

The Efficacy of Vectored Thermal Pulsation System (Lipiflow®) for Meibomian Gland Dysfunction

Research Question: To what extent is a vectored thermal pulsation system more effective for patients suffering from meibomian gland dysfunction than the traditional warm compress and antibiotic treatments?

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Introduction

Dry eye disease affects millions of people worldwide and is a general term encompassing many causes and expressions (Dry Eye: Symptoms, Common Causes & Treatment, 2022). Dry eye disease is when the eyes do not have adequate lubrication from tears. There are various causes behind the lack or unstableness of tears. Meibomian gland dysfunction (MGD) is the leading cause of dry eye, encompassing any disorder linked to meibomian gland abnormalities (O'Neil et al., 2019). The risk of dry eye and MGD increases with age; the International Dry Eye Workshop predicts around 38-68% of people over forty suffer from some degree of MGD (Tomlinson et al., 2011). Although the concept of dry eye has existed and documented for a long time, the modern understanding of the disease was only developed in 1973 (Karpecki, 2015). MGD has two subclassifications depending on the delivery of meibum from the glands, a substance that helps prevent the evaporation of tears. The most common type of MGD is an obstruction of the meibomian gland, which falls under the classification of low delivery. Treatment for this type of MGD aims to clear the obstruction and increase the secretion of meibum (Chhadva et al., 2017). There are no cures for MGD, as there is currently no way to prevent the obstruction from reoccurring. Current treatments include maintaining eyelid hygiene, using antibiotics, eye drops, or surgical options (Pitts & Lievens, 2009). Despite the variety of treatments, they all come with their limitations in terms of efficacy and side effects. LipiFlow® System refers to an automated vectored thermal pulsation system, which presents itself as a breakthrough in efficacy and safety. It simultaneously applies heat therapy and massage to the eyelid (Qiao & Yan, 2013). However, there is skepticism and debate on the effects and claims. Thus, the following research question is developed: **To what extent is a vectored thermal pulsation system more effective for patients suffering from meibomian gland dysfunction than the traditional warm compress and antibiotic treatments?**

Methodology

Many studies have been conducted testing the VTP system over varying periods. The studies analyzed for this paper all originate from PubMed. The most common and recommended treatment of MGD before the development of VTP is using warm compresses (WC) to relieve the obstructions (Schubert & Murakami, 2015). Many studies use WC as a control. In this paper, the first three studies assess the short-term and long-term effects of VTP (Lane et al., 2012) (Blackie et al., 2016) (Greiner, 2016). The fourth compares VTP against antibiotic treatments (Hagen et al., 2018). The last study targets the Asian population, who are most at risk for MGD (Zhao et al., 2016).

Each study has its own inclusion and exclusion criteria. Most studies required that subjects be above eighteen, and usually defined by the criteria of SPEED score over six, and MGS score below twelve. Patients had no other co-existing conditions or additional risks. Extreme inflammation or infection was also excluded.

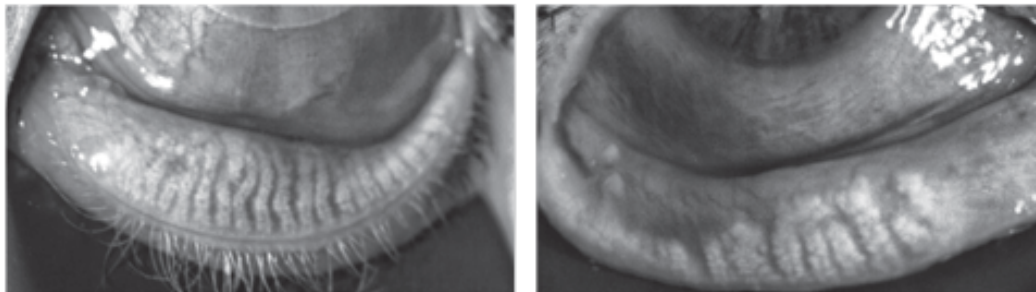
The Biology of Meibomian Gland Dysfunction

The meibomian glands are large sebaceous glands in the eyelid that secrete meibum, a lipid compound (Abelson et al., 2016). It is responsible for coating the aqueous layer of the ocular surface and providing stability to the tear film layer. The tear film protects against the evaporation of natural tears. MGD impacts ocular surface health and changes the tear film's composition, subsequently leading to increased tear evaporation, inflammation and tear hyperosmolarity (salt concentration in tears). The result is visual discomfort. The pathophysiology of MGD includes aging, environmental stress and ethnicity (Chhadva et al., 2017). Aging leads to cell atrophy, which in turn decreases lipid production and changes the meibum composition. Additionally, increased age leads to decreased meibocyte differentiation, meibocyte cell renewal, and gland size. These changes are associated with reduced expression

of peroxisome proliferator-activated receptor gamma (PPAR γ), a nuclear receptor protein (Hwang et al., 2017) (Lee et al., 2021). This protein plays a critical role in regulating meibocyte differentiation and the formation/function of meibomian glands. Low humidity is one of several environmental stresses that are related to meibocyte-associated abnormalities. It has also been recorded that those with Asian ancestry are about three times more likely to get MGD than Europeans.

As stated previously, the broadness of dry eye and MGD results in many possible causes. For a healthy eye, microbiota density is low and there are limited types of microbes (Vernhardsdottir et al., 2022). Tears contain secretory IgA, lysozyme, and lactoferrin which are antimicrobial proteins. They are responsible for preventing microbes from adhering to the epithelia, being toxic to bacteria, and decreasing nutrients for microbial growth respectively. When the tear film homeostasis is disrupted, the ability to defend against microbial invasion decreases. The above demonstrates the wide range of factors that can lead to MGD, but also the range of issues that fall under this disease. Thus, a cure or solution is difficult to reach.

Figure 1: The comparison of eyes with healthy meibomian glands (left) and eye with MGD (right) (Olennikov et al., 2016)



Current Treatments

Antibiotics

Antibiotics are one conventional therapy for MGD (Lonsberry, 2014) (Vernhardsdottir et al., 2022). Doctors can prescribe doxycycline, which is a class of tetracycline antibiotic medication. Doxycycline in particular is often chosen due to its limited side effects and longer half-life. It targets bacteria by preventing its growth and spread. It holds the property to inhibit matrix metalloproteinases (MMP), enzymes that degrade proteins like connective tissue in the extracellular matrix. In addition, tetracyclines have an anti-inflammatory role. Doxycycline can be used to help patients manage MGD due to its antimicrobial in addition to its anti-inflammatory properties. However, doxycycline is only used as an adjunctive therapy for managing the disease as it can not remove existing obstructions. Like using any antibiotics, this path of treatment comes with the risk of developing microbial resistance (*Side Effects of Doxycycline - NHS*, 2022).

Warm Compresses

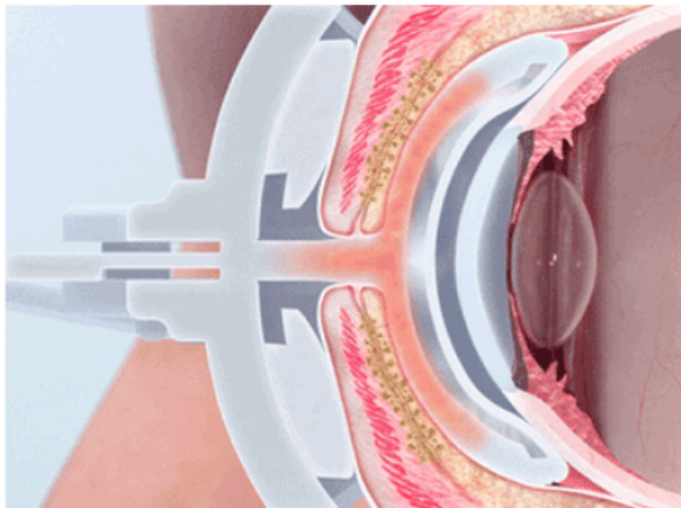
Warm compresses are meant to be supplementary therapy; they do not remove obstructions caused by MGD but soften the material blocking the gland instead. The material is consequently allowed to melt away (Schubert & Murakami, 2015). It results in a more stabilized tear film and improves its evaporative stress defence. This is not a clinical procedure and relies on the patient's application. The problem with this method stems from the lack of personal results. The effects of this process are only temporary, and the application process can be considered laborious. There is also a lack of information on optimizing the efficacy of this method; if the temperature is not high enough, the warm compress will not be effective. Alternatively, if the temperature is too high, it can cause skin scalding or corneal injury. When the meibum has been melted, it must be excreted. However, patients often can not tolerate the

pain that comes with the squeezing. Otherwise, massaging the lids after a warm compress will help express meibum (Pitts & Lievens, 2009).

The New Treatment

LipiFlow® thermal pulsation attempts to look into treating obstruction caused by MGD, as treating the eyelid margin, the portion of the eyelid that is the orifice of the meibomian glands, and ocular surface inflammation is not enough to provide sufficient relief (Qiao & Yan, 2013) (Zargar, 2023). It is a combination of heat therapy and massaging. The breakthrough made in this new treatment is its ability to clear meibomian gland obstruction without any of the limitations presented in the traditional warm compress method. This device's lid warmer simultaneously heats the internal surface of the upper and lower eyelid. This warmer directly touches the inner surface, which minimizes heat transfer. The eye cup, which has an inflatable air bladder, can massage the eyelids to squeeze the glands. The temperature and the pressure can be precisely controlled. The temperature is often set to 42.5°C, as studies suggest that this is the optimal temperature for breaking down the blockages (Schubert et al., 2015).

Figure 2: The LipiFlow® device inserted into the eye (Elliot-Pohl, 2021)



The standard procedure begins with anesthetic drops being placed in the eye. The LipiFlow® warmer will be inserted under the eyelids while the cup is placed over the eyelids (*LipiFlow® Thermal Pulsation System*, 2019). The twelve-minute procedure then begins, as constant pressure is applied for two minutes as it warms. The obstructions in the glands will begin to dissolve in this stage. The continued application of pressure and warmth leads to the natural flow of oils to begin again.

Studies

Overview

Most trials will use warm compresses as a control group, as it is the most traditional and conventional method of treatment. The length and frequency of warm compresses will vary from study to study, although most will opt for a ten-minute warm compress session once a day (Schubert & Murakami, 2015).

MGD can be assessed in a multitude of ways. Some common parameters used to measure the effectiveness of treatment include meibomian gland secretion/assessment (MGS), tear break-up time (TBUT), and recording dry eye symptoms (Xiao et al., 2019) (Vislisel, n.d.). MGS uses a Meibomian Gland Evaluator to measure the expressed secretion characteristics of the fifteen glands along the lower eyelid margin. TBUT inserts fluorescein dry eye test strips onto the ocular surface, measuring the amount of time before a dry spot can be recorded on the strip. Dry eye symptoms are typically assessed using two questionnaires, SPEED and OSDI (Hwang & Bunya, 2023). SPEED assesses the frequency and severity of symptoms experienced, while the OSDI assesses the frequency and severity of symptoms in specific contexts. OSDI (scale of 0-100) and SPEED (scale of 0 to 28) have lower scores as fewer symptoms experienced.

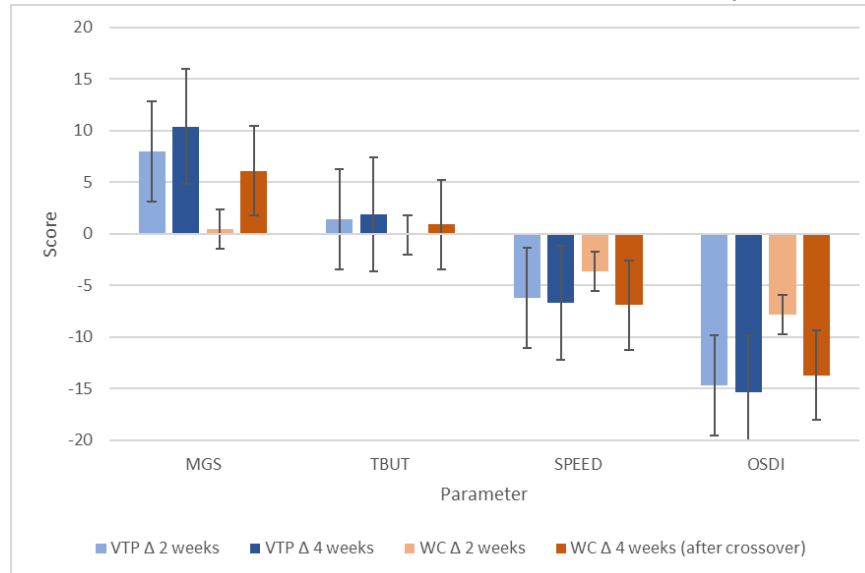
Study 1

In a study published in 2012, the researchers performed an open-label, randomized, crossover multicenter clinical trial (Lane et al., 2012). The patients were randomly selected from the eligible population and had knowledge of which treatment option they were going under. This short-term trial had Lipiflow patients receive a twelve-minute treatment, with reassessment at one day, two weeks and four weeks. The control subjects began with a five-minute warm compress treatment they performed for two weeks before switching over to LipiFlow. MGS, TBUT and dry eye symptoms were all recorded in this trial. The trial had a total of 139 participants, with both eyes being tested.

Table 1: The change in Study 1 parameters (MGS, TBUT, SPEED, and OSDI) in VTP and WC treatments compared to the baseline value after two and four weeks

Parameter	VTP		WC	
	Δ 2 weeks	Δ 4 weeks	Δ 2 weeks	Δ 4 weeks (after crossover)
MGS	8	10.4	0.5	6.1
TBUT	1.4	1.9	-0.1	0.9
SPEED	-6.2	-6.7	-3.6	-6.9
OSDI	-14.7	-15.4	-7.8	-13.7

Graph 1: The change in MGS, TBUT, SPEED, and OSDI after two and four weeks for VTP and WC treatments compared to the baseline values in Study 1*



*Error bars are Standard Deviation

The outcome after the first two weeks for the LipiFlow group showed a statistically significant mean increase in MGS and TBUT. In contrast, the control group saw no improvement in either of the parameters, proving that LipiFlow has a far greater effect in this short-term period. When observing the improvement of symptoms at this time, the recorded improvement for the LipiFlow® group was 76%, compared to 56% for the control group. After four weeks, the LipiFlow group saw continued improvement in all the parameters recorded. While the effect change became less dramatic between weeks two and four, there is still a statistically significant improvement in MGS, TBUT and dry eye symptoms compared to the baseline. The notable methodology used in this trial was the use of a crossover group. After recording the data for the warm compress method, they switched over to also receiving LipiFlow® treatment. A statistically significant improvement was only noted after the crossover, indicating the treatment's success over the warm compress (Lane et al., 2012).

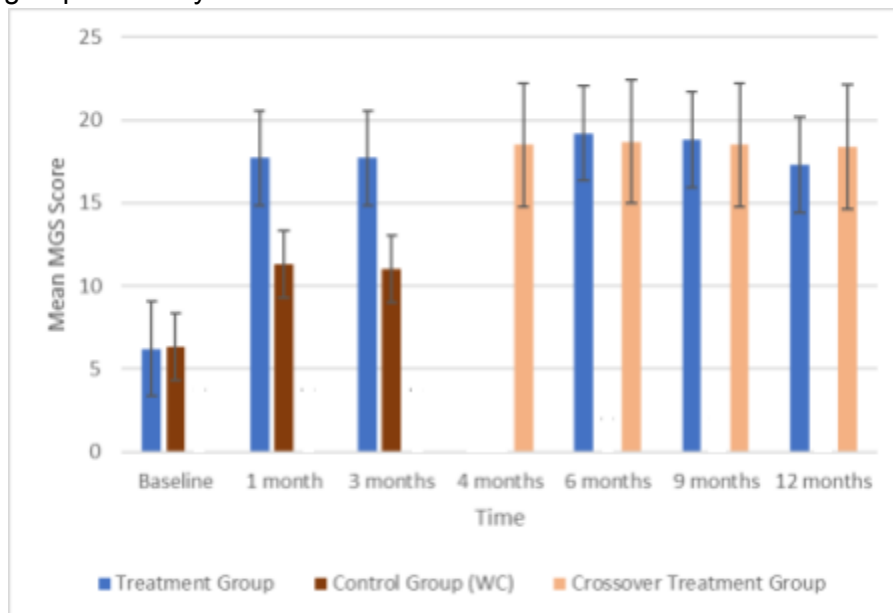
Study 2

When assessing the long-term effects, a similar trial was done studying its effectiveness over twelve months against a warm compress control group (Blackie et al., 2016). This was an open-label, randomized controlled study, with a crossover group after three months (stage two). The participants were further divided into three subgroups after the three-month mark based on a physician's assessment of whether additional treatment was necessary for symptom relief. Most subjects in both the control and LipiFlow® groups received a single twelve-minute vectored thermal pulsation (VTP) treatment, another received two VTP treatments and the last group received a combination treatment (VTP and another treatment). The subjects' mean age was 56.3 years, with 71% of them being females. 97% of the subjects were White or Caucasian race. This study's parameters were MGS and the OSDI Questionnaire.

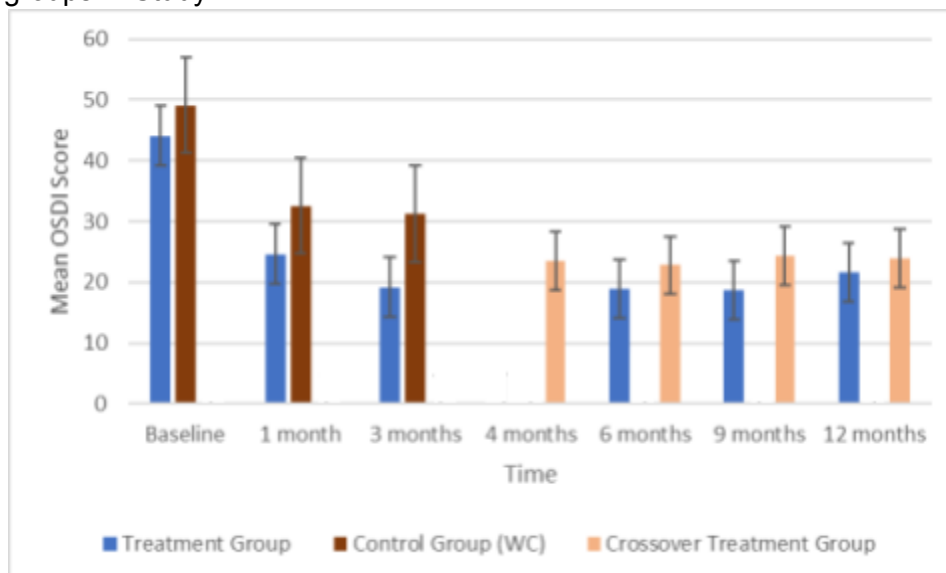
Table 2: The mean MGS and OSDI values at 0, 1, 3, 4, 6, 9, and 12 months for VTP and WC Crossover groups in Study 2

		Baseline	1 month	3 months	4 months	6 months	9 months	12 months
Mean MGS Score	1 VTP Treatment Group	6.2	17.7	17.9	-	19.2	18.8	17.3
	Control Group (WC)	6.3	11.3	11.0	-	-	-	-
	Crossover Treatment Group	-	-	-	18.5	18.7	18.5	18.4
Mean OSDI Score	Treatment Group (VTP)	44.1	24.6	19.2	-	18.9	18.7	21.6
	Control Group (WC)	49.1	32.6	31.3	-	-	-	-
	Crossover Treatment Group	-	-	-	23.5	22.8	24.4	24.0

Graph 2: The mean MGS values after 1, 3, 4, 6, 9, and 12 months for VTP and WC Crossover groups in Study2*



Graph 3: The mean OSDI value after 1, 3, 4, 6, 9, and 12 months for VTP and WC Crossover groups in Study 2*



*Error bars are Standard Deviation

The treatment group saw greater statistically significant mean improvement in both parameters. After twelve months, significant and sustained mean improvement was seen in the MGS score and fewer symptoms were observed through the OSDI Questionnaire for most of the treatment (LipiFlow) group with one VTP treatment. For the control (warm compress) group,

mean MGS was improved during the first three months, but saw greater improvement after the crossover, with statistics similar to the one-month mark of the treatment group. It was also noted that shorter duration from the time of diagnosis and treatment or lower baseline MGD saw greater improvements in MGS scores within the first three months (Blackie et al., 2016).

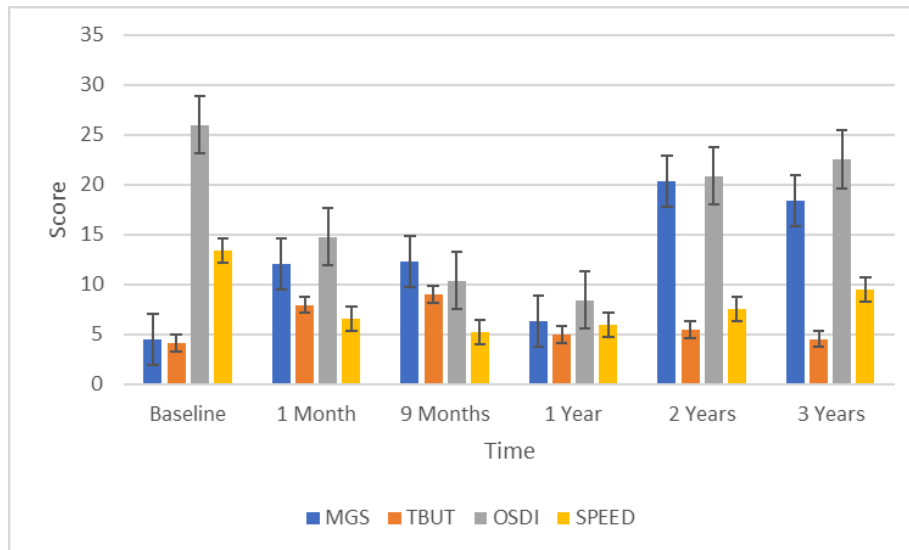
Study 3

The third study looked at the three-year effects of one thermal pulsation treatment (Greiner, 2016). This study was an extension of a one-month trial. A subcohort of twenty subjects received a twelve-minute VTP treatment. As part of the original trial, the patients were examined nine, twelve, and twenty-four months post-treatment. This study added examination after three years. MGS, TBUT, SPEED and OSDI questionnaires were all used as study parameters.

Table 3: The MGS, TBUT, OSDI, and SPEED values for VTP treatment measured at 0, 1, 9, 12, 24, and 36 months in Study 3

Parameter	Baseline	1 Month	9 Months	1 Year	2 Years	3 Years
MGS	4.50	12.00	12.27	6.32	20.29	18.40
TBUT	4.11	7.94	8.99	4.95	5.45	4.51
OSDI	25.96	14.74	10.35	8.43	20.87	22.52
SPEED	13.38	6.53	5.23	5.95	7.50	9.47

Graph 4: The MGS, TBUT, OSDI, and SPEED values for VTP treatment measured at 0, 1, 9, 12, 24, and 36 months in Study 3*



*Error bars are Standard Deviation

The study found that TBUT levels increased, getting better up until the nine-month mark, but returned to baseline values at the one-year mark. Likewise, OSDI scores showed symptom relief increasing for one year before quickly jumping back to the baseline values. SPEED scores show that the most symptom relief came at the one-year mark before slowly returning to the baseline; however, there is still a significant improvement when comparing the baseline and three-year scores (Greiner, 2016).

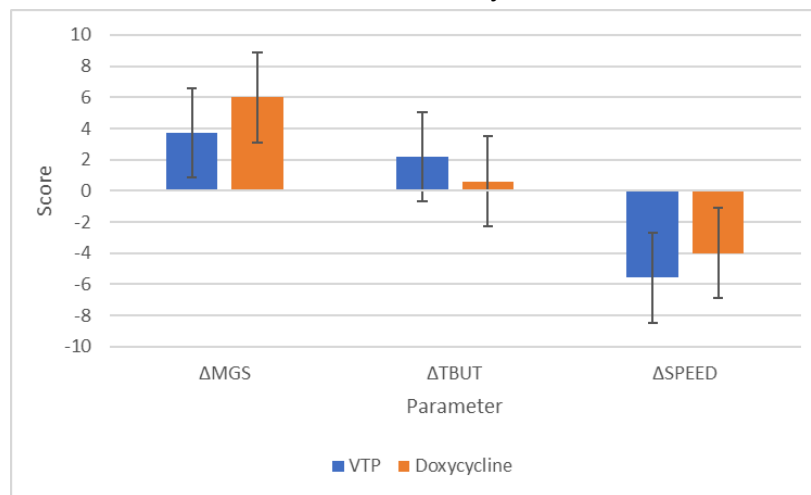
Study 4

The other discussed traditional treatment was antibiotics (Hagen et al., 2018). A different study used daily oral doxycycline as the control group for a three-month VTP treatment. This study included twenty-eight subjects in total. The study used MGS, SPEED, and TBUT as the parameters. LipiFlow® subjects were treated with one twelve-minute cycle treatment. The doxycycline subjects were administered daily oral doxycycline (100mg bidaily for the first two weeks, then once a day for the remaining three months). The mean age for the VTP and doxycycline groups was 41.7 and 50.4 years respectively.

Table 4: The change in MGS, TBUT, and SPEED values for VTP and Doxycycline treatments after three months in Study 4

Parameter	VTP	Doxycycline
Δ MGYLS	3.73	6.00
Δ TBUT	2.18	0.59
Δ SPEED	-5.58	-4.00

Graph 5: The change in MGYLS, TBUT, and SPEED values for VTP and Doxycycline treatments after three months in Study 4*



*Error bars are Standard Deviation

At the three-month mark, the VTP group saw statistically significant improvement in all parameters, whereas the doxycycline group only saw statistically significant improvement in SPEED and MGS scores. The only big difference was the VTP had significantly better mean SPEED scores (Hagen et al., 2018).

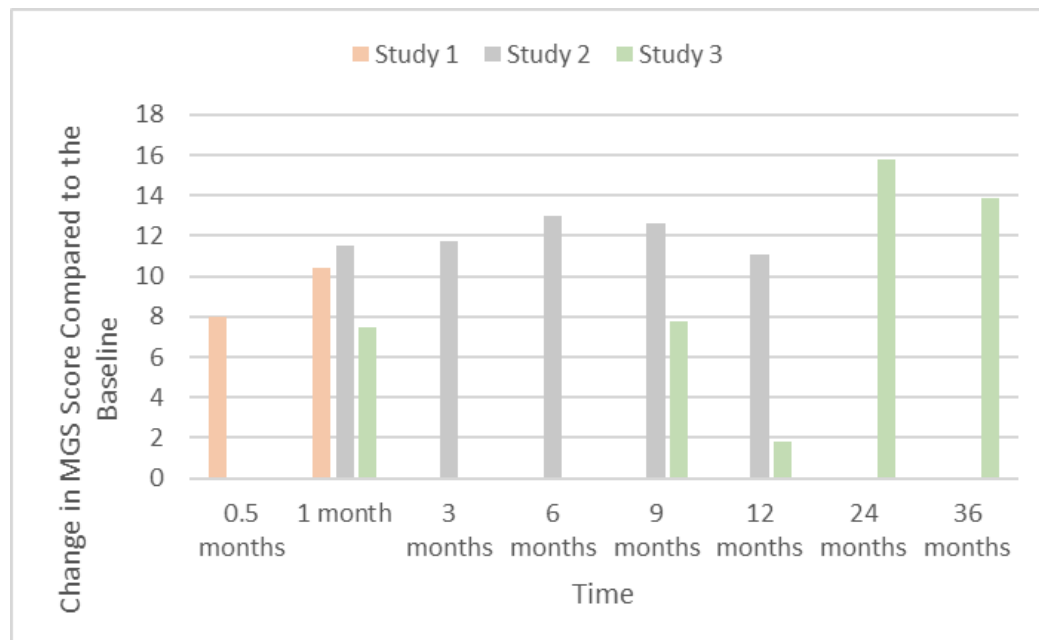
Study 5

In a Singapore tertiary eye hospital, a trial was conducted to observe the effects of LipiFlow® after three months (Zhao et al., 2016). The mean age of the participants in this trial was 56.4 years for the warm compress group and 55.6 in the LipiFlow® group. It is also significant to note that this trial consisted of mostly females, making up 76% of the sample. The

trial was also conducted to target its efficacy in Asian populations, with the sample size being similar to the reported profile of patients from Singapore National Eye Center's dry eye clinic. Twenty-five patients were placed in each group, all being tested for baseline characteristics before any intervention. TBUT was recorded at this time, as well as a SANDE symptom score which is similar to the other questionnaires. The LipiFlow® group received one twelve-minute treatment session, while the control group was instructed to do two sessions of ten-minute warm compresses each day. While there was no raw data posted for this study, results and observations were recorded. In both arms, the symptoms recorded showed a significant reduction, but without significant difference between the two arms. When assessing TBUT, there was a significant change in the LipiFlow® group, but not a statistically significant difference between the two groups (Zhao et al., 2016).

Discussion

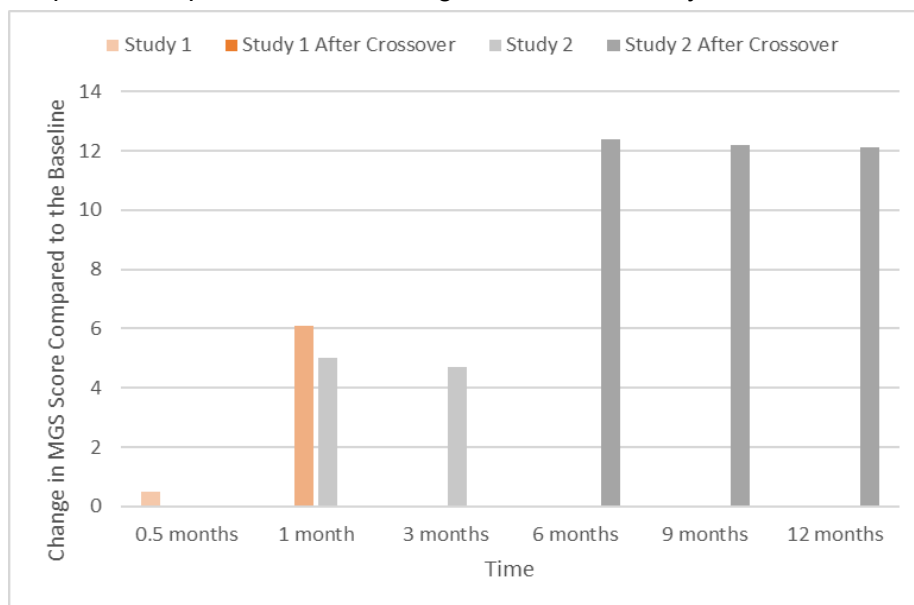
Graph 6: Comparison of the change in MGS for VTP treatments in Studies 1-3



MGS was a common parameter used throughout studies 1-4, as it directly measures the blockage of the glands. The graph shows greater symptom relief as time passes. Study 2 shows

a trend where the relief is relatively consistent after the treatment, with the relief slowly decreasing after the six-month mark. However, Study 3 shows symptom relief is relatively consistent for nine months before a sudden dip and increase in value. This may be attributed to the small sample size and original intent of the study. Study 3 was originally not designed to last for three years, thus the interim data (months 9, 12, 24) are taken from a different study with the same participants (Greiner, 2012). This introduces several errors, as it indicates the participants took part in other studies, thus altering the factors that led to the decrease in blockage. The one-month mark shows a comparison of the three studies. Study 2 has consistently higher change in MGS scores, which may be due to adjunctive treatments being allowed in the study.

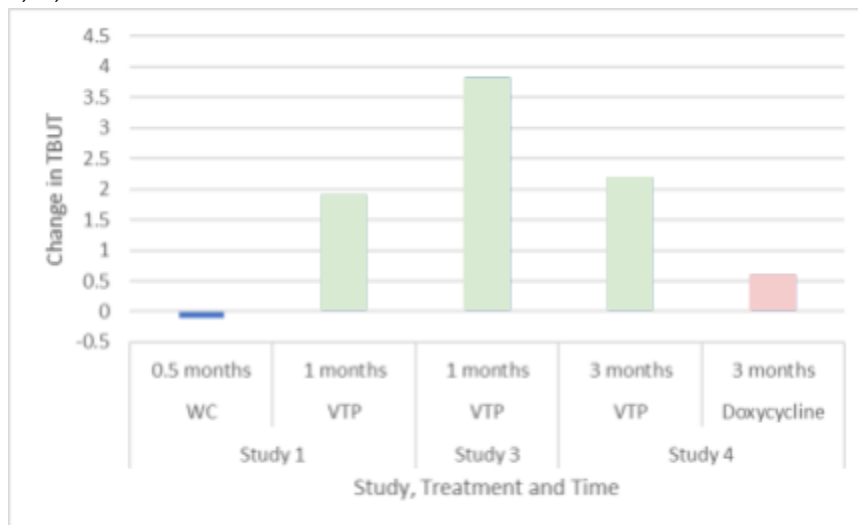
Graph 7: Comparison of the change in MGS for Study 1 and 2 WC treatment



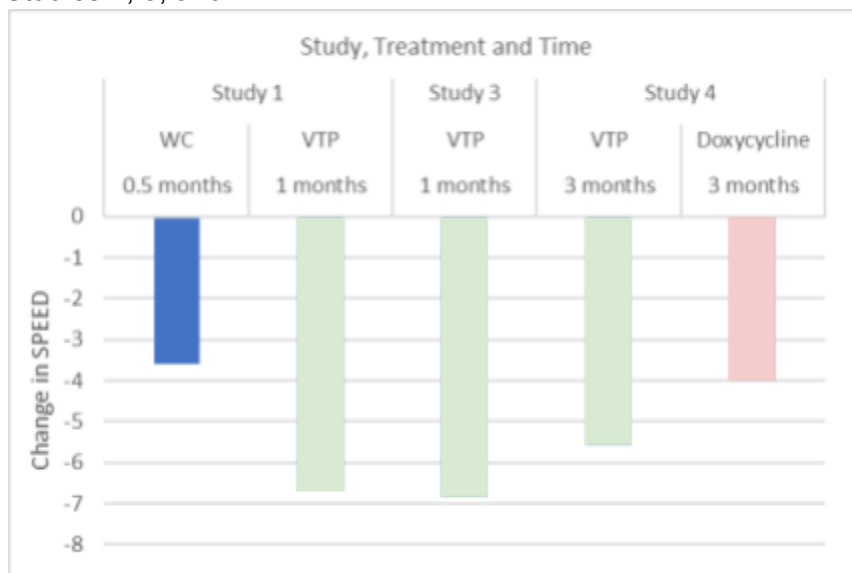
The graph above compares the two crossover groups from studies 1 and 2. The relief from VTP in Study 1 is comparable to the warm compress in Study 2. The two studies used different methods of warm compress. Study 1 opted for a five-minute treatment for at least ten of the fourteen days (using the iHeat portable Warm Compress System) (Lane et al., 2012). Study 2 opted for ten-minute treatments twice daily, accompanied by eyelid hygiene treatment (using

OTC EyeGiene® Insta-Warmth™ System) (Blackie et al., 2016). The stricter and more intensive warm compress routine results in significantly better symptom relief. Both show improvement in MGS after receiving VTP, suggesting VTP is better at clearing blockages.

Graph 8: Comparison of change in TBUT for VTP, WC and Doxycycline treatments from Studies 1, 3, and 4



Graph 9: Comparison of change in SPEED for VTP, WC and Doxycycline treatments from Studies 1, 3, and 4



The two graphs above compare the three types of treatments in terms of TBUT and SPEED scores, however, the studies did not record results at the same time intervals.

Regardless, all treatments show significant improvement in both the amount of time for the eye to produce a dry spot, and the frequency and severity of symptoms. From the data present, the results from study 4 show lesser changes in symptoms, perhaps due to its allowance of previous adjunctive treatments, lowering the baseline scores and thus the change in scores. Graph 8 suggests VTP is best at restoring tear film stability, most likely due to its ability to release meibum. The failure of the warm compress may be due to this specific study's methodology, as it uses a less intense and effective procedure; it could also be due to the short timeframe.

Overall

The first study was a study on the short-term effects of the treatment (Lane et al., 2012). Its crossover design allowed for the patients' responses to both treatments to be compared while removing patient variation. The subjects in this study reported mild discomfort, with 97% rating it equal or lower than 4 on a scale of 0-10. LipiFlow® is a better option for patients who struggle in terms of pain and time.

The second study concludes symptom relief drastically improves in the first month before stabilizing and sustaining the effects for a year (Blackie et al., 2016). This study took into account the duration of MGD diagnosis and duration of dry eye symptoms: the longer the patient had MGD saw less change in MGS over the initial three months. VTP treatments see higher efficacy if early intervention is possible. 86.2% of patients did not need to receive any other therapy during the twelve months, demonstrating its lasting and powerful effect.

In the third study, all the parameters peaked and began decreasing (Greiner, 2016). The most notable difference was in the OSDI and SPEED questionnaires: SPEED results suggested continued symptomatic relief while OSDI did not. It suggests that at three years, symptom relief will continue unless the patient is faced with adverse environmental situations. Low humidity and windy conditions can lead to more symptoms for patients. Patient subjective reports led to

other dry eye symptoms being revealed at the three-year follow-up. It is possible that LipiFlow® treatment can unmask other underlying conditions.

The fourth study demonstrated the positive effects doxycycline can have while also highlighting its complications (Hagen et al., 2018). While doxycycline showed greater improvement in MGS and comparable improvement in SPEED scores, the side effects must be noted. Two subjects had to drop out of the study due to stomach pain, which is in line with the many gastrointestinal problems associated with oral doxycycline (*Side Effects of Doxycycline - NHS*, 2022). The study concluded that VTP in comparison has a better safety profile, and can be a better course of treatment due to its short treatment time and similar outcomes, with better TBUT improvement as well.

The last study followed the trend seen in other three-month Lipiflow trials, in which there is significant symptomatic improvement recorded at the one-month mark which is sustained for the three months. This is the only trial that suggested that Lipiflow had statistically similar efficacy as warm compresses over the three months, likely due to the Asian demographic of patients. Asians are observed to have greater severity of dry eye symptomology (Craig et al., 2019). Genetically, Asians show a higher degree of MGD and incomplete blinking (Zheng et al., 2022). Incomplete blinking is when the eyelid does not fully cover the pupil when blinking, leading to insufficient meibum being released over time. Meibomian gland dropout levels are significantly higher in Asians, meaning more meibomian gland loss. More severe symptoms can lead to the treatment being less effective, which is likely what occurs with Asian patients. Fewer meibomian glands may also contribute to a less effective treatment on Asian patients, seeing that meibum production can not be improved to the extent that Caucasian patients do (Zhao et al., 2016). However, this treatment still presents its benefits of being a one-session treatment rather than the two sessions a day that warm compresses call for.

Evaluation

A strength of this essay is the source of the studies; the studies all stem from PubMed, a highly authoritative database of medical research. LipiFlow® is a relatively new treatment, so the experiments are all performed at a similar time. The studies also have similar inclusion and exclusion criteria. All require patients to be over eighteen and can not have any other conditions or medications that could alter results, like pregnancy or eye abnormalities. All of these studies only included patients who had medium cases of dry eye disease. The criteria help define a consistent range of patients. Another strength of the essay is the variety of purposes of the studies. Short and long-term effects, differing target populations, and control comparisons were used in each study, thus gaining a broader understanding of LipiFlow's efficacy.

Limitations of this essay include the different parameters and methodology in each study. The lack of consistency in parameters made it difficult to compare the results of the studies. The OSDI and SPEED parameters are subjective, as they rely on personal experience. The altered methodologies, particularly in how warm compresses are performed and the frequency of recording data. Variables are controlled in different manners causing inconsistencies between studies to arise. Lastly, the expression of MGD and dry eye disease will alter from person to person, varying in severity, cause, and adjunctive conditions. The efficacy of LipiFlow® for every person will differ, and every study result will be distinct due to the population. Some of the studies use small sample sizes, thus not properly representing the big variety of populations that can receive the treatment.

These studies only use the lower lid for MGS measurements. The functionality of the upper lid could not be evaluated due to the lack of standardized technique. The effects of this treatment on the upper lid meibomian glands are unknown. This is especially significant as there are more meibomian glands on the upper lid. There is greater uncertainty when trying to

compare the relationship with observed parameters, like the MGS score, and symptoms felt by the subject.

An extension to this investigation is to find studies targetting specific types and progression of MGD to determine where LipiFlow® is most effectively applied. The studies focused on milder cases of MGD, so the effect of LipiFlow® on more extreme cases could be considered. More studies targeting the short and long-term effects, different demographics, and comparisons to current treatments should also be researched to better determine a trend and definite conclusion on its efficacy. Alternatively, more research can be put into determining how to optimize the efficacy of LipiFlow; multiple rounds of VTP or receiving VTP in conjunction with other treatments may have a stronger or longer-lasting effect.

Conclusion

When taking all the data together, LipiFlow® can be concluded to be an effective treatment for MGD. The efficacy proves to be greater than the traditional warm compresses. The studies prove that when it is used in crossover trials, significant improvements in parameters are only seen when the crossover happens. In direct comparisons, VTP consistently shows greater improvement. When compared to doxycycline, the efficacy is comparable in MGS and SPEED, but it showed significant TBUT improvement. What gives VTP treatment the edge over doxycycline is its decreased side effects and shorter treatment time. LipiFlow® presents itself as a favourable treatment, however, there is a limit to its effectiveness. At the three-year mark, many parameters began to return to the baseline value, showing that VTP treatments may need to be continuous, although not frequent. Based on the data shown, the development of VTP is a step towards better treating MGD and dry eye disease.

Bibliography

Abelson, M. B., Ousler, G., Shapiro, A., Rimmer, D., & Mass, A. (2016, May 10). The Form and Function of Meibomian Glands. Review of Ophthalmology – Monthly Publication for Ophthalmologists.

<https://www.reviewofophthalmology.com/article/the-form-and-function-of-meibomian-glands#:~:text=The%20Anatomy.-Both%20upper%20and&text=Secretions%20from%20these%20glands%20protect.50%20on%20the%20upper%20lid>

Blackie, C. A., Coleman, C. A., & Holland, E. J. (2016). The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. *Clinical ophthalmology (Auckland, N.Z.)*, 10, 1385–1396.

<https://doi.org/10.2147/OPTH.S109663>

Chhadva, P., Goldhardt, R., & Galor, A. (2017). Meibomian Gland Disease: The Role of Gland Dysfunction in Dry Eye Disease. *Ophthalmology*, 124(11S), S20–S26.

<https://doi.org/10.1016/j.ophtha.2017.05.031>

Craig, J. P., Lim, J., Han, A., Tien, L., Xue, A. L., & Wang, M. T. M. (2019, January 1). Ethnic Differences Between the Asian and Caucasian Ocular Surface | PracticeUpdate. PracticeUpdate; The Ocular Surface.

<https://www.practiceupdate.com/content/ethnic-differences-between-the-asian-and-caucasian-ocular-surface/74854#:~:text=Asian%20participants%20exhibited%20more%20severe,predisposition%20towards%20dry%20eye%20development>

Dry Eye: Symptoms, Common Causes & Treatment. (2022, November 28). Cleveland Clinic. <https://my.clevelandclinic.org/health/diseases/24479-dry-eye>

Elliot-Pohl, K. (2021). Lipiflow Mechanism of Action from Johnson & Johnson. Lipiflow for Dry Eye. Optical Studio. Retrieved 2024, from <https://opticalstudio.ca/lipiflow-for-dry-eye/>

Greiner J. V. (2016). Long-Term (3 Year) Effects of a Single Thermal Pulsation System Treatment on Meibomian Gland Function and Dry Eye Symptoms. *Eye & contact lens*, 42(2), 99–107.

<https://doi.org/10.1097/ICL.0000000000000166>

Hagen, K. B., Bedi, R., Blackie, C. A., & Christenson-Akagi, K. J. (2018). Comparison of a single-dose vectored thermal pulsation procedure with a 3-month course of daily oral doxycycline for moderate-to-severe meibomian gland dysfunction. *Clinical ophthalmology (Auckland, N.Z.)*, 12, 161–168. <https://doi.org/10.2147/OPTH.S150433>

Hwang, F. S., & Bunya, V. Y. (2023, October 2). Dry Eye Syndrome Questionnaires - EyeWiki (V. Y. Bunya, Ed.). EyeWiki; American Academy of Ophthalmology.

https://eyewiki.aao.org/Dry_Eye_Syndrome_Questionnaires

Hwang, H. S., Parfitt, G. J., Brown, D. J., & Jester, J. V. (2017). Meibocyte differentiation and renewal: Insights into novel mechanisms of meibomian gland dysfunction (MGD). *Experimental eye research*, 163, 37–45. <https://doi.org/10.1016/j.exer.2017.02.008>

Karpecki, P. M. (2015, January 15). The Evolution of Dry Eye. Review of Optometry – The Magazine Read Most by Optometrists.

<https://www.reviewofoptometry.com/article/the-evolution-of-dry-eye>

Lane, S. S., DuBiner, H. B., Epstein, R. J., Ernest, P. H., Greiner, J. V., Hardten, D. R., Holland, E. J., Lemp, M. A., McDonald, J. E., 2nd, Silbert, D. I., Blackie, C. A., Stevens, C. A., & Bedi, R. (2012). A new system, the LipiFlow, for the treatment of meibomian gland dysfunction. *Cornea*, 31(4), 396–404. <https://doi.org/10.1097/ICO.0b013e318239aaea>

LipiFlow® Thermal Pulsation System | Johnson & Johnson Vision. (2019, December 20). Johnson & Johnson Vision. <https://www.jnjvisionpro.ca/products/lipiflow-treatment>

Lee, Y. H., Bang, S. P., Shim, K. Y., Son, M. J., Kim, H., & Jun, J. H. (2021). Association of tear matrix metalloproteinase 9 immunoassay with signs and symptoms of dry eye disease: A cross-sectional study using qualitative, semiquantitative, and quantitative strategies. *PloS one*, 16(10), e0258203. <https://doi.org/10.1371/journal.pone.0258203>

Lonsberry, B. (2014, February 15). Doxycycline: Do's and Don'ts. Review of Optometry – The Magazine Read Most by Optometrists; Review of Optometry.

[https://www.reviewofoptometry.com/article/doxycycline-dos-and-donts#:~:text=For%20example%20E2%80%93E2%80%93these%20medications%20have.matrix%20metalloproteases%20\(MMP\).&text=Rosacea%20is%20typically%20managed%20with%2050mg%20to%20100mg%20doxycycline%20QD%20to%20BID](https://www.reviewofoptometry.com/article/doxycycline-dos-and-donts#:~:text=For%20example%20E2%80%93E2%80%93these%20medications%20have.matrix%20metalloproteases%20(MMP).&text=Rosacea%20is%20typically%20managed%20with%2050mg%20to%20100mg%20doxycycline%20QD%20to%20BID)

O'Neil, E. C., Henderson, M., Massaro-Giordano, M., & Bunya, V. Y. (2019). Advances in dry eye disease treatment. *Current opinion in ophthalmology*, 30(3), 166–178.

<https://doi.org/10.1097/ICU.0000000000000569>

Olennikov, L., Cunningham, D., & Whitley, W. (2016). Comparison of Eye with healthy Meibomian Glands and Eye with Meibomian Gland Dysfunction. Improve Your Understanding of Meibomian Gland Function —and Dysfunction. Review of Optometry. Retrieved 2024, from <https://www.reviewofoptometry.com/article/improve-your-understanding-of-meibomian-gland-function-and-dysfunction>

Pitts, J., & Lievens, C. (2009, September 16). Put the Squeeze on Meibomian Gland Disease. Review of Optometry – The Magazine Read Most by Optometrists.

<https://www.reviewofoptometry.com/article/put-the-squeeze-on-meibomian-gland-disease#:~:text=Warm%20compresses..and%20helps%20soften%20lash%20debris>

Qiao, J., & Yan, X. (2013). Emerging treatment options for meibomian gland dysfunction. *Clinical ophthalmology (Auckland, N.Z.)*, 7, 1797–1803. <https://doi.org/10.2147/OPHTH.S33182>

Schubert, J. R., & Murakami, D. K. (2015, August 12). Using warm compresses to treat meibomian gland disease. *Optometry Times*; Optometry Times.

<https://www.optometrytimes.com/view/using-warm-compresses-treat-meibomian-gland-disease>

Side effects of doxycycline - NHS. (2022, January 19). Nhs.Uk.

<https://www.nhs.uk/medicines/doxycycline/side-effects-of-doxycycline/>

Tomlinson, A., Bron, A. J., Korb, D. R., Amano, S., Paugh, J. R., Pearce, E. I., Yee, R., Yokoi, N., Arita, R., & Dogru, M. (2011). The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. *Investigative ophthalmology & visual science*, 52(4), 2006–2049. <https://doi.org/10.1167/iovs.10-6997f>

Vernhardsdottir, R. R., Magno, M., Hynnekleiv, L., Lagali, N., Dartt, D. A., Vehof, J., Jackson, C. J., & Utheim, T. P. (2022, October). Antibiotic treatment for dry eye disease related to meibomian gland dysfunction and blepharitis – A review - ScienceDirect. ScienceDirect.Com | Science, Health and Medical Journals, Full Text Articles and Books.; The Ocular Surface. [https://www.sciencedirect.com/science/article/abs/pii/S1542012422000829#:~:text=Local%20or%20systemic%20antibiotics%2C%20including.anti%2Dinflammatory%20properties%20\(Fig.](https://www.sciencedirect.com/science/article/abs/pii/S1542012422000829#:~:text=Local%20or%20systemic%20antibiotics%2C%20including.anti%2Dinflammatory%20properties%20(Fig.)

Vislisl, J. (n.d.). Atlas Entry - Tear breakup time (TBUT). Retrieved February 1, 2024, from <https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/TBUT/index.htm>

Xiao, J., Adil, M.Y., Olafsson, J. *et al.* (2019) Diagnostic Test Efficacy of Meibomian Gland Morphology and Function. *Sci Rep* 9, 17345 . <https://doi.org/10.1038/s41598-019-54013-4>

Zargar, R. (2023, July 27). LipiFlow, IPL, & RF Treatments: How Are They Different? Eye Doctors | Richmond Hill, ON | Dr. Zargar Eyecare. <https://drzargareyecare.com/2023/07/27/lipiflow-ipl-radiofrequency-treatments-how-are-they-different/>

Zhao, Y., Veerappan, A., Yeo, S., Rooney, D. M., Acharya, R. U., Tan, J. H., Tong, L., & Collaborative Research Initiative for Meibomian gland dysfunction (CORIM) (2016). Clinical Trial of Thermal Pulsation (LipiFlow) in Meibomian Gland Dysfunction With Pretreatment Meibography. *Eye & contact lens*, 42(6), 339–346. <https://doi.org/10.1097/ICL.0000000000000228>

Zheng, Q., Wang, L., Wen, H., Ren, Y., Huang, S., Bai, F., Li, N., Craig, J. P., Tong, L., & Chen, W. (2022). Impact of Incomplete Blinking Analyzed Using a Deep Learning Model With the Keratograph 5M in Dry Eye Disease. *Translational vision science & technology*, 11(3), 38. <https://doi.org/10.1167/tvst.11.3.38>