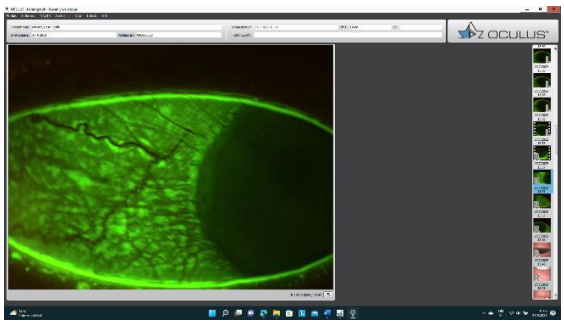


Figure 61 Conjunctival Staining Right Eye temp

Figure 62 Conjunctival Staining Right eye nasal

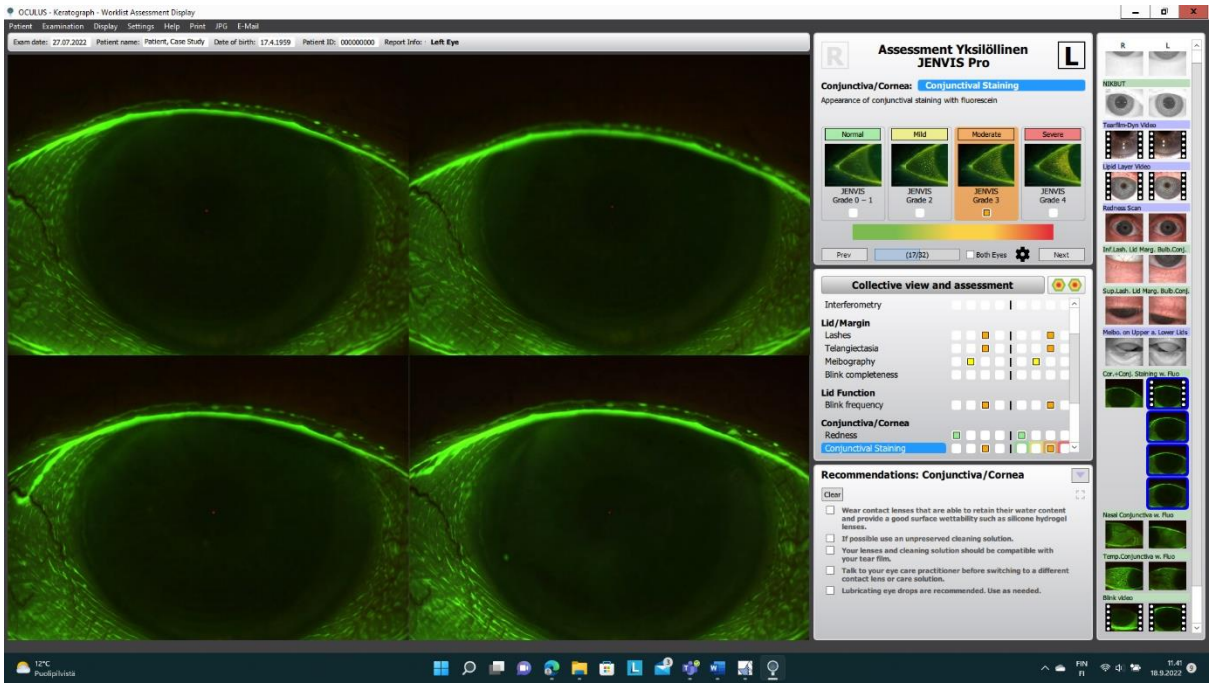


Figure 63 Conjunctival Staining Right and Left Eye

Additional imaging on the cornea and conjunctiva was performed using fluorescein and analyzed using Jenvis Scale.

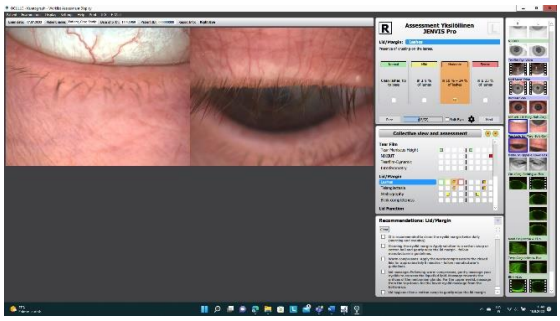


Figure 64 Lids and Lashes Right Eye

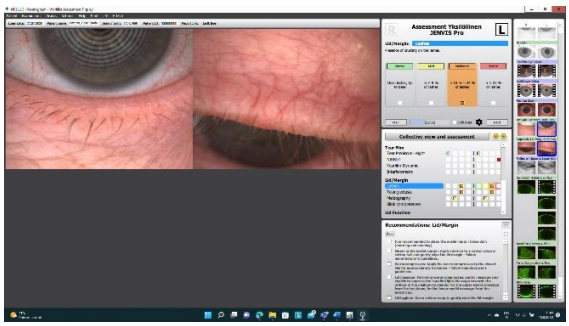


Figure 65 Lids and Lashes Left Eye

Also, lids and lashes were documented and analyzed using Jenvis Scale.

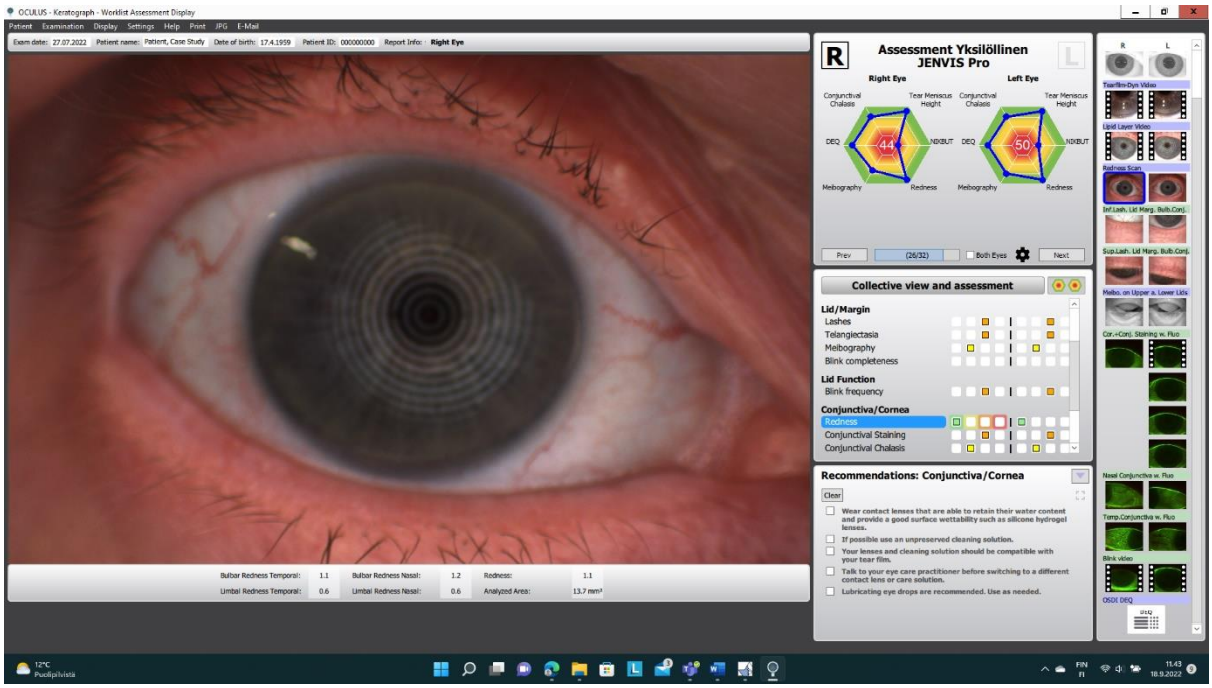


Figure 66 Jenvis Pro numerical value on the Dry Eye status Right Eye and Left Eye

Jenvis Pro Dry Eye analysis was made using the following parameters: Tear Meniscus Height, NIKBUT, Tear Film Dynamic, Lipid Layer, Redness, Lashes, Telangiectasia, Meibography, Blink completeness, Corneal staining, Conjunctival Staining, Conjunctival Chalasis, and OSDI. Jenvis Pro Dry Eye analysis collects all the measured parameters and gives a single number. The scale is between 0 to 100, and the smaller the number, the more severe the dry eye. Here the values are 44 on the right eye and 50 on the left eye.

The slit lamp examination was performed after the K5M measurement, including the fluorescein staining. There were no changes on the lids, lashes, conjunctiva, and cornea, the fluorescein break-up time (FBUT) was 6 seconds on the right eye and 6 seconds on the left eye.

4.1.27 The measurements on the 13th of September, 2022

The last measurements were made on the 13th of September 2022 to evaluate the effect of Rexon Eye therapy on this patient. The patient suffered from the Covid-19 virus starting on the 1st of September 2022 and was still recovering from the Covid-19 virus at the time of the measurements.

Oculus K5M measurements showed the following results:

OSDI was 21.

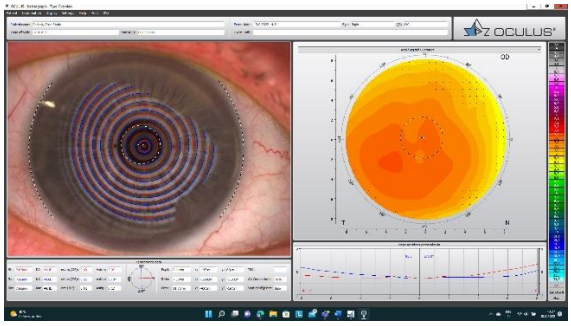


Figure 67 Topography Right Eye

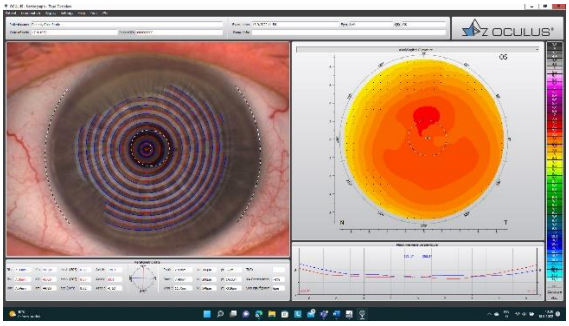


Figure 68 Topography Left Eye

Topography Right Eye K1 7,65 mm 3 degrees, K2 7,66 mm 93 degrees

Topography Left eye K1 7,58 mm 178 degrees, K2 7,50 mm 88 degrees

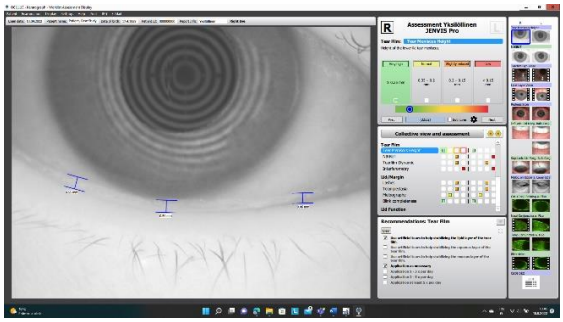


Figure 69 TMH Right Eye

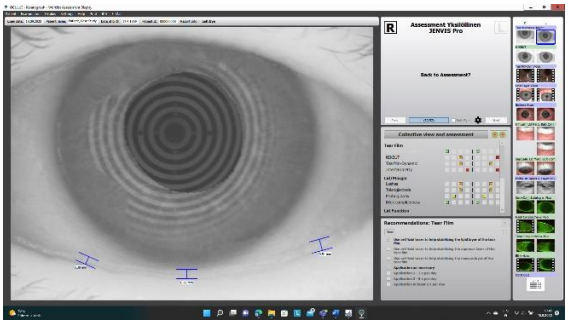


Figure 70 TMH Left Eye

The tear meniscus was measured from the three locations at 6 o'clock, 8 o'clock, and 4 o'clock.

Right eye 0,54 mm, 0,55 mm, and 0,46 mm

Left eye 0,42 mm, 0,38 mm, and 0,51 mm

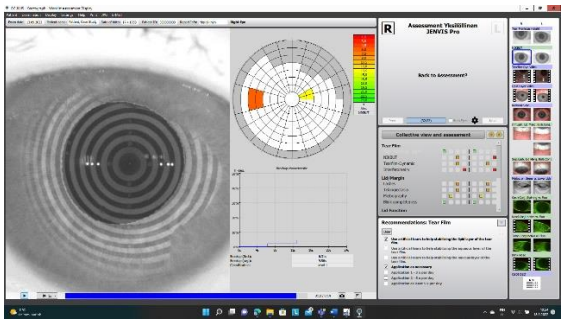


Figure 71 NIKBUT Right Eye

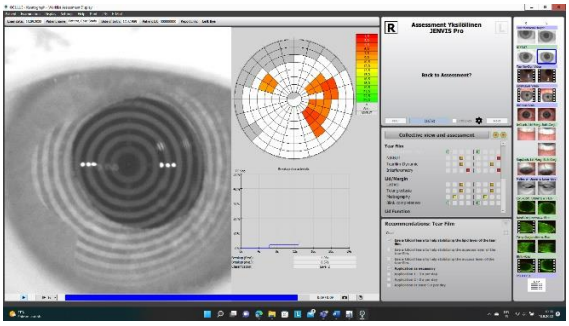


Figure 72 NIKBUT Left Eye

NIKBUT's right eye first break at 6,31 seconds, break-up medium at 9,56 seconds, level 1 (Jenvis Scale), and first blink in 14 seconds.

NIKBUT left eye first break at 4,08 seconds, break-up medium at 6,57 seconds, level 2 (Jenvis Scale), and first blink in 9 seconds.

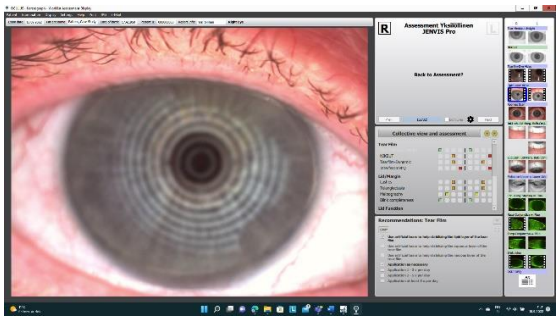


Figure 73 Lipid Layer Right Eye

Figure 74 Lipid Layer Left Eye

LIPID LAYER very pale-whitish hue on both eyes, significant lipid deficit

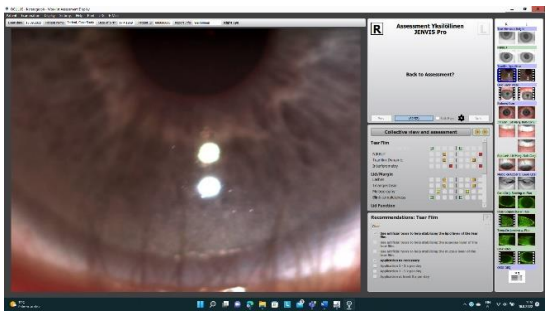


Figure 75 TF Dynamics Right Eye

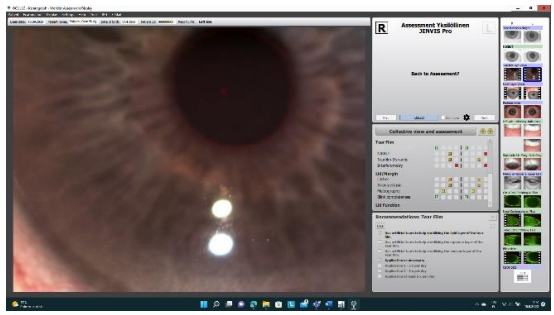


Figure 76 TF Dynamics Left Eye

TF DYNAMICS both eyes showed slow flow, viscous tear film, and change in previous measurements.

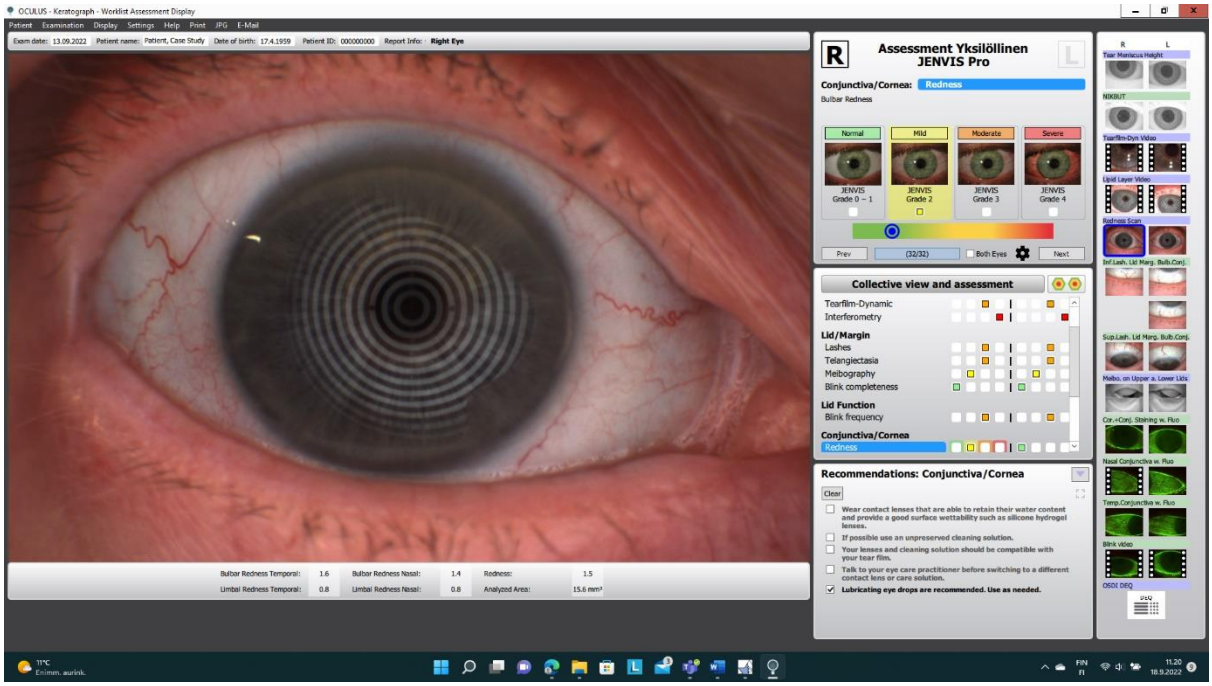


Figure 77 Redness Right Eye

Redness Right Eye

Bulbar redness temporal 1,6, nasal 1,4

Limbal redness temporal 0,8, nasal 0,8

Bulbar redness 1,5, analyzed area 15,6 mm2

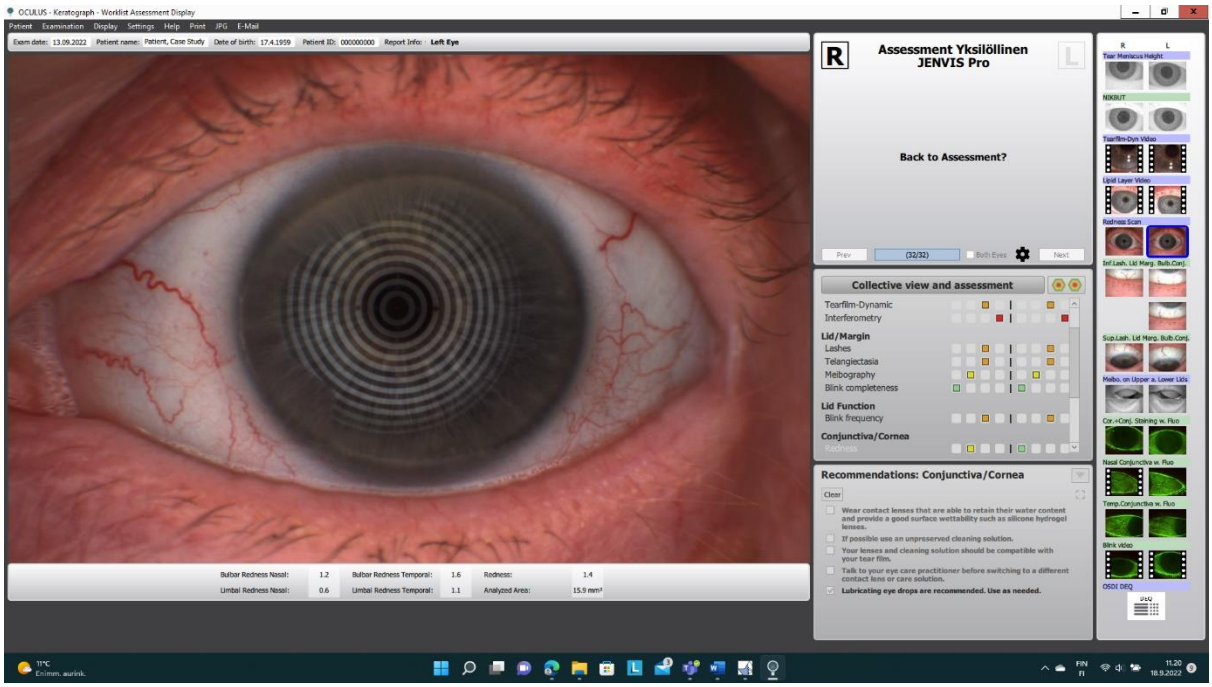


Figure 78 Redness Left Eye

Redness Left Eye

Bulbar redness temporal 1,7, nasal 1,3

Limbal redness temporal 1,1, nasal 0,6

Bulbar redness 1,4, analyzed area 15,9 mm2

Figure 79 Meibo Scan Right Eye

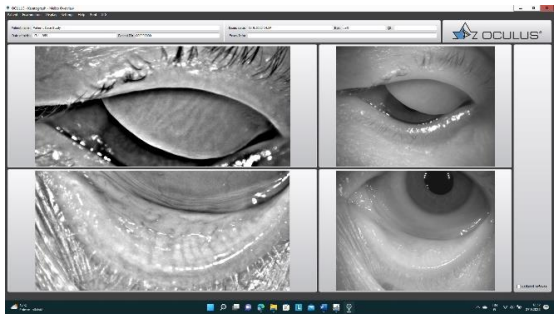


Figure 80 Meibo Scan Left Eye

Meibo Scan using Jenvis grading scale right eye, the estimated value is 1,0 on the upper lid, 1,3 on the lower lid, and left eye on the upper lid, the estimated value is 1,0 on both upper and lower lid. Hence, there is a change after measurement made on the July 27th, 2022.

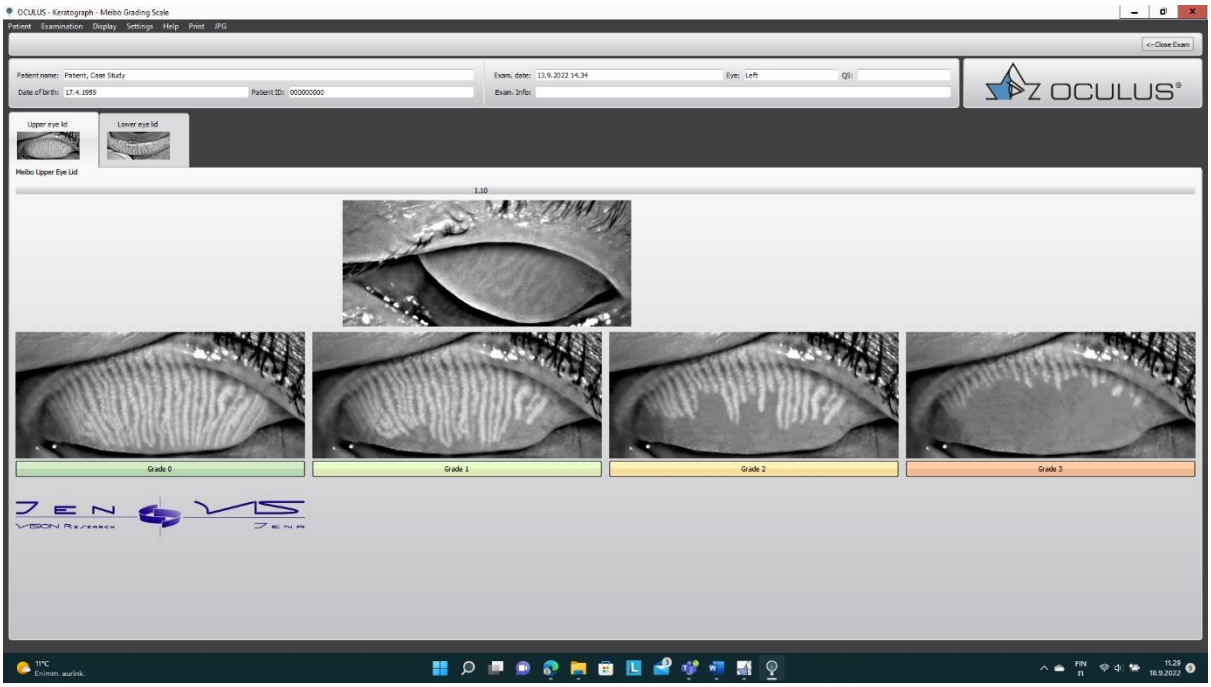


Figure 81 Meibo Scan Jenvis Scale Right Eye

Left eye shows Jenvis Scale, that was used.

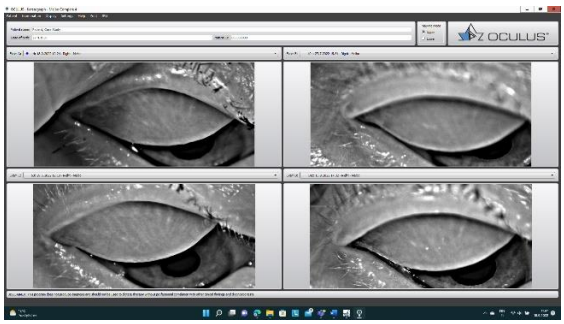


Figure 82 Meibo Scan comparison Right Eye

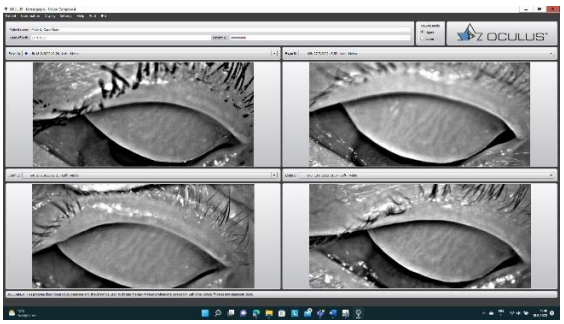


Figure 83 Meibo Scan comparison Left Eye

Here are the results on both eyes on four different dates.

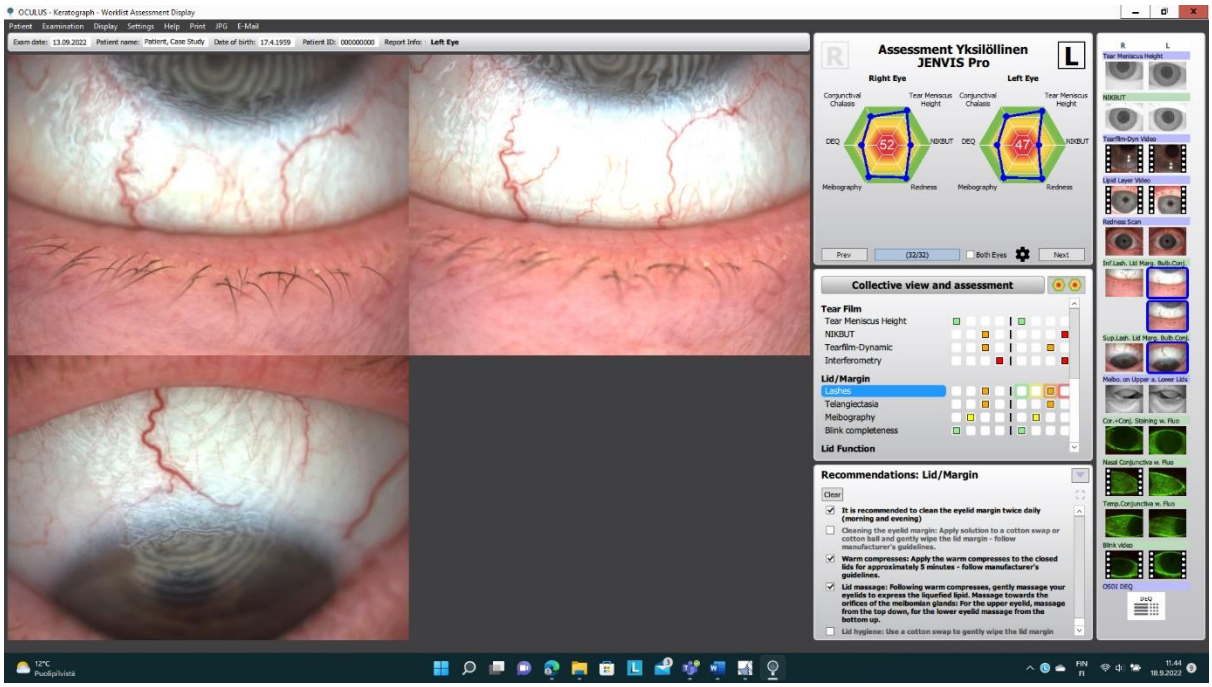


Figure 84 Jenvis Pro numerical value on the Dry Eye status Right Eye and Left Eye

Jenvis Pro Dry Eye analysis was 52 on the right eye and 47 on the left eye.

The slit lamp examination was performed after the K5M measurement, including the fluorescein staining. Both upper lids were reddish lid wiper showed blepharitis; the lashes were regular, conjunctiva, and cornea as last time, the fluorescein break-up time (FBUT) was 9 seconds on the right eye and 8 seconds on the left eye.

4.2 Discussion

This thesis introduces a case study on a patient with Meibomian Gland Dysfunction and presents reviews of the literature on Dry Eye Disease. Dry eye is a multifactorial disease with the loss of tear film homeostasis. It is accompanied by different ocular symptoms, in which hyperosmolarity, tear film instability, ocular inflammation, and neurological abnormalities are present. The main risks for dry eye disease are age, female sex, medications, low humidity environment, smoking, computer use, and eye surgeries—proper assessment and management based on the pathophysiology play a vital role in DED. The most important key to resolving the problematic dry eye is to find the etiological cause, break the vicious circle and restore homeostasis.

After the complete anterior ocular surface evaluation using a slit lamp and digital imaging devices Oculus K5M and Topcon Myah, dry eye disease, including blepharitis, was confirmed in this patient. However, there were no signs of other ocular surface diseases.

The management is suggested to be done yearly to follow up on the progress of the dry eye disease and use imaging tools to motivate the patient about decreasing screen time and taking good care of lid hygiene. The Rexon Eye treatment was suggested to be done yearly to keep the homeostasis steady on the ocular surface. This management was chosen due to the satisfaction of the case study patient and the user-friendly therapy operation. The price of both therapies is quite similar. Due to the limitations of this study, the vast generalization should not be used for guidelines for the DED treatment.

The research development work has tried to be objective, honest, careful, open, and respecting the patient in all the processes. The methods are used daily, and cooperation with the private clinics has been excellent.

The results of this study correlate with the previous studies presented in the research development work. The effectiveness of the assessment and management using existing devices shown in the case study correlates well with the protocol suggested by DEWS II.

4.3 Conclusions

Dry eye disease patients feel their symptoms differently. Proper assessment and management of are essential in the dry eye disease. The imaging tools are good assistants for evaluations and follow-ups, but the slit lamp examination is the crucial instrument for dry eye assessment. Artificial tear eyedrops are a handy tool to manage dry eye, but they do not affect the disease itself, only relieving the symptoms.

It is vital to inform the patients of the new possibilities for treating dry eye for the long-term benefit of the patients. Dry eye assessment and management should also be considered parts of ophthalmological operations like cataract and refractive surgeries. Cataract surgeons often focus more on the surgery than the possibility of dry eye. Existing dry eye can also lead to IOL miscalculations. Especially Patients with multifocal IOLs can be unsatisfied with the outcome after surgery due to dry eye. The steps for the successful surgery outcome could be the following: include the slit lamp examination with dry eye assessment in the routine of the eye surgery procedure. While there is

an increased risk of dry eye, these patients should be treated before surgery. For assessment and management assistance, the Oculus K5M JenvisPro analysis, IPL, and Rexon Eye therapies are valuable tools for improved customer satisfaction before and after eye surgeries.

5 TIMELINE AND BUDGET

The case study patient came to the first appointment on the 18th of February, 2022, where the comprehensive eye examination, including the slit lamp examination, was made, followed by Oculus Keratograph 5M and Topcon Myah measurements and first IPL therapy. On the 24th of March, 2022, the second slitlamp examination, K5M, and Topcon Myah measurements were made, followed by IPL therapy. On the 29th of June, 2022, the third slit lamp examination, K5M, and Topcon Myah measurements were made without the IPL therapy. On the 20th of July, the first Rexon Eye therapy was performed. The fourth measurements on the slitlamp and K5M without Topcon Myah were made on the 27th of July, 2022, one week after the first Rexon Eye dry eye therapy. The Rexon Eye therapy was also given on the 27th of July, 2022, as well as on the 3rd of August and the 11th of August. The last slitlamp and K5M measurements were made on the 13th of September, 2022.

There was no budget for the case study; it was self-funded.

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