A Study of Contact Lens Comfort in Patients Wearing Comfilcon A Soft Contact Lenses Compared to Their Habitual Soft Contact Lenses

Thesis

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Abstract

Contact lens discomfort, especially contact lens-related ocular dryness, is a major cause of contact lens wear discontinuation. Many studies have evaluated different contact lens materials for their comfort in both normal patients and sufferers of contact lens-related dry eye. This study seeks to evaluate a new silicone hydrogel soft contact lens material (comfilcon A) in terms of comfort, measurable tear film parameters, and total contact lens-extracted lipid in normal and contact lens-related dry eye contact lens wearers as compared to their habitual contact lenses. Thirty-four participants completed this study consisting of two visits—the first with participants wearing their habitual soft contact lenses and the second with the study contact lenses. Interferometric measurements of the pre-lens tear film thinning rate (PLTF thinning rate), the lipid layer thickness (LLT), and the initial pre-lens tear film thickness (PLTF) were recorded, the Contact Lens Dry Eye Questionnaire (CLDEQ) was performed, and the participants’ lenses were collected for lipid analysis at each visit. The CLDEQ scores at the first study visit of the non-dry eye and dry eye group were shown to be significantly different from one another (p < 0.0001). Total extracted lipid amounts showed a significant difference for the non-dry eye group between the first and second study visits (p = 0.01) but not for the dry eye group (p = 0.10). A significant correlation was found between LLT and PLTF thinning rate for the first visit (r = 0.39, p = 0.03), but not for the second visit (r = 0.14, p = 0.43).
significant correlation was found between CLDEQ score and PLTF thinning rate for the
dry eye group \( r_s = -0.55, p = 0.03 \) but not for the non-dry eye group \( r_s = 0.11, p = 0.71 \) at the first visit. A significant correlation was found between CLDEQ score and LLT for
the non-dry eye group \( r_s = -0.53, p = 0.04 \) but not for the dry eye group \( r_s = -0.18, p = 0.53 \) at the first visit. A significant correlation was found between contact lens-extracted
lipid quantity and number of days for which the habitual contact lenses were worn \( r = 0.37, p = 0.03 \). One month of wear of comfilcon A silicone hydrogel contact lenses did
not significantly improve subjective dryness symptom severity in either normals or
contact lens-related dry eye sufferers as compared to their habitual lens materials. Further
research is needed to determine a quantifiable tear film parameter or other marker by
which to diagnose or grade contact lens-related dry eye and is also needed to find or
develop a soft contact lens material that can be comfortably worn by contact lens-related
dry eye sufferers.
Dedication

Dedicated to Aaron, Sandy, John, Kristin, Ivory, Louisa, Jeronimo, Gregg, and Sharon.
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Chapter 1: Introduction

Much research is currently devoted to the classification and study of dry eye syndrome and methods by which it might be diagnosed or quantified. Dry eye syndrome is a widespread and visually detrimental condition. Contact lens-related ocular dryness also poses a problem for many patients—some who might not otherwise be symptomatic of ocular dryness. In clinical practice, it is a challenge to fit these patients with contact lenses that are satisfactory for ocular comfort and visual performance.

The advent of silicone hydrogel contact lenses has given clinicians new materials to employ when trying to combat the issue of contact lens-related dryness in their patients, but many practitioners, like their patients, become frustrated with the process of refitting soft contact lenses multiple times in an attempt to provide optimal comfort and vision. It is often a time-consuming process for both parties with varied end results, and, in many cases, there has been no published research to indicate whether certain materials might perform better or worse in relation to other materials.

This study seeks to evaluate the appropriateness of a new silicone hydrogel material, comfilcon A, for alleviating dryness symptoms in contact lens-related dry eye sufferers and to compare these data and those of another group of non dry-eye patients to data on the performance of the participants’ habitual soft contact lenses. Various tear parameters are also measured as are the quantities of total extractable lipid deposits from
the contact lenses in order to assess these factors for any association with contact lens-related dry eye symptoms.

1.1 Tear Film

The pre-ocular tear film provides lubrication, protection, and optical regularity to the eye. Early theories of its structure divided the tear film into three distinct layers: the inner mucin layer, the middle aqueous layer, and the outer lipid layer (Holly 1980; Albarran, Pons et al. 1997). This three layer conception of tear film structure has since been replaced with a two-layer model comprised of an outer lipid layer with a thicker underlying layer of aqueous containing free mucins and membrane-bound mucins on the ocular surface (Tiffany 2008).

The mucin components of the tear film are secreted by the goblet cells and the Crypts of Henle, the aqueous components originate in the lacrimal gland, and the lipid layer is deposited on the front of the eye predominantly by the meibomian glands but also by the glands of Zeiss (Albarran, Pons et al. 1997).

The mucins and the aqueous portion of the tears account for 90% of the tear film thickness (Albarran, Pons et al. 1997). The aqueous layer contains bactericidal proteins and electrolytes, and helps to provide a smooth refractive surface on the front of the eye.

The outermost lipid layer of the tear film itself is believed to consist of two layers—the outer hydrophobic non-polar layer and the inner hydrophilic surfactant polar layer (McCulley and Shine 2004). The non-polar layer helps to prevent moisture loss from the tear film through evaporation, and the polar layer stabilizes the overall lipid layer through its interaction with and spreading over the watery inner tear film.
1.2 Tear Film Lipids: Composition and Production

The precise composition of the lipid layer has a high inter-personal variability. Early in the study of meibum components, Tiffany found no consistent meibomian gland secretion composition between individuals (Tiffany 1978). It was able to be determined, however, that all samples collected contained wax esters, cholesterol esters, and triglycerides. This work has not been contradicted and confirms other studies.

In 1982, Nicolaides and Ruth were able to identify more specifically three groups of high molecular weight ω-hydroxy fatty acids in the meibomian gland (Nicolaides and Ruth 1982). These were thought to aid lipid spreading over the tear film. Nicolaides also analyzed pooled samples of total human meibum in both unhydrolyzed and hydrolyzed states using thin layer chromatography and gas chromatography finding endogenous hydrocarbons, sterol esters, wax esters, triacyl glycerols, free cholesterol, phospholipids, and free fatty acids in the unhydrolyzed portion and unsubstituted fatty acids, alpha-hydroxy fatty acids, and omega-hydroxy fatty acids of the hydrolyzed portion (Nicolaides 1986). Ninety percent of human meibomian lipid was found to be comprised of a variety of esters in this study, via gas chromatography-mass spectrometry.

Nichols et. al. have used electrospray mass spectrometry to identify fatty acids and fatty acid amides in meibomian gland secretions from 16 normal individuals (Nichols, Ham et al. 2007). This group identified oleamide, stearamide, palmitamide, myristamide, and erucamide in these samples with oleamide consistently as the
predominant positive-ion mode lipid found. A new group of diacylglycerol lipids has recently been found in meibomian secretions (Butovich, Uchiyama et al. 2007).

There do appear to exist patterns of meibomian secretion differences between certain demographic groups. Increasing age was found to be associated with significant alterations in meibomian gland secretions, and it is hypothesized that these changes may contribute to the age-related increase in the prevalence of tear film hyperosmolarity and dry eye (Sullivan, Evans et al. 2006). Chronic blepharitis is also associated with abnormalities in the tear film lipid layer as well as meibum abnormalities (McCulley and Shine 2003).

More is probably known about the way that meibomian glands manufacture and secrete ocular lipids than about the exact composition of these secretions. The meibomian glands are considered to be modified sebaceous glands (Jester, Nicolaides et al. 1981). Meibomian glands are single-duct branched tubulo-acinar glands embedded within the tarsal plate with orifices located at the lid margin just anterior to the mucocutaneous junction. Acini are found along the length of the main duct, which is approximately as long as the tarsal plate. Meibum is produced via holocrine secretion of the glands, is produced 24 hours per day, and is released from the meibomian glands via the squeezing action of binking (Bron and Tiffany 2004). In the act of blinking, meibomian glands are squeezed by a combination of the muscles of Riolan and the orbicularis oculi (Linton, Curnow et al. 1961).

The amount of meibomian secretions is also variable across generalized patient demographics. Using a Meibometer, a modified skin lipid measuring device, Chew et al. found that casual levels of meibomian lipids on the lid margin were
indistinguishable between males and females both below the age of 14 years and above the age of 50 years (Chew, Hykin et al. 1993). A general trend of increasing levels of meibomian secretion with increasing age was observed up to age 60-69 in males and 70-79 in females with males showing a greater rise in meibum levels between the ages of 20-29 and with females showing the greater rise between the ages of 30-50. Chew and coworkers’ study of 421 normal subjects excluded contact lens wearers, symptomatic patients, wearers of eye cosmetics, women using oral contraceptives, and users of eye drops.

In addition to parasympathetic control of secretions, human meibomian glands show vasoactive intestinal polypeptide (a peptide hormone) innervation in direct contact with acinar cells (McCulley and Shine 2004). The acinar cells also express both estrogen and androgen receptors, suggesting possible androgen hormonal regulation of meibum secretion.

1.3 Tear Film Thickness and Thinning

The thickness of the tear film is very dependant on the method of measurement that is being performed and where on the ocular surface the measurement is being taken. Some of these methods include wavelength-, thickness-, and angle-dependant fringes, optical coherence tomography, fluorometric techniques, optical pachometry, and confocal microscopy (King-Smith, Fink et al. 2004). It is common to take tear film thickness measurements over the visual axis for the clinical importance of this location visually, the ease of ocular alignment, and for the consistency of the location.
Until about one second following the blink, the tear film thins inferior-centrally as it thickens superiorly over the visible corneal surface (King-Smith, Fink et al. 2004). After about two seconds following the blink, the tear film begins to thin at a slower and constant rate. The precise reason for the superior flow of the tear film is uncertain, but the general thinning of the tear film during the inter-blink interval does seem to be at least partially attributable to evaporation (Mathers 2004). These factors make it important to measure the tear film thickness at a specific point in time after the blink or over a specific interval of time between blinks to obtain an average tear film thickness measurement. The refractive interface that causes reflections that are being recorded also has an effect on the measured thickness value. Reported average tear film thickness values range from wavelength-dependent fringe measurements as low as 2.7µm to confocal microscope measurements as high as 46µm. King-Smith et. al. (King-Smith, Fink et al. 2004) propose a value of 3µm as the most accurate thickness in normal subjects.

Tear film lipid layer interferometry readings in a double-masked study have shown increases in lipid layer thickness with both Soothe® (107% increase over baseline, p<0.0001) and Systane® (16% increase over baseline, p<0.0001) lubricating eye drops over a 15 minute time period (Korb, Scaffidi et al. 2005). Systane®, from Alcon Laboratories, containing hydroxypropyl guar, creates a gel on the eye intended to allow cell repair on the surface of the eye. Soothe®, from Bausch & Lomb (formerly from Alimera Sciences), contains a metastable oil in water emulsion and a dual surfactant system. This is designed to create an increased lipid layer on the surface of the eye.
In another study, Refresh® Dry Eye Therapy lubricating eye drops, from Allergan, were similarly shown to increase tear film lipid layer thickness as measured by interference patterns (Scaffidi and Korb 2007). The same study also showed again the tear film lipid layer thickening properties of Systane®. Both studies infer that a thicker lipid layer alleviates dry eye symptoms.

One of the major factors that can effect the thickness of the tear film is contact lens wear. In contact lens wearers, the tear film thickness is divided into the post-lens tear film (PoLTF) thickness and the pre-lens tear film (PLTF) thickness. Reported PoLTF thicknesses include wavelength-dependent fringe measurements as low as 2.3\(\mu\)m to optical pachometry measurements as high as 11.5\(\mu\)m (King-Smith, Fink et al. 2004). Nichols and King-Smith (Nichols and King-Smith 2003) have used interferometry to record an average PoLTF thickness of 2.34\(\mu\)m. In the same study, these researchers reported an average PLTF thickness of 2.31\(\mu\)m. A different interferometric study by this group demonstrated a significant thinning of the PLTF (with a fairly stable PoLTF thickness) over the first 30 minutes of soft contact lens wear (Nichols and King-Smith 2004). Nichols et. al. proposed three methods of PLTF thinning: evaporation, absorption into the ocular surface, and flow parallel to the ocular surface (Nichols, Mitchell et al. 2005). Pre-lens tear film differs from the pre-ocular tear film in that it contains less polar lipids and more non-polar lipids (Maissa, Guillon et al. 2002). Polar lipid groups are responsible for tear film spreading in the pre-ocular tear film, and their absence in the pre-lens tear film may contribute to the decreased tear-film thinning rate as well as subjective feelings of contact lens-related dryness.
The PoLTF under high water content soft contact lenses has been shown to thin over time in response to dehydrating environmental conditions (Little and Bruce 1995). These factors may impact both the fit and the comfort of a given contact lens (Little and Bruce 1995). This thinning of the PoLTF as well as dehydration of the soft contact lens itself tends to stabilize within the first few minutes of hydrogel lens insertion (Fornasiero, Prausnitz et al. 2006). This is thought to be due to the net flux of tear water from the PoLTF through the contact lens to the contact lens surface where evaporation occurs (Fornasiero, Prausnitz et al. 2006). The rate of PoLTF depletion was found to be faster when measuring it under thinner contact lenses (Fornasiero, Prausnitz et al. 2006). Morgan and Efron found that the amount of on-eye dehydration of one silicone hydrogel contact lens material (PureVision) was less than that of a hydrogel material (etafilcon), though, interestingly, the oxygen permeability of the silicone hydrogel lens increased in its dehydrated state whereas that of the hydrogel lens decreased (Morgan and Efron 2003).

Some contact lens care solutions have been shown to be associated with a thicker PLTF in contact lens wearers without dryness symptoms (Nichols, Mitchell et al. 2005).

1.4 Dry Eye

Dry eye is estimated to effect between 14 and 33% of people worldwide and can have significant adverse effects on vision-related quality of life by effecting tasks such as reading and driving (Behrens, Doyle et al. 2006; Miljanovic, Dana et al. 2007).
The National Institutes of Heath/Industry Workshop in 1995 published the definition of dry eye disease that would be followed for the next 12 years. This described dry eye disease to be a “disorder of the tear film due to tear deficiency or excessive tear evaporation that causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort” (Lemp 1995). This description included two possible etiologies for the disease.

In 2007, the International Dry Eye WorkShop amended this definition, stating that dry eye disease was a multifactorial condition (DEWS 2007). The new definition included the symptom of visual disturbance often reported by dry eye patients, and it included the signs of increased tear film osmolarity and ocular surface inflammation that accompany dry eye disease.

The two major types of dry eye disease remain evaporative and aqueous-deficient dry eye (DEWS 2007). Aqueous-deficient dry eye can have autoimmune, mechanical, or pharmaceutical components, and involves a decreased volume of the aqueous component of the tears. Evaporative dry eye can also be attributable to many different causes. Some of these include meibomian gland dysfunction, lid disorders, and contact lens wear.

One of the major confounding aspects of the study of dry eye is the often poor repeatability of tests to quantify the disease (Nichols, Mitchell et al. 2004). Repeatability can be affected by the lack of adherence to a standard protocol for each test and the order in which different tests are performed on any given patient among other factors (Nichols, Mitchell et al. 2004). Severity of dry eye disease can also impact test repeatability. Schirmer tests, for example, tend to show better repeatability
for more severe cases of dry eye disease than for mild to moderate dry eye (Nichols, Mitchell et al. 2004). The measure of dry eye that does seem to have the best repeatability is patient-reported symptoms, though it is difficult to grade the severity of dryness based on these more subjective data (Nichols, Mitchell et al. 2004). Additionally, patient-reported symptoms have been shown to correlate poorly with more objective clinical tests that measure signs of dryness such as the Schirmer and phenol red thread tests, tear film break-up time, corneal staining, and meibomian gland assessment (Nichols, Nichols et al. 2004). Patient surveys such as the McMonnies’ questionnaire, the Short Questionnaire for Dry Eye Syndrome, and the Contact Lens Dry Eye Questionnaire (CLDEQ) have been developed to be used clinically in the evaluation of subjective symptoms of ocular dryness and to standardize their reporting (Nichols, Mitchell et al. 2002; Gulati, Sullivan et al. 2006).

Concentrations of pro-inflammatory markers such as interleukins 1α and β and matrix metalloproteinase-9 have been shown to be increased in the tears of patients with dry eye disease (Schultz and Kunert 2000; Solomon, Dursun et al. 2001). Additionally, the levels of secreted immunoglobin A, an anti-pathogen substance, in the tears of contact lens wearers has been shown to be significantly reduced and the levels of interleukin-6, another pro-inflammatory mediator, significantly elevated as compared to those levels in non contact lens wearers (Wilcox and Lan 1999; Schultz and Kunert 2000). Cyclosporine A, in a 0.05% emulsion, has been shown to reduce the levels of pro-inflammatory interleukin-6 in the conjunctival epithelium of dry eye patients and has also been shown to reduce contact lens intolerance in lens wearers suffering from ocular dryness (Turner, Pflugfelder et al. 2000; Hom 2006).
1.5 Contact Lens-Related Dry Eye

Contact lens discomfort is the leading reported cause of contact lens discontinuation (Young, Veys et al. 2002). Dryness and discomfort are the ocular symptoms reported most frequently by individuals who first limit and then discontinue contact lens wear (Richdale, Sinnott et al. 2007). In one large-scale study, 34% of contact lens wearers were found to have discontinued lens wear at least once for reasons of lens-related discomfort (Pritchard, Fonn et al. 1999). Young et. al reported that, after a period of six months, 55% of patients who had formerly ceased contact lens wear for reasons of discomfort and had been subsequently refit with contact lenses were still actively wearing the refit contact lenses (Young, Veys et al. 2002). The majority of the patients who discontinued contact lens wear for a second time in this study again reported the reason for discontinuation to be discomfort, and the majority those reporting discomfort attributed it to dryness.

Symptoms of ocular discomfort related to dryness have been shown to be reported significantly more frequently while wearing contact lenses than while not wearing contact lenses for the same individuals (Begley, Caffery et al. 2000). Contact lens wearers are 5 times more likely than spectacle wearers and 12 times more likely than emmetropes to report dry eye (Nichols and Sinnott 2006). Dry eye symptoms among contact lens wearers have been shown to be as high as 52.3% and tend to be more frequent than dryness symptoms in non-contact lens wearers (Nichols, Ziegler et al. 2005). One reason for this increased occurrence of dryness complaints in contact lens wearers may be dewetting of the contact lens surface. Successful contact lens wear requires a stable tear film for hydration and lubrication of the contact lens on the
eye (Foulks 2003). In addition to contact lens-related discomfort, short PLTF breakup times have been shown to be associated with a significant reduction in high and middle spatial frequency contrast sensitivity (Thai, Tomlinson et al. 2002). Lipid deposition on contact lenses may play a role in dewetting and increased PLTF evaporation rates.

Non-invasive tear film break-up time and tear meniscus height have been found to be significantly reduced in contact lens-intolerant patients while the number of ocular symptoms reported by these patients has been found to be significantly increased (Glasson, Stapleton et al. 2003; Glasson, Stapleton et al. 2006). These factors have been shown to have high sensitivity but low specificity in predicting whether an individual will experience contact lens intolerance (Glasson, Stapleton et al. 2003). In another study, Glasson et. al. found non-invasive tear film break-up time to be statistically different between tolerant and intolerant contact lens wearers prior to but not after 6 hours of wear of a group IV hydrogel soft contact lens (Glasson, Stapleton et al. 2006). This group also found statistically higher tear flow rates as well as phenol red thread test results in the contact lens tolerant group both before and after the six hours of lens wear (Glasson, Stapleton et al. 2006).

Some tear film components are altered by contact lens wear. Mucin levels in long-term contact lens wear are not found to be altered, but protein levels in the tears are decreased—possibly due to loss of protein via deposition on the contact lens surface or to the occurrence of reflex tearing during the tear collection process for these measurements (Hori, Argueso et al. 2006). A greater amount of degraded lipid was found in the tear film of intolerant than that of tolerant contact lens wearers,
which may be associated with a tenfold greater level of reactive aldehydes in the tear film of these individuals causing lipid oxidation (Glasson, Stapleton et al. 2002).

Contact lens wear has been found to be a risk factor for patient-reported symptoms of dryness (Guillon and Maissa 2005). Though dry eye trends indicate that females and older individuals are more likely to suffer from ocular dryness in general, du Toit et. al. found that contact lens wear may be a stronger influence on dry eye symptoms than either age or gender (du Toit, Situ et al. 2001).

1.6 Contact Lens Material Properties

Contact lens deposition may play a large role in many clinical problems related to lens wear. These include reduced acuity, poor comfort, decreased lens wettability, and increased ocular inflammatory conditions (Jones, Mann et al. 2000). The amount and type of deposition on the contact lens surface is usually predicted by which of the four FDA groups the lens material falls. The four groups are group I, low water content and non-ionic, group II, high water content and non-ionic, group III, low water content and ionic, and group IV, high water content and ionic (Bontempo and Rapp 1994).

Non-ionic and high water content (group II) soft contact lenses show increased lipid deposition (Bontempo and Rapp 1994). Group II soft contact lenses incubated and stirred in an artificial tear solution containing only lipids normally found in the tears—cholesterol, oleic acid, triolein, oleic acid and methyl ester, and cholesterol ester—have been shown with chromatography to bind more lipid than soft contact lenses from the other three groups in vitro (Bontempo and Rapp 1994).
Another study showed that when an artificial tear solution containing lipids and proteins normally found in the tears was used in place of the lipid-only artificial tear solution, group IV (high water content and ionic) soft lenses deposited more lipid than in the original study, and proteins replaced some of the polar lipids bound to group II soft lenses (Bontempo and Rapp 1997). Theoretically, this is due to proteins adhering to group IV lenses numerously enough to create an overall surface charge strong enough to attract lipid binding and to lipids adhering to group II numerously enough to neutralize the overall surface charge, thereby attracting protein binding.

It has been shown that the protein deposition onto group IV materials plateaus over the first 1 to 7 days of lens wear, and lipid deposition on these lenses levels off after one day of wear (Jones, Mann et al. 2000). The deposition of lipid and protein onto the surface of group II materials appears to occur less quickly but does not level off over time (Jones, Mann et al. 2000). The total amount of protein deposited on the lenses has not been shown to be correlated with patient discomfort levels during contact lens wear (Lever, Grooemminger et al. 1995).

Silicone hydrogel contact lenses in particular have been shown to deposit high levels of lipids and low levels of lysozyme compared with hydrogel contact lens materials (Jones, Senchyna et al. 2003). The lysozyme adsorbed to silicone hydrogel contact lenses, however, tends to be highly denatured compared to other group II contact lens materials. This can be a contributive factor to giant papillary conjunctivitis development in silicone hydrogel wearing patients (Jones, Senchyna et al. 2003).
Lipid deposition is thought to be a major problem accompanying silicone hydrogel contact lens wear. The amount and type (polar or non-polar) lipid adsorbed into the lens depends greatly on the lens polymer material (Carney, Nash et al. 2008). Adsorption was found to increase with increasing contact lens water content (Carney, Nash et al. 2008). Either a smooth lens surface with less areas of permeability for lipid materials or a coating on the surface of the contact lens to improve biocompatibility helps to prevent at least some lipid adsorption; this coating may be more important than the FDA grouping in predicting lipid deposition on any given type of silicone hydrogel contact lens (Carney, Nash et al. 2008).

Silicone hydrogel lenses do offer some advantages over hydrogel contact lenses in many cases. Symptomatic hydrogel soft contact lens wearers have reported less discomfort after being refitted into senofilcon A silicone hydrogel lenses (Dumbleton, Keir et al. 2006; Riley, Young et al. 2006). Bulbar hyperemia has also been shown to improve in many cases when the patient is refit into a silicone hydrogel contact lens from a hydrogel lens (Dumbleton, Keir et al. 2006).

Deposits causing hydrophobic areas on the lens surface can lead to a decreased pre-lens tear film thinning time—a factor which has been shown to be related to contact-lens related dry eye (Nichols and Sinnott 2006). Similarly, the pre-lens tear film (PLTF) thickness has been shown to be greater in tolerant contact lens wearers (Nichols and Sinnott 2006). Shorter PLTF thinning time was found to be significantly associated with contact lens-related dry eye (Nichols and Sinnott 2006). Decreased PLTF thinning time could be associated with evaporation and dewetting; tangential tear flow across the lens surface, surface tension gradients, or hydrophobic regions on
the lens surface are all potential causes of contact lens surface dewetting (Nichols and Sinnott 2006). Thinner lipid layers of the PLTF of contact lens wearers suffering from dryness versus PLTF lipid layers of non-dry eye contact lens wearers were found, and these may be associated with lipid binding on the surface of the contact lenses (Nichols and Sinnott 2006). The lipid layer of the tears is generally less than 100nm (Nichols and Sinnott 2006). Subjects wearing low water content contact lenses were shown to have a significantly less dry eye (Nichols and Sinnott 2006). Water content, free water content, and free-to-bound water content ratio were not found to be predictors of on-eye hydrogel soft contact lens dehydration (Tranoudis and Efron 2004).

Low tear potassium levels, one possible cause of tear film instability, have been indicated in cases of heavy lipid deposition on hydrogel contact lenses (Hart, Lane et al. 1987). High dietary protein intake may also contribute to large “jelly bump” lipid deposits on these lenses, possibly due to the body’s conversion of excess protein into lipid and expression of excess lipid via the meibomian glands (Hart, Lane et al. 1987).

Not only material properties but also replacement schedule can impact the comfort of contact lenses. One high water content, nonionic hydrogel soft contact lens was found to be significantly less wettable after three months of wear than after one month of wear in a cross-over study on successful contact lens wearers without dry eye (Jones, Franklin et al. 1996). The lenses worn for only a single month were found to have 60% less protein and 44% less lipid deposition than the lenses worn for three months (Jones, Franklin et al. 1996). There is evidence that protein deposition is an
electrostatic process (Soltys-Robitaille, Ammon et al. 2001). Ionic group III and IV lenses tend to deposit higher quantity of proteins while nonionic group I and II lenses, in particularly group II lenses, tend to deposit the highest quantity of lipids (Jones, Evans et al. 1997). Lysozyme tends to deposit most on group IV lenses, and it tends to deposit least frequently on first-generation silicone hydrogel contact lenses, though that which is deposited is largely denatured—possibly contributing to giant papillary conjunctivitis in silicone hydrogel wearers (Jones, Evans et al. 1997; Suwala, Glasier et al. 2007). Mucins adhere to contact lenses in long-term contact lens wear (Hori, Argueso et al. 2006).

Lens surface coatings, such as polyethylene glycol, have been shown to improve the wettability of the contact lens surface and may help to prevent lysozyme and protein deposition on the lenses (Cheng, Muller et al. 2004). While levels of lipid deposition on silicone hydrogel lenses are much higher than those on regular hydrogel lenses, the level of lysozyme deposited on the silicone hydrogels is much lower than that of hydrogel lenses (Jones, Senchyna et al. 2003). The lysozyme deposited on silicone hydrogels, however, is far more likely to be in a denatured state (Jones, Senchyna et al. 2003).

Contact lens cleaning and soaking solutions may also help to increase the wearability of the lenses by helping to remove debris from the lens surface. Increased PLTF thinning time and better on-eye lens wettability have been observed for hydrogel contact lenses soaked in a multipurpose solution containing hydroxypropyl methylcellulose, a lubricant (Thai, Tomlinson et al. 2002). The amount of subjective improvement in comfort with this solution, however, was not significant; the
participants chosen for this study were all tolerant established soft contact lens
wearers (Thai, Tomlinson et al. 2002). Additionally, Lakshman et al. have found that
use of Opti-Free® RepleniSH™ rewetting drops (Alcon, Fort Worth, TX) reduced
deposition of lysozyme and protein a silicone hydrogel material contact lens
compared to that of a control group (Subbaraman, Bayer et al. 2006). Lenses worn in
conjunction with the use of this rewetting drop also showed less denatured lysozyme
(Subbaraman, Bayer et al. 2006).

1.7 Comfilcon A Material Lenses

Comfilcon A, while classified into FDA group I (non-ionic, water content <
50%), has a water content of 48%. Of the silicone hydrogel materials currently on the
market, these lenses are some of the highest water content available. The
manufacturers of Biofinity, a comfilcon A material lens, claim that this relatively high
water content helps to improve on-eye comfort for wearers. Comfilcon A silicone
hydrogel contact lenses have been shown to be subjectively preferred to both
lotrafilcon A and balafilcon A in regard to visual performance and end-of-day lens
comfort, respectively (Brennan, Coles et al. 2007).

This study seeks to determine whether this claim of superior contact lens
comfort translates to a measurable difference in tear parameters, a decrease in
subjective ocular dryness symptoms, or a measurable difference in total contact lens-
extracted lipid quantity for a group of participants who either do or do not report
suffering from contact lens-related dry eye. Better comfort is expected with these
lenses, and, based on previous studies, this comfort is expected to be related to a decreased PLTF thinning rate.
Chapter 2: Methods

2.1 Participant Selection

Current soft contact lens wearers either experiencing or not experiencing contact lens-related ocular dryness and over the age of 18 years were recruited via email, flyer, and word-of-mouth advertising. All potential participants were asked whether or not they felt that they had contact lens-related dryness in their habitual contact lenses via face-to-face contact or phone interview with the examiner at the time that the first study visit appointment was made. Definitive classification of participants into the non-dry eye group or the contact lens-related dry eye group (referred to as “dry eye group” hereafter) was based on the participants’ scores on an ocular dryness survey, the Contact Lens Dry Eye Questionnaire (CLDEQ), at the time of the first visit. Female volunteers were asked whether they were currently pregnant or lactating; those that responded positively to either question were not included in the study. Subjects already wearing comfilcon A soft contact lenses (Biofinity™ DW by CooperVision®, San Francisco, CA), having myopia exceeding -10.00 diopters or less severe than -0.50 diopters in either eye, having hypermetropia in either eye, or having astigmatism exceeding -0.75 diopters in either eye were excluded from the study. Dry eye or non-dry eye status was confirmed using the CLDEQ where 1.29 was used as a cutpoint to categorize participants into the dry eye
group. All participants gave signed informed consent in accordance with the Declaration of Helsinki and signed a HIPAA agreement before they were enrolled.

Thirty-five total participants were enrolled. Seventeen participants experiencing contact lens-related dryness and 17 normal contact lens wearers completed the study. One normal contact lens wearer dropped out of the study due to an unrelated health concern. Interferometry data from two normals and two contact lens-related dry eye participants was lost due to an equipment misalignment, but CLDEQ and lipid analysis data from these participants was available for analysis.

2.2 Study Visits

The study consisted of a total of two visits per participant separated by 28 ± 4 days.

2.2a Visit 1

The participants reported to the first visit wearing their habitual soft contact lenses. Their contact lens-corrected monocular visual acuities were measured using a projected Snellen chart. The wearing schedules, replacement schedules, and brand name of each participant’s habitual soft contact lenses were recorded according to self-report. The Contact Lens Dry Eye Questionnaire Short Form (CLDEQ) was administered, interferometry was performed, and each participant’s habitual lenses were collected.

After collection of the participant’s contact lenses, a balanced sphero-cylindrical refraction was performed prior to a biomicroscopic evaluation of the anterior ocular health including the use of sodium fluorescein (BioGlo™ Fluorescein Sodium Ophthalmic Strips by Wilson Ophthalmics, Mustang, OK) to assess the corneal surface health. The fluorescein was then rinsed from the eye with sterile saline, and the comfilcon
A study lenses were fit according to the refraction results and assessed via biomicroscope. The material, brand name, and manufacturer of the study contact lenses were withheld from participants until the end of the second study visit as not to help prevent possible bias.

2.2b Visit 2

The participants reported for the second study visit wearing the study contact lenses. Contact lens-corrected monocular visual acuities were measured with a projected Snellen chart, a second CLDEQ was administered, interferometry was performed, and the study lenses were collected.

2.3 Lens Care System and Contact Lens Wearing Schedule

The participants were given a 30 day supply of OptiFree® RepleniSH® Multi-Purpose Disinfecting Solution (by Alcon Laboratories, Inc., Fort Worth, TX) and verbally instructed to clean the study lenses nightly by the rinse (“no rub”) method detailed on the solution packaging, which the participant was also given. These directions included rinsing each side of the lens with solution for 5 seconds and soaking the lenses for at least 6 hours in fresh solution. Each participant was instructed to use a new sterile screw top contact lens case, which was provided. Finally, participants were reminded of the daily wear wearing schedule of the study contact lenses and told not to use the lenses for overnight wear. The participants were instructed to wear the study lenses with the same frequency (excluding overnight wear) and for the same daily duration as they would normally wear their habitual lenses. No restrictions on topical ocular lubricants or medications were imposed on participants.
2.4 Primary Outcome Data: Pre-Lens Tear Film Thinning Rate, Lipid Layer Thickness, and Initial Pre-Lens Tear Film Thickness

Pre-lens tear film thinning rate (PLTF thinning rate), lipid layer thickness (LLT), and initial pre-lens tear film thickness (PLTF thickness) were measured using interferometry. Two interferometry calibration readings were performed before and after each participant’s interferometry reading was recorded. A calibration reading was first performed using a plano convex lens (PCX), and then a background reading was performed with no lens in place. For the initial study visit of the first ten participants, only the PCX reading was taken; this was due to a change in interferometer use protocol during the course of the study. All other visits, including the second study visits of the aforementioned ten participants, both the PCX and background measurements were made. After the two calibration measurements were recorded, two interferometry measurements were taken on the right eye only of each subject while wearing either their habitual soft contact lenses (first study visit) or the study lenses (second study visit). At the beginning of each measurement, each participant was instructed to blink once and then hold their eyes open until the end of the automated twenty second measurement period. The interferometer recorded 10 PLTF thickness and LLT readings per second for a total of 200 readings per measurement. All readings were taken under the same room illumination conditions, and the temperature and relative humidity of the room was recorded for each interferometry reading.

The interferometer measures the reflection of a beam of light off of the different refractive interfaces on the ocular surface—specifically the outermost lipid layer reflection, the interface between the lipid layer and the aqueous/mucin PLTF layer, and
off of the surfaces of the contact lens and cornea (Nichols and King-Smith 2003; Nichols,
Mitchell et al. 2005). Depending on the thicknesses of these different layers, the
reflections cause varying degrees of constructive or destructive interference in the
reflected beams. These data can be recorded and analyzed to determine the thicknesses of
the different layers of the tear film.

The interferometry data was processed by Fourier transform software and
analyzed with data analysis software (SigmaPlot® by Systat Software, Inc., San Jose,
CA) to determine the average PLTF thinning rate, LLT, and PLTF thickness of each
participant. The average PLTF thinning rate was taken to be the average of the PLTF
thinning rates of the two interferometry readings recorded on the right eye of each
participant. Each of these PLTF thinning rates was read beginning two seconds after the
blink to the end of the 20 second measurement interval. The average LLT was taken to be
the average LLT of the two interferometry readings at each visit. The average PLTF
thickness was taken from the two PLTF thickness values as recorded by the
interferometer at two seconds after the blink (or the first valid PLTF thickness value per
interferometry reading) for each visit. PLTF thinning rate, LLT, and PLTF thickness
values deviating from the mean for either group at each visit by an absolute value
exceeding four standard deviations were considered outliers and were excluded from data
analysis.
2.5 Secondary Outcome Data: Contact Lens Dry Eye Questionnaire (CLDEQ)

Results

The Contact Lens Dry Eye Questionnaire Short Form (CLDEQ) was administered to each participant at both the first and second study visit. The CLDEQ is a survey designed to assess the presence or absence of contact lens-related dryness in individuals and consists of three questions (Nichols, Mitchell et al. 2002; Chalmers and Begley 2006). The participant is asked to subjectively rate the frequency and severity of their dryness and photophobia symptoms (if any) during periods of contact lens wear over the course of the two preceding weeks. The participant is also asked to state whether they feel that they experience contact lens-related dry eye the third question—they may answer “yes,” “no,” or “unsure.” For the purposes of this study, an answer of “unsure” was treated as an answer of “no.” The survey is then scored using a fixed scoring protocol, and each participant is thereby assigned a status of non-dry eye or experiencing contact lens-related dryness.

Possible CLDEQ scores range from 0.08 to 2.30. Scores over 1.29 were classified as contact lens-related dryness as were scores over 0.03 if the patient also responded “yes” to the third question.

2.6 Tertiary Outcome Data: Total Contact Lens-Extracted Lipid Analysis

2.6a Lens Collection

Both the habitual (first visit) and study soft contact lenses (second visit) were collected from the participants’ right eyes only by a gloved examiner using alcohol-sterilized plastic forceps. These were placed into labeled clear glass screw-top collection
vials and stored immediately in a cooler of ice until the end of each study visit (no longer than 25 minutes), at which time they were transported to a -80 degree Celsius freezer until lipid analysis was performed.

### 2.6b Lipid Extraction

The frozen contact lens samples in their vials were first allowed to thaw for 30 minutes at room temperature. Lipids were then extracted from each lens by pipetting 250µL of a 1:1 chloroform/methanol solution into each clear glass vial. The solution was allowed to interact with the lens for 30 seconds in the closed vial under gentle agitation, and then 100µL of the solution was pipetted into screw-top amber glass collection vials using a fresh pipette tip for each sample. These samples were allowed to air dry in uncovered vials under a ventilation hood overnight and then covered and frozen until the lipid assay was performed. The contact lenses in the clear glass vials were discarded.

### 2.6c Lipid Standard Preparation

Oleamide was used as the standard lipid for the lipid assay. A stock solution of 10mg oleamide in 100mL chloroform was used to make oleamide/chloroform dilutions directly in screw-top amber glass collection vials identical to those used in the lipid extraction process above. Two vials were produced each containing one of following six microgram amounts of oleamide: 5.0µg, 2.0µg, 1.0µg, 0.5µg, 0.25µg, 0.0µg. These, like the lipid samples, were allowed to air dry in uncovered vials under a ventilation hood overnight and then covered and frozen until the lipid assay was performed.
2.6d Lipid Assay

All lipid samples and the oleamide standards were allowed to thaw at room temperature for 30 minutes. Twenty µL of 34N sulfuric acid solution was then pipetted into each amber vial. The vials were then incubated at 100 degrees Celsius for ten minutes and subsequently cooled to room temperature in a water bath for an additional ten minutes. One hundred µL of the assay reagent, 1.2mg/mL vanillin in 68% phosphoric acid, was then pipetted into each vial and mixed by low speed vortex for 1-2 seconds. The reagent was then allowed to react at room temperature for 45 minutes.

At the end of this time, 90µL was pipetted from each vial (using a new pipette tip each time) into one well of the assay plate (Corning® 96 Well Clear Round Bottom UV-Transparent Microplate, by Corning Incorporated, Corning, NY). The assay plate was then inserted into the reader (Infinite M 200, by TECAN Systems, Inc., San Jose, CA) and the absorbance read at 530nm.

The absorbance of the standard blank (0.0µg oleamide) was subtracted from each standard and lipid sample absorbance value. The average of each duplicate oleamide standard was then used to generate a lipid standard curve. From this curve, the total lipid (in µL) was calculated for each lipid sample.

2.7 Statistical Methods

2.7a Comparisons of Means

The Wilcoxon Signed Rank Test was used to compare means within groups, T-Test was used to compare means between study visits, and the Mann-Whitney Test was used to compare means within study visits for each set of data save total contact lens-
extracted lipid for which the T-Test was not necessary as no between study visit comparison of means was warranted.

2.7b Correlations

As the only significant differences found between the non-dry eye and dry eye groups were CLDEQ scores at the first study visit, Pearson correlation was used to determine the relationships between LLT and PLTF thinning rate, LLT and PLTF thickness, LLT and contact lens-extracted lipid quantity, and LLT and the number of days for which each participants’ habitual contact lenses were worn. These correlations were each determined for the entire study sample at both the first and second study visits except for the last, which was only determined for the first study visit.

As a significant difference was found between the non-dry eye and dry eye groups’ CLDEQ scores at the first study visit, Spearman Correlations were used to determine the relationships between CLDEQ score and PLTF thinning rate, CLDEQ score and LTT, CLDEQ score and PLTF thickness, and CLDEQ score and contact lens-extracted lipid quantity for this visit. Pearson correlations were used to evaluate the equivalent relationships for the second study visit, as no significant differences were found between the two groups at this visit.

As the only significant differences found between the non-dry eye and dry eye groups were CLDEQ scores at the first study visit, Pearson correlation was used to determine the relationships between contact lens-extracted lipid quantity and PLTF thinning rate (determined for the entire study sample at both the first and second study visits) and between contact lens-extracted lipid quantity and number of days for which
the habitual contact lenses were worn (determined for the entire study sample for the first study visit only).
Chapter 3: Results

3.1 Subject Characteristics

Thirty five participants provided informed consent and were enrolled in this study. Of these participants, 34 completed both the first study visit as well as the second study visit. One participant completed only the first study visit and had to discontinue participation due to an unrelated medical condition. Five subjects (14.3%) were male. Participants ranged in age from 19 to 50 with an average age of 27.0 ± 7.1 years. The average time lapse between the first and second study visits was 27.4 ± 1.4 days.

3.2 First Study Visit Habitual Contact Lens Characteristics

The brands of habitual contact lenses worn at the first study visit are summarized in Figure 1. The FDA groupings of the habitual contact lens materials are summarized in Figure 2. The average number of days that the habitual contact lenses had been worn at the time of the first study visit was 14.4 ± 11.9 days.
Figure 1. Summary of habitual contact lens brands worn at first study visit.
Figure 2. Summary of habitual contact lens material by FDA grouping worn at first study visit.

3.3 Primary Outcome Data: Pre-Lens Tear Film Thinning Rate (PLTF Thinning Rate), Lipid Layer Thickness (LLT), and Initial Pre-Lens Tear Film Thickness (PLTF Thickness)

Interferometry was performed on each participant at each study, and PLTF thinning rate, LLT, and PLTF thickness values were calculated from these measurements.
3.3a Within Group Comparisons Between Study Visits

The mean PLTF thinning rates for the non-dry eye and dry eye groups at the first study visit were 8.50 ± 5.28 µm/min and 6.79 ± 6.07 µm/min, respectively; they were 8.40 ± 6.79 µm/min and 8.61 ± 5.05 µm/min at the second study visit. No significant differences were found between the first and second study visits within each group (Z = -0.04, p-value = 0.97 for non-dry eye group, Z = -1.70, p-value = 0.09 for dry eye group). These data are summarized in Table 1 for the non-dry eye group and Table 2 for the dry eye group.

The mean LLT for the non-dry eye and dry eye groups at the first study visit were 21.55 ± 9.32 nm and 28.25 ± 18.70 nm, respectively; they were 20.12 ± 6.77 nm and 23.26 ± 11.52 nm at the second study visit. No significant differences were found between the first and second study visits within each group (Z = -0.59, p-value = 0.55 for non-dry eye group, Z = -0.68, p-value = 0.50 for dry eye group). These data are summarized in Table 1 for the non-dry eye group and Table 2 for the dry eye group.

The mean PLTF thickness for the non-dry eye and dry eye groups at the first study visit were 3.44 ± 1.72 nm and 2.87 ± 0.84 nm, respectively; they were 3.41 ± 1.37 nm and 2.46 ± 1.02 nm at the second study visit. No significant differences were found between the first and second study visits within each group (Z = -0.73, p-value = 0.46 for non-dry eye group, Z = -0.97, p-value = 0.33 for dry eye group). These data are summarized in Table 1 for the non-dry eye group and Table 2 for the dry eye group.
Table 1: Summary of PLTF thinning rates, LLT, and PLTF thicknesses between the first and second study visits for non-dry eye group and within group p-values.¹

<table>
<thead>
<tr>
<th>Non-Dry Eye Group</th>
<th>Study Visit</th>
<th>Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTF Thinning Rate (µm/min)</td>
<td>First n = 15</td>
<td>8.50 ± 5.28</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>Second n = 17</td>
<td>8.40 ± 6.79</td>
<td></td>
</tr>
<tr>
<td>LLT (nm)</td>
<td>First n = 15</td>
<td>21.55 ± 9.32</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>Second n = 17</td>
<td>20.12 ± 6.77</td>
<td></td>
</tr>
<tr>
<td>PLTF Thickness (µm)</td>
<td>First n = 15</td>
<td>3.44 ± 1.72</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Second n = 17</td>
<td>3.41 ± 1.37</td>
<td></td>
</tr>
</tbody>
</table>

¹ Interferometry was performed on each participant at each study visit according to the method described previously except for participant 18, who completed only the first study visit. The first visit interferometry readings were unusable for participants 2, 3, 4, and 13 due to a misalignment of the device. The interferometry values for the second study visit for participant 27 were the only values excluded for this reason.

Table 2: Summary of PLTF thinning rates, LLT, and PLTF thicknesses between the first and second study visits for dry eye group and within group p-values.

<table>
<thead>
<tr>
<th>Dry Eye Group</th>
<th>Study Visit</th>
<th>Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTF Thinning Rate (µm/min)</td>
<td>First Visit n = 15</td>
<td>6.79 ± 6.07</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Second Visit n = 17</td>
<td>8.62 ± 5.05</td>
<td></td>
</tr>
<tr>
<td>LLT (nm)</td>
<td>First n = 15</td>
<td>28.25 ± 18.70</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Second n = 17</td>
<td>23.26 ± 11.52</td>
<td></td>
</tr>
<tr>
<td>PLTF Thickness (µm)</td>
<td>First n = 15</td>
<td>2.87 ± 0.84</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Second n = 17</td>
<td>2.46 ± 1.02</td>
<td></td>
</tr>
</tbody>
</table>
Figure 3. Boxplot showing the difference in PLTF thinning rate (second visit – first visit) between the first and second study visits within each group.
Figure 4. Boxplot showing the difference in LLT (second visit – first visit) between the first and second study visits within each group.
3.3b Entire Study Sample Comparison Between Study Visits

The mean PLTF thinning rates for the first and second study visits for the entire study sample were 7.65 ± 5.66 µm/min and 8.51 ± 5.89 µm/min respectively. The PLTF thinning rates for the entire study sample showed no significant difference between the two study visits (t = 0.60, 28 df, p = 0.56). This data is summarized in Table 3.

The mean LLT for the first and second study visits for the entire study sample were 24.90 ± 14.91 nm and 21.69 ± 9.44 nm respectively. The LLT for the entire study
sample showed no significant difference between the two study visits \((t = 1.06, 28 \text{ df}, p = 0.30)\). This data is summarized in Table 3.

The mean PLTF thicknesses for the first and second study visits for the entire study sample were \(3.16 \pm 1.36 \, \mu m\) and \(2.93 \pm 1.28 \, \mu m\) respectively. The PLTF thicknesses for the entire study sample showed no significant difference between the two study visits \((t = 0.49, 28 \text{ df}, p = 0.63)\). This data is summarized in Table 3.

<table>
<thead>
<tr>
<th>Study Visit</th>
<th>Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTF Thinning Rate ((\mu m/min))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First (n = 30)</td>
<td>7.65 ± 5.66</td>
<td>0.56</td>
</tr>
<tr>
<td>Second (n = 34)</td>
<td>8.51 ± 5.89</td>
<td></td>
</tr>
<tr>
<td>LLT (nm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First (n = 30)</td>
<td>24.90 ± 14.91</td>
<td>0.30</td>
</tr>
<tr>
<td>Second (n = 34)</td>
<td>21.69 ± 9.44</td>
<td></td>
</tr>
<tr>
<td>PLTF Thickness ((\mu m))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First (n = 30)</td>
<td>3.16 ± 1.36</td>
<td>0.63</td>
</tr>
<tr>
<td>Second (n = 34)</td>
<td>2.93 ± 1.28</td>
<td></td>
</tr>
</tbody>
</table>

3.3c **Within Study Visit Comparisons Between Groups**

No significant difference was found between the PLTF thinning rates of the non-dry eye and dry eye groups for either the first or second study visits \((U = 77.0, p = 0.14\) for first visit, \(U = 137.0, p = 0.80\) for second visit). The test also showed no significant difference between the LLT of the groups at either visit \((U = 91.0, p = 0.37\) for first visit, \(U = 134.0, p = 0.72\) for second visit). Finally, no significant difference between the PLTF thicknesses of the non-dry eye and dry eye groups for either visit \((U = 95.0, p = 0.47\) for
first visit, \( U = 90.0, p = 0.06 \) for second visit). The PLTF thinning rate, LLT, and PLTF thickness means and test statistics for the first visit are summarized in Table 4, and those for the second visit are summarized in Table 5.

Table 4: Summary of PLTF thinning rates, LLT, and PLTF thicknesses between the non-dry eye and dry eye groups for the first study visit and within visit p-values.

<table>
<thead>
<tr>
<th>First Study Visit</th>
<th>Study Visit</th>
<th>Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTF Thinning Rate (( \mu \text{m/min} ))</td>
<td>Non-Dry Eye</td>
<td>8.50 ± 5.28</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>6.79 ± 6.07</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LLT (nm)</td>
<td>Non-Dry Eye</td>
<td>21.55 ± 9.32</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>28.25 ± 18.70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLTF Thickness (( \mu \text{m} ))</td>
<td>Non-Dry Eye</td>
<td>3.44 ± 1.72</td>
<td>0.47</td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>2.87 ± 8.38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5: Summary of PLTF thinning rates, LLT, and PLTF thicknesses between the non-dry eye and dry eye groups for the second study visit and within visit p-values.

<table>
<thead>
<tr>
<th>Second Study Visit</th>
<th>Study Visit</th>
<th>Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTF Thinning Rate (( \mu \text{m/min} ))</td>
<td>Non-Dry Eye</td>
<td>8.40 ± 6.79</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>8.62 ± 5.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LLT (nm)</td>
<td>Non-Dry Eye</td>
<td>20.12 ± 6.77</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>23.26 ± 11.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLTF Thickness (( \mu \text{m} ))</td>
<td>Non-Dry Eye</td>
<td>3.41 ± 1.37</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>2.46 ± 1.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 6. Boxplot showing PLTF thinning rates for non-dry eye and dry eye groups at (a) the first and (b) the second study visits.

Figure 7. Boxplot showing LLT for non-dry eye and dry eye groups at (a) the first and (b) the second study visits.
3.4 Contact Lens Dry Eye Questionnaire (CLDEQ) Scores

The CLDEQ, as previously stated, was administered to each participant at both the first and second study visits.

3.4a Within Group Comparisons Between Study Visits

The mean CLDEQ scores at the first study visit were 0.68 ± 0.37 for the non-dry eye group and 1.54 ± 0.55 for the dry eye group. The mean CLDEQ scores at the second visit were 0.87 ± 0.61 for the non-dry eye group and 1.37 ± 0.89 for the dry eye group. CLDEQ scores within the non-dry eye and dry eye groups showed no significant differences between the first and second study visits (Z = -1.28, p = 0.20 and Z = -0.57, p = 0.57 for the non-dry eye and dry eye groups respectively). This data is summarized in Table 6.
Table 6: Summary of CLDEQ scores between the first and second study visits within each group and within group p-values.

<table>
<thead>
<tr>
<th></th>
<th>CLDEQ</th>
<th>Mean Score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Dry Eye Group</td>
<td>First Visit n = 18</td>
<td>0.68 ± 0.37</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>Second Visit n = 17</td>
<td>0.87 ± 0.61</td>
<td></td>
</tr>
<tr>
<td>Dry Eye Group</td>
<td>First Visit n = 17</td>
<td>1.54 ± 0.55</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>Second Visit n = 17</td>
<td>1.37 ± 0.89</td>
<td></td>
</tr>
</tbody>
</table>

Figure 9. Boxplot showing the change in CLDEQ score between the first and second study visits (second visit – first visit) within each group.
3.4b Entire Study Sample Comparison Between Study Visits

The mean CLDEQ scores for the first and second study visits for the entire study sample were 1.10 ± 0.64 and 1.12 ± 0.79 respectively. The CLDEQ scores for the entire study sample showed no significant difference between the two study visits (t = -0.12, 33 df, p = 0.91). This data is summarized in Table 7.

Table 7: Summary of CLDEQ scores and p-value for entire study sample between the first and second study visits.

<table>
<thead>
<tr>
<th></th>
<th>Mean Score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Visit CLDEQ</td>
<td>1.10 ± 0.64</td>
<td></td>
</tr>
<tr>
<td>n = 35</td>
<td></td>
<td>0.91</td>
</tr>
<tr>
<td>Second Visit CLDEQ</td>
<td>1.12 ± 0.79</td>
<td></td>
</tr>
<tr>
<td>n = 34</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.4c Within Study Visit Comparisons Between Groups

The CLDEQ scores at the first study visit of the non-dry eye and dry eye group were shown to be significantly different from one another (U = 28.0, p <0.0001). No significant difference was found between the CLDEQ scores of the two groups for the second study visit (U = 91.5, p = 0.07). These data are summarized in Table 8.
Table 8: Summary of CLDEQ scores between the non-dry eye and dry eye groups within each study visit and within visit p-values.

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>Mean Score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Visit CLDEQ</td>
<td>Non-Dry Eye</td>
<td>0.68 ± 0.37</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>n = 18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>1.54 ± 0.55</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second Visit CLDEQ</td>
<td>Non-Dry Eye</td>
<td>0.87 ± 0.61</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dry Eye</td>
<td>1.37 ± 0.89</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 10. Boxplots showing CLDEQ scores within each group (a) at the first study visit and (b) at the second study visit.

3.5 Total Contact Lens-Extracted Lipid Analysis

Contact lens collection procedures and lipid analysis techniques were performed.

3.5a Within Group Comparisons Between Study Visits

The mean amount of contact lens-extracted lipid at the first study visit was 0.12 ± 0.18 µg/lens for the non-dry eye group and 0.17 ± 0.34 µg/lens for the dry eye group. The mean contact lens-extracted lipid at the second study visit was 0.30 ± 0.20 µg/lens for the
non-dry eye group and 0.28 ± 0.18 μg for the dry eye group. Total extracted lipid amounts showed a significant difference for the non-dry eye group between the first and second study visits (Z = -2.69, p = 0.01) but not for the dry eye group (Z = -1.66, p = 0.10). This data is summarized in Table 9.

Table 9: Summary of extracted lipid quantities between the first and second study visits within each group and within group p-values.²

<table>
<thead>
<tr>
<th></th>
<th>Study Visit</th>
<th>Mean Lipid</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Dry Eye Group (µg/lens)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First n = 18</td>
<td></td>
<td>0.12 ± 0.18</td>
<td>0.01</td>
</tr>
<tr>
<td>Second n = 17</td>
<td></td>
<td>0.30 ± 0.20</td>
<td></td>
</tr>
<tr>
<td><strong>Dry Eye Group (µg/lens)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First n = 17</td>
<td></td>
<td>0.17 ± 0.34</td>
<td>0.10</td>
</tr>
<tr>
<td>Second n = 17</td>
<td></td>
<td>0.28 ± 0.18</td>
<td></td>
</tr>
</tbody>
</table>

² Lenses were collected for each participant at both the first and second study visits save for participant 18, who completed only the first study visit.
3.5b Within Study Visit Comparisons Between Groups

No significant difference was found between the total contact lens-extracted lipid quantities of the two groups for either the first or the second study visits (U = 141.0, p = 0.67 for first visit, U = 132.5, p = 0.68 for second visit). These data are summarized in Table 10.
Table 10: Summary of total contact lens-extracted lipid quantities between the non-dry eye and dry eye groups within each study visit and within visit p-values.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Lipid</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Visit Lipid</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(µg/lens)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Dry Eye n = 18</td>
<td>0.12 ± 0.18</td>
<td>0.67</td>
</tr>
<tr>
<td>Dry Eye n = 17</td>
<td>0.17 ± 0.34</td>
<td></td>
</tr>
<tr>
<td><strong>Second Visit Lipid</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(µg/lens)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Dry Eye n = 17</td>
<td>0.30 ± 0.20</td>
<td>0.68</td>
</tr>
<tr>
<td>Dry Eye n = 17</td>
<td>0.28 ± 0.18</td>
<td></td>
</tr>
</tbody>
</table>

(a) Figure 12. Boxplots showing total contact lens-extracted lipid quantities within each group (a) at the first study visit and (b) at the second study visit.

3.6 Relationship Between Lipid Layer Thickness (LLT) and Pre-Lens Tear Film Thinning Rate (PLTF Thinning Rate), Pre-Lens Tear Film Thickness (PLTF Thickness), Contact Lens-Extracted Lipid Quantity, and Number of Days for Which the Habitual Contact Lenses Were Worn

A significant correlation was found between LLT and PLTF thinning rate for the first visit ($r = -0.39$, $p = 0.03$), but not for the second visit ($r = -0.14$, $p = 0.43$). No
significant correlations were found between LLT and PLTF thickness at either visit (r = 0.11, p = 0.55 and r = -0.10, p = 0.57, respectively). No significant correlations were found between LLT and contact lens-extracted lipid quantity at the first (r = 0.00, p = 0.99) or second (r = 0.18, p = 0.31) visits. Finally, no significant correlation was found between LLT and the number of days for which each participants’ habitual contact lenses were worn at the first study visit (r = 0.14, p = 0.48). These results are summarized in Table 11, and scatterplots of these data are shown in Figure 13.

Table 11: Summary of correlations between LLT and PLTF thinning rate, LLT and PLTF thickness, and LLT and contact lens-extracted lipid quantity for each study visit, and between LLT and the number of days for which each participants’ habitual contact lenses were worn for the first study visit.

<table>
<thead>
<tr>
<th>First Visit Correlations (n = 30)</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLT PLTF Thinning Rate</td>
<td>-0.39</td>
<td>0.03</td>
</tr>
<tr>
<td>PLTF Thickness</td>
<td>0.11</td>
<td>0.55</td>
</tr>
<tr>
<td>Extracted Lipid</td>
<td>0.00</td>
<td>0.99</td>
</tr>
<tr>
<td>Days Habitual Lenses Worn</td>
<td>0.14</td>
<td>0.48</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second Visit Correlations (n = 34)</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLT PLTF Thinning Rate</td>
<td>-0.14</td>
<td>0.43</td>
</tr>
<tr>
<td>PLTF Thickness</td>
<td>-0.10</td>
<td>0.57</td>
</tr>
<tr>
<td>Extracted Lipid</td>
<td>0.18</td>
<td>0.31</td>
</tr>
</tbody>
</table>
Figure 13. Scatterplots showing the correlations between (a) LLT and PLTF thinning rate for the first visit, (b) LLT and PLTF thinning rate for the second visit, (c) LLT and PLTF thickness for the first visit, (d) LLT and PLTF thickness for the second visit, (e) LLT and contact lens-extracted lipid quantity for each the first visit, (f) LLT and contact lens-extracted lipid quantity for each the second visit, and (g) LLT and the number of days for which each participants’ habitual contact lenses were worn for the first study visit.
Figure 13 continued

3.7 Relationship Between Contact Lens Dry Eye Questionnaire (CLDEQ) Scores and Pre-Lens Tear Film Thinning Rate (PLTF Thinning Rate), Lipid Layer Thickness (LLT), Pre-Lens Tear Film Thickness (PLTF Thickness), and Contact Lens-Extracted Lipid Quantity

A significant correlation was found between CLDEQ score and PLTF thinning rate for the dry eye group ($r_s = 0.55$, $p = 0.03$) but not for the non-dry eye group ($r_s = -0.11$, $p = 0.71$) at the first visit. A significant correlation was found between CLDEQ score and LLT for the non-dry eye group ($r_s = -0.53$, $p = 0.04$) but not for the dry eye
group \( (r_s = -0.18, \ p = 0.53) \) at the first visit. No significant correlations were found for either group between either CLDEQ score and PLTF thickness \( (r_s = 0.01, \ p = 0.96 \) for the non-dry eye group; \( r_s = 0.00, \ p = 1.00 \) for the dry eye group) or between CLDEQ score and contact lens-extracted lipid quantity \( (r_s = -0.35, \ p = 0.16 \) for the non-dry eye group; \( r_s = -0.14, \ p = 0.60 \) for the dry eye group) at the first visit. These results are summarized in Table 12, and scatterplots of these data are shown in Figure 14.

No significant correlations were found between CLDEQ score and PLTF thinning rate \( (r = 0.11, \ p = 0.53) \), between CLDEQ score and LLT \( (r = -0.12, \ p = 0.51) \), between CLDEQ score and PLTF thickness \( (r = -0.31, \ p = 0.08) \), or between CLDEQ score and contact lens-extracted lipid quantity \( (r = 0.02, \ p = 0.91) \) at the second visit. These results are summarized in Table 13, and scatterplots of these data are shown in Figure 15.

Table 12: Summary of correlations between CLDEQ score and PLTF thinning rate, CLDEQ score and LTT, CLDEQ score and PLTF thickness, and CLDEQ score and contact lens-extracted lipid quantity for each group at the first visit.

<table>
<thead>
<tr>
<th>First Visit Correlations</th>
<th>Non-Dry Eye Group</th>
<th>Dry Eye Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r_s )</td>
<td>p-value</td>
</tr>
<tr>
<td>CLDEQ PLTF Thinning Rate ( (n=15) )</td>
<td>-0.11</td>
<td>0.71</td>
</tr>
<tr>
<td>LLT ( (n=15) )</td>
<td>-0.53</td>
<td>0.04</td>
</tr>
<tr>
<td>PLTF Thickness ( (n=15) )</td>
<td>0.01</td>
<td>0.96</td>
</tr>
<tr>
<td>Extracted Lipid ( (n=18 ) for Non-Dry Eye Group; ( n=17 ) for Dry Eye Group)</td>
<td>-0.35</td>
<td>0.16</td>
</tr>
</tbody>
</table>

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Table 13: Summary of Pearson Correlations between CLDEQ score and PLTF thinning rate, CLDEQ score and LTT, CLDEQ score and PLTF thickness, and CLDEQ score and contact lens-extracted lipid quantity for the entire study sample at the second visit.

<table>
<thead>
<tr>
<th>Second Visit Correlations (n = 34)</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLDEQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLTF Thinning Rate</td>
<td>0.11</td>
<td>0.53</td>
</tr>
<tr>
<td>LLT</td>
<td>-0.12</td>
<td>0.51</td>
</tr>
<tr>
<td>PLTF Thickness</td>
<td>-0.31</td>
<td>0.08</td>
</tr>
<tr>
<td>Extracted Lipid</td>
<td>0.02</td>
<td>0.91</td>
</tr>
</tbody>
</table>
Figure 14. Scatterplots showing the correlations between CLDEQ score and PLTF thinning rate for the non-dry eye (a) and dry eye (b) groups at the first study visit, CLDEQ score and LTT for the non-dry eye (c) and dry eye (d) groups at the first study visit, CLDEQ score and PLTF thickness for the non-dry eye (e) and dry eye (f) groups at the first study visit, and CLDEQ score and contact lens-extracted lipid quantity for the non-dry eye (g) and dry eye (h) groups at the first study visit.
Figure 14 continued
Figure 15. Scatterplots showing the correlations between (a) CLDEQ score and PLTF thinning rate, (b) CLDEQ score and LTT, (c) CLDEQ score and PLTF thickness, and (d) CLDEQ score and contact lens-extracted lipid quantity for the entire study sample at the second visit.

3.8 Relationship Between Contact Lens-Extracted Lipid Quantity and Pre-Lens Tear Film Thinning Rate (PLTF Thinning Rate) and Number of Days for Which the Habitual Contact Lenses Were Worn

No significant correlation was found between contact lens-extracted lipid quantity and PLTF thinning rate at either the first \( (r = -0.11, p = 0.57) \) or second \( (r = 0.30, p = 0.09) \) study visits. A significant correlation was found, however, between contact lens-
extracted lipid quantity and number of days for which the habitual contact lenses were worn \( (r = 0.37, \ p = 0.03) \). These results are summarized in Table 14, and scatterplots of these data are shown in Figure 16.

Table 14: Summary of correlations between total contact lens-extracted lipid and PLTF thinning rate at the first study visit, total contact lens-extracted lipid and the number of days for which each participants’ habitual contact lenses were worn for the first study visit, and total contact lens-extracted lipid and PLTF thinning rate at the second study visit.

<table>
<thead>
<tr>
<th>First Visit</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracted Lipid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLTF Thinning Rate (n = 30)</td>
<td>-0.11</td>
<td>0.57</td>
</tr>
<tr>
<td>Days Habitual Lenses Worn (n = 34)</td>
<td>0.37</td>
<td>0.03</td>
</tr>
<tr>
<td>Second Visit</td>
<td>r</td>
<td>p-value</td>
</tr>
<tr>
<td>Extracted Lipid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLTF Thinning Rate (n = 34)</td>
<td>0.30</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Figure 16. Scatterplots showing the correlations between (a) total contact lens-extracted lipid and PLTF thinning rate at the first study visit, (b) total contact lens-extracted lipid and PLTF thinning rate at the second study visit, (c) and total contact lens-extracted lipid and the number of days for which each participants’ habitual contact lenses were worn for the first study visit.
Chapter 4: Discussion

4.1 Pre-Lens Tear Film Thinning Rate (PLTF Thinning Rate), Lipid Layer Thickness (LLT), and Initial Pre-Lens Tear Film Thickness (PLTF Thickness)

No significant differences were found within group, between study visits, or within study visits for the non-dry eye and dry eye PLTF thinning rates, LLT, or PLTF thicknesses. These findings are interesting in that many researchers have studied relationships between these parameters and the presence or absence of dry eye symptoms. Nichols, et. al (Nichols, Nichols et al. 2004) found no relationship between the frequency of signs and symptoms of dryness in dry eye disease sufferers when subjective symptomology, tear meniscus height, meibomian gland health, tear film break-up time, sodium fluorescein and rose bengal staining, and Schirmer and phenol red thread tear volume were tested. It has been found that patient surveys are the most repeatable test for dry eye (Begley, Caffery et al. 2000).

One confounding factor that may have influenced these data is that, though the study sample consisted of non-dry eye and dry eye participants according to self-reported dry eye status, current contact lens wear was a prerequisite to enrollment in this study. In this way, even those participants that were categorized as contact lens-related dry eye sufferers were still able to wear and were actively wearing soft contact lenses at the time.
of the study. One theory is that those dry eye sufferers with even greater severities of symptoms had already discontinued contact lens wear. It is possible that, had the study been designed in such a way as to include a group of former contact lens wearers that had discontinued lens wear due to dryness symptoms, a correlation between one or more of these tear parameters and ocular dryness status may have been found.

A study by Glasson, et. al. (Glasson, Stapleton et al. 2006) conducted on tear film and other ocular characteristics of a group of discontinued contact lens wearers including both “tolerant” (able to wear lenses comfortably for at least 6 hours) and “intolerant” (preferring not to wear lenses for longer than 6 hours) former wearers. In their study, no significant change was found in the non-invasive tear film break-up time of the intolerant wearers over the course of a 6 hour wearing period; the non-invasive tear film break-up time of the tolerant wearers, however, was no longer distinguishable from that of the intolerant group at the end of the 6 hour wearing period and was significantly different from the baseline reading. The time of day was recorded for each of the interferometry readings in the current study, but data on the total number of contact lens wearing hours prior to these recordings were not collected. Standardizing these values may have made the data in this study more uniform and more directly comparable. An earlier and similar study, again by Glasson et. al. (Glasson, Stapleton et al. 2003), also found lower non-invasive tear film break-up times, a higher number of dryness symptoms, and lower tear volumes to be characteristic of intolerant lens wearers and predictors of contact lens intolerance.

Contact lens care solutions have been evaluated as to their influence on PLTF thickness on non-dry eye sufferers (Nichols, Mitchell et al. 2005), but it seems unclear as
to whether or to what extent the PLTF thickness plays a role in dryness symptomology. Others researchers have suggested that contact lens drying on the eye may lead to ocular surface drying via depletion of the post-lens tear film due to evaporation and diffusion of the watery component of the tears to the outer surface of the lens (Fornasiero, Prausnitz et al. 2006).

A significant correlation was found between LLT and PLTF thinning rate in the current study at the time of the first visit only (p = 0.03); as the thickness of the LLT increases the PLTF thinning rate decreases. This data is in good agreement with the current theory of the outermost lipid layer’s functional role as an evaporation retardant for the underlying aqueous layer of the tear film (McCulley and Shine 2004). The relatively much thinner lipid layer acts to prevent loss of the aqueous layer of the tear (90% of the tear film thickness) (Albarran, Pons et al. 1997). It has previously been demonstrated that evaporative dry eye is exacerbated in the presence of altered lipids in cases of chronic blepharitis, presumably because this altered lipid layer cannot perform the spreading function that it normally would (McCulley and Shine 2003).

### 4.2 Contact Lens Dry Eye Questionnaire (CLDEQ) Scores

The CLDEQ scores at the first study visit of the non-dry eye and dry eye group were shown to be significantly different from one another (p <0.0001), with the dry eye group scoring higher (indicating more severe dryness symptoms). This finding was as expected and allowed a valid differentiation of participants into either the non-dry eye or the dry eye group. Interestingly, there was no longer a significant difference between the CLDEQ scores of the two groups at the second study visit (p = 0.07), nor were there
significant differences within each group between the two study visits \((p = 0.20\) for non-dry eye, \(p = 0.57\) for dry eye group) or within the entire study sample between the two study visits \((p = 0.91)\). It is possible that, as all participants were wearing the same brand of contact lens at the second study visit, contact lens material had some equalizing effect on the sample, obscuring the initial difference in subjective symptom reporting.

Similarly, the number of days that the contact lenses were worn for was more consistent across the sample at the second study visit than at the first.

Other explanations for the loss of statistically different CLDEQ scores between the first and second study visits include patient bias. Participants, having been informed that this study was being performed to assess the performance of a new silicone hydrogel contact lens on contact lens-related dry eye and non-dry eye patients, may have been biased to expect an alleviation of dryness symptoms with the new lens. Additionally, regression to the mean may have occurred at the second study visit. In this way, the participants, initially chosen and assigned to groups based on self-reported ocular dryness status, may have reflected something closer to the population mean CLDEQ score at the second visit.

The possibility that regression to the mean accounts for the loss of a significant difference between the two groups from the first study visit to the second is supported by studies that have found the CLDEQ and similar dryness questionnaires (including oral questioning of patients) to be valid and repeatable tools for classifying patients into dry eye and non-dry eye groups (Nichols, Mitchell et al. 2002; Nichols, Mitchell et al. 2004; Gulati, Sullivan et al. 2006).
At the first visit only, a significant positive correlation was found between CLDEQ score and PLTF thinning rate for the dry eye group (p = 0.03). With faster PLTF thinning rates, CLDEQ scores were found to be higher (corresponding to more severe dryness symptoms), which supports the findings of studies that have related faster PLTF thinning rates (and decreased tear break-up times) to ocular dryness and dryness symptoms (Glasson, Stapleton et al. 2003; Glasson, Stapleton et al. 2006). Why this difference was not also found for this group at the second study visit is unknown but may also be subject to the effect of a possible regression to the mean on CLDEQ scores.

A significant correlation was found between CLDEQ score and LLT for the non-dry eye group (p = 0.04) at the first visit but not at the second. This finding that the CLDEQ scores indicate less subjective dryness when the LLT is thicker, like the correlation between thinner LLT and faster PLTF thinning rates at the first visit for the entire study sample, was expected. However, the above correlation was found for the non-dry eye group. That there should be a significant correlation between one tear film parameter and the subjective symptom reports for a subgroup of participants who were classified as asymptomatic in comparison to the other subgroup seems out of the ordinary. Ultimately, it would be interesting to see if these results are repeatable, especially in light of the fact that the correlation was no longer found at the second study visit for this group.

It is interesting to note, however, that five of the participants classified into the non-dry eye group via CLDEQ scores at the first study visit were classified as dry eye at the second study visit. Three of the participants classified into the dry eye group at the first visit were classified as non-dry eye at the second visit.
4.3 Total Contact Lens-Extracted Lipid Analysis

Total contact lens-extracted lipid quantities were significantly different (greater) only for the non-dry eye group between the first and second study visits ($p = 0.01$ non-dry eye, $p = 0.10$ dry eye). No difference was found between the amounts of extracted lipid between the two groups within either study visit. These are inconclusive as to whether total contact lens-extracted lipid quantity has an effect on subjective dryness symptoms reported by patients, as has been proposed in the literature (Hart, Lane et al. 1987; Jones, Senchyna et al. 2003; Carney, Nash et al. 2008). As silicone hydrogel contact lens materials, to varying degrees, have been shown to accumulate more lipid deposits than ionic hydrogel contact lens materials, it might be expected that the study of silicone hydrogel contact lenses would have shown greater lipid deposition in comparison to the various habitual contact lens materials in both groups, but perhaps the fact that the comfilcon A lenses are FDA group I lenses and not FDA group II lenses (the most notoriously lipid-attractive materials) had a mitigating factor on the results—especially when the great variety of habitual contact lens materials is taken into account (Bontempo and Rapp 1994; Jones, Senchyna et al. 2003; Carney, Nash et al. 2008).

A significant positive correlation was found between contact lens-extracted lipid quantity and number of days for which the habitual contact lenses were worn ($p = 0.03$). This may be explained by a greater contact time with the tear film and thus greater lipid deposit accumulation. The maximum amount of contact lens-extracted lipid, however, may have been mediated by other lens surface deposits, such as proteins (Bontempo and Rapp 1997). This interaction has been shown to occur on the surfaces of FDA group II and group IV contact lens materials. Total contact lens-extracted lipid was the only
deposit measured in the current study. Also, the cleaning and disinfecting solution used by the participants was standardized by the time of the second study visit, and though the participants may not all have been using the same contact lens solution at the time of the first study visit, this information was not collected.
Chapter 5: Conclusion

One month of wear of comfilcon A silicone hydrogel contact lenses did not significantly improve subjective dryness symptom severity in either normals or contact lens-related dry eye sufferers as compared to their habitual lens materials. It also did not increase the severity of these symptoms. Correlations were found between LLT and PLTF thinning rate in this study, and further study of relationship may help solidify theories about the interaction of the different layers of the tear film. Also of note was the association found between increased PLTF thinning rate and increased subjective symptom severity for the dry eye group at the first visit.

It must be taken into account that as this study was pilot in nature, many of these analyses may lack sufficient power to make firm statements about the nature of this contact lens material as it relates to subjective symptoms and quantifiable signs of dry eye and discomfort.

More research is needed on contact lens materials and their effects on different ocular surface and tear film interactions to help find or develop an ideal material that can provide maximal comfort to the majority of contact lens-related dry eye sufferers.
References


Foulks, G. N. (2003). "What is dry eye and what does it mean to the contact lens wearer?" Eye Contact Lens 29(1 Suppl): S96-100; discussion S115-8, S192-4.


Nicolaides, N. (1986). Recent findings on the chemical composition of the lipids of steer and human meibomian glands. The Preocular Tear Film: In Health, Disease, and contact Lens Wear. F. J. Holly. Lubbock, TX, Dry Eye Institute: 570-96.


