Universidade do Minho
Escola de Ciências

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Tear Film Parameters and Clinical Performance of Daily Disposable Contact Lenses

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Tear Film Parameters and Clinical Performance of Daily Disposable Contact Lenses

Dissertação de Mestrado
Mestrado em Optometria Avançada

Trabalho realizado sob a orientação do
Professor Doutor José Manuel González-Méijome

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DECLARAÇÃO

Nome: Rute Juliana Ferreira Macedo de Araújo

Endereço eletrónico: rjfmaraujo@gmail.com

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Tear Film Parameters and Clinical Performance of Daily Disposable Contact Lenses
Parâmetros Lacrimais e Desempenho Clínico de Lentes de Contacto Descartáveis Diárias

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“The most exciting phrase to hear in science,

the one that heralds the most discoveries,

is not 'Eureka! ' (I found it!) but 'That's funny... '”

(Isaac Asimov)

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ABSTRACT

Contact lenses (CLs) are an alternative to the traditional optical correction that is suffering constant and challenging developments. In fact, eye care professionals have observed changes in the anterior ocular surface since the first CL insertion, with visible signs and reported symptoms. The discomfort caused by CL wear is an important and widely-spoken theme that largely affects the CL wearers. When placed on eye, CLs divide the tear film into two layers: the pre-lens tear film (PLTF) and post-lens tear film (PoLTF). This division causes the well-known tear film destabilization and many other biophysical and biochemical changes that can affect the integrity of the tear film.

Stating this, it is important to know what mechanisms lead to the discomfort and if the symptomatology could be reduced with the adaptation of new soft daily disposable CL materials, as well as assess the differences in tear film, visual quality performances' and clinical parameters between different lenses. For this assessment, Delefilcon A and Stenfilcon A lenses were used in a randomized, double-masked and contralateral way. After a 5 days trial, the two lenses used proved their effectiveness in reducing ocular symptomatology, which was shown by the reduction in total score of OSDI questionnaire, answered at baseline visit and at the final outcome visit, in both lenses. There were few differences between the two lenses in tear film, optical quality and clinical parameters. The high and low-contrast visual acuities were similar between the lenses, as well as the subjective optical quality and pre-lens NIBUT. Dynamic topography and dynamic wavefront aberrometry proved to be sensitive in the assessment of tear film's temporal changes, although the second technique has shown some limitations. Clinical parameters measured with slit lamp showed some differences between the two lenses as well as dehydration, with Stenfilcon A having a greater dehydration values than Delefilcon A in both morning and afternoon visits. In average, the comfort assessment during the dispending consultations showed a slightly better performance for Delefilcon A lens, with a significant improved comfort from day 1 to day 3. In a global evaluation, patients have preferred Delefilcon A lens. So, the aim that daily disposable contact lenses can reduce ocular symptomatology was supported by this work.

RESUMO

As lentes de contacto (LC) são uma alternativa à correção ótica tradicional que tem vindo a sofrer bastantes desenvolvimentos. De facto, os profissionais dos cuidados de visão têm vindo a observar mudanças na superfície ocular anterior desde a primeira inserção de uma LC, reportando-se sinais visíveis e sintomas. O desconforto causado pelo uso de LC é um tema importante e muito falado que afeta os usuários. Quando colocada no olho, a LC divide o filme lacrimal em duas camadas: o filme lacrimal pré-lente e o filme lacrimal pós-lente. Esta divisão causa uma maior destabilização do filme lacrimal, bem como outras mudanças biofísicas e bioquímicas que podem afetar a integridade do filme lacrimal.

Assim, torna-se importante saber qual o mecanismo que leva ao desconforto e se a sintomatologia pode ser reduzida com a adaptação de novos materiais de LC descartáveis diárias presentes no mercado, assim como avaliar as diferenças nos desempenhos do filme lacrimal, clínicos e visuais entre diferentes lentes. Para esta avaliação, foram usadas as lentes Delefilcon A e Stenfilcon A num estudo aleatório, duplo-cego e contralateral. Após 5 dias de uso das LC, as duas mostraram ser efetivas em reduzir a sintomatologia ocular, uma vez que houve uma redução significante do valor do OSDI que foi efectuado na visita baseline e no final da última visita de seguimento. À parte desta avaliação, houve poucas diferenças entre as duas lentes. A acuidade visual de alto e baixo contraste foi bastante similar entre as lentes, assim como a qualidade ótica subjetiva e o NIBUT pré-lente. A topografia e a aberrometria dinâmicas mostraram ser sensíveis em detetar as mudanças temporais no filme lacrimal, embora a segunda tenha demonstrado algumas limitações. Foram encontradas algumas diferenças no exame de lâmpada de fenda e na desidratação, com a lente Stenfilcon A a mostrar maiores níveis de desidratação nas visitas da manhã e da tarde. Em média, a avaliação do conforto mostrou uma pequena preferência pela lente Delefilcon A, que mostrou ter um melhor desempenho ao longo dos dias. Globalmente, os pacientes preferiram a Lente Delefilcon A. Assim, a ideia que as LC descartáveis diárias conseguem reduzir a sintomatologia, foi apoiada por este estudo.

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ABBREVIATIONS AND ACRONYMS

BUT: Break-up Time

CCLRU: Cornea and Contact Lens Research Unit Grading Scale

CL: Contact lens

CLD: Contact Lens Discomfort

CLDEQ: Contact Lens Dry Eye Questionnaire

CLIDE: Contact Lenses Induced Dry Eye

CLs: Contact lenses

DEQ: Dry Eye Questionnaire

ETDRS: Early Treatment of Diabetic Retinopathy Study

EWC: equilibrium water content

HCDVA: High contrast distance visual acuity

HCVA: High contrast visual acuity

HOA: High Order Aberrations

IBI: Interblink Interval

IDEEL: Symptoms of Dryness

LCDVA: Low contrast distance visual acuity

LCVA: Low contrast visual acuity

LE: Left Eye

LOA: Low Order Aberrations

LogMAR: Units of measurement of visual acuity by the Logarithm of the Minimum Angle of Resolution

NIBUT: Non-Invasive Tear Break-up Time

OSDI: Ocular Surface Disease Index

p: Statistical significance

PLTF: Pre-lens tear film

PoLTF: Post-lens tear film

POTF: Pre-ocular tear film

PRO: Patient Reported Outcomes

RE: Right Eye

RML: relative mass loss

RPG: rigid gas permeable

SAI: Surface Asymmetry Index

SD: Standard deviation

Si-Hy: Silicone Hydrogel

SOQ: Subjective Optical Quality

SRI: Surface Regularity Index

TBUD: Tear Break-up Dynamics

TBUT: Tear Break-up Time

TSAS: Tear Film Stability Analysis System

TFOS: Tear Film and Ocular Surface Society

TFSQ: Tear Film Surface Quality

VA: Visual Acuity

VAS: Visual Analogue Scale

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1. LITERATURE REVIEW

Contact lenses (CL) are an alternative to the traditional optical correction that is suffering constant and challenging developments, making this a constant hot topic for researchers.

Although Leonardo da Vinci (1452-1519) is traditionally considered the inventor of the first device in contact with the eye, is to Thomas Young (1773-1829) that is attributed the first method of changing the ocular refraction in contact with the eye. Only later, around the year 1888, began to emerge scientific publications about CLs by Adolf Fick, Eugene Kalt and August Muller, showing already some consequences of its use. Almost a century later (1975) and after the appearance of soft contact lens in the 1970s, more than 2 million people worldwide were already using CLs.[1] Currently, more than 140 million people wear CLs throughout the world[2] (Figure 1.1), and some perspectives pointed to an increase to about 202 million for the last year 2010.[1]

Despite this great numbers, there's still a dark side: CL wear discontinuation which is a significant problem for the clinicians and for the industry. In fact, patients continue to complain about ocular dryness and related symptoms (such as discomfort), affecting about 35 to 60% of CL users, and contributing to CL drop-out.[3] There are many factors that can lead to this situation and all will be discussed in the introduction of this thesis.

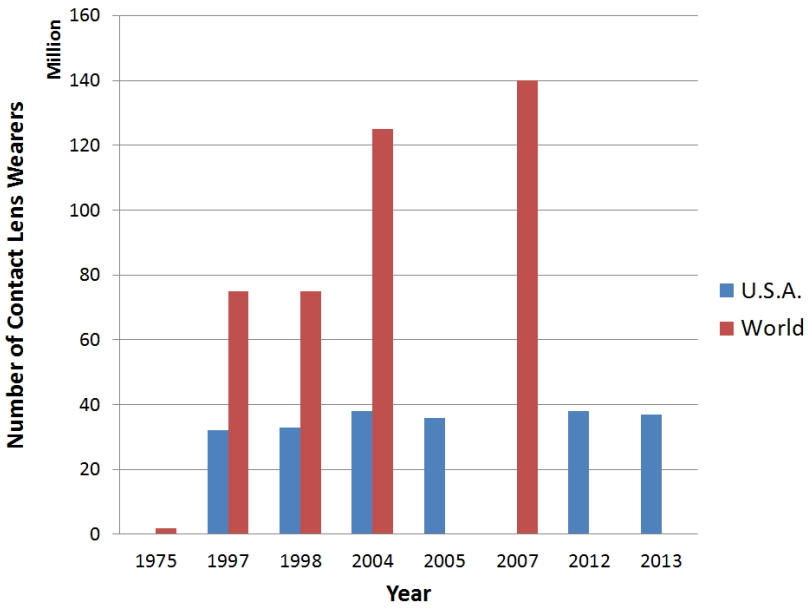


Figure 1.1. Estimated number of contact lens wearers throughout the world (red bars) and in USA (blue bars) over the years.

As is known, the last decades have been very important for CL industry, with the development and emergence of new CL materials in order to enhance wearer's comfort and to decrease drop-out percentages. After the invention of soft lenses in the 1970s, the emergence of silicone hydrogels (SiHy) in 1998 is undoubtedly the most significant and exciting breakthrough in lens material technology, as seen in Figure 1.2. This lead to an inclusion of a significant proportion of siloxy groups which contains the element silicon directly linked to oxygen and carbon atoms, generating an increase in both oxygen permeability and hydrophobicity, worsening lens wettability.[4] This material also attracts more lipids and lipophilic proteins from tears, causing tear film destabilization.[4] Although the original intent for SiHy was for extended wear because of its enhanced oxygen permeability [5], they quickly became available for daily wear. Daily disposable CLs have emerged in the mid-1990s and since then they have experienced constant increases (Figure 1.3). These new modality theoretically provides enhanced comfort[6], decreased lens deposition and improved ocular health.[7] Solomon *et al* [8] compared daily disposables to conventional wear and frequent replacement CLs during a 3-year study and concluded that daily disposable was the most trouble-free option of wearing CLs, with fewer symptoms of redness and cloudy vision, fewer surface deposits and complications and better vision.

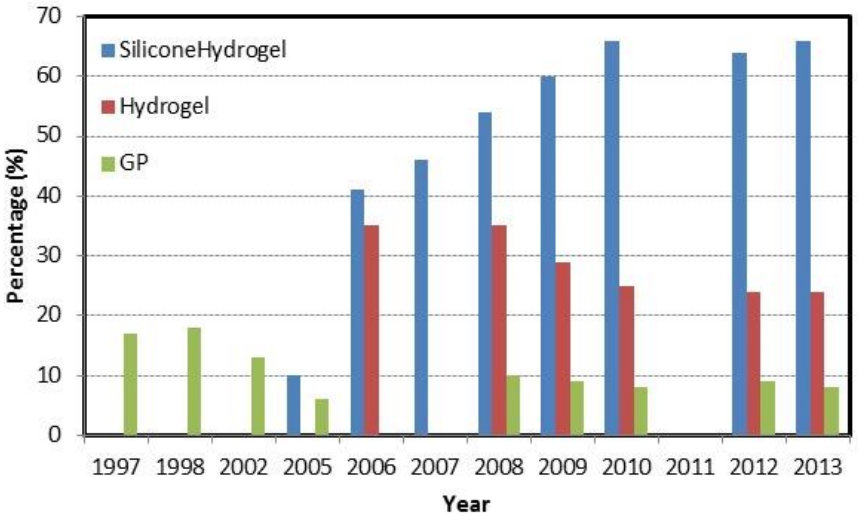


Figure 1.2 Distribution of material classes used in fittings and re-fittings throughout the years. Data from contact lens spectrum annual reports.

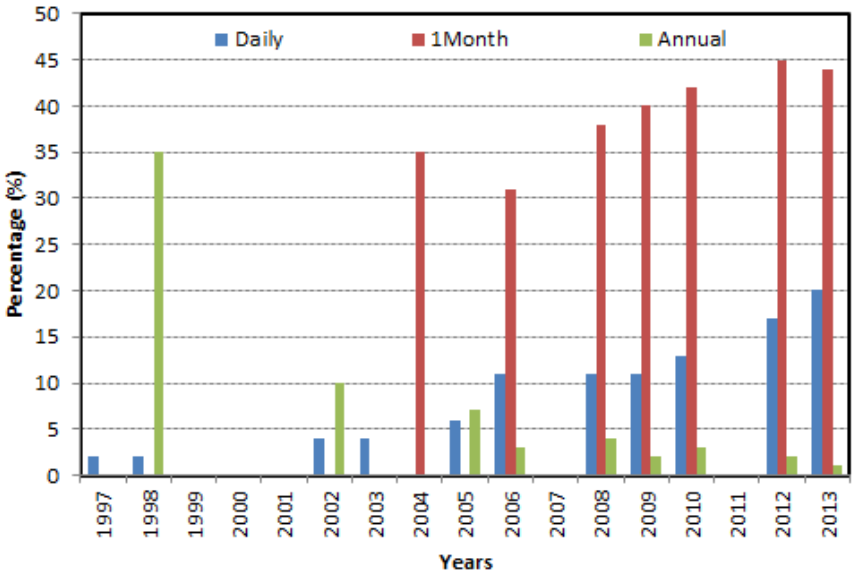


Figure 1.3 Distribution of replacement schedules used in fittings and refits by year. Data from contact lens spectrum annual reports.

1.1 Pre-ocular and Pre-lens Tear Film

To ensure a healthy and comfortable functioning of all ocular surface many things deserve attention. In fact, the ocular surface involves a wider concept with several structures involved. Initially, it was described as an integrated unit comprising the cornea, conjunctiva, lacrimal glands and eyelids.[9] This concept was extended by Gipson [10] that said that "*ocular surface includes the surface and glandular ephitelia of the cornea, conjunctiva, lacrimal gland, accessory lacrimal glands, meibomian glands, and their apical (tears) and basal (connective tissue) matrices; the eyelashes with their associated glands of Moll and Zeiss; those components of the eyelids responsible for the blink and the nasolacrimal duct".*

The tear film and their respective glands seem to have an important role in the proper functioning of the ocular surface. The pre-ocular (POTF) or pre-lens tear film (PLTF) are the first structures that light encounters when reaching the eye, making this air-tear interface the first refractive surface responsible for focusing the light rays. That said, it can be concluded that little irregularities in this interface can affect substantially the quality of vision[11] (more in section 1.1.4).

The tear film structure and stability will be briefly reviewed in this chapter, as well as the differences between an intact tear film and a tear film disrupted by a CL interphase.

1.1.1 Tear Film Characteristics

Tear film is an important optical element with vital contributions to proper visual functions. There are two models for the tear film structure. The model traditionally more accepted was enunciated by Wolf in 1946, and has been described as a three-layered liquid film with each layer deriving from a distinct origin with a thickness ranging between 7 and 11μm[12] (Figure 1.4), but with differences between studies and the technique used. In this model, the most superficial layer is the **lipid film** with a thickness between 0.05μm and 0.2μm (about 0.1μm), representing about 0.02% of the total POTF thickness. This layer inhibits the evaporation of the aqueous components, since it separates the exterior ambient from aqueous layer, delaying the tear break-up time. It consists of several lipids that varies between subjects and is secreted by meibomian glands at the rim of the eyelids. Lipid layer is also determining in some issues related to CL wear, because it can be significantly altered by the CL presence and cause changes in the sensation of dryness and discomfort.[13;14]

The intermediate and also thickest layer is the **aqueous layer**, with approximately 7μm, representing about 99.78% of POTF thickness. It is mostly secreted by the main lacrimal gland and can dissolve all the nutritive products, so the tear film can maintain a good function. Its major function is the hydration of ocular surface.

Finally, the **mucous layer** is in contact with the corneal and conjunctival epithelium. It has about 0.02μm to 0.8μm, representing about 0.2% of all POTF thickness and is secreted by globet cells of the conjunctiva. Among its functions, the decreasing surface tension and the increase in surface energy of the corneal epithelium and conjunctiva can be highlighted, so the TF can be spread over these surfaces. [13]

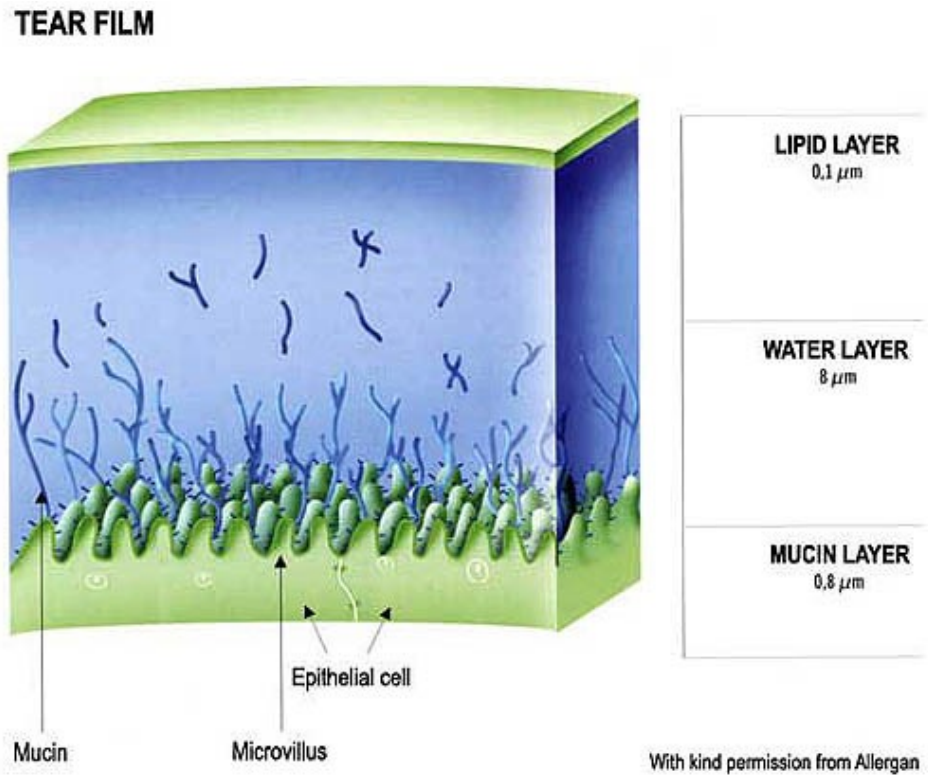


Figure 1.4 Schematic representation of tear film structure in three-layers and its' respective thickness. (http://www.lea-test.fi/en/eyes/images/pict7b.jpg).

Recent findings in tear film research suggest that there might be no sharp boundaries between the aqueous and mucin layers. Until recently, it was thought that there were insoluble mucins in the first layer, hence this can be considered a separate layer.[15;16] However, today's knowledge seems to ensure that the mucins secreted are soluble and disperse into the aqueous layer, making the tear film a two-layered structure. [15;16]

Despite these findings, tear film layers continue to have a specific and particular function and the overall good functioning of the tear film depends on the contribution of the smooth functioning of all the layers separately, by means of good and balanced quantity and quality of all structures. Knowing the multiple function of POTF can help us to better understand many problems, namely those who are related to the CL wear discontinuation, as CL wearers have more ocular symptoms than non-wearers.[17] The POTF has an optical function, maintaining a homogenous surface between the air and the anterior eye surface, coating small corneal irregularities. This can prevent light scattering and blurred vision.[18] POTF also promotes a smooth contact between the conjunctiva and eyelids/ocular

globe, lubricating this surfaces and allowing a tolerable CL use. Drying of the eye can lead to discomfort, epithelial erosions and even ulcerations.[19] The antimicrobial protection function can prevent ocular infections, because of the immunological defense carried out by proteins, antibodies, phagocytic cells and others. Tear film also has a physical protection as the superficial lipids repel dust particles and some types of bacteria.[20] The POTF has also a nutritive function, allowing the transition of oxygen, glycose, minerals, amino acids, vitamins and others, into the corneal epithelium. In other way the cornea won't receive these nourishing components because of its avascular tissue. There are some metabolic products derived from cornea, such as carbon dioxide and lactate that must be removed from ocular surface. The POTF takes care of eliminating them, and also does limit the passage of contaminant substances from the environment to the ocular surface, acting as a cleaning function. [13]

However, all these functions only act in a normal tear film. The absence or lack of tears can cause the augment of debris in ocular surface, with discomfort, decreased quality of vision, weakness of corneal and conjunctival epithelia and increased risk of infection.[13]

The CL insertion interrupts the normal functioning of the tear film. In the next sub-section, the modifications in tear film caused by CL wear will be discussed.

1.1.2 Contact Lens Interactions with Tear Film

A known cause of tear film destabilization is the CLs' presence. When placed on the eye, CLs divide the tear film in two layers: the pre-lens tear film (PLTF) and post-lens tear film (PoLTF) (Figure 1.5). The PLTF provides a regular surface to the lens for an adequate interaction with the eyelids and offer a good refraction. This layer consists of a lipid layer and a reduced aqueous layer with approximately 2μm at 3 minutes after lens insertion (measured both with interferometry and ultra-high resolution OCT), and about 6μm right after lens insertion, because of reflex tearing.[21] Consequently, the PoLTF is constituted by aqueous layer and mucinic layer, and is about 1-3μm.[22] This division varies according to the individual characteristics of each subject and the characteristics of the lens material and design, and can have potential negative effects on patient comfort and tolerability.

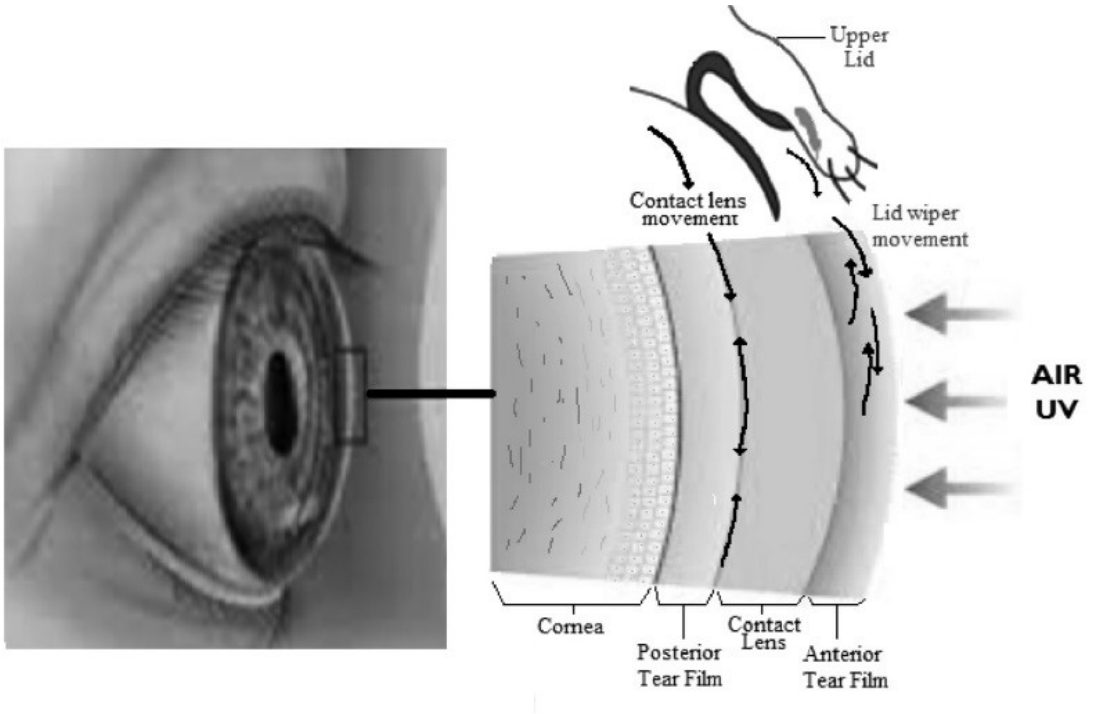


Figure 1.5 The place of contact lens and the tear film division. Image reproduced from Mann. [4]

In fact, eye care professionals have observed changes in the anterior ocular surface since the first CL insertion (1888), with visible signs and symptoms. The biophysical and biochemical changes that can affect the integrity of the tear film after CLs' insertion are many. The biochemical changes require sophisticated laboratory techniques and contemplate changes in biochemistry (lipidome, proteome, mucins and glycocalyx, and others[19]), changes in cellular content of tears and external components; on the other hand the biophysical phenomena of lens-tear interactions can be directly observed using clinical techniques and contemplate a series of phenomena listed below.

- Blink frequency: evidences that blinking frequency plays an important role in comfort and CL wear date back to 1971 and 1984, that already have shown that subjects with CL-related dry eye have an increased blinking frequency (from 15.5 blinks/minute to 20.3 blinks/minute).[23;24] However, the blinking frequency may be decreased in some tasks essentially related to near vision, increasing the interblink interval (IBI) and exposing the CL surface.[19] In fact, the blinking rate is reduced when reading or using a computer (4 to 8 blinks per minute) [25] and there are more incomplete blinks, increasing the IBI and exposing the CL surface and conjunctiva, that might result in increased evaporation and a deficient spread of lipid layer over the ocular surface.

- Lipid Layer: CLs divide the tear film into two layers and if the aqueous layer at PLTF becomes too thin, the lipid layer will interact directly with CLs' surface. This can lead to formation of lipid deposits. This is particularly problematic in SiHy lenses because of non-wettable hydrophobic silicone moieties. This can lead to impaired optical quality and non-wettability of lens surface, accelerating TBUT. [26]
- Tear Film Stability: Tear film is seriously affected with CL use and configures an important part of this thesis. The disruption of lipid layer[22;27] and reduced tear film thickness[28] are some of the consequences of CL use. Although tear thinning is significantly faster on the surface of a CL than in corneal surface[29], this could not be explained by means of the thinner PLTF. In fact, it has been proposed that "*even when the PLTF and POTF are similar in thickness, the PLTF is still considerably less stable*". [12] More information of tear film stability can be found on the 1.1.3 section of the present thesis.
- Tear Film Evaporation: The normal tear film is lost from the ocular surface by evaporation, absorption and drainage.[19] The CL presence increase the rate of tear film evaporation,[30] by means of lipid layer disruption that lead to a more exposure of aqueous layer. These increased evaporation rates can lead to dryness and discomfort symptoms.[19] There are some evidences that CLs increase tear evaporation by 1.2x to 2.6x compared to non-lens wearing, with no relation to lens material or water content.[31] However, a recent study conducted by Kojima *et al* [32] found significant increases in evaporation rate in hydrogel wearers but not in silicone hydrogel wearers, and a relationship between this evaporation and discomfort.
- Tear Film Temperature: The normal tear film temperature is in the order of 32-36ºC.[33] When a CL is placed on the eye, the temperature of the PLTF becomes colder[34] and the PoLTF becomes higher, when compared to the non-CL wearing eye.[35] High water content materials have lower lens surface temperature than low water contents.[34]
- Tear Film Thickness: Tear Film Thickness is altered with CL insertion once it divides the tear film into two layers. The PLTF is about 2µm but can be altered by the instillation of eye-drops, although transiently.[21] PoLTF maintains its thickness after the instillation of artificial tears.[21]
- Tear Production/Turnover: Technically, it's difficult to measure tear production. Some studies (the primaries) failed to encounter differences in tear production between CL wearers and non-wearers. With a new technique, some differences between these two groups were encountered.[19]
- Tear Volume: A reduced tear meniscus volume was found on CL surface when compared to the same measures on the ocular surface, using an OCT.[21] Tear volume also decreases over time with

CL use.[36] There is some evidences on the existing studies that decreased tear meniscus volumes are related to ocular discomfort at the end of the day.[37]

- Tear Film Profile at the edge of a soft CL: This tear meniscus seems to change with CL insertion. It is smaller in soft CL edge when compared to hard lens edge and augment when artificial tears are instilled.[38]
- Tear Exchange: Tear exchange can be regulated by lens diameter and movement, the blink and tear replenishment rate. It seems to be affect by lens diameter, with lesser exchange the bigger the diameter. [39]
- Osmolarity: Osmolarity is a clinical and objective measurement that indicates the balance between tear production and their elimination (evaporation, drainage and absorption). A balanced tear production and elimination is important for tear film stability and maintain a normal osmolarity.[40] CL wear changes tear osmolarity, showing a possible role in the reduction of lens movement and increase contact lens adherence.[40] The CL insertion leads to a reduction on tear osmolarity because of reflex tearing with a subsequent increase.[41] This increase can occur because of the reduced tear production (reduced corneal sensitivity) and because of excessive evaporation caused by a disrupted tear film and consequent reduced tear film stability.[42]
- Ferning: Tear ferning is an indicator of tear functionality. Abnormal tear functionality by means of significant increased tear ferning can be seen in contact lens wearers.[43]
- pH: The pH of a normal tear film is about 6.5 – 7.8, and is more acid in CL wearers with decreases of about 0.27 and 0.53 pH units.[44] This decrease is attributed to the lens preventing CO_2 loss from the eye. [44]
- Viscosity: The effect of CL wear on tear viscosity is still unknown; however there are reports of differences in this parameter in dry eye disease.[45]
- Surface Tension: The surface tension also plays an important role in tear film stability, with less stability the bigger the surface tension.[46] There are no studies contemplating the changes of CL wear in surface tension.[19]

All these parameters mentioned are tear biophysical changes. When biophysical and biochemistry are seen together, we can highlight the removal or reduce of some components of the tear film and the augment of the tear film, stimulating the influx of new components or increasing the level of specific existing components.[4] This alteration of lacrimal production has two phases. Initially, the CL

causes a hypersecretion of tears because of the mechanical stimulus. In a long-term, the CL wear cause less tear secretion because of the reduced friction between eyelids and ocular surface and the reduction in corneal sensitivity because of the nervous hyper-stimulation caused by the CL (more notice in rigid gas permeable (RPG) lens).[13]

Among the different components that can affect the lens-tear interactions, we can highlight the properties of the lens: ionicity, water content, moduli, and surface properties, and the characteristics of the individual wearer and the wear schedule.[4] In addition, the comonomers, manufacturing process, rate of deposition of the tear film components and the wearers' tear film must be taken into account, once all are related to the wetting nature of the lens material.[47] Although we can change some of the mechanisms mentioned above, the patients' tear film is a non-modifiable factor and it seems to be a major determinant of successful CL wear.[48]

There are many studies that concluded that CL wear can lead to different and various changes in the structure of ocular adnexa. Nichols *et al*[49] have concluded that CL wear could damage and change the structure of the meibomian glands, changing their production. This can lead to alterations in the lipid layer thickness, tear film instability, increased tear osmolality and dehydration of hydrogel lenses.

To mitigate these effects and for a perfect biocompatibility with the eye, the lens should be completely surrounded by tears, having two tear film layers both in front of the eye (PoLTF) and after CL (PLTF), mentioned before.[13]

1.1.3 Tear Film Stability

Many factors can affect tear film stability. A known and already mentioned factor is the CL presence. Also, tear film stability is not constant throughout the day, with decreased values of TBUT immediately after awakening[50] and at the end of the day[51] in non-CL wearers which may contribute to the increased end of the day discomfort felt by CL wearers. There are evidences that TBUT is reduced in females, [17;52] and decreases with age,[52;53] with greater temporal changes in females.[54] Ocular surgery also impacts tear film dynamics because of the irregularities caused or changes in some tear

components, caused by ocular/palpebral surgery.[55] Although these known changes, it's important to have into account the environmental conditions such as temperature, humidity, air conditioning and pollution, and others.[55]

Young and Efron[56] demonstrated that tear break-up occurred within 3-10s on the front of hydrogel lenses. Also, they found longer TBUT in high water content CLs, which is consistent with the thicker aqueous layer proportioned by this lenses. Other authors concluded that tears begin to break-up within 2-3s on the front surface of a rigid permeable CL and 5-6s on soft contact lens.[28]

1.1.3.1 Measuring Tear Film Stability

As we can see by the analysis in the last section, the tear film plays an important role mainly when CL wear is under discussion. Nowadays there are many ways to measure it quantity, stability, and osmolality. In this section the methods for measuring the tear film stability will be reviewed.

Many methods have been developed for measuring tear film stability. In reality, we measure the tear film instability to assess its stability. Some of the principal methods and techniques are listed above.

- Tear Break-up Time (TBUT): TBUT was first described by Norm in 1969.[57] Since then, TBUT have been the most frequently test used for evaluate tear film stability.[58] In testing TBUT, sodium fluorescein is instilled into the tear film by means of a sterile strip or a pipette. The patient is instructed to do a complete blink and then avoid blinking for a period of time. The examiner is observing the tear film through a biomicroscope with a cobalt blue light and a wratten #12 yellow filter[55], and reports the time (in seconds) between the last complete blink and the appearance of the first break, dry spot or discontinuity on the tear film. The longer it takes, the more stable the tear film. Tear film is considered abnormal if TBUT is less than 10s[59]; if TBUT values are between 5-10s they are considered marginal and if less than 5s is indicative of dry eye syndrome.[60] Table 1.1 shows the values of TBUT reported by some studies.

The location of the spot of the first break can be also analyzed. In healthy subjects, TBUT occurs most frequently in the inferior or central corneal quadrants and less frequently in the superior quadrant.[61;62]

Although its' wide use, TBUT is known by its' poor reproducibility since the 70s[63] In fact, it can be affected by many factors such as the observer experience, incomplete blinks, illumination techniques,[64] and by the characteristics of fluorescein instilled.[65] TBUT is dependent on the volume of fluorescein solution instilled before measurement as well as its' concentration, pH, and type of fluorescein used. Some studies show an improved repeatability and reproducibility with less volume of fluorescein instilled.[66;67] In 1998, Cho *et al*[68] observed that the first measure was always significantly different from the second and third. Because of this, is recommended to do multiple measures and then take the mean of them.

An application of TBUT, also with the fluorescein instillation, is the tear film break-up dynamics (TBUD). This technique videotapes changes in fluorescein pattern after the first break in the tear film.[69] The images are converted in greyscale and analyzed with MATLAB. This allows the assessment of the total area of TBUT and the maximum IBI. Although this technique is highly correlated to patients' symptoms when compared to TBUT, it also allows the detection of distinct break-up patterns: amorphous (26%), linear (22% - most frequently associated with dry eye), spot (20%), fractured (20%) and wispy (12%).[70]

Table 1.1 Summary of results of recent studies evaluating the TBUT.

Author/ Year	Sample/ Age	TBUT (s) Mean±SD
García-Resúa *et al*[62] (2005)	n=31 21.19±1.84 y	13.12±2.21
Gumu *et al*[71] (2011)	n=45 48.20±16.55 y	9.12±0.97
Szczesma *et al*[72] (2011)	n=34 20-68 y	14.3±12.6
Ibrahim *et al*[73] (2011)	n=107 Study 44.6±13.7 Control 38±12.2	8.3±2.9
Unlu *et al*[74] (2012)	n=35 29.09±6.73 y	(4 to 18) 11.37±3.69
Lira *et al*[51] (2011)	n=51 21.1±2.2 y	6.68±2.62 M 4.47±1.99 A

M, Morning; A, Afternoon; S, Seconds;

- Non-Invasive Break-Up Time (NIBUT): According to Szczesna and Iskander[75] a method is considered non-invasive if there is no instillation of fluorescein, natural blinking, no contact between the instrument and the eye or adnexa, and the methodology must not alter the normal ocular environment. So, non-invasive techniques basically focus on observing a reflected grid pattern on the ocular surface. NIBUT is the time (in seconds) between the last blink and the appearance of the first irregularity/dry spot on the reflected target.[76-78] Thus, NIBUT can be evaluated using the reflected mires of keratometers, topographers and other approaches, like tearscope (will be explained in: Interferometry of lipid layer) or other custom made techniques based on the same basis. In 1989 Hirji *et al*[9] added a fine grip to the keratometer and concluded that the detection of tear break-up was easier with this technique and recommended the use of the mean of five measurements for a great reproducibility. Others have joined a hemispherical bowl to the biomicroscope to assess the entire cornea for better measurements of NIBUT.[80]

Although its inter-observer differences,[55] NIBUT is generally longer than TBUT and they are poorly correlated.[81] One explanation could be the tear film destabilization caused by the instillation of fluorescein for the TBUT measures. Nevertheless, this effect of fluorescein on tear stability is not well known yet.

Table 1.2 Summary of results of studies evaluating NIBUT.

Author/Year	Sample/Age	NIBUT (sec.) Mean±SD	Method
Fonn *et al*[82] (1999)	n=20 AS n=20 S	8.6 AS (0h) 8.7 AS (5h) 9.5 S (0h) 6.5 S (5h)	PLTF Slit-lamp biomicroscope
Glasson *et al* (2006)	n=11 AS 25-39 y n=9 S 23 – 40 y	21.3±5.7 AS (0h) 13.7±4.3 AS (5h) 13.7±2.8 S (0h) 12.7±4.6 S (6h)	Costum made tearscope + slit lamp
Glasson *et al*[48] (2003)	n=20 AS n=18 S	20±5.6 AS 13.2±3.2 S	Costum made tearscope + slitlamp
García-Resúa *et al*[62] (2005)	n=31 AS 21.19±1.84 y	17.50±3.06 AS	PCTF TearScope
Lira *et al*[51] (2011)	n=51 NCLW 21.1±2.2 y	6.58±2.62 (Morn.) 5.38±2.53 (Aftern.)	PCTF Helmholtz
Nichols *et al*[49] (2006)	n=161 AS n=199 S	11.03±8.63 AS 8.23±5.67 S	Interferometry
Guillon *et al*[83] (1997)	n=55 NCLW n=184 CLW	16.9±13.5 NCLW 15.3±13.1 CLW	PCTF TearScope

AS, asymptomatic; S, symptomatic; NCLW, non-contact lens wearers; CLW, contact lens wearers; PLTF, pre-lens tear film; PCTF, pre-corneal tear film

Studies using non-invasive techniques have found shorter tear film break-up times (TFBUTs) on SiHy lenses compared with hydrogel lenses.[84;85] As seen in Table 1.2, Fonn *et al*[82] conducted a study which aimed to compare the pre-lens NIBUT values between symptomatic and asymptomatic CL wearers during the day. Before 5h of CL use, they found a decreased NIBUT values, mainly in symptomatic group. Guillon *et al* found a value of 14.7±12s for symptomatic and 15.7±14s for asymptomatic, with p=0.014.

- Interferometry of lipid layer: This technique is used for asses tear lipid layer thickness and more recently for NIBUT, by observing interference patterns generated by the light reflected from the surface of the lipid layer and from the interface between that layer and aqueous layer of the tear film. Recent approaches and modifications led to the development of TearScope Plus, a non-invasive instrument capable of measure NIBUT by means of specular reflection and a flexible grid.[86] Its' cold light source decreases the possible reflex tearing caused by high intensity light sources.

- Topographical analysis systems. Videokeratoscopy: Tear film stability can be evaluated through the analysis of some topographic indices as the surface regularity index (SRI) and surface asymmetry index (SAI)[87;88]. The topographer can capture several images for some seconds. Thus, the time that the tear film takes to build-up and reach its' more regular state can be taken (3 to 10s tear film buil-up time).[89]

All of these as resulted in a commercially available non-invasive and objective method: the Tear Film Stability Analysis Software (TSAS).[90-92] This software automatically capture consecutive corneal surface images every second for a 10 seconds examination routine and later determine the tear stability by analyzing the changes in corneal topography over time (SAI and SRI).

Other studies used videokeratoscopy to assess the tear film surface quality (TFSQ) of different soft CLs. They are based on the assumption that the quality of the ring reflection is associated to the quality of tear film surface[93] and can differentiate between lenses type/material.[94] Others have used the SAI and SRI indexes to characterize the corneal surface of CL wearers and no-wearers but not to assess their tear film stability.[95]

- Confocal microscopy: Despite the high costs, confocal microscopy is a high-resolution, three-dimensional tool that allows the measurement of morphological changes present in TBUT phenomena and better understanding the underlying mechanisms.[96] Other variants allow the observation of real-time images of tear film and its dry spots.

- Visual Acuity Testing: Tsubota and colleagues don't found differences between the best corrected VA between normal and dry eye subjects.[97] However, dry eye patients continue to report reduced VA, mainly while reading, driving and watching TV.[98] These are visually demanding tasks that require attention: and it's known that this lead to a reduced IBI and more incomplete blinks. So, the reported loss of VA can be explained by tear instability caused by deficient blinks.[55]

- Functional Visual Acuity: The concept of Functional Visual Acuity arises because of the anteriorly mentioned problems in dry eye patients referring decreased VA despite normal conventional VA measure. This consists in measuring VA during and after a period of volunteering sustained eye opening, which is more representative of real-life activities. Despite all the critics that this technique has received because of the time that the patient needs to be with the eye open, it's a widely used method for assessing visual disturbances in dry eye patients.[99] In 2005, Ishida *et al*[100] developed a device that allows continuous monocular VA measurements during 30s without blinking.

- Wavefront Aberrometry: Wavefront aberrometry is a non-invasive technique that can assess the tear film stability. The non-uniform tear thickness caused by tear break-up lead to additional corneal and high-order aberrations.[101] However, the real contribution of tear-film in these aberrations is still unknown due of the accommodation microfluctuations.[75] More information about the utility of wavefront aberrometry will be showed in the 1.1.4 section (Tear film and quality of vision).

1.1.4 Tear film and Optical Quality with Contact Lenses.

Despite the famous advances in CL industry over the years, little has been done to improve the quality of vision in soft CL wearers, occasionally inferior to spectacles and RPG. The quality of vision of CL wearers is influenced by several factors that include the aberrations induced by the eye optics and CL optical properties, the interactions between eye and CL (cornea and tear film) and the manufacture process, material, water content and optical design.[102] As Montes-Micó said, "...*the optical quality of the human eye is dynamic and is affected by the tear film, in addition to accommodation, age, gaze, lens, vitreous cavity, keratometry, and pupil size."*[103]

As previously said, little irregularities in the air-tear film interface can affect substantially the quality of vision, as this is the first structure that light encounters when reaching the eye[11] and is the most powerful optical surface once is associated to the largest changes in refractive index (step between air and tear film).[104] If the tear film remains uniform in thickness, the cornea/tear combination will have almost the same power as the cornea alone: if we consider that the tear film thickness can reach the 20μm[12], and if the tear film only changes its surface radius (uniform thickness), the maximum power increase will be about 0.10 D (because it can only change up to 20 μm). Considering only this example, where the tear film remains uniformly thick, we can assume as true the common belief that the PCTF has little optical impact. On the other hand, and has been demonstrated by other studies[64;80], the tear film does not remain uniform in thickness between blinks (tear break-up), occurring local variations that will introduce aberrations into the optical system.[11;105] Notwithstanding, if the tear breaks totally, the irregular corneal surface will be exposed, which may increase optical scatter.[105] Concluding, tear film disruption can cause optical changes that contribute to the reduction in retinal image quality and consequently in visual function.[106] So, a smooth and regular tear film is important to have high-quality retinal images.[11]

1.1.4.1 Wavefront Aberrometry for assessing tear film

Many techniques such as wavefront sensing, double-pass optical method, videokeratoscopy, interferometry and retroilumination analysis have been developed to quantify the role of the tear film in optical quality. The wavefront aberrometry is the objective technique most used that allows monitoring the through-time evolutions: and has been called the most useful technique to evaluate the optical quality of CL-eye. [107;108] Defocus and astigmatism are low order aberrations (LOA) and are known as the main responsible for decrease vision. But there also are high order aberrations (HOA), as spherical aberration (0.1±0.1μm for a 6mm-pupil)[109] that is the HOA that affects the image quality the most.[110] However, we have to take into account that under the light of previous studies, differences in spherical aberration between the lens-eye combinations will be the difference in spherical aberration between the lenses themselves.[111]

In normal eyes, after a trends towards reducing right before a blink (tear build up), there is a gradual increase in optical aberrations a few seconds before (Figure 1.6), which lead to a progressive reduction of the optical quality of the eye (mean increase 21%±8%).[104] The aberrations seem to be lowest approximately after 6 seconds after a blink.[103] So, if the IBI is of about 4 seconds is unlikely that the changes in aberrations will produce detectable effects on vision. These changes in optical aberrations are associated to irregularities in tear film, namely caused by break-up. Nevertheless, the microflutuations of accommodation deserve attention, as well as the age, gaze, lens, vitreous cavity, keratometry, and pupil size which may contribute to changes in dynamics of optical quality of the human eye.[103]

In their introduction to this topic, Montés-Mico *et al*[102] referred a few studies[112;113] that intent to assess the optical quality of *ex vivo* CL, stating that these data could not be enough to predict the optical performance of CL when they are in an *in vivo* ambient. When the CL is placed on the eye, multiple interactions may occur. In fact, the non-CL wear has no diurnal variations in wavefront aberrations when compared to the joint CL + eye, which has some diurnal variations in optical quality.[102] They attributed these changes to the optical properties of the CL and to its interactions with the eye, especially with the tear film. In the same study, the best optical quality and most stable results over time were obtained for Dailies Total1.

Hong *et al* [114] demonstrated that wavefront aberrations have significantly higher values in patients wearing hydrophilic CL or glasses, compared to RPG wearers. These results are justified by the reduction of asymmetrical aberrations and positive spherical aberrations caused by gas permeable CLs. Using a double-pass method, Albarran *et al*[11] have observed a significant reduction in image quality after tear break-up with and without soft CLs, being these reduction greater when soft CLs were worn.

Dry-eye patients have increased optical aberration values by a 2.5 factor when compared to normal eyes, namely in spherical aberration. These values are caused by tear-film irregularities in ocular surface, with larger vertical coma values than horizontal coma values.[101] The mentioned changes in spherical aberration may be due to the tendency of tear film thin at a different rate in the center of the cornea and at its periphery, with a thinner central tear film inducing more positive spherical aberrations, in both normal and dry eye patients.[103] The instillation of artificial tears seems to improve the optical quality in patients with dry eye.[115]

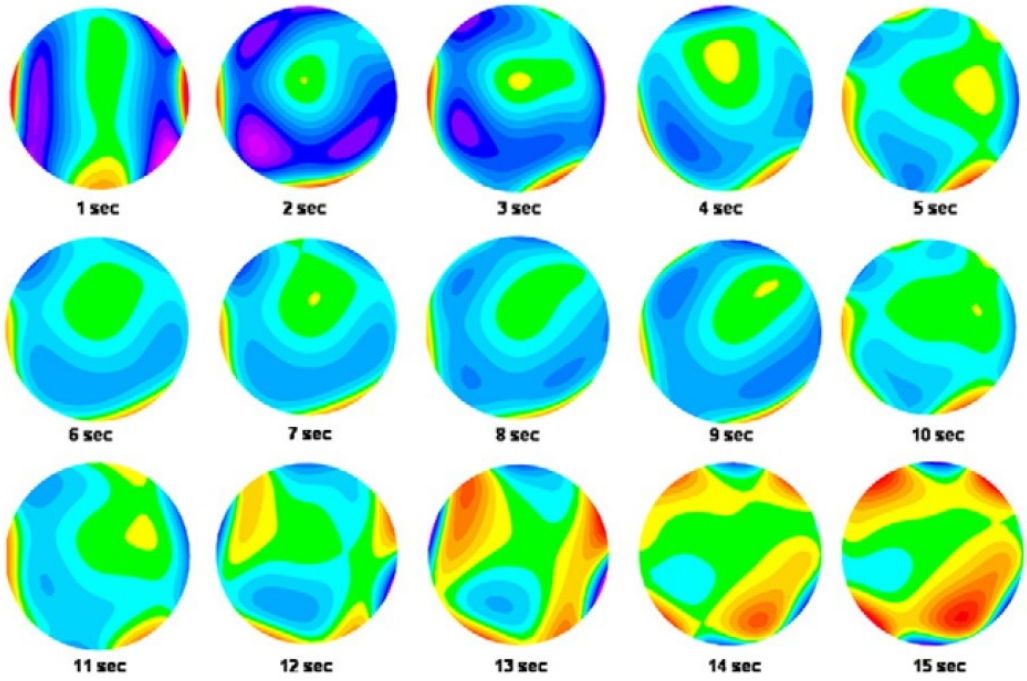


Figure 1.6 Change in corneal wavefront aberrations in different times after a blink (1 to 15 sec after blink). Image reproduced from Montés-Micó *et al* (2007), [103] who referred that, for this image *"Contour line step, 1µm; pupil diameter, 7mm; Only high order aberrations (3th to 6th) are shown; Piston prism defocus, and astigmatism have been compensated by canceling the corresponding 1st and 2nd- order Zernike coefficients."*

Although the utility of these measures is arguably necessary, increasingly subjective measures should be included in research protocols, where the patients have the principal role. It is important to meet patients' problems and understand if the objective data can be comparable to the patient's comfort and vision (more in sections 1.2 and 1.3).

1.2 Discomfort with Contact Lenses

A comfortable CL wear is not always possible. Is a very common situation subjects without signs or symptoms of dry eye suffering of CL discomfort (CLD). For many years there has been lack of consensus about this term and until a short time ago there was no approved or agreed definition for CLD. In the "International Workshop on Contact Lens Discomfort", published in 2013, the "Definition and Classification" subcommittee created a definition for this problem: "*the contact lens discomfort (CLD) is a condition characterized by episodic or persistent adverse ocular sensations related to lens wear either with or without visual disturbance, resulting from reduced compatibility between the contact lens and the ocular environment, which can lead to decreased wearing time and discontinuation of contact lens wear".*[116] As shown in Table 1.6, CLD seems to be more prevalent in females and cover between 28 and 50% of CL wearers.[117;118] Discomfort is the CL related factor which further lead more CL drop-outs (between 43 and 72%).[119]

CL wearers have some biophysical changes in common with dry eye disease patients, being some subclinical indicators of dry eye amplified when CL is placed on eye.[120;121] This discomfort can be due to CL inherent factors such as the design (edge, base curve), material (lubricity, water content, wettability), fit and wear (modality and lens interactions) and lens care (care solutions). There are also factors related to the environment, such as factors inherent to the patient (age and gender), modifiable factors (medications), ocular environment (blink, tear stability) and external environment (humidity, air quality).[116]

The comfortable wearing time is an important clinical consideration. This situation refers to the time that the patient can wear the lens with comfort, being the "comfort" term used for the "no-lens wear" feeling. Most clinicians and scientists use this term to determine if the lens is compatible with the eye. Thus, this includes:

- The ability to wear lens without sensation (lack of awareness);
- Maintain visual acuity;
- Have complete tolerance, including the ability to wear lenses as long as desired without problem.

So, this leads to other important term commonly reported by CL wear patients: the end of the day discomfort. This can occur with any lens material type, but is often associated with soft contact lens, both conventional and silicone hydrogel, as they are the CLs more used nowadays.[116] There are many

clinical signs to diagnose CLD, though they are poorly correlated with patients' symptoms.[122] They include assessments of pre-lens tear film[48], meibomian glans, hyperemia[123], and staining.[124] Young *et al* [125] contended that poor lens wettability and decreased TBUTs and NIBUTs are seen in around 40% of symptomatic patients.

As said before, the destabilization caused by CL presence is a known factor to take into account; however, there are other factors that deserve interest, as the unknown effect of long-term CL wear and if the effects persist once the lens has been removed for a long time.[83] All these changes were already known in 1986, when McMonnies concluded that dry eye symptoms are more frequent in CL wearers than in non-wearers, stating that the CL wear is a provocative condition for dry eye.[123] In an epidemiologic study conducted in 1996 by Caffery *et al* [126], a prevalence between 20-30% were found for dry eye in CL wearers. Two years later, the same authors confirmed that dry eye symptoms were more prevalent in CL wearers, with half of them (50.1%) experienced dry eye symptoms compared with the just 21.7% of non-wearers.[127]

Although a study have found no differences between hydrogels and Si-Hy lenses in comfort or dryness ratings,[128] other found that Si-Hy lenses were more comfortable and led to less dryness symptoms than hydrogels.[129] Others have not encountered differences in comfort scored between lens types.[130] Other study conducted by Efron and colleagues compared the initial comfort (after 5min of lens wear) of low, medium and high water content CLs and faced a significant negative correlation between lens comfort and lens water content, that is: low water content were more comfortable than high water content lenses.[131]

A successful CL wear is expected when the patient has a normal ocular surface, normal lid function and when the CL is compatible with eye lids, ocular surface and does not interfere adversely with tear film (excessive evaporation, surface dehydration, etc). [132]

Table 1.3 Results of prevalence of CLD from Population-based studies (in a natural population setting, most preferred for epidemiological studies) and Clinical Practice/Hospital-based.

Author/ Year	Sample/ Age	Prevalence	Study type
Doughty *et al*[117] (1997)	n=3285 CLW 10-80 y	50.1% CLD (M + F)	Population-based
Uchino *et al*[133] (2011)	n=105 CLW ≥40 yrs	28% CLD M 35% CLD F	Population-based
Uchino *et al*[118] (2008)	n=1298 CLW 15-18 yrs	36.8% CLD M 37.4% CLD F	Population-based
Brennan *et al*[134] (1989)	n=104 SCLW 24±9 yrs	75% Dryn	Clinical Practice
Guillon *et al*[83] (1997)	n=184 SCLW 31±7 yrs	44% Symp	Clinical Practice
Riley *et al*[135] (2006)	n=1092 SCLW 18-42 yrs	28% Dryn 17%discomfort 31% RCWT	Clinical Practice
Gonzalez-Meijome *et a* (2007)	n=71 SCLW 24.9±5.5 yrs	Symptoms often 24%	Clinical Practice
Young *et al*[137] (2011)	n=932 SCLW <20 to >61 yrs	31% Dryn	Clinical Practice

CLW, Contact lens wearers; SCLW, Soft Contact lens wearers; M, Male; F, Female; Dryn, Dryness; Symp, Symptomatic; RCWT, Reduced comfortable wearing time.

1.2.1 Dehydration and its relation with discomfort

It was believed that the higher the water content, the more wettable and comfortable the lens were.[138] Conversely, quickly it turn into light that high water content CLs suffer more dehydration.[139]

Dehydration can be assessed with *in vitro* and *ex vivo* methods, with *in vitro* dehydration being limited in predicting on-eye dehydration. In order to equilibrate the hydration in the new environment, CLs begins to dehydrate as soon as they are placed on eye, and continues during the day with greater or lesser intensity.[140] In hydrogel lenses, dehydration results in loss of lens mass and volume, affecting lens size and shape (decreased diameter, steeper base curve, and decreased lens movement after insertion) and affecting their clinical performance.[141] Also, the water content changes overtime can lead to some impact in oxygen transmissibility, namely in hydrogel lenses. This effect has less impact in silicone hydrogels, once their oxygen performance is less dependent in water content.[142] Dehydration is also influenced by several factors such as characteristics of the material, thickness, palpebral aperture, blink rate, tear film quality and environmental conditions.[143] Despite this assumption, a study that investigated the CL dehydration in controlled environmental conditions concluded that lens dehydration was unaffected by extreme environment conditions, stating that the eye may compensate this situation by increasing the blink rate and tear production.[144]

The TFOS International Workshop on Contact Lens Discomfort also focused on the "Dehydration" topic, concluding that "...*considering the body of literature available (...) it is not likely that a causative or associative relation exists between on-eye bulk dehydration of materials and discomfort using the current methods used to capture either dehydration or subjective comfort".*[138] As said before, the major complaints reported by CL wearers are dryness and discomfort, being them the main factors for CL discontinuation.[145] This led to a relationship between dehydration and discomfort, mainly at the end of the day, although the literature is equivocal in this area.[146] In the Contact Lens Materials, Design and Care of the TFOS Workshop, they justified this connection between dehydration and discomfort by *"... 1) the potential correlation between lens thickness and desiccation staining, 2) the potential correlation between corneal staining and discomfort, and 3) the increased friction presumably induced by dehydrated, dry lens surfaces."*

In the 80s, the high water content and thin lenses were already perceived as the greatest cause of lens dehydration.[147-149] In 1988, Efron and Brennan[150] completed these findings, showing that the lenses of patients who refer less dry symptoms were high water content CLs, and the lenses of those who often experienced dryness had less water content. Other study that intended to correlate CL dehydration and discomfort, dryness and NIBUT in asymptomatic and symptomatic patients failed to correlate dehydration with subjective sensation of comfort and dryness.[82] Although Etafilcon A dehydrated less after 7h of CL wear in asymptomatic (-3.9±2.3) when compared to symptomatic (-4.6±2.5), the same does not happened in Omafilcon A, with a greater water content loss in asymptomatic (-1.8±1.2 and -1.6±0.8, respectively). Other studies have failed to show this association.[151.144] Although these findings, a significant negative correlation was found in another study between dehydration and comfort, after 12 hours of CL wear.[152]

1.3 Clinical Performance of Soft Contact Lenses

Tear and vision related techniques are important, but the contact lens interactions with the eye have also great significance. Ocular and clinical performance can be dependent of material and surface properties of the lens and the design-material interactions with the eye. The clinical performance of SCL can be evaluated by slit lamp examinations and subjective assessments such as anamnesis and questionnaires.

1.3.1 Subjective Assessment of Comfort

The subjective assessment of CLs has demonstrated to be very important as the current clinical tests are not good at predicting CL wearers' symptoms. Thus, patient-reported outcomes (PRO) are gaining greater importance.[153] This comprises the specific questionnaires that can measure and diagnose dry eye symptoms and can reflect patient's viewpoints. To determine subject's dry eye symptoms, many questionnaires are available:

- Dry Eye Questionnaire (DEQ); [154]
- Contact Lens Dry Eye Questionnaire (CLDEQ), the only exclusively designed for CL wearers; [154]
- Ocular Surface Disease Index (OSDI); [155]
- McMonnies Dry Eye Index; [156]
- Frequency of Dryness Score, or Subjective Evaluation of Symptoms of Dryness (SESoD); [157]
- Impact of Dry Eye on Everyday Life Questionnaire (IDEEL). [158]

There are other questionnaires or PRO. A review conducted in 2013 found 121 PRO instruments in ophthalmic area, and constructed a top-8 higher-quality PRO, being in second the OCI (Ocular Comfort Index) that is similar to OSDI, for ocular surface symptoms assessment and its severity in dry eye and ocular surface disease. A study conducted by Michel *et al* [159] compared the OCI and McMonnies for the Contact Lens Induced Dry Eye (CLIDE) detection and concluded that the McMonnies performs better in predicting CLIDE. In the fourth place is Contact Lens Impact on Quality of Life (CLIQ), but this questionnaire only assessing the quality of life instead of symptomatology.[153] In the same study, the Ocular Disease Surface Index (OSDI), used in the present thesis, was "*not recommended by the*

authors for use in its original version because it violated the condition of unidimensiolality". Despite this, OSDI is notable among other similar questionnaires for having undergone psychometric testing and having been accepted by the US FDA as an outcome measure for use in dry eye trials.[155] But, once again, it is criticized because the inconstant step of difficulty between categories and by the no-comparable nature of the difficulty of all questions, which may result in a no-linearly scale related to symptom severity.[160]

In 2005, Guillon *et al* [161] applied the McMonnies questionnaire to ascertain the best questions that could be done to patients to know their symptoms, and concluded that the more predictive question for the detection of dry eye was frequency of ocular dryness instead of scratchiness; burning symptoms and sensitivity to cigarette and make-up products were lesser important.

1.3.2 Biomicroscopy

The slit-lamp evaluation with the proper use of clinical grading scales is important to assess the response of the eye to new CL materials, modalities or through-time changes. The eye can respond to CL wear by different forms. One of them comprises the engorging of limbal vasculature known has limbal redness.[162] This is considered a local response and is not affected by hypoxia at the central cornea, as soft lens wearers show a greater limbal injection than hard lens wearers, which have a vasculature similar to non-wearers.[163] This is a situation to be considered, since the chronic vessel dilation in soft CL wearers can lead to new vessel growth,[163] causing neovascularization namely in low Dk CL wearers.[164] More recent studies have found no differences in limbal redness between high Dk/t Si-Hy wearers and no-lens wear,[165] but there are differences between them and low Dk/t Si-Hy lenses.[166]

Other common clinical sign is bulbar hyperemia. This answer is also noticed in asymptomatic soft and rigid CL wearers,[84] but the changes in this parameter have not been significant over a 10 month period in soft CL wear.[167] These changes can be due to the damage that CL wear causes to the conjunctival vasculature by direct vaso-occlusion, once there are more conjunctival abnormalities in CL wearers than in non-wearers, with increased vessel diameter and contour over the lens edge.[168]

Other sign is the conjunctival staining. In CL wearers is often seen 2-mm from the limbus, which is the soft CL edge,[169] and is thought to happen because of CL movements and changes in the tear film

at the lens edge.[84] Conjunctival staining is most often encountered in CL wearers than in non-wearers, namely in Si-Hy[84] and symptomatic wearers and non-wearers,[124] so it can be correlated to some ocular symptoms.[170] These reactions are indicative of conjunctival damage caused by CL edges and by the evaporation caused by destabilization of the tear film,[124] but also include changes in lens parameters, CL modulus or poor lens fit.[171]

Corneal staining can occur in CL wearers but also in non-wearers.[172] The corneal staining may be due to several factors, such as mechanical effects (poor lens quality, such as rough edge), inflammatory, exposure, metabolic, toxic, allergic, and infectious.[19] Nichols and colleagues have concluded that there are many factors related to increased corneal staining, such as larger daily wear times, CL deposition, increased tear meniscus height and decreased hydrogel water content, and concluded that the use of Si-Hy lenses improved the corneal staining value.[173]

A recent study concluded that daily disposable Si-Hy CL have different ocular responses, maybe because of lens materials, surface properties, designs and packaging solutions.[166] For example Etafilcon A exhibited statistically higher limbal redness grades when compared to the other daily-disposable CLs used, and Senofilcon A the higher corneal staining extent and type.[166] A study who hypothesized that daily wear could improve CL related-symptoms in symptomatic CL wearers, found significant improvements in signs of limbal redness, bulbar redness and conjunctival staining at 2 and 4 weeks of daily disposables wear when compared to habitual CLs.[6]

2. HYPOTHESIS AND OBJECTIVES OF THE STUDY

2.1 Problem formulation

Although CL industry has increased considerably in the past years, there are many people that still drop-out CL wear because of discomfort. Thus, it is important to know what mechanisms lead to this discomfort and know if the new CL materials can reduce the symptoms presented. In this study are used two recent daily disposable CLs to investigate if there are any changes in visual, tear film and subjective parameters, in symptomatic CL wearers

2.2 Hypothesis

The hypothesis of this thesis is to know if new soft daily disposable CL materials can reduce the symptomatology throughout the day by means of a better PLTF stability and better optical quality.

2.3 Objectives

The main goals of this thesis are:

1. To investigate if there are any improvements in symptomatology with the lenses tested.
2. To analyze the PLTF stability, optical quality, and dehydration during the day of 2 lenses exposed to the same conditions (contralateral study), and compare them.
3. Assess the ocular surface response to the lenses.
4. Know if dynamic topography and aberrometry can measure PLTF stability.

3. MATERIAL AND METHODS

3.1 Study design

This study was a prospective, double-masked, randomized contralateral study which intended to compare two different daily disposable CLs with respect to their dehydration and differences in the quality of vision and tear quality during the day.

The research was conducted in the Clinical and Experimental Optometry Research Lab (CEORLab) at the University of Minho (Braga, Portugal). All the instruments used in this study were available in the CEORLab. The protocol of the study was reviewed and approved by the Subcomité de Ética para as Ciências da Vida e da Saúde / Ethics Submcomittee for Health and Life Sciences (SECVS) of the University of Minho. Following the guidelines of the Declaration of Helsinki, all subjects signed a Consent Form once the objectives and procedures of the study were fully explained to them.

3.2 Participants and Sample Size

Sample size calculation was done by means of online software (http://hedwig.mgh.harvard.edu/sample_size/js/js_crossover_quant.html). This was calculated for NIBUT and a total sample size of 18 subjects was needed.

In order to recruit participants for this study, it was sent an email to all academic community of the University of Minho. All the patients must had between 18 and 40 years of age, must be CL users even occasionally and must have symptoms of ocular discomfort. It was required transparent ocular media, no ocular pathology or surgery, and taking no ocular or systemic medications with ocular affectation. Subjects should present with a best corrected VA of 0.00 logMAR units or better, with refractive cylinder below 1.00D. The difference in VA between both eyes must be of less than 0.1 logMAR units and having less than 1.00D of anysometropia. All subjects that answered to the email and volunteered to participate underwent a full optometric examination to assess suitability to enter the study.

Thirty-one (31) subjects answered the email and came to an initial consultation, however 11 of them were unable to complete the experimental session: one (1) of them was asymptomatic (OSDI < 15); one (1) has been subjected to corneal refractive surgery before; one (1) did not feel comfortable with the CL involved in the trial despite the attempts to use CL before; three (3) of them had incompatibilities in scheduling all the follow-up visits; and five (5) had high astigmatism (>1.25D).

Twenty (20) subjects completed the study protocol. All measurements were done at the CEORLab at the University of Minho following the procedures described below in section 3.3.

3.3 Experimental Procedure

3.3.1 Contact Lenses Used

The daily disposable soft contact lenses used were Dailies Total1 (Alcon) and MyDay (CooperVision). The first one is a silicone hydrogel CL (Delefilcon A, <80% equilibrium water content (EWC)) which is the first-ever water gradient CL designed to feature an increase from 33% at the lens core to more than 80% water content from core to surface (Figure 3.1).

MyDay (Stenfilcon A, 54% EWC) is a daily disposable CL with a new chemical structure known as SmartSilicone™. These lenses have efficient channels for oxygen passage to the cornea, so they need less silicone in their material to enhance the desired oxygen permeability. This leads to a better humectability of lens surface, increased water content and lower modulus of elasticity.

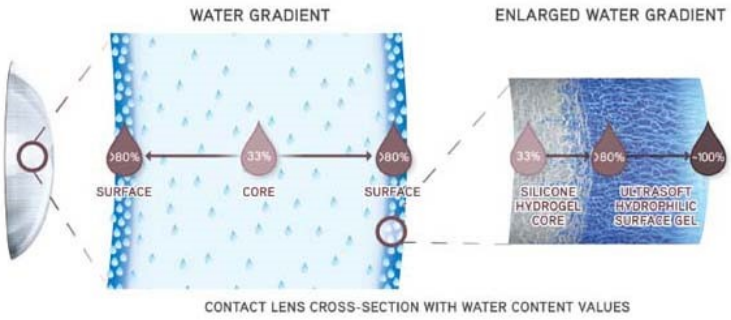


Figure 3.1 Cross-sectional illustration of Dailies Total1 water gradient. Image from Contact Lens Spectrum.[174]

Table 3.1 Parameters of Contact Lenses Used in Study

	Material	Diameter (mm)	Base Curve (mm)	Centre Thickness (mm)	Water Content (%)	DK/t	Modulus (MPa)
Total1	Delefilcon A	14.1	8.5	0.09	>80% at surface 33% at core	156	0.7
MyDay	Stenfilcon A	14.2	8.4	0.08	54%	100	0.4

3.3.2 Ocular Surface Disease Index (OSDI)

The Ocular Surface Disease Index (OSDI) developed by the Outcome Research Group at Allergan Inc (Ivrine, Calif)[175], is a 12-item questionnaire designed to provide a rapid assessment of the symptoms of ocular irritation consistent with dry eye disease and their impact on vision-related functioning. The OSDI has good to excellent reliability, validity, sensitivity, and specificity.[155] This questionnaire allows the diagnosis of any form of dry eye and its severity, as well as conduct a rapid assessment of ocular irritation due to dry eye and its impact on related visual functions. The questionnaire has 12 items graded on a scale of 0 to 4, where 0 indicates the absence of symptoms (none of the time); 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time. The total OSDI score was calculated on the basis of the following formula: OSDI= [(sum of scores for all questions answered) X 100] / [(total number of questions answered) X 4]. This was built on a 0 to 100 scale, with higher scores indicating greater disability. Similarly to other studies, we use a cut off value of 15 to group patients into asymptomatic and symptomatic CL wearers.[155]

This questionnaire specifically investigates the symptoms that the patient felt during the previous week and was used to measure the patients' symptoms at the start and after 5 days of contralateral use of the two CLs in the present study.

The OSDI has been validated for the Portuguese language in 2012, however it was only adapted for the Brazilian population. A preliminary analysis showed that the translation was weakly related with

the vocabulary currently used in Portugal. Thus, we choose to do a translation from the approved English and Spanish versions of OSDI to Portuguese people.

3.3.3 Patient Questionnaire

This questionnaire was developed at CEORLab (University of Minho). It is a visual analogue scale (VAS) that allows the simultaneous comparison of two different contact lenses used contralaterally (one in the RE and other in the LE). The patient is asked about the comfort felt right after lens insertion and at 4 and 8 hours of use, the dryness degree during the day and after 8 hours and about the quality of vision during the day and 8h after CL wear. The patients may assign a value between 0 and 10 in a continuous scale in each item, and answers for both eyes simultaneously. The questionnaire is included in Appendix 1.

The questionnaire also contains "forced choices" questions with respect to comfort and quality of vision, where the patient must choose between the lenses used in the right or left eye. This questionnaire was answered 3 times, in each final of the day visits.

3.3.4 Clinical Examination Routine

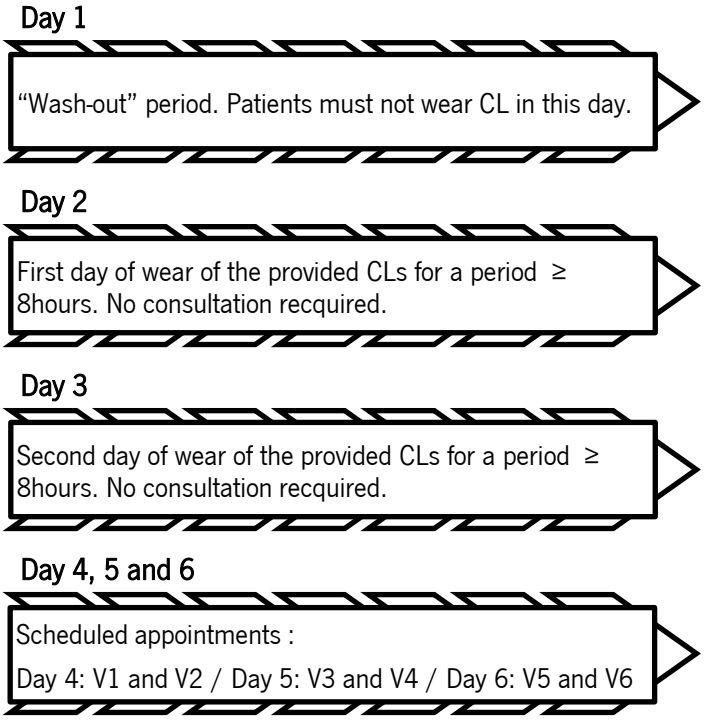
Once the subjects were selected to participate in this study, one baseline visit was scheduled according to the subject's availability and the protocol requirements. In the first visit (V0) the subjects underwent a full optometric examination, which included anamnesis, OSDI, refraction, logMAR HCDVA, topography, NIBUT with Tearscope, and slit-lamp examination with instillation of fluorescein. This visit was performed in the morning (between 9 and 12 a.m) and the patient was instructed to only insert the CL after de consultation.

Once the subjects were selected to participate in this study, an informed consent was signed and other 6 visits were scheduled. These visits were done in three days of the same week, one visit in the morning, 1 to 2h after CL insertion, and the other in the late afternoon after 7 to 9h of lens wear.

The lenses were masked by a third person so that neither the subject nor the examiner knew which lens the subject would be using in each eye. The subject must use the lens assigned with “OD” in the right eye and “OE” in the left eye (Figure 3.2). All subjects agreed to attend the 6 visits according to the protocol as illustrated in Table 3.2.

Figure 3.2 The masked blisters as they were provided to the subjects. The subjects were instructed to wear the “OD” lenses in the right eye and “OE” lenses in the left eye.

Table 3.2 Scheme of the 6 days of the study.



On the first day, each subject should not use any contact lens: 24h of "wash-out" period. The next day the subject would wear the first pair of lens provided by the examiner for a period equal or greater than 8h. The same should be done in the next day, with a new pair of lenses. In these 2 days was not necessary attend to any consultation. By the fourth day, the subject should attend the scheduled consultations: one in the morning, V1 (1 to 2h after lens insertion) and the other in the afternoon, V2 (7 to 9h of CL wear). So, the measures were done in the day 4 (V1 and V2), day 5 (V3 and V4) and day 6 (V5 and V6). The same parameters were evaluated in all visits and are listed above.

3.3.5 Visual Acuity

High contrast (100%) visual acuity (HCVA) and low contrast (10%) visual acuity (LCVA) were measured with the Logarithmic Visual Acuity Chart EDTRS (Precision Vision. IL) at 4 meters (as recommended by the manufacturer. The EDTRS distance chart is constituted by 14 lines with 5 letters each, and measure VA between 1.0 LogMAR units (that is equivalent to 0.1 in decimal scale) and -0.3 LogMAR units (2.0 in decimal scale). The line of 20/20 (or 1.0 in decimal scale) is equivalent to 0.0

(zero) in LogMAR scale. Each letter read means -0.02 and so VA is better if it is more negative or less positive. VA was evaluated under high (100%) (CAT No 2110) and low (10%) contrast (CAT No 2153) conditions using Cabinet Illuminator No 2425. All measures were taken monocularly and binocularly in the referred conditions. Room luminance was kept at photopic levels (85cd/m^2) during the whole examination.

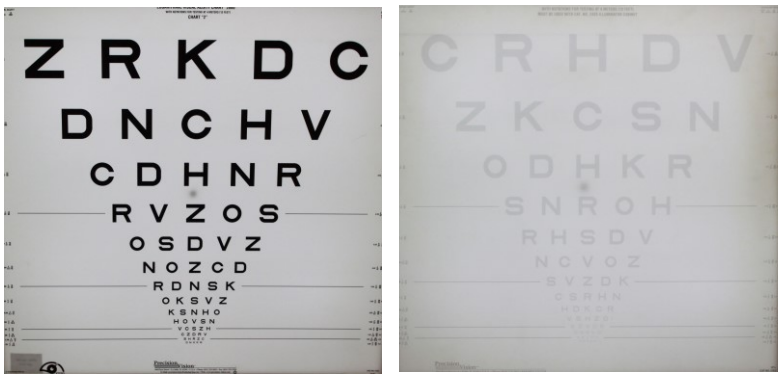


Figure 3.3 EDTRS chart for HCVA measure (right) and LCVA (left).

3.3.6 Subjective Optical Quality

This procedure was monocular and after obtaining the maximum low contrast distance VA with the EDTRS. The patient was instructed to fixate the VA line inmediatelly inferior to his maximum acuity (i.e. 0.1 if the patient's visual acuity was 0.0 logMAR), blink 3 or 4 times and maintain the eye open. After a few seconds, the patient must warn that stooped seeing the letters. The time between the last blink and the patient warning was recorded with a stopwatch. There were made three repetitions of this measure in each eye, in each one of the follow-up visits.

3.3.7 Non-Invasive Tear Break-Up Time (NIBUT)

3.3.7.1 Tearscope

The Tearscope (Keeler, Windsor, UK) allows the evaluation of the quality of the tear film by the projection of a grid into the anterior ocular surface (cornea). The instrument uses a cold cathode light which minimizes the ocular dryness during the procedure. The patient is asked to blink several times and then to open both eyes (although we evaluate only one at a time), the maximum time that is possible, until the observer sees the rupture. The time between the last blink and the appearance of the first distortion in the lines is registered and is known as the break-up time using the instrument's stopwatch. Three measures were performed in each eye and the mean was calculated.

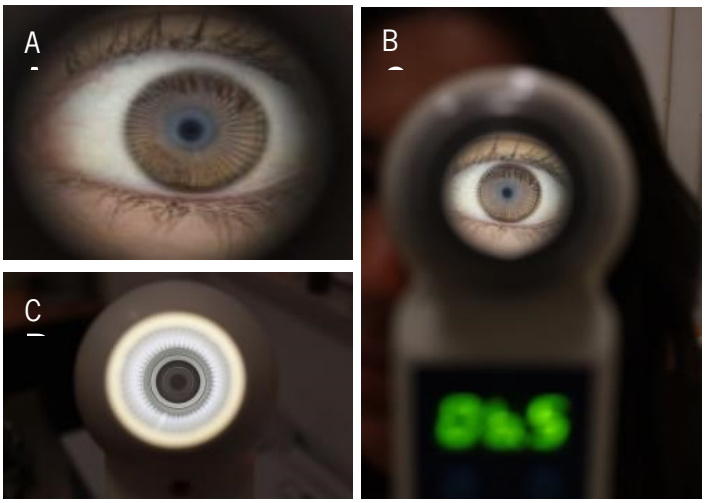


Figure 3.4 View of the observer through the Tearscope during the measurements (A and B) and view of the Tearscope's grid of (C).

The location were the first rupture was seen was taken for each measure, as shown in Figure 3.5.

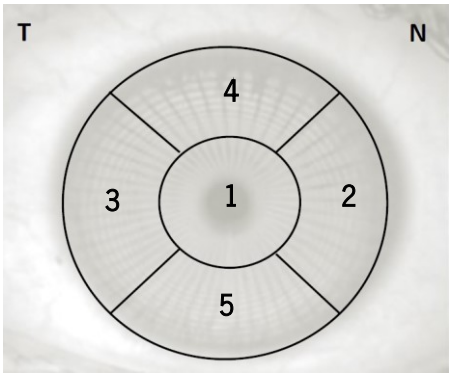


Figure 3.5 Schematic representation of the diagram used to note the location of the first rupture of the tear film. 1, Central; 2, Nasal; 3, Temporal; 4, Superior; 5, Inferior.

3.3.7.2 Dynamic Topography

Dynamic topography was obtained from a corneal topographer (Medmont E300, Australia) and with the lens *in situ*. In the "video" option, the 50 frames routine was chosen. This was chosen to avoid failures / not captures of images in some "instants" when another routines were chosen. After the measurement, the examiner must choose one of five images taken in each second, getting a total of 11 images: second 0, right after the blink; and seconds 1 to 10. The criterion used depended on the chosen image at 0 sec. If the investigator chose the 0.25sec, for example, the next image should be the 1.25sec or as close as possible.

For the measurement, the subject was comfortably set in the chin up of the instrument and the mires focused. The subject was instructed to blink several times and then open the eye for about 10 seconds. During this time, the examiner controls the joystick to ensure the maximum centering. Only one measure per visit was done.

Figure 3.6 Corneal Topographer Medmont and respective patients' view.

After choosing the images, the Surface Asymmetry Index (SAI) and Surface Regularity Index (SRI) values were taken for each second. The irregularities caused by tear film disruption can distort the topographic images and can be quantified with these two indexes.[89]

The SAI value is a global measure of corneal asymmetry with respect to the visual axis. In a perfect sphere the SAI value should be zero and should increase when the corneal power distribution becomes more asymmetrical. Technically, this index is based on power differences (centrally weighted average) between corresponding points located 180 degrees apart of the same chord. This is measured in the 4 central rings (Figure 3.7A). Basically, SAI detects alterations in corneal symmetry and will detect off-centre keratoconus apices by comparing areas of the corneal 180 degrees apart. So, SAI will not increase with regular astigmatism or centrally located cones, but will detect irregular astigmatism and decentered cones.[88;176] Its normal values range 0.10 to 0.42.[176]

The SRI value characterizes local fluctuations in corneal power and measures the central corneal optical quality, with lower values being related to a smooth corneal surface and increased values to an augmented central corneal irregularity (Figure 3.7B). They can predict the optical outcome that might be expected based on corneal topography, with normal values ranging 0.0 to 0.56.[176] SRI analyses the area of entrance pupil in standard lighting conditions. This is based on a comparative analysis of dioptric powers of adjacent points in 256 hemi-meridians in the 10 central-rings.[88] The predicted

power at a point is calculated as the average of the value of its rectilinear neighbors. The differences between the predicted power and the actual power are averaged over the central 4mm chord area.

In summary, SAI and SRI represent variations in corneal contour and can provide information about the relation of the corneal and tear film status.[90] In the context of the present study it is expected that SRI would be more sensitive to detect tear film break points due to the local specificity of these tear changes and the density and extension of the analyzed area.

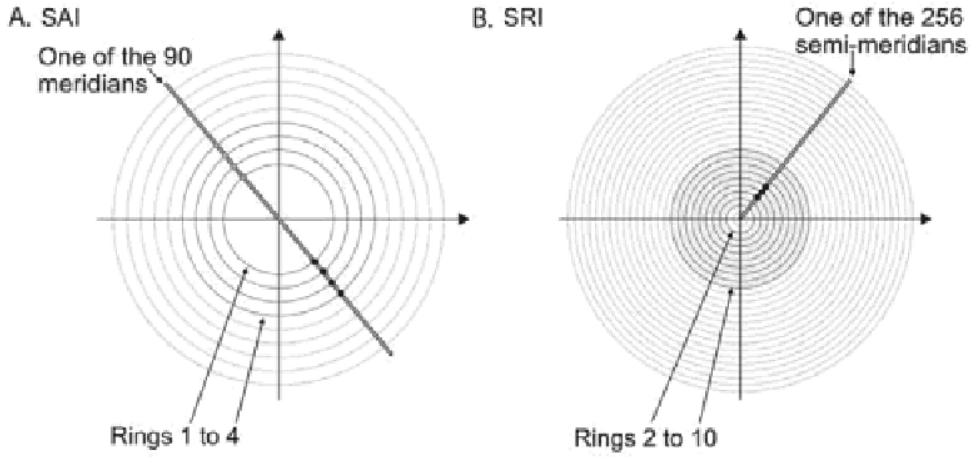


Figure 3.7 The analysed topographic indexes. A: SAI; B: SRI. Image from *Corneal Topography: From theory to practice.* [177]

For a better assessment, the TSRI (difference between maximum and minimum SRI values at each measure) and TSAI (difference between the maximum and minimum values at each measure) were also assessed and discussed.

3.3.7.2.1 Dynamic Aberrometry

Dynamic aberrometry was measured using IRx3 (ImaginEyes, France) and with the lens *in situ*. Twenty measurements of ocular wavefront were taken during a 28 seconds, with a blink at 14 seconds (between the 10th and the 11th measure). So, the patient must blink several times and then maintain the eye open for approximately 14 seconds, perform a fast complete blink and then continue with the eye wide open for another 14 seconds. The aberrometer takes the measures for a slightly different time in the different subjects. Table 3.2 shows the mean time in which each measure was taken. Ocular high order aberrations (HOAs) were recorded in mesopic conditions without any pharmacological mydriasis. The analysis of the Zernike polynomials up to the sixth order was done for a 3-mm pupil diameter.

Repeatability problems may be due to fixation errors and variation in the ocular aberrations themselves, caused by microfluctuations in accommodation, tear film instability or small eye movements. These factors affect more the horizontal and vertical coma.[178] Some studies applied topical anesthesia to prevent blinking and minimize patient discomfort.[179] Despite its unquestionable usefulness, the drop instillation can alter the tear film organization and then influence the outcomes.

Table 3.3 Time in which each measure was taken. Measures presented in millisecond (ms) and mean±SD.

M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
0.00± 0.00	1374± 53.72	2894± 93.87	4329± 127.31	5781± 175	7213± 220	8606± 239	10011± 280	11420± 340	12860± 394

M: Measure

Only the first 10 measures of 9 patients were considered for the analysis of this data, due to some problems with the pupil diameter in the other patients. There were some complications with these measures. The collection of dynamic aberrometry data could only be done for the minimum pupil size of each dynamic measure (20 aberrometry measures). So, if there were some "error" in any of the measures and the aberrometer considered the pupil with only 1mm, all the measures would be collected for 1-mm pupil. In other cases, patients could not keep the eye wide open during all the measurement, so there were not 20 measures in all visits for all patients. So, the measures of the third day (more days adapted to the lenses) were preferred. Only 9 patients fulfilled the criteria of: 3mm-pupil and 10 or more measures in day 3.

3.3.8 Biomicroscopy

For this evaluation on morning and afternoon visits the lenses were removed and were weighed (section 3.3.9) and then placed in saline.

For hyperemia assessment the Efron graphic scale was used (Figure 3.8). The superior, inferior, nasal and temporal quadrants were assessed individually and the final result was obtained by the sum of the 4 quadrants.

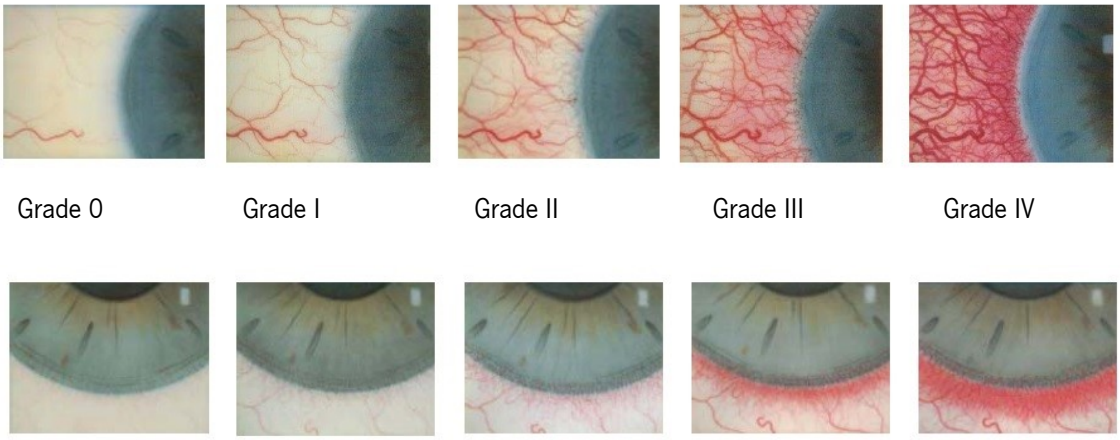


Figure 3.8 Efron Graphic Scales for Bulbar and Limbal Hyperemia

This was followed by fluorescein instillation. The Fluorescein Sno Strips (Chauvin) with saline solution (Avizor) were used and were placed in the superior fornix of conjunctiva. This instillation was done carefully in order to not instill too much fluorescein or even cause excessive reflex tearing, which could influenced the results. This was done for TBUT and both corneal and conjunctival staining assessment. Together with the fluorescein, the slit lamp with cobalt blue filter, 10x of magnification and yellow filter Wratten #12 (Eastman Kreak Company, Rochester, USA), for augment contrast, were needed. The evaluation was done 2min after fluorescein instillation. First, the TBUT was measured. The time interval between the last blink and the appearance of the first black spot was noted. Three measures were done and later the mean.

After it, the assessment of corneal staining extent was done with the assistance of Cornea and Contact Lens Research Unit (CCLRU) grading scale (5 zones) with: Grade 0 (nothing); Grade 1 (1 to 15% area with staining); Grade 2 (16 to 30% are with staining); Grade 3 (31 to 45% are with staining); Grade 4 (>45% area with staining). The assessments were done in steps of 1.[180] In the end, it was made the sum of five areas, where total corneal surface with complete staining was equivalent to 20 units. The conjunctival staining was assessed with Efron scale, with a 4-zone division (superior, inferior, nasal e temporal) and the sum of all scores was taken. After these evaluations, an "eye wash" was done with saline, so it does not interfere with the CL.

3.3.9 Ex-Vivo Dehydration

Before slit lamp evaluation, a third person performed the weighing of lenses. The principal investigator could not accomplish this task, because of the double-blind nature of this study and because the lenses can easily be distinguished by professionals by its coloration and handling. The material weight was assessed using a gravimetric method. The digital analytical balance was KERN ABT 220-5DM (Figure 3.9). This analytical balance is capable of measuring within 0.0001 g. The lenses were removed from the patient's eye and placed directly on the analytical balance. Only one measurement per visit was performed, for a total of 3 in the morning and 3 in the afternoon over the three days.

For establish a comparison with these *ex vivo* data, *in vitro* baseline measures were subsequently done for new lenses of the same optical powers. For these *in vitro* measurements, 3 lenses of each power of the lenses used by the subjects were taken. There were 12 different powers for each brand (12 for Total1 and 12 for MyDay). Each lens was measured 3 times, totaling 9 measures per power and brand. The same analytical balance was used for *in vitro* and *ex vivo* measurements.

Figure 3.9 Analytical balance used for lens' weight measures.

The balance was calibrated before each measure according to manufacturer's recommendations. For the weight measure, lenses were removed from the blister and the excess of water was removed from each surface before measurement, by blotting with a Whatman n°1 filter paper, preventing overestimated values. After it, the lens was placed on the balance and weighed. The total time that the lenses were exposed to air prior to measurement was less than 5 seconds in order to minimize dehydration before the first reading. After the lenses were placed on the balance, there was an additional 2-3 seconds until the digital scale of the balance stabilized. After each measurement the balance was cleaned with alcohol until it evaporates. It avoids the overestimation of the weight by small drops of water that could be in the base. After this, the balance was calibrated and then other measure was done. The values obtained were recorded and the mean of the 9 measures of the 3 lenses of the same power mas taken. Later, they were compared against the morning and afternoon visits, by the use of Relative Mass Loss (RML, %).

$$\%\, RML = \frac{\text{Baseline Weight} - \text{Weight 2}}{\text{Baseline Weight}} \text{ X } 100$$

3.4 Statistical Analysis

Statistical analysis was performed with SPSS Statistic software version 22.0 (SPSS Inc, Chicago, IL). The descriptive data are presented in terms of mean ± standard deviation. The normality of all variables was evaluated using the Shapiro-Wilk test, since the sample was <30. In the normality test, if the parameter of statistical significance (p) was less than 0.05, the null hypothesis was rejected, meaning that there were differences in the distribution of the sample compared to a sample with normal distribution. If the alternative hypothesis was accepted, is because there are no differences to the normal distribution and the variable in question has a normal distribution. For comparisons between the three visits, comparison of means was analyzed using ANOVA and Friedman test if the variable presented a normal or non-normal distribution, respectively. When only 2 visits were compared, for example the comparisons morning – afternoon, the Paired Samples T-Test was used for variables with normal distribution and Wilcoxon for those who do not fulfill this assumption of normality.

For the questionnaires, the VAS answers were done with Friedman test for multiple comparisons, because of the no-parametric nature of variables. The Wilcoxon test was done for morning-afternoon assessment. The second parts of questionnaire (forced-choices) were analyzed with Chi-square test. To compare between two questions, the Spearman Chi-Square test was used.

The correlations were performed by Pearson test if the sample had a normal distribution; otherwise the Spearman correlation was used. The correlations were considered strong if >0.80, moderately strong if between 0.5 and 0.8, fair if between 0.3 and 0.5 and poor if <0.30.[181]

The level of significance of the study was set at α=0.05.

4. RESULTS

4.1 Sample Characteristics (Baseline visit)

The characteristics of the sample (Table 4.1) are based on the baseline visit. All baseline visits were done in the morning, between 9 and 12 a.m. and the patients should not wear CL before this visit.

Table 4.1 Demographic characteristics of the sample.

Parameter	Description
N	20
Gender	13 F (65%) 7 Ma (35%)
Age (years)	26.75±6.28 Ma+F 26.92±6.4 F 26.42±6.6 Ma
Habitual refraction (D)	Pre-Total1 Eye -1.97±1.14 DS -0.11±0.27 DC Pre-MyDay Eye -1.88±1.15 DS -0.16±0.33 DC
Keratometry	Pre-Total1 Eye: 7.71±0.26 (D) Pre-MyDay Eye: 7.79±0.26 (D) **p=0.033** (Paired Sample T-Test)
Habitual correction	**Glasses and sporadic CL wear**: 5 **Sporadic CL wear only**: 2 **Daily disposable CL wear**: 5 **Monthly CL (daily wear):** 8
NIBUT (seconds)	Pre-Total1 Eye: 7.73±2.2 s Pre-MyDay Eye: 8.3±2.9 s p=0.09 (Paired Sample T-Test)
OSDI	32.95±9.82 (Range: 16.67 to 56.25) 33.36±9.7 F 32.70±10.9 Ma p=0.398 (Wilcoxon)

F, Female; Ma, Male; M, Equivalent Sphere; Pre-Total1 Eye, eye that receive Total1 lens, by randomization; Pre-MyDay Eye, Eye that receive MyDay lens, by randomization; DS diopters of sphere; DC, Diopters of cylinder. Age, refraction, NIBUT and OSDI expressed in mean±SD.

Similarly to other studies[49;83], the male/female ratio of the study population were representative of the general CL wearers, with a higher number of females.

There was a statistical difference in the keratometry values between the two eyes, but with no clinical significance to suggest a differnet behavior between both lens fittings. The values obtained are in agreement with the mean value of 7.77±0.2 mm measured with Medmont E300, in a study using a sample of 92 subjects with mean age of 24 years.[182] NIBUT was measured with Tearscope Plus, and there were no differences between the two eyes, being them strongly correlated (r=0.892, Pearson). All subjects had a monocular VA $\geq$ 0.00 LogMAR with the best correction in sphere.

Since the population was integrated by symptomatic CL wearers, the OSDI scores ranged from 16.67 to 56.25, with a slightly higher score in females when compared to males, but with no statistical significance. Figure 4.1 shows OSDI scores grouped by the modality of CL wear. Although there were no statistical differences between any of them (Wilcoxon), an increased symptomatology is present by those who only use CL sporadically. OSDI scores are inversely but poorly correlated to baseline NIBUT values (Spearman correlation of r=-0.193, p=0.415).

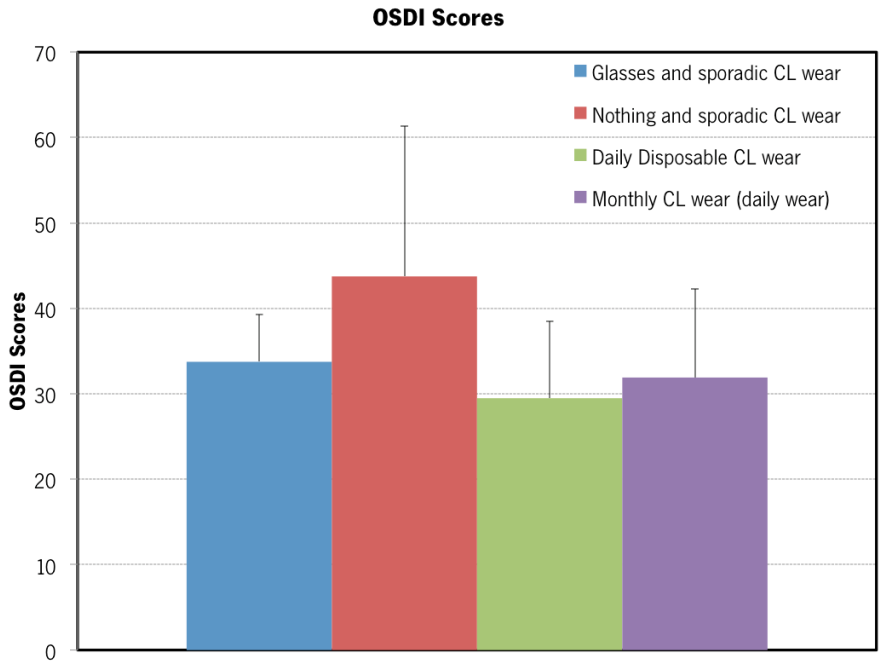


Figure 4.1 OSDI scores grouped by subjects' habitual CL modality.

Table 4.2 Slit lamp examination results (Limbal and bulbar hyperemia, BUT, corneal and conjunctival staining). The results shown are the sum of the different quadrants, except for BUT that is the mean of three measures.

	Limbal Redness	Bulbar Redness	BUT	Corneal Staining	Conjunctival Staining
Pre-Total1 Eye	1.7±1.50	3.05±2.03	4.22±1.94	0.55±0.83	1.9±2.19
Pre-MyDay Eye	1.85±1.70	2.65±1.46	4.15±1.60	0.25±0.55	1.85±1.91
p	*0.606* [·]	*0.176* [+]	*0.753* [+]	*0.068* [·]	*0.782* [·]

[·] Wilcoxon

[+] Paired Samplte T-test

The slit lamp examinations results are shown in Table 4.2. There were no statistically significant differences in all parameters between the eye that will wear Total1 nor MyDay lenses.

The next sections will show the results of each visit of the study. Primarily, the consistency between different days and in the same day will be shown for each lens separately and after the comparison between the two lenses will be done.

4.2 Visual Acuity

The results of monocular HCVA and LCVA changes for Total1 are shown in Table 4.3. VA is represented in LogMAR units, so the lower the better, with 0.00 indicating 1.0 or 20/20 visual acuity. There are no statistical differences between the different morning visits (V1, V3 and V5), contrary to afternoon visits (p=0.021, Friedman), being this differences between Day 1 and Day 3 (p=0.015, Wilcoxon). For LCVA there also are statistical differences only for afternoon visits (p=0.043, Friedman), between Day 1 and 2 (p=0.026, Wilcoxon) and Day 1 and 3 (p=0.029, Wilcoxon). As shown, there was a slight improvement of VA from Day 1 to 3 in both 100% and 10% VA for both morning and afternoon visits.

Table 4.3 also shows monocular HCVA and LCVA results for MyDay lens. In general, there are no differences between the three morning or afternoon visits for HCVA or LCVA. The only statistically significant difference was obtained in Day 1 between the morning and afternoon visit, with a better LCVA at the end of the day (p=0.024, Paired Sample T-test). There is a little improvement for LCVA,

namely in the morning visits. For binocular vision there was also a statistically significant difference in Day1 for LCVA.

Figure 4.2A shows the differences in HCVA between Total1 and MyDay lenses. In the morning visits, Total1 has better HCVA in all visits when compared to MyDay, but there were no statistically significant differences between the lenses in none of the visits. In the afternoon visits (Figure 4.2B) the behaviour is not so consistent, but Total1 lens seems to undergo an improvement relatively to MyDay lens reaching a better HCVA in the last day, as shown in Table 4.3. Once again, there are no statistically significant differences between the two lenses for any visit.

Table 4.3 Monocular and binocular High Contrast Visual Acuity and Low Contrast Visual Acuity (LogMAR scale) for the Total1 and MyDay lenses, measured over 3 days, in the morning and by the afternoon visits. Results are expressed in Mean±SD.

		HCVA				LCVA			
		Day1	**Day2**	**Day3**	**Mean p (a)**	**Day1**	**Day2**	**Day3**	**Mean p (a)**
TOTAL1	**Morning**	-0.05±0.07	-0.05±0.10	-0.07±0.11	-0.06±0.08 *0.821**	0.17±0,10	0.16±0.11	0.13±0.12	0.16±0.10 *0.081+*
	Afternoon	-0.03±0.10	-0.05±0.10	-0.08±0.10	-0.05±0.09 ***0.021+***	0.17±0.12	0.14±0.10	0.13±0.12	0.15±0.10 ***0.043+***
	Difference p (b)	-0.02±0.06, *0.144**	0.00±0.07, *0.984+*	0.01±0.06, *0.425**		0.00±0.07 *0.950**	0.02±0.06, *0.079**	0.00±0.06, *0.801**	
MYDAY	**Morning**	-0.04±0.09	-0.04±0.11	-0.06±0.11	-0.04±0.09 *0.771**	0.17±0.09	0.15±0.12	0.12±0.09	0.15±0.08 *0.196**
	Afternoon	-0.05±0.10	-0.05±0.10	-0.06±0.09	-0.05±0.09 *0.877**	0.14±0.11	0.12±0.08	0.12±0.11	0.13±0.09 *0.766**
	Difference p (b)	0.01±0.06 *0.468**	0.01±0.08 *0.484**	0.00±0.08 *0.769**		0.04±0.06 ***0.024****	0.04±0.12 *0.304+*	0.00±0.05 *0.729**	
BINOCULAR	**Morning**	-0.15±0.17	-0.12±0.07	-0,14±0.08	-0.14±0.09 *0.513+*	0.09±0.06	0.06±0.07	0.04±0.05	0.06±0.05 *0.068**
	Afternoon	-0.12±0,08	-0.13±0.06	-0.12±0.08	-0.13±0.07 *0.921**	0.06±0.06	0.05±0.05	0.05±0.06	0.05±0.05 *0.461+*
	Difference p (b)	-0.02±0.16, *0.636+*	0.01±0.04, *0.280**	-0.01±0.07, *0.452+*		0.03±0.05, ***0.029****	0.01±0.05, *0.267**	-0.01±0.04, *0.391**	

Statistical significant differences between the groups are presented in bold;
p(a): (*)ANOVA; (+) Friedman.
p(b): (*) Paired Sample T-test; (+) Wilcoxon.

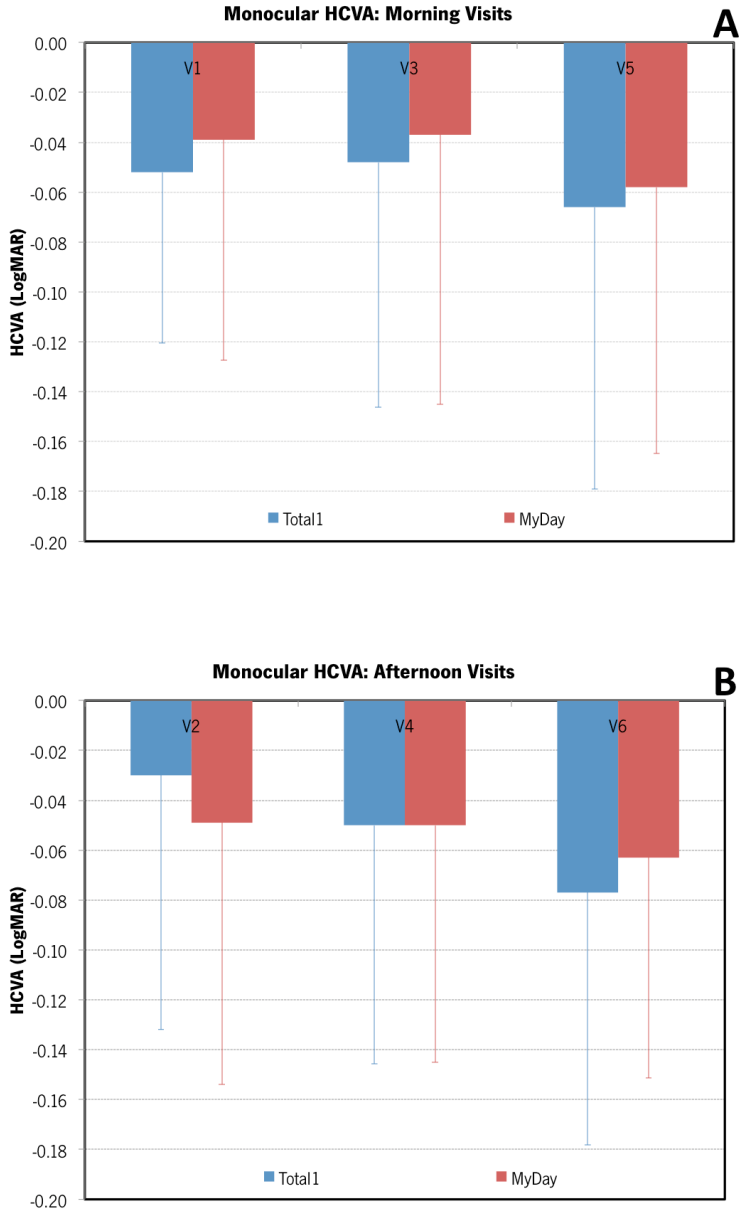


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Figure 4.2 Differences in High Contrast Visual Acuity (LogMAR scale) between Total1 and MyDay lenses in the morning visits (A) and afternoon visits (B). No statistical differences were found between the two lenses during the visits.

For monocular LCVA (Figure 4.3) the two lenses seem to have a very similar behaviour in the morning visits, with a better LCVA for MyDay lens in V3 and V5. In the afternoon visits MyDay shows a better LCVA since day 1. There are no statistically significant differences between the lenses in any visit.

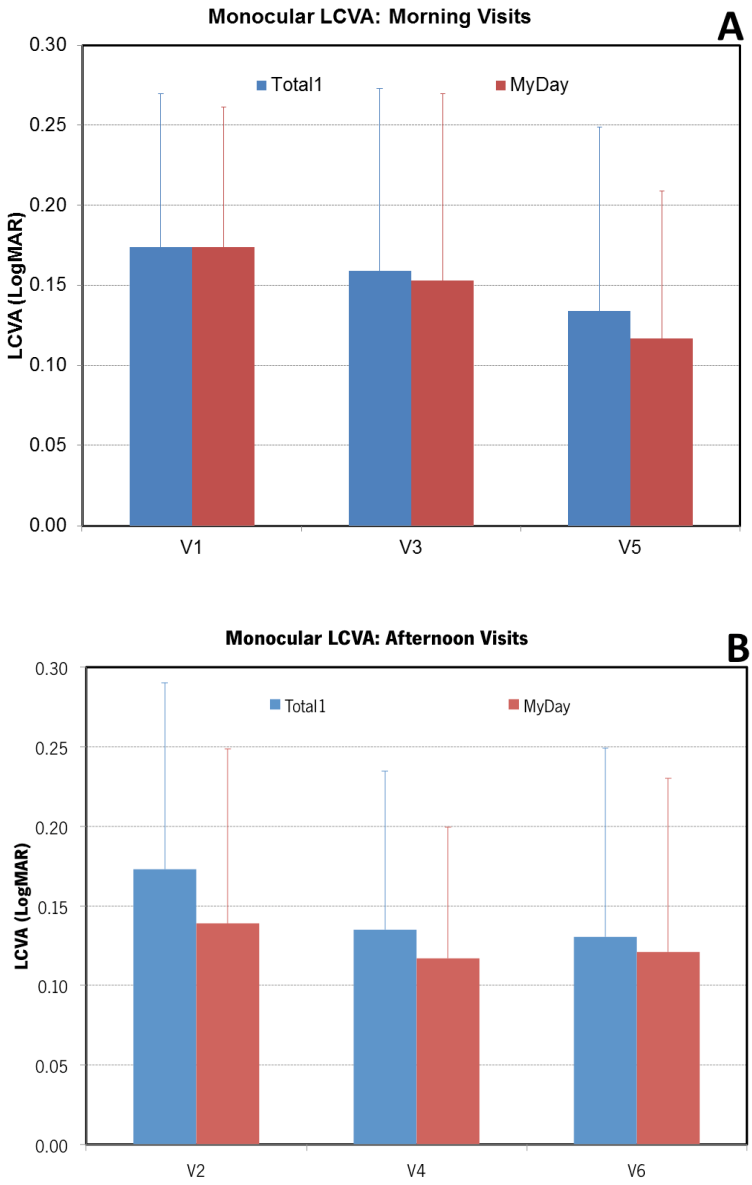


Figure 4.3 Differences in Low Contrast Visual Acuiry (10%) between Total1 and MyDay lenses in the morning visits (A) and afternoon visits (B). No statistical differences were found between the two lenses during the visits.

4.3 Subjective Optical Quality

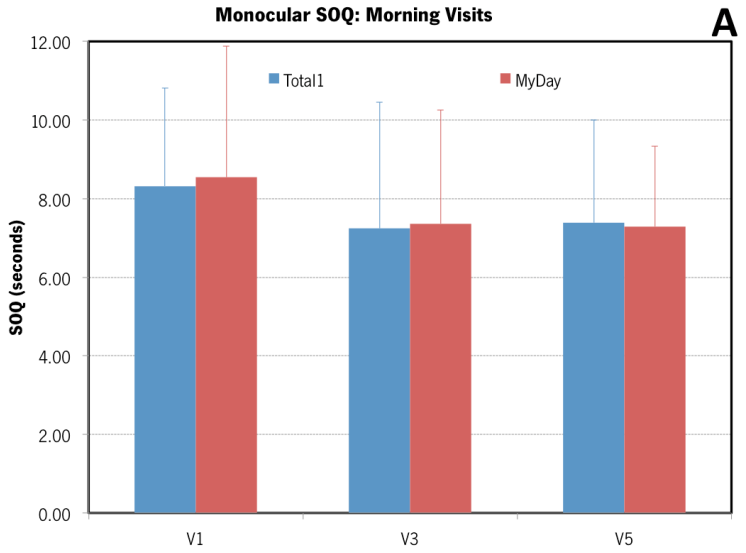
Table 4.4 shows the time (in seconds) between a blink and the disappearance of the letters of the line above the best LCVA: subjective optical quality (SOQ). The results show a worsening in this parameter between the morning visits and between the afternoon visits for both lenses (throughout the days). This worsening in SOQ values have statistical significance only for Total1 morning visits (p=0.043, Friedman) and in the afternoon visits for MyDay (p=0.026, Friedman). A worsening is also noticed during the day, with a better SOQ in the morning visits (except V3 of MyDay), but with no statistical significance in none of the lenses.

Table 4.4 Subjective Optical Quality (seconds) for Total1 and MyDay lenses. Results are expressed in Mean±SD.

		Day1	Day2	Day3	Mean p (a)
TOTAL1	**Morning**	8.31±2.51	7.24±3.20	7.39±2.61	7.65±2.26 ***0.043+***
	Afternoon	7.38±3.18	7.19±2.53	7.05±2.96	7.21±2.59 *0.705+*
	Difference p (b)	0.93±2.67, *0.100+*	0.05±3.67, *0.911+*	0.33±2.15, *0.751+*	
MYDAY	**Morning**	8.55±3.32	7.36±2.90	7.29±2.05	7.73±2.29 *0.387+*
	Afternoon	7.73±3.02	7.38±3.20	7.03±3.18	7.38±2.56 ***0.026+***
	Difference p (b)	0.82±2.57, *0.172**	-0.02±2.73, *0.976**	0.25±2.37, *0.636**	

Statistical significant differences between the groups are presented in bold;
p (a) *ANOVA; + Friedman Test
p (b) *t-test, + Wilcoxon

The same results are also shown in Figure 4.4 for comparison between the two lenses. There are no statistical differences between the two lenses in any of the visits, with both lenses showing a very similar behavior with approximate values.



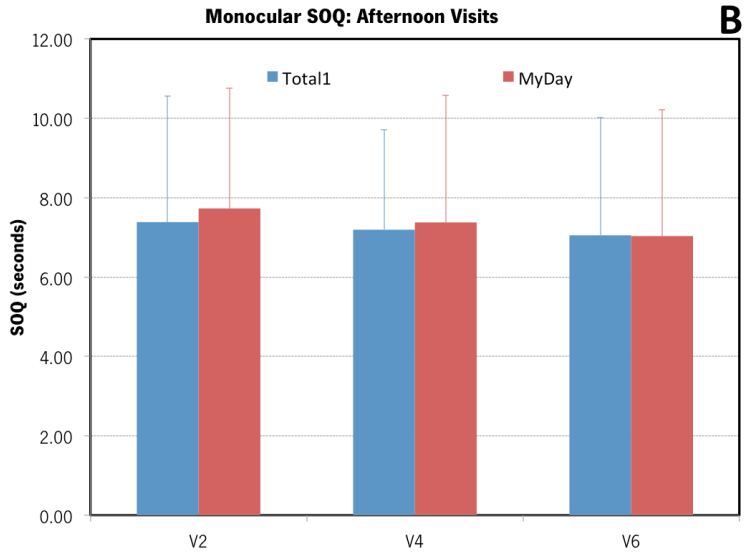


Figure 4.4 Subjective optical quality for morning visits (A) and afternoon visits (B). No statistical differences between the 2 lenses during the 3 days.

4.4 Tear Film

4.4.1 Pre-lens NIBUT

Table 4.5 shows the NIBUT values (in seconds) measured with Tearscope. The values seem to be consistent between the three morning and the three afternoon visits for both lenses, with no statistical significant differences (p>0.05, ANOVA or Friedman Test, depending on the distribution of each variable). Although there is a decreased NIBUT for Total1 between all morning and afternoon visits, the difference only has statistical significance in Day 3, between V5 and V6 (p=0.048, Wilcoxon). For MyDay lenses, the decrease in NIBUT for morning to afternoon has statistical significance in all days. Although these differences throughout the day in both lenses, they don't reach 1 second, making this values clinical insignificants.

Table 4.5 Monocular Pre-lens NIBUT (seconds) for Total1 and MyDay lenses. Results are shown in Mean±SD.

		Day 1	Day 2	Day 3	Mean (s) p (a)
TOTAL1	**Morning**	5.94±1.58	5.27±1.33	5.57±1.31	5.59±1.05 *0.387+*
	Afternoon	5.21±0.82	4.80±0.86	4.83±1.17	4.95±0.63 *0.326**
	Difference **p (b)**	0.73±1.63 *0.102+*	0.47±1.22 *0.101**	0.74±1.58 ***0.048+***	
MYDAY	**Morning**	5.97±1.58	5.45±1.15	5.66±1.43	5.69±1.21 *0.165+*
	Afternoon	5.07±0.79	4.87±1.32	4.93±1.95	4.96±0.93 *0.200+*
	Difference **p (b)**	0.89±1.29 ***0.006****	0.58±0.99 ***0.017****	0.74±1.90 ***0.007+***	

Statistical significant differences between the groups are presented in bold;
p (a), difference between the three visits: (*) ANOVA; (+) Friedman

p (b): (*) Paired Samplte T-test; (+) Wilcoxon

Figure 4.5 shows the same values for direct comparison between the two lenses. Both lenses seem to have a similar behavior in all visits, with no differences between the two lenses in any visit.

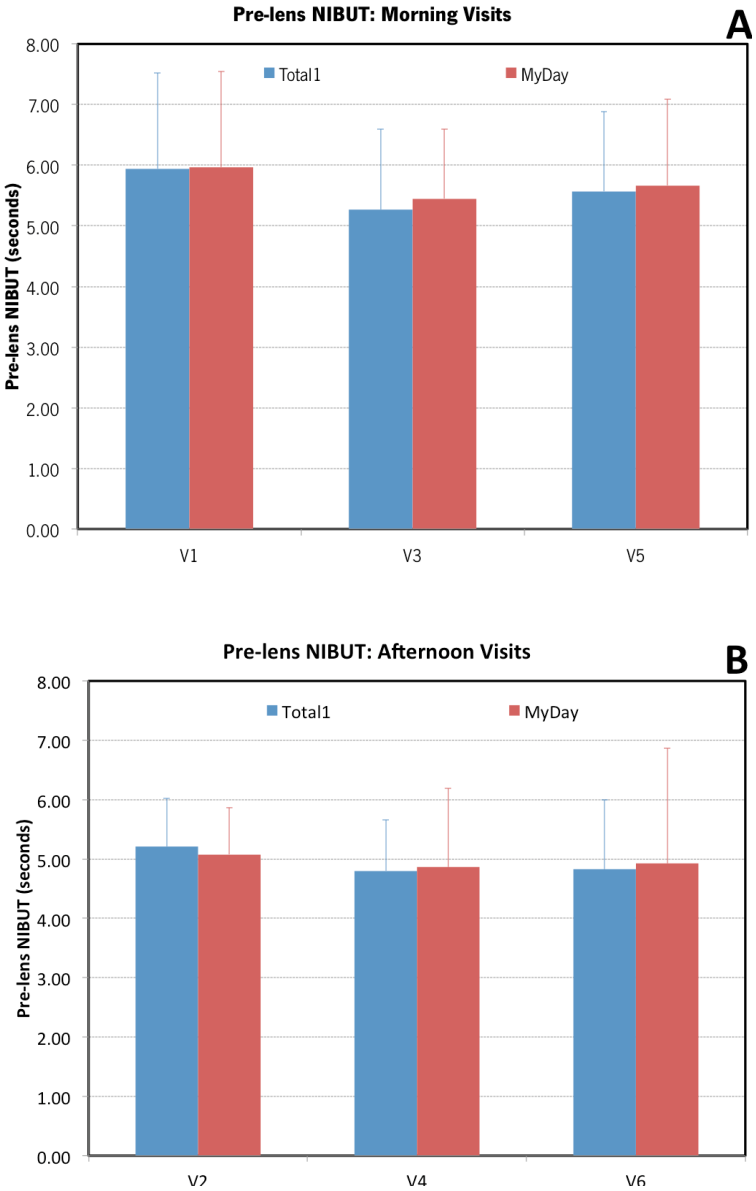


Figure 4.5 Pre-lens NIBUT (seconds) for morning visits (A) and afternoon visits (B). No statistical differences between the 2 lenses.

These NIBUT values are poorly correlated to SOQ values, being all correlations statistically insignificant.

The mean of the locals of the first tear film disruption in morning and afternoon visits are shown in Figure 4.6.

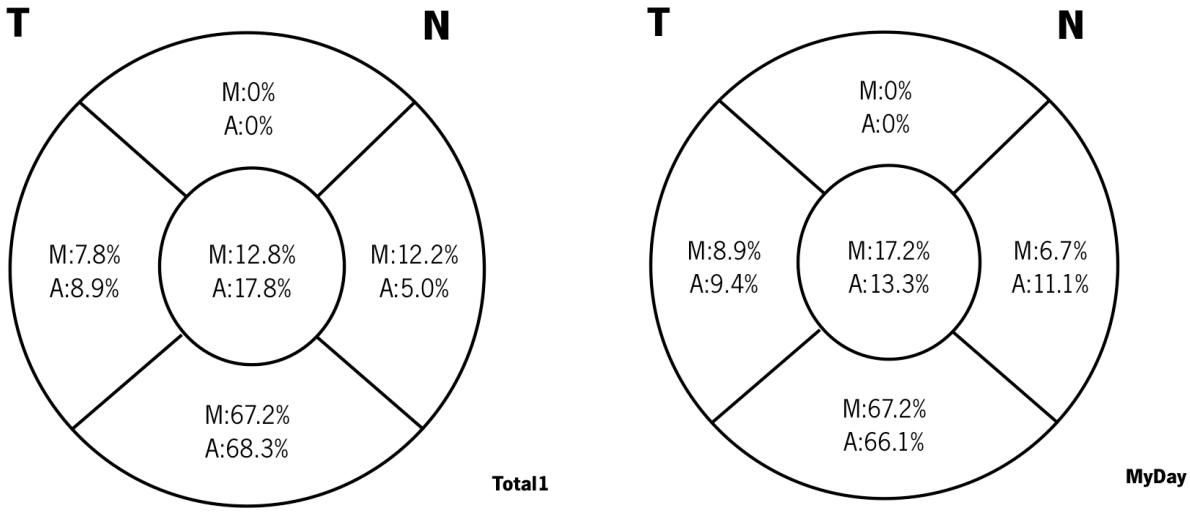


Figure 4.6 Local of the first tear film disruption in Total1 lens (left) and MyDay lens (right). Results are expressed in percentage of the mean of morning visits and mean of afternoon visits. M: Morning Visits; A: Afternoon Visits.

In the majority of times, the lens zone where tear breaks first is the inferior zone in all visits and for both lenses. The tear has never disrupted in the superior zone. The measures were always performed by the same observer.

There are some differences between morning and afternoon for both lenses. In Total1 there are differences mainly in the central and nasal zones; the number of measures in which the tear has disrupted in the central zone has augmented and has decreased in nasal zone for morning to afternoon. In the other zones (temporal and inferior) the frequencies remained very similar. There are differences in the frequency of times that each zone was observed in the morning and in the afternoon visits ($p=0.045$, Pearson Chi-square). In MyDay lenses the scenario is the opposite; the frequency of tear film disruption in the central zone has decreased from morning to afternoon, and has augmented

in the nasal zone, with no statistical significance. Despite this mentioned difference, both lenses seem to have similar performance, with disruption in inferior zone occurring between 67.2-68.3% in Total1 and 66.1-67.2% in MyDay lenses. There are no differences between Total1 and MyDay lenses neither for morning visits nor afternoon visits (p=0.051 and p=0.070, Pearson Chi-Square).

4.4.2 Dynamic Topography

Figure 4.7 shows the SRI values for Total 1 lens in the morning visits (A), in the afternoon visits (B) and the difference between the maximum and minimum SRI value in each measure: TSRI (C). In all the three morning visits is a very similar and regular performance up to 4 seconds, and an increase between 4 and 10 seconds. There are higher values namely from 5 to 10 seconds at V1, and more consistent values between V3 and V5 but also with a trend to increase. There is also an augment in standard deviation after the 5 seconds, evidencing a more variability in the values at higher times with the eye open. Despite this, there are no differences between the three morning visits. In the afternoon visits the values are lower when compared to morning visits, but with no statistical significance. By the afternoon, SRI values seem to be stable up to 2 seconds, and then is an increase until the 10 seconds. Total 1 lens seems to have a more stable behavior in the afternoon visits, with more consistent values and no statistical significant differences between the three visits.

The TSRI shows the difference between the maximum and the minimum value at each measure, indicating the stability in the measures during the 10 seconds measurement. For Total1 lens, greater TSRI values are shown in V1 and V5 (both morning visits) evidencing a less stable tear film in these two visits. Despite this, only a statistical significant difference between V1 and V2 were obtained (p=0.040, Wilcoxon), with Total1 showing a better performance in the afternoon. In the second day (V3 and V4), the values are very similar.

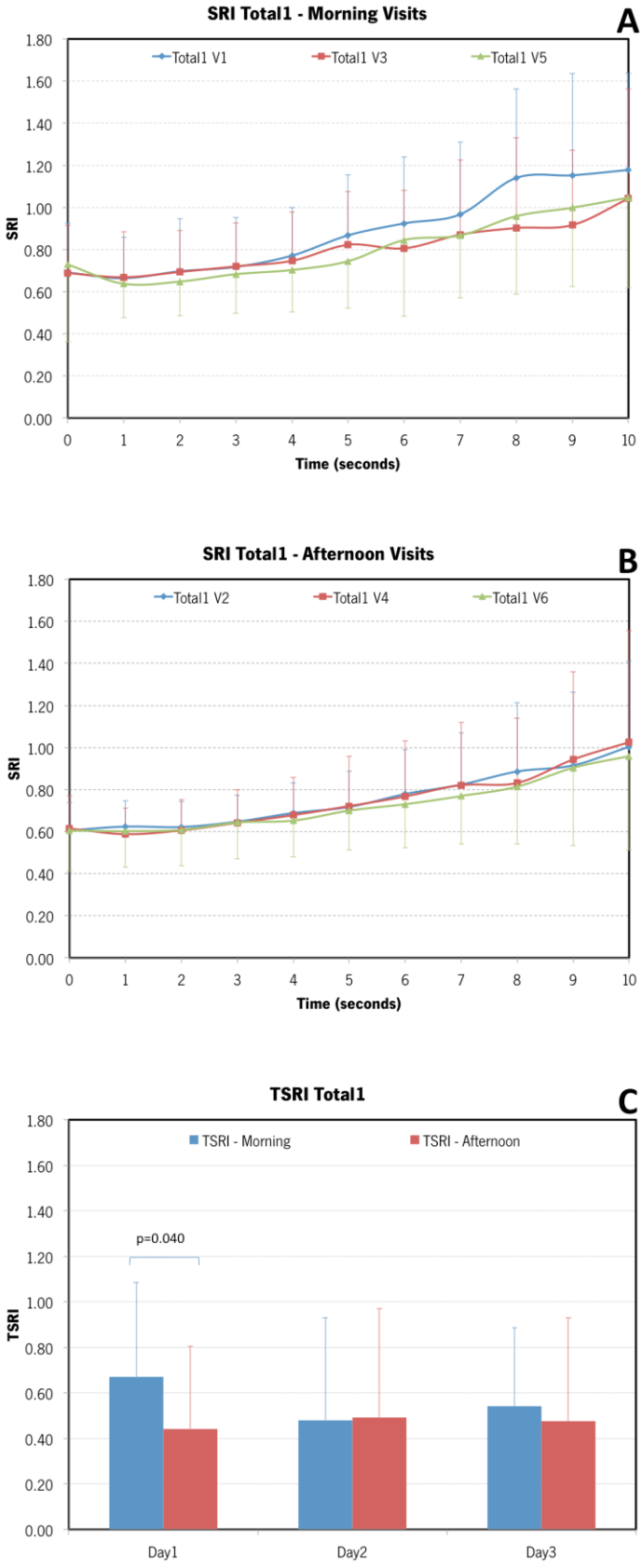


Figure 4.7 SRI values for Total1 lens in the morning (A) and afternoon (B) visits. The (C) represents the TSRI that is the maximum-minimum value for each visit.

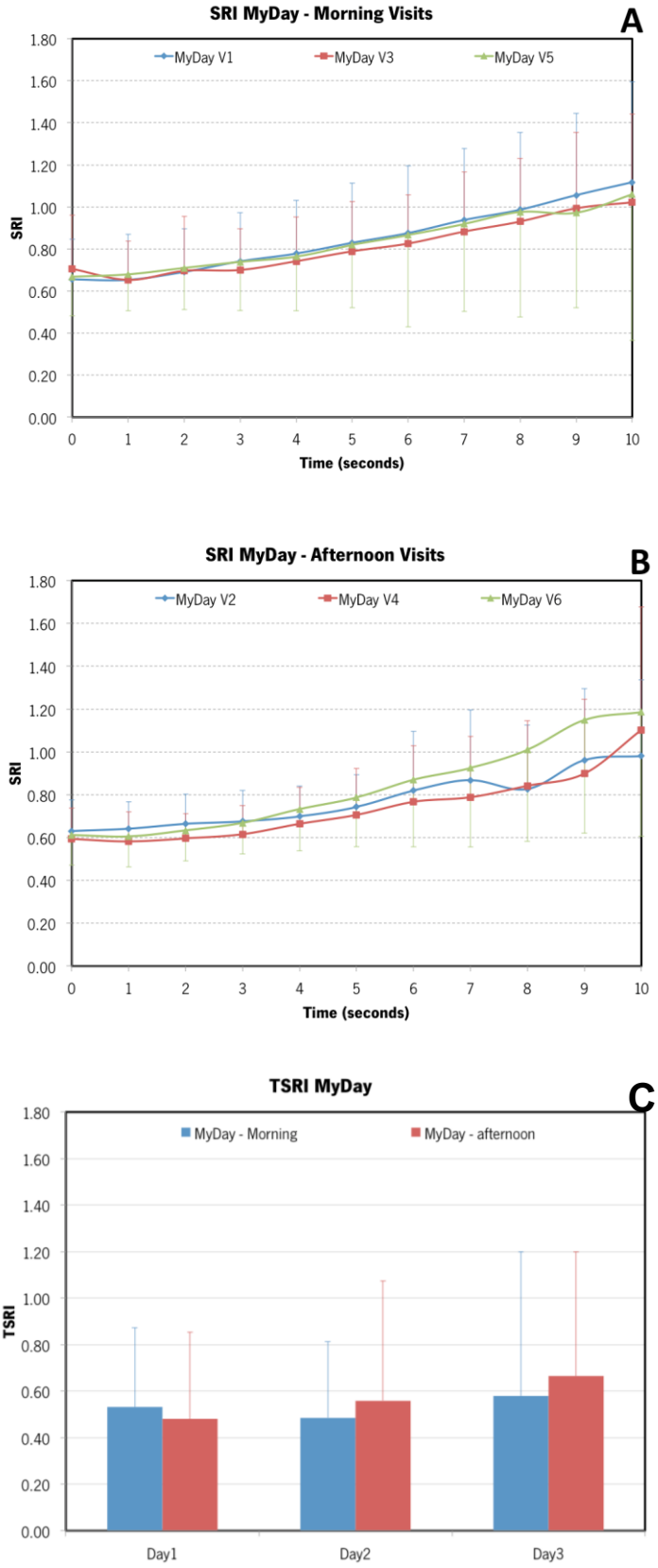


Figure 4.8 SRI values for MyDay lens in the morning (A) and afternoon (B) visits. The (C) represents the TSRI that is the maximum-minimum value for each visit.

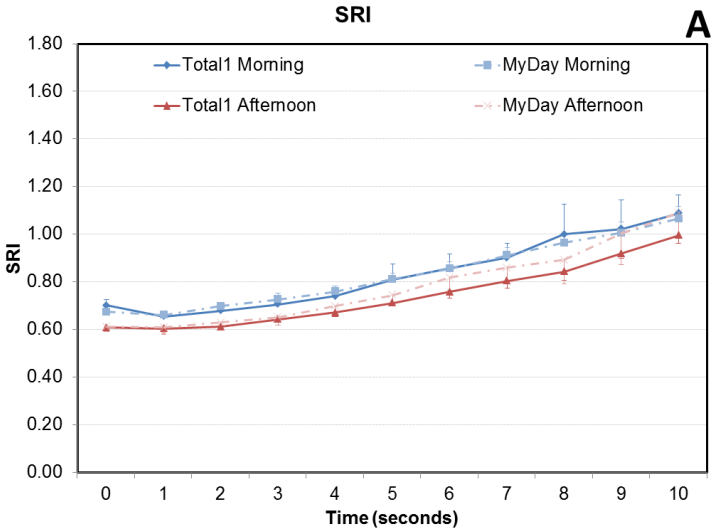
SRI values for MyDay lenses are shown in Figure 4.8. SRI values are very consistent during the three morning visits (Figure 4.8A) with no statistical differences between them ($p>0.05$, Friedman). The performance worsens right after the 2 seconds in all visits, continuing its degradation until the 10 seconds.

More irregular values are found between 5 and 10 seconds in the afternoon visits (Figure 4.8B) when compared to morning visits, but with no statistical significant differences between them ($p>0.05$, Wilcoxon) nor between the three afternoon visits ($p>0.05$, Friedman). In all visits (V1-V6) is an augment in SRI values over the time, showing a higher irregularity in MyDay surface the higher the time the eye is open. This increase is more noticed in V6. Contrary to the morning visits, this augment seems to be more noticed only after the 3 seconds (against the 2 seconds in the morning).

Higher TSRI values (Figure 4.8C) were found in the afternoon visits of Day2 and Day3, representing a less stable tear film in these visits. There are no statistical significant differences between morning and afternoon visits.

Figure 4.9 shows the comparison between Total1 and MyDay lenses for SRI values. As the values were very similar throughout the days, the mean of the three morning and three afternoon visits was done to compare the two lenses. The two lenses have a very similar behaviour in the morning visits (lines in blue). By the afternoon, Myday seems to have higher values of SRI, although there are no differences between the two lenses, neither for afternoon nor morning visits. As seen previously in Figure 4.7 and Figure 4.8, the SRI values are higher the higher the time the eye is open, suggesting a more irregular surface, with the increases being after the 2 seconds.

Analysing TSRI values (Figure 4.9B), a better performance is obtained for MyDay lens by the morning, but a much better for Total1 by the afternoon. Total1 seems to improve their stability during the day, when compared to MyDay, although there is no statistical significant difference between the two lenses. Contrary, MyDay worsens their performance from morning to afternoon. The SAI values of Total1 lens are presented in Figure 4.10.



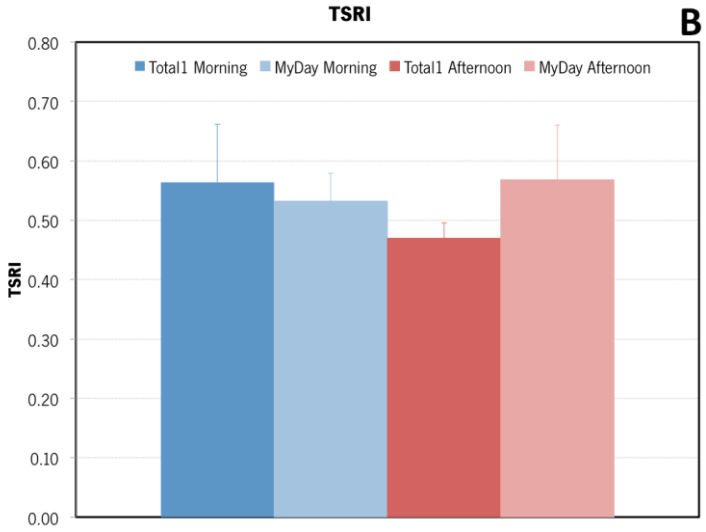


Figure 4.9 Differences in SRI (A) and TSRI (B) in morning and afternoon visits between the two lenses.

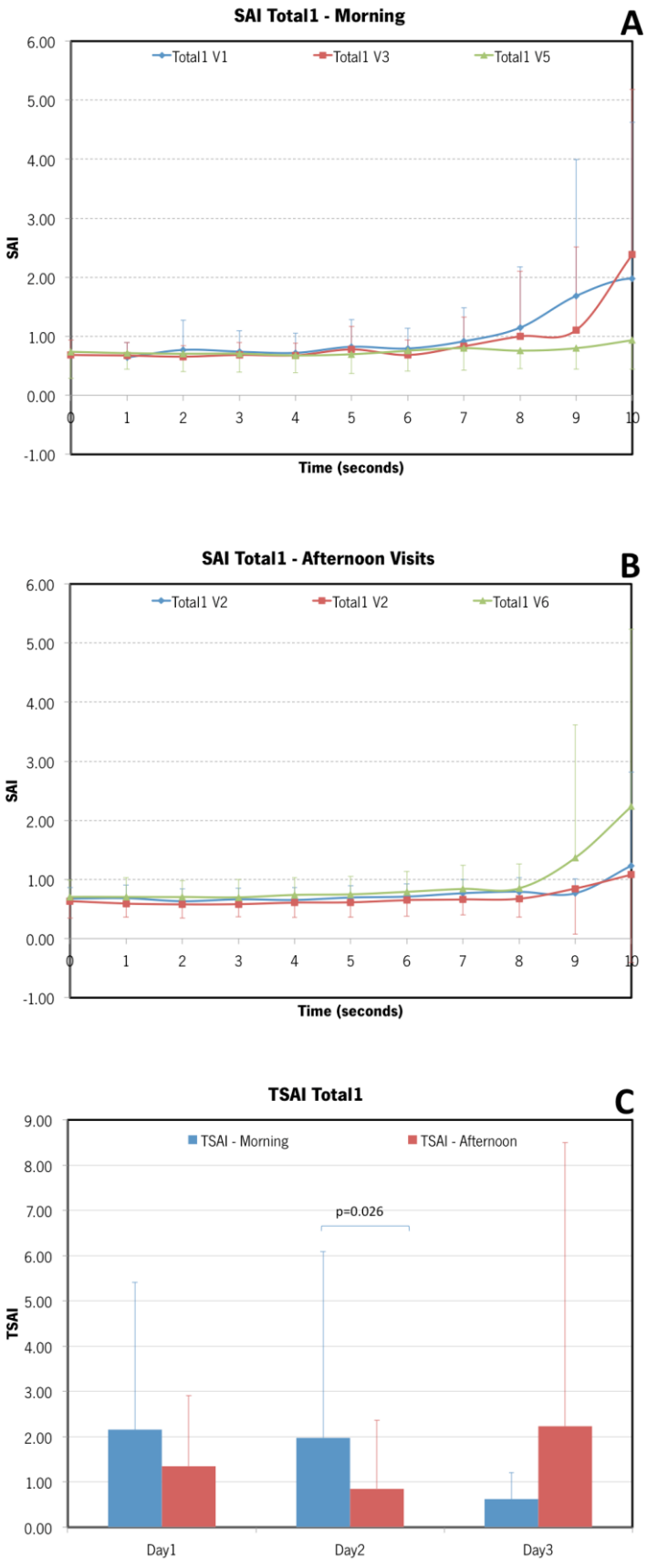
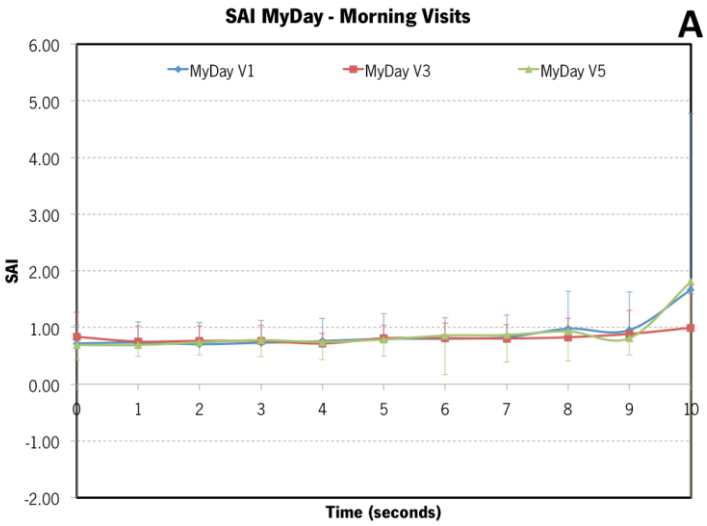


Figure 4.10 SAI values for Total1 lens. (A) morning visits; (B) afternoon visits; (C) TSAI value.

In the morning visits, SAI values for Total1 lens (Figure 4.10A) were very similar and constant up to the 7 seconds, where the V1 values start to increase. In V3 the increase is only noticed after 9 seconds of open-eye. There are statistically significant differences between the three morning visits (p=0.044, Friedman), more specifically between V1 and V5 (p=0.025, Wilcoxon). In the afternoon visits (Figure 4.10B), SAI values were more stable with a little increase after 8 seconds, namely for V6. Similarly to what happened in SRI values, the standard deviation is higher, the higher the sustained eyes open. No statistical differences were encountered between none of the afternoon visits, neither for SAI or TSAI.

TSAI values for Total1 lens (Figure 4.10C) present inconsistent values. Although in Day1 and Day2 there is a better performance in the afternoon, the same not happened in Day 3, with higher TSAI in the afternoon visit (V6). There is only a statistical significant difference between V3 and V4 (p=0.026, Wilcoxon). When the three afternoon visits are compared, there are differences between V2 and V4 (p=0.003, Wilcoxon) and between V2 and V6 (p=0.021, Wilcoxon). There are no differences between the three morning visits.



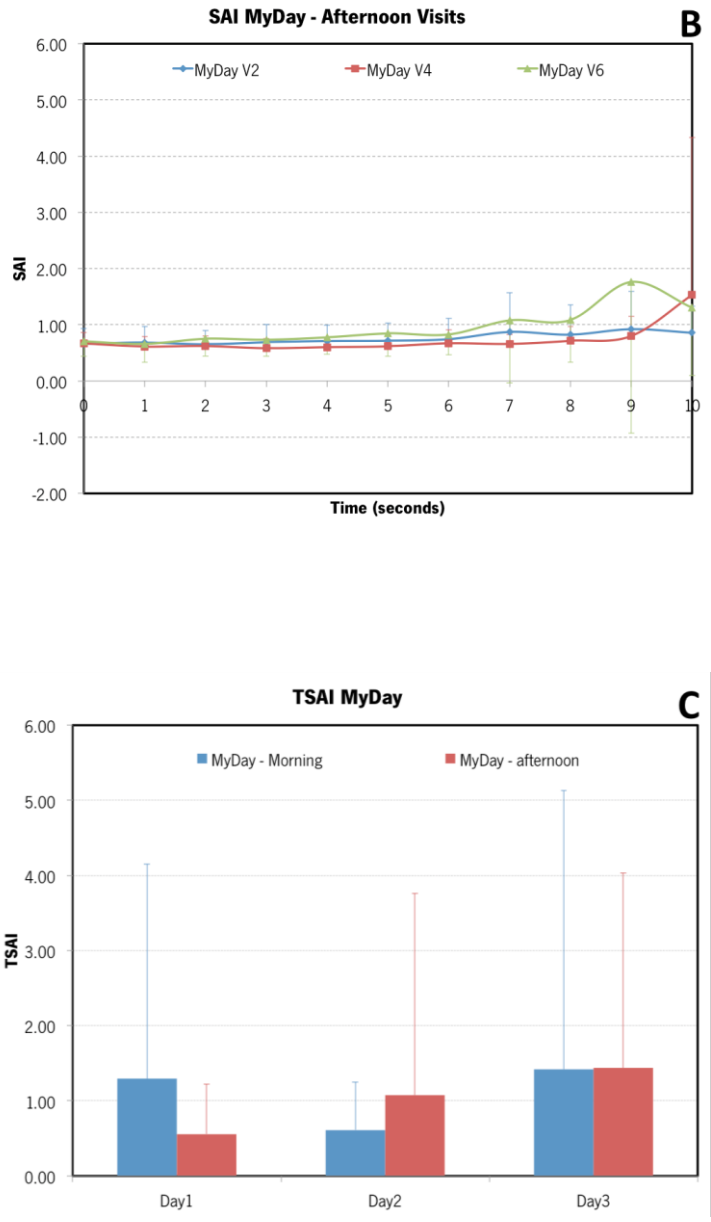


Figure 4.11 SAI for MyDay lenses. (A) morning visits; (B) afternoon visits; (C) TSAI value.

MyDay lens shows stable and coherent values between the three morning visits, with no statistically significant differences between them. Values are consistent until the 9 seconds. In the afternoon visits, V6 presents higher values after 8 seconds, but with no statistical differences when compared to the other visits. There were also no differences between morning and afternoon visits.

The TSAI values for MyDay (Figure 4.11C) lens show different behaviours throughout the days. Although in Day1 the TSAI were higher in the morning visit (V1), in Day2 the less stability was in V4 (afternoon) and in the last day, the values were similar in the two phases of the day.

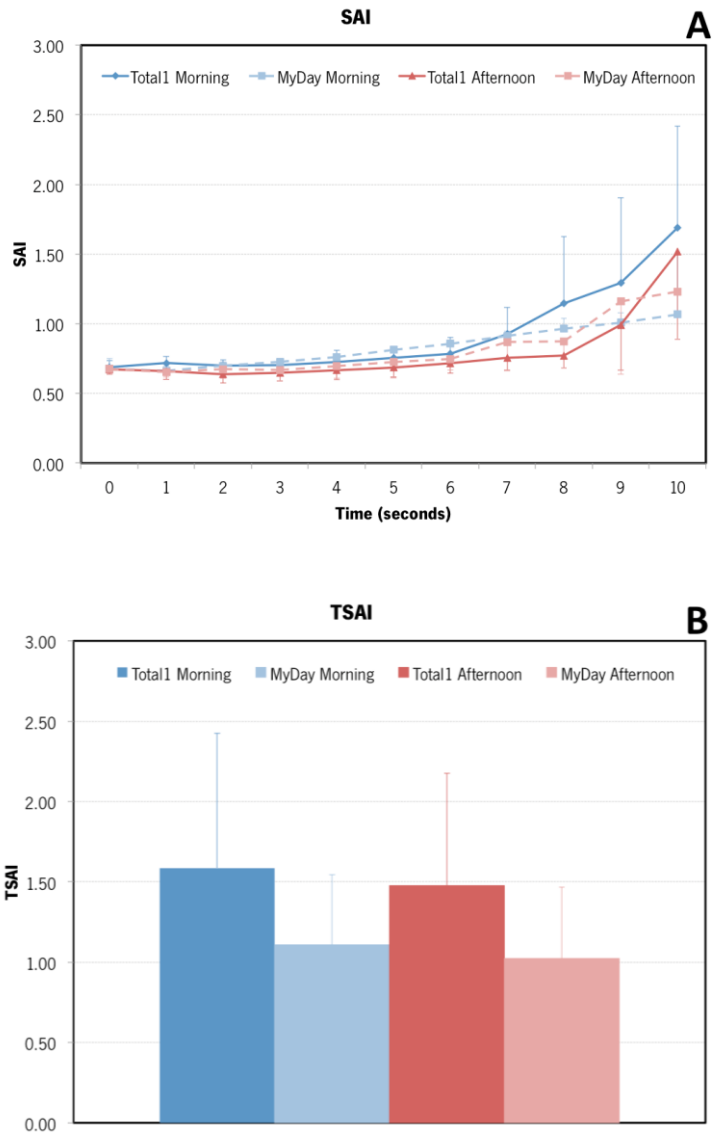


Figure 4.12 Differences in SAI values and TSAI values between the two lenses.

Again, as the SAI values were similar in the three morning and three afternoon visits, Figure 4.12 only shows the mean of the visits. SAI values (Figure 4.12A) are higher for Total1 lens by the morning, when compared to MyDay lens in the same visits. By the afternoon, the results are opposite, with

Total1 showing lower values until the 9 seconds. These results suggest that Total1 as a worst performance in the morning (especially from 7 seconds) and better in the afternoon, when compared to MyDay lens. As shown in Figure 4.10 and Figure 4.11, Total1 performs better in the afternoon compared to morning and MyDay performs better in the morning until 8 seconds. Despite this, there are no statistical significant differences between the two lenses.

Analysing TSAI (Figure 4.12) we can see a better performance for MyDay lens, but there are no statistical significant differences between the two lenses. So, there are more difference between the lower and highest SAI values in Total1 lens, making this lens appear less stable.

When pre-lens NIBUT was compared to the time that topographic values start to increase more, little correlations are found. Only a correlation of r=0.526 (p=0.017, Spearman) is found when NIBUT and the time that SRI reaches its maximum for Total1 morning visits are compared. There are no more statistically significant correlations between these two variables, neither between NIBUT and the time that the SAI values reach their maximum values in none of the lens.

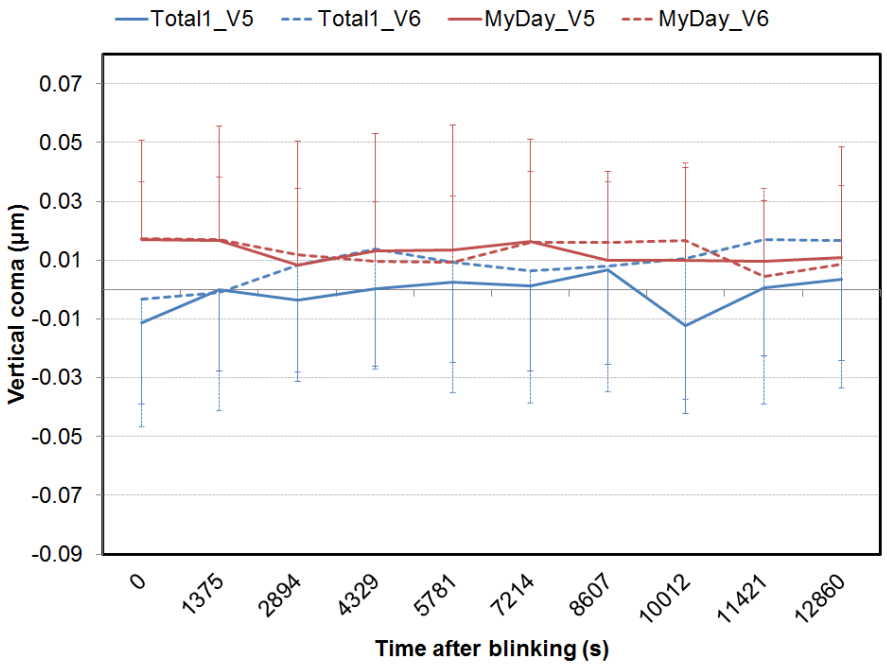
The pre-lens NIBUT was also compared to the mean SRI and SAI values. For Total1 lens, there was only a negative and fair correlation between pre-lens NIBUT and mean SAI value (r=-0.448, p=0.047, Spearman) in afternoon. The other correlations are weak and with no significance. For MyDay lens, there are two significant, negative and moderately strong correlations. One is between NIBUT and the mean SRI value in the morning visits (r=-0.503, p=0.024, Pearson) and the other between NIBUT and mean SRI of the afternoon visits (r=-0.512, p=0.021, Spearman).

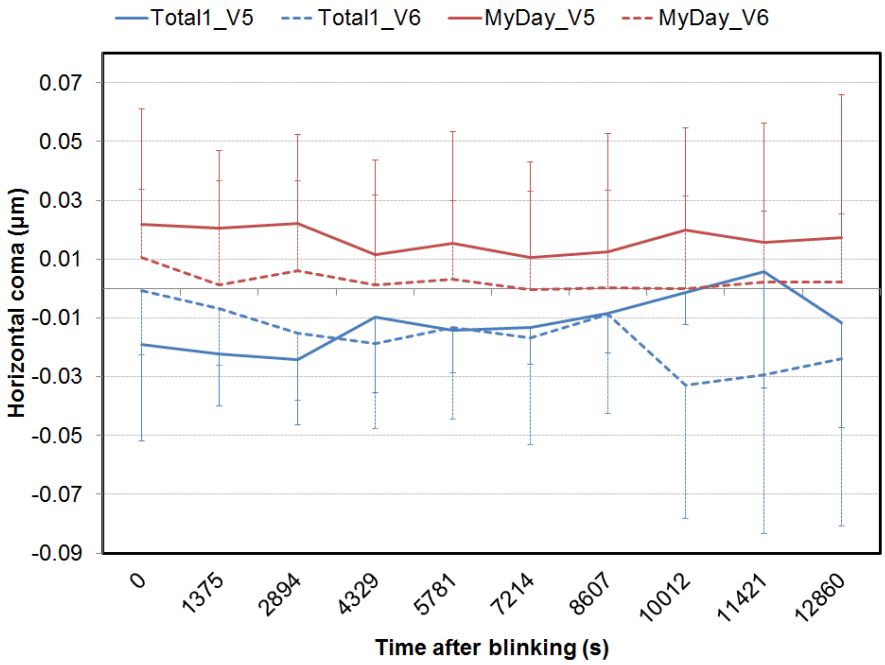
4.5 Wavefront aberration dynamics.

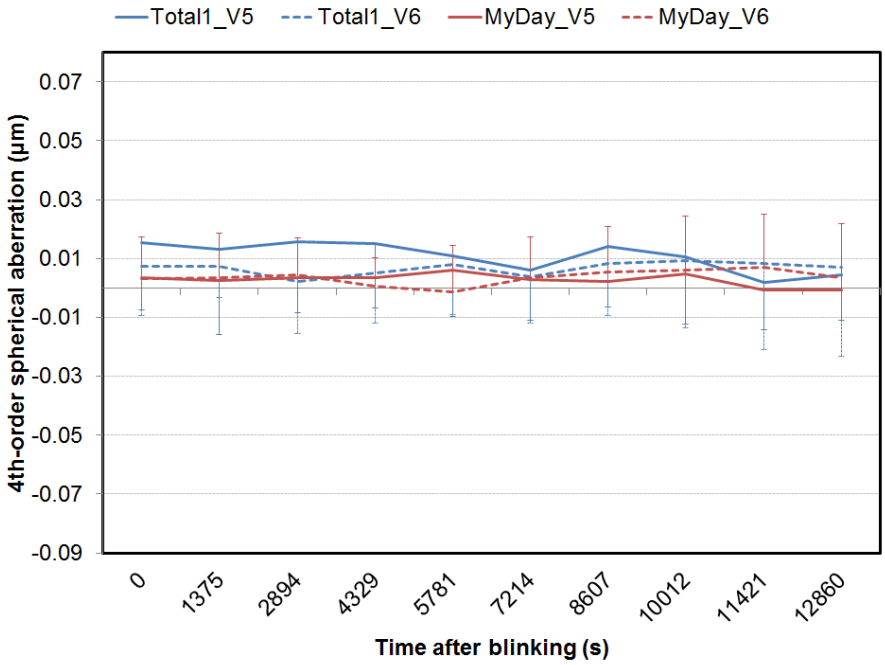
Only the measures of 3mm-pupil of 9 patients of the third day (V5 and V6) were considered for this analysis. There were considered only up to the 12 seconds measurement (before the intermediate blink).

In average, there are statistical significant differences between morning and afternoon for the vertical coma in Total1 lens ($p=0.002$, Paired Sample T-test) and for the horizontal coma in MyDay lens ($p<0.001$, Paired Sample T-test). Between the two lenses, there are statistical significant differences in the morning for vertical coma ($p<0.001$, Paired Sample T-test), horizontal coma ($p<0.001$, Paired Sample T-test) and Spherical aberration ($p<0.001$, Paired Sample T-test). In the afternoon, the differences are in horizontal coma ($p<0.001$, Paired Sample T-test) and spherical aberration ($p=0.011$, Paired Sample T-test).

The RMS values from 3rd to 6th order are presented in Figure 4.13D. It is observed some disparity between morning and afternoon for Total1 lenses (blue lines).




Total1_V5
Total1_V6
MyDay_V5
MyDay_V6
Horizontal coma (µm)
0.07
0.05
0.03
0.01
-0.01
-0.03
-0.05
-0.07
-0.09
0
1375
2894
4329
5781
7214
8607
10012
11421
12860
Time after blinking (s)


Total1_V5
Total1_V6
MyDay_V5
MyDay_V6
4th-order spherical aberration (µm)
0.07
0.05
0.03
0.01
-0.01
-0.03
-0.05
-0.07
-0.09
0
1375
2894
4329
5781
7214
8607
10012
11421
12860
Time after blinking (s)

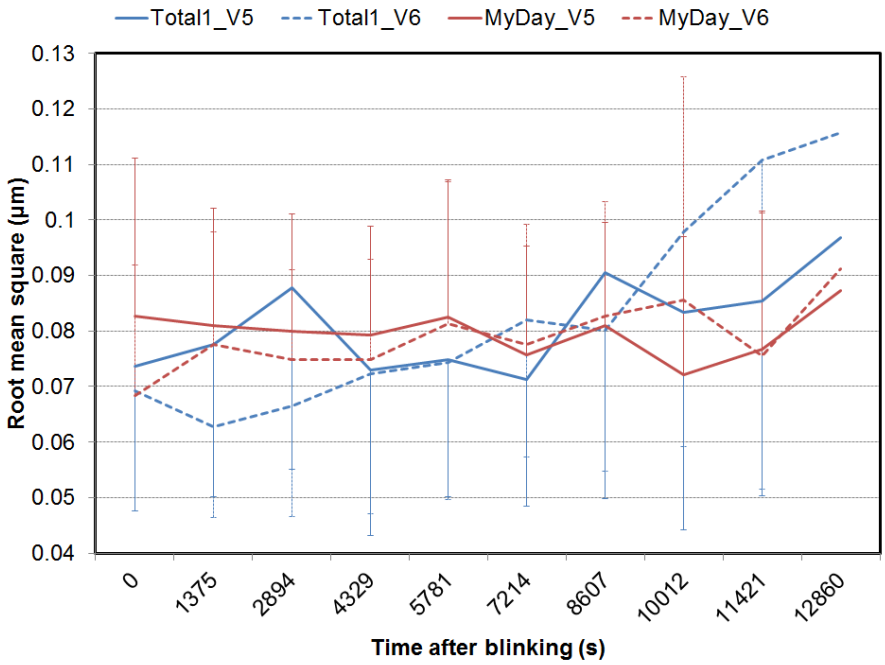


Figure 4.13 Comparative analysis of wavefront aberration dynamics (3mm-pupil) between Total1 and MyDay lenses and between morning (V5) and afternoon (V6) visits of the third day. A: Vertical coma; B: Horizontal coma; C: Spherical aberration; D: RMS of 3rd to 6th order. Data from 9 patients and throughout 12 seconds (10 steps) after a complete blink.

The correlations encountered between NIBUT and the time that aberrations reach their maximum or minimum value for Total1 lenses, was only found between NIBUT and the time that spherical aberration reaches its maximum value in morning visits (r=-0.766, p=0.016, Pearson); and also between afternoon NIBUT and the time that spherical aberration reach its maximum value in afternoon (r=-0.684, p=0.042, Pearson). The other correlations have no statistical significance. For MyDay lens, there are no significant correlations between these two variables in the morning visit, and in the afternoon visit only a significant correlation is found between afternoon NIBUT and the time that vertical coma reaches its minimum value (p=-0.799, p=0.010, Pearson). The other moderate correlation is found between afternoon NIBUT and the time that the vertical coma reaches its maximum value (r=0.653, p=0.056, Pearson). Despite these two, the other correlations are poor.

4.6 Biomicroscopy

The lenses were removed before slit lamp examination. Thereby, we will name "Total1 eye" to the eye that had Total1 lens and "MyDay eye" to the eye that used MyDay lens.

The results of the parameters measured during slit lamp examination are shown in Table 4.6. For Total1 eyes, higher values of limbal hyperemia are found in the morning visits when compared to the afternoon ones, with statistical difference only between in Day 3 (p=0.034, Wilcoxon). For bulbar hyperemia and corneal staining the scores are very similar between the morning and afternoon visits for this lens, with no statistical significant differences. For conjunctival staining, the highest values are found in afternoon visits except for Day 3, but again with no differences.

For MyDay eyes, there are differences between the three morning visits for the limbal hyperemia with the highest value in Day 1 and the lower in Day 3. These differences are between V1 and V3 (p=0.044, Wilcoxon) and V1 and V5 (p=0.005, Wilcoxon). Morning limbal hyperemia shows high values when compared to the afternoon visits, but with no statistical significant differences. Both limbal and bulbar hyperemia have suffered a decrease from Day 1 to Day 3 in both morning and afternoon visits. Contrary to Total1, corneal staining has high values in Day 1 and Day 2 morning visits when compared to afternoon visits in MyDay eyes, but with no statistical differences. The opposite happens in conjunctival staining, with afternoon visits having highest values, being these differences statistical significant for Day 3 (p=0.028, Wilcoxon).

Table 4.6 Values of Limbal Hyperemia, Bulbar Hyperemia, Corneal Staining and Conjunctival Staining for Total1 and MyDay eyes in morning and afternoon visits. The results are shown in Mean±SD. p-value is shown in italics and statistical significant differences in bold.

		Day 1	Day 2	Day 3	p(a)
		Limbal Hyperemia			
Total1	MORNING	1.55±1.96	2.25±2.07	2.00±2.08	*0.615*
	AFTERNOON	1.80±1.90	1.60±1.96	1.30±1.38	*0.113*
	p(b)	*0.360*	*0.171*	***0.034***	
MyDay	MORNING	2.90±2.57	2.00±2.77	1.45±1.79	***0.010***
	AFTERNOON	2.05±2.09	1.65±1.72	1.50±1.60	
	p(b)	*0.248*	*0.441*	*0.830*	
		Bulbar Hyperemia			
Total1	MORNING	2.95±1.96	3.35±2.16	2.50±1.88	*0.526*
	AFTERNOON	3.05±1.70	3.15±1.87	2.50±1.40	*0.554*
	P(b)	*0.705*	*0.644*	*1.000*	
MyDay	MORNING	3.30±2.61	3.15±2.21	2.25±1.30	*0.169*
	AFTERNOON	2.85±1.31	2.65±1.87	2.35±1.50	*0.504*
	p(b)	*0.472*	*0.417*	*0.731*	
		Corneal Staining			
Total1	MORNING	0.40±0.75	0.21±0.53	0.32±0.59	*0.368*
	AFTERNOON	0.32±0.58	0.31±0.48	0.45±0.94	*0.717*
	P(b)	*0.414*	*0.317*	*0.414*	
MyDay	MORNING	0.15±0.37	0.26±0.73	0.00±0.00	*0.223*
	AFTERNOON	0.05±0.23	0.21±0.41	0.35±0.81	*0.212*
	p(b)	*0.317*	*0.739*	*0.066*	
		Conjunctival Staining			
Total1	MORNING	0.85±1.92	0.95±1.47	1.00±1.56	*0.519*
	AFTERNOON	1.42±1.87	1.21±1.90	0.95±1.54	*0.337*
	p(b)	*0.085*	*0.287*	*1.000*	
MyDay	MORNING	1.45±1.73	1.26±1.59	0.89±1.44	*0.058*
	AFTERNOON	1.95±2.22	1.47±2.14	1.60±2.26	*0.423*
	p(b)	*0.162*	*0.688*	***0.028***	

p(a) Friedman

p(b) Wilcoxon

Table 4.7 represents the statistical differences (p-value) between Total1 and MyDay eyes in all visits (V1-V6). There are statistical significant differences in V1 for limbal hyperemia (p=0.014, Wilcoxon) with a highest value for MyDay eyes (1.55±1.96 for Total1 and 2.90±2.57 for MyDay), and in V5 in corneal staining (p=0.034, Wilcoxon) with a highest value for Total1 eyes (0.32±0.59 for Total1 and 0.00±0.00 for MyDay). The other differences were in conjunctival staining in V1 (p=0.012, Wilcoxon), in V2 (p=0.048, Wilcoxon) and in V6 (p=0.030, Wilcoxon), always with highest values for MyDay. In average, Total1 has lowest values for limbal hyperemia and conjunctival staining for both morning and afternoon visits, and highest for corneal staining in morning and afternoon. Bulbar hyperemia is very similar in the two eyes.

Comparatively to baseline visit, there are only statistical significant differences for conjunctival staining in both Total1 and MyDay eyes (p=0.03 and p=0.01, respectively).

Table 4.7 Representation of the differences found between Total1 and MyDay lenses in all visits for the parameters measured in slit lamp.

	V1	V2	V3	V4	V5	V6
Limbal Hyperemia	***0.014***	*0.374*	*0.423*	*0.748*	*0.096*	*0.344*
Bulbar Hyperemia	*0.365*	*0.531*	*0.305*	*0.05*	*0.569*	*0.755*
Corneal Staining	*0.206*	*0.05*	*0.705*	*0.317*	***0.034***	*0.414*
Conjunctival Staining	***0.012***	***0.048***	*0.161*	*0.405*	*0.763*	***0.030***

Table 4.8 represent the BUT values after fluorescein instillation. As seen, the Total1 has a lesser BUT than MyDay in all visits, although they are no statistical differences between them. Also, Total1 eyes show a great difference between morning and afternoon, with a mean difference of 0.295seconds between these visits, with just 0.180seconds for MyDay. These values have no statistical differences and no clinical relevance. Despite this, the changes in BUT during the day are minimal in the two eyes. There are no statistical differences between these values and baseline visit in both eyes.

Table 4.8 Mean BUT values for Total1 and MyDay lenses in all visits. p-value is shown in italics. No statistical significant differences were found.

	V1	V3	V5	p(b)	V2	V4	V6	p(b)
Total1	4.60±1.35	4.23±0.81	4.25±0.81	4.37±0.84 *0.241* [·]	4.15±0.77	3.81±0.96	4.24±1.10	4.07±0.70 *0.062* [+]
Myday	4.41±1.37	4.30±1.10	4.60±1.45	4.45±1.10 *0.504* [+]	4.34±0.93	4.09±1.09	4.31±1.27	4.26±0.89 *0.841* [+]
p(a)	*0.430* [·]	*0.778* [+]	*0.218* [+]		*0.322* [·]	*0.206* [+]	*0.926* [+]	

p(a): [·]Paired Sample T-Test; [+] Wilcoxon

p(b): [·]ANOVA; [+] Friedman

4.7 Dehydration

Dehydration values are shown in percentage, by mean of relative mass lost (RML, %). Data show the difference between the CL mass in the baseline (*in vitro*) measure, and in the *ex-vivo* measure performed in all visits. Later, the results will express the RML between the morning visits (*ex vivo measure*) and afternoon visits (*ex vivo measure*).

Figure 4.14 show the RML values for Total1 lens. Despite the negative value (-0.083%) found in V3 (Day 2 - morning) which means that the *ex vivo* measure was higher than the *in vitro*, there are no statistical significant differences between the three morning visits (p=0.537, ANOVA). In the afternoon visits, the values are very similar, ranging from 0.880±3.9% in V2 to 0.654±3.1% in V6, being the differences found between visits not statistical significant (p=0.385, Friedman).

Total1 lenses show a higher dehydration after 8 hours (afternoon) of CL wear than in the morning visit (2 hours), when compared to the baseline (*in vitro*) measures, but the differences were not statistical significant in none of the cases (p>0.05, V1 vs V2: Wilcoxon; V2-V4 and V5-V6, Paired Sample T-Test).

For MyDay lenses (Figure 4.14B) the performance is somewhat different. There are no statistical significant differences between the three morning visits (p=0.549, Friedman) nor between the three afternoon visits (p=0.528, ANOVA). Comparing the morning and afternoon visits, some differences appear. In the 3 days, MyDay lenses present higher RML values in the afternoon than in the morning visits, when compared to *in vitro* measures, like Total1 lenses. In Day 1, the difference between V1

and V2 is from 1.69±3.9% and 2.22±3.7%, being this difference statistical significant (p=0.008, Wilcoxon). The difference is higher in Day 2, with RML values with 2.22±4.03% in the morning, reaching 3.94±4.3% in the afternoon. The different between these two visits were statistical significant (p<0.001, Paired Sample T-Test). In the third day, the difference between the two visits was also statistical significant (p=0.002, Paired Sample T-Test), with values ranging from 1.64±3.78% in the morning and 2.64±4.13% in the afternoon.

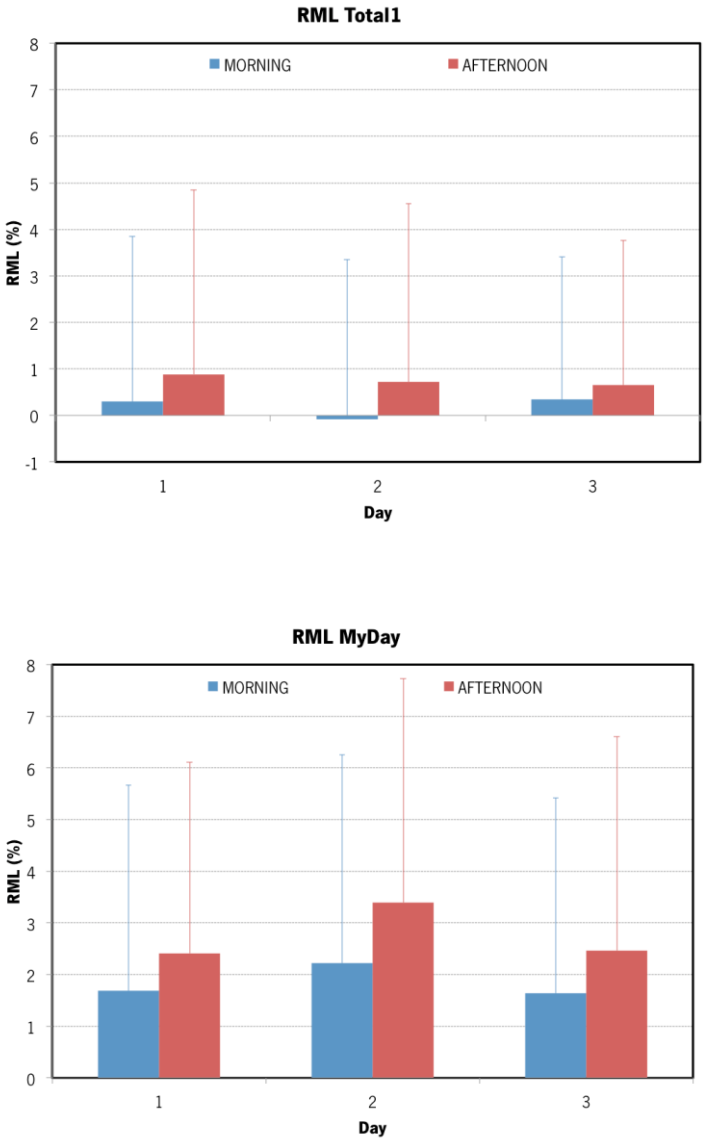
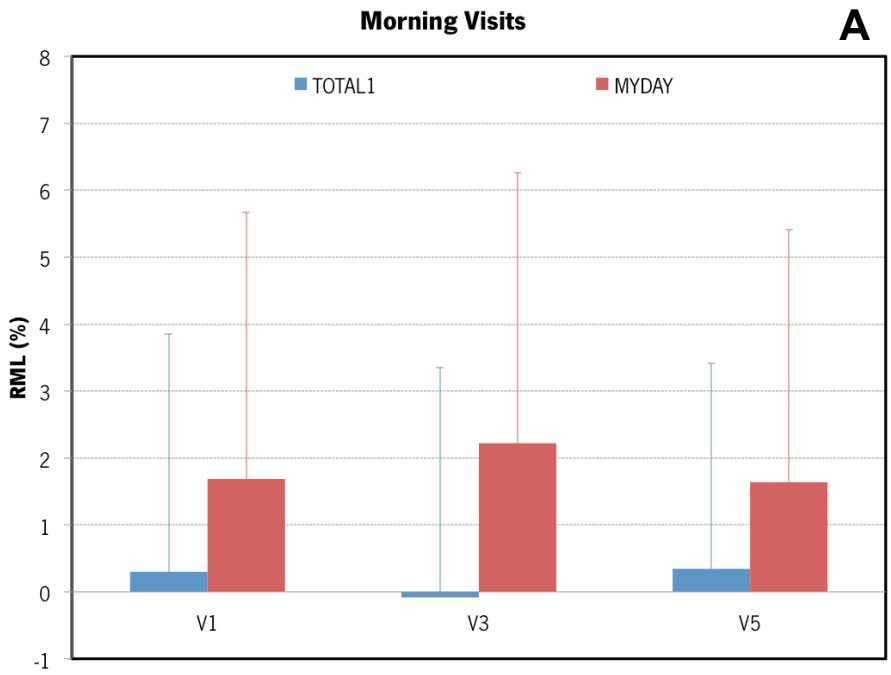


Figure 4.14 Relative Mass Loss (RML, %) Total1 (up) and RML MyDay (down).

The direct comparison of the two lenses can be seen in Figure 4.15 for morning (A) and afternoon visits (B). It can be seen that MyDay has higher RML values for both morning and afternoon visits. Despite the differences shown between the lenses in morning visits, there is only one with statistical significance in V3 (p=0.030, Wilcoxon), with RML values ranging from -0.083±3.4% in Total1 and 2.22±4.03% in MyDay. In the afternoon visits, the differences remain and statistical significant differences between the two lenses are found in V4 (p=0.033, Paired Sample T-Test) and V6 (p=0.049, Paired Sample T-Test).

For a more direct comparison between the two lenses, the mean of the three morning and the three afternoon visits were done (Figure 4.15C). In these results, a difference between the morning and afternoon visits was evidenced for Total1 lens (p=0.027, Paired Sample T-Test) and for MyDay lens (p<0.001, Wilcoxon separately, there are differences in all visits). There also are differences between the two lenses in the morning visits (p=0.044, Paired Sample T-Test) and also in the afternoon visits (p=0.037, Wilcoxon).



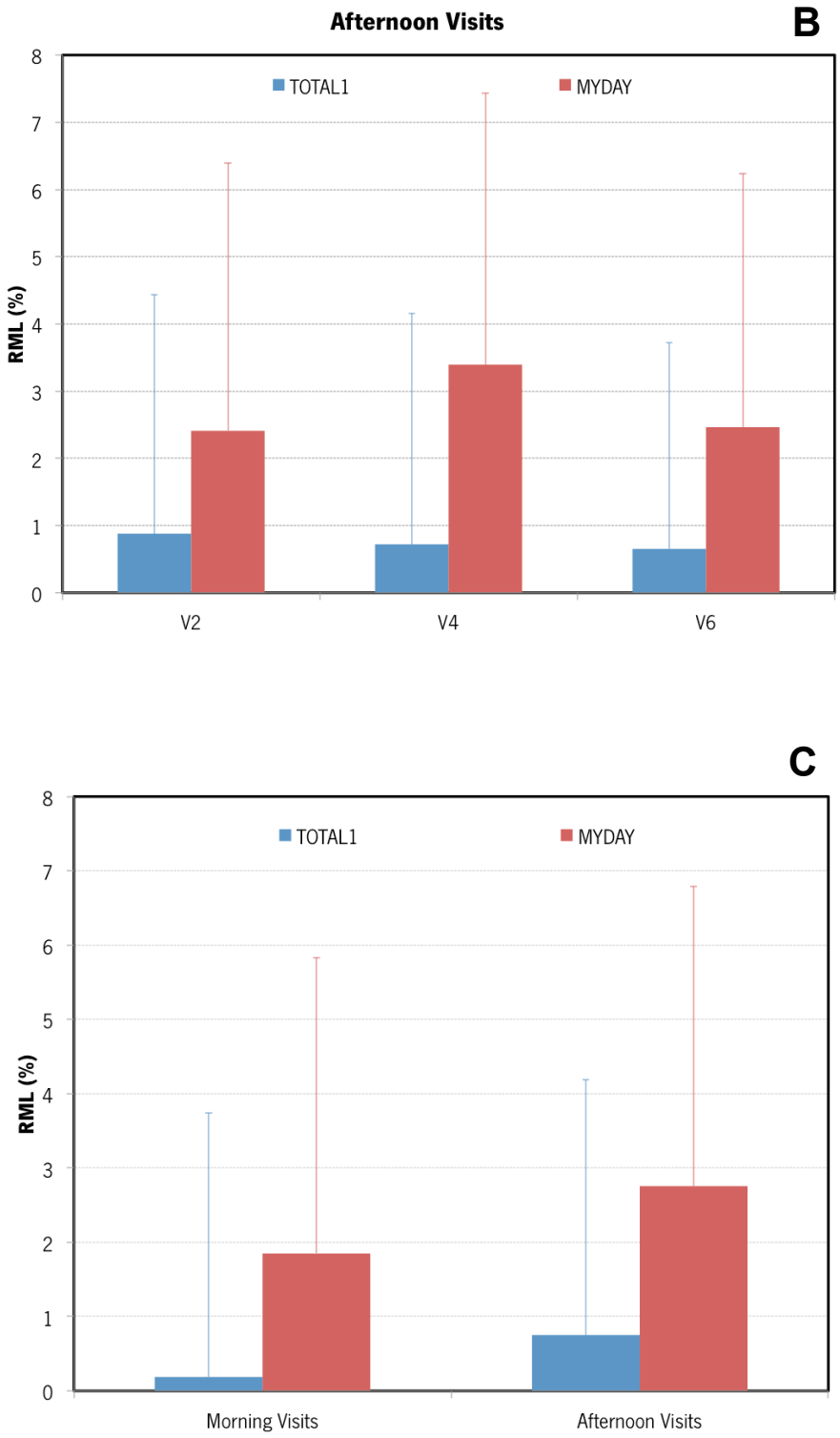


Figure 4.15 Comparison between the two lenses: (A); afternoon (B); mean of the three morning and three afternoon visits (C).

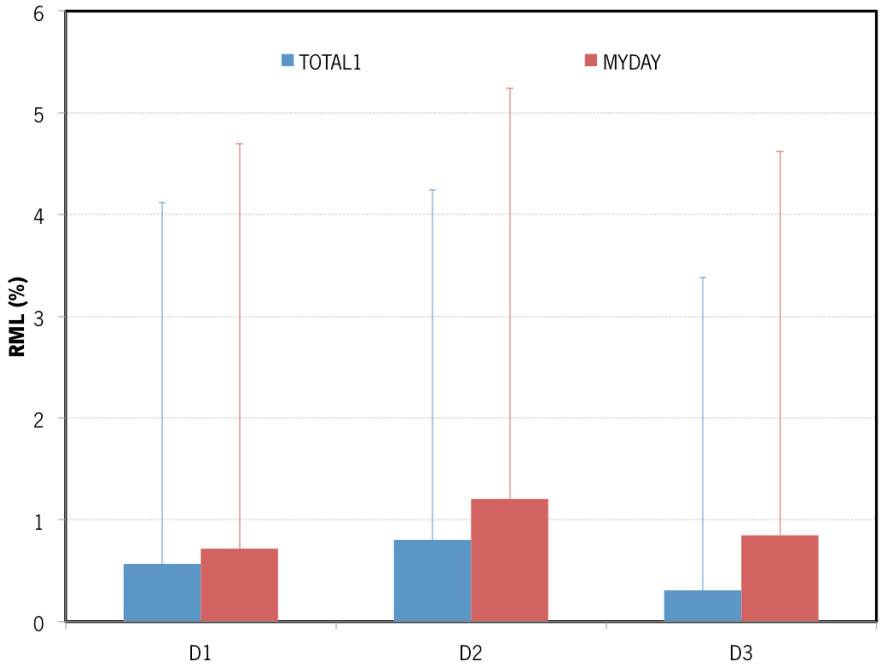


Figure 4.16 Dehydration from 2h to 8h (morning and afternoon visits). For this graphic, the baseline values were not considered.

For the construction of the graphic present in Figure 4.16, it was only used the *ex vivo* measures for assessing the differences between morning and afternoon visits and also the differences between the two lenses. The *ex vivo* only refer to the 2h measure (morning) and the 8h measures (afternoon), so the difference between them do not contemplate the baseline measure, performed *in vitro*. There are no differences in dehydration throughout the three days, neither for Total1 nor for MyDay lenses (p=0.705 and p=0.446 (Friedman), respectively). Once again, it can be seen a greater dehydration shown by RML values in MyDay lenses when compared to Total1, but with no statistical significant differences.

There are no statistical significant correlations between dehydration and conjunctival or corneal staining (in none of the zones) in none of the lens and in none of the visits.

4.8 Questionnaires

4.8.1 OSDI

OSDI (Ocular Surface Disease Index) was answered in baseline visit and in the last visit (V6). In baseline visit OSDI was answered by place an "X" in the local desired, as indicated by the developers of the questionnaire. In the last visit the patients were instructed to answer the same questionnaire but differentiating the two eyes: they should place "OD" for right eye and "OE" for left eye. These results are shown in Figure 4.17. There was a mean value of 32.95±9.82 for the baseline OSDI, and 16.11±11.94 and 19.68±12.68, for the final questionnaire of Total1 and MyDay lenses, respectively. There were statistical significant differences between the OSDI answered in the baseline visit and the OSDI answered for the Total1 lens in the final visit ($p<0.001$, Wilcoxon) and for the MyDay lens ($p<0.001$, Paired Sample T-Test), meaning a reducing in symptomatology with the two lenses used. When the two final OSDI were compared, a statistical difference of $p=0.046$ (Wilcoxon) was obtained, with a lower OSDI value for the Total1 lens (meaning lower symptoms). As the baseline OSDI was answered without distinguish the two eyes, the mean of the two final OSDI was done, obtaining a value of 17.90±11.77. This value has a statistical significant difference between the OSDI baseline ($p<0.001$, Paired Sample T-Test).

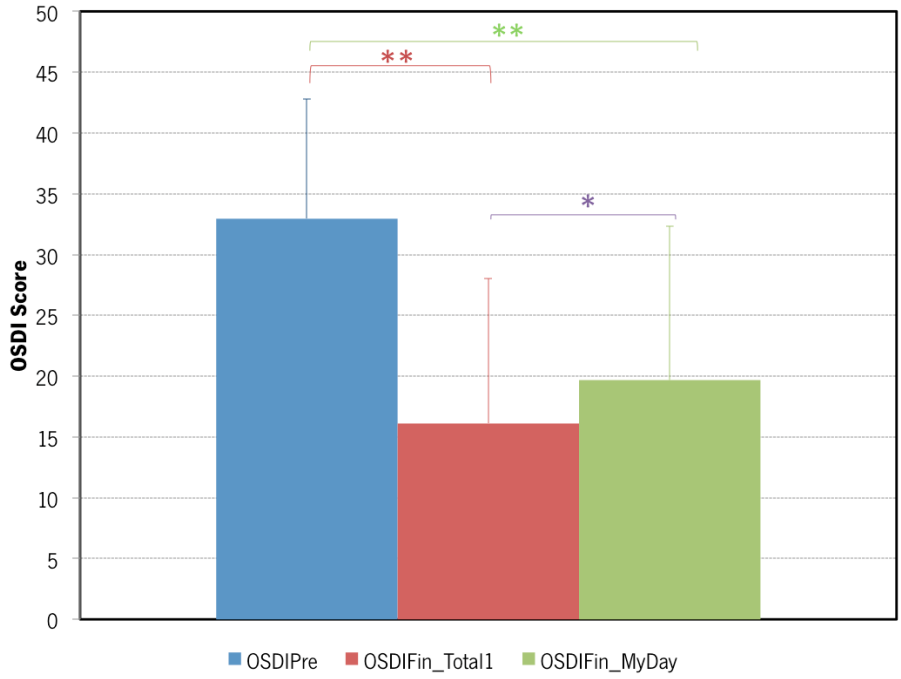


Figure 4.17 Comparison between OSDI Score from baseline visit and OSDI score in the final visit for Total1 and MyDay lenses separately. * p<0.05 ; ** p<0.001.

4.8.2 Patient Daily Questionnaire

Table 4.9 shows the results of VAS daily questionnaire, answered in all the afternoon visits. For the ease of handling the lens question, there were differences during the three days for Total1 but not for MyDay, although the two lenses have showed an improvement during the three days. There were no differences between the two lenses in none of the days, suggesting that the handling is similar in the two lenses, but with better scores for Total1 lens in Day 2 and Day 3. It seems that the comfort after insertion improves during the three days for both lenses, with higher values for Total1 but with no differences between the lenses. For the comfort at 4 and 8 hours of wear there are differences between the two lenses, with a higher score (more comfort) for Total1 lens by the 4 hours and for the MyDay lens at the 8 hours of CL wear. These differences are noticed in Day 2 and Day 3. Despite

these differences, the scores have improved during the three days for both lenses, suggesting an improvement in comfort.

The level of dryness throughout the day has also improved from Day 1 to Day 3 in both lenses, but the differences between the three days or between the lenses are not statistical significant. For the eye wearing Total1 lenses the dryness sensation after 8h of CL wear have improved from Day 1 to Day 3 (p=0.028, Friedman). A less improvement is shown for the eye wearing MyDay lenses, but there were no differences between the two lenses in this parameter.

There are also differences in the vision during the day between the two lenses, namely in Day 1 and 2 (p=0.0458 and p=0.042: Wilcoxon, respectively), with Total1 lens showing a better quality of vision in all visits. The same happened in the punctuation of the next question (vision after 8h), but with no statistical differences between Total1 and MyDay. Notice that the score is lower when the question remains to the vision after 8h, comparing to the vision throughout the day (for both lenses).

If we analyse the total score of this questionnaire, a difference between the day 1 and 2 (p=0.008, Wilcoxon) and the day 1 and 3 (p=0.004, Wilcoxon) is observed for Total1, with an improvement score throughout the days (p=0.004, Friedman). Although the MyDay lens also showed an improvement in the total score throughout the three days, there were no statistical differences between the days. When the two lenses are compared, only one statistical difference appears in the third day, with a higher score for Total1 lens.

Table 4.9 Scores of Daily Questionnaire with a VAS scale.

		Day 1	Day 2	Day 3	p (a)
Ease of handling the lens	**Tot1**	7.61±3.34	8.96±1.53	9.17±1.40	***0.027***
	MyD	7.99±2.51	8.79±1.69	9.07±1.43	*0.469*
	p (b)	*0.4049*	*0.6741*	*0.8927*	
Comfort with lenses upon insertion	**Tot1**	8.82±1.73	9.22±1.19	9.15±0.96	*0.521*
	MyD	8.42±1.73	8.78±1.69	9.03±0.99	*0.212*
	p (b)	*0.3246*	*0.1230*	*0.6219*	
Comfort with lenses after 4 hours of wear	**Tot1**	8.39±1.56	8.81±0.99	8.94±0.86	*0.246*
	MyD	8.15±1.57	8.46±1.07	8.50±1.13	*0.545*
	p (b)	*0.3615*	***0.0187***	***0.0107***	
Comfort with lenses after 8 hours of wear	**Tot1**	8.15±1.57	8.46±1.07	8.50±1.13	*0.061*
	MyD	7.96±1.37	8.51±1.10	8.50±0.94	*0.591*
	p (b)	*0.6813*	***0.0407***	***0.0279***	
Level of dryness throughout the day	**Tot1**	7.68±1.86	8.05±1.44	8.22±1.29	*0.219*
	MyD	7.57±1.98	7.88±1.49	7.86±1.36	*0.936*
	p (b)	*0.73*	*0.25*	*0.07*	
Level of dryness after 8 hours of wear	**Tot1**	7.56±1.85	7.63±1.66	8.01±1.09	***0.028***
	MyD	7.56±2.01	7.53±1.68	7.67±1.19	*0.442*
	p (b)	*0.9441*	*0.4959*	*0.0913*	
Vision with the lenses throughout the day	**Tot1**	8.79±1.29	9.01±0.95	8.94±1.20	*0.843*
	MyD	8.53±1.45	8.58±1.39	8.55±1.37	*0.892*
	p (b)	***0.0458***	***0.0420***	*0.0749*	
Vision with the lense after 8 hours of wear	**Tot1**	8.40±1.49	8.61±0.98	8.72±1.19	*0.346*
	MyD	8.20±1.52	8.42±1.25	8.31±1.53	*0.915*
	p (b)	*0.3441*	*0.3552*	*0.0845*	
Total Score	**Tot1**	65.19±9.87	68.78±8.47	69.63±6.96	***0.004***
	MyD	64.20±10.65	66.58±9.21	66.76±8.46	*0.368*
	p (b)	*0.5871*	*0.0575*	***0.0385***	

p(a) –Friedman test

p(b) e (c) – Wilcoxon

The comfort ratings were correlated to the dehydrations values. For Total1 lens, the RML was weakly correlated to the values of comfort and vision (question of daily questionnaire). For MyDay lens, some correlations appeared, namely between morning RML and comfort with the lens after 4h of wear (r=0.462, p=0.40, Pearson), level of dryness throughout the day (r=0.548, p=0.012) and level of dryness after 8h of CL wear (r=0.558, p=0.011).

Comfort was also compared to NIBUT values. For Total1 lens, the correlations found were between NIBUT and comfort with the lenses upon insertion (r=0.523, Spearman), comfort with the

lenses after 8h of lens wear (r=0.556, Pearson), level of dryness after 8h of lens wear (r=0.513, Pearson), vision with the lenses throughout the day (r=0.626, Pearson), and vision with the lenses after 8h of lens wear (r=0.631, Pearson). There also are statistical significant correlations between afternoon NIBUT and comfort with the lens upon insertion (r=0.523, Spearman), comfort with the lenses after 8h of wear (r=0.556, Pearson), level of dryness after 8h of wear (r=0.513, Pearson), vision with the lenses throughout the day (r=0.626, Pearson), and vision with the lenses after 8h of wear (r=0.631).For MyDay lens, only one fair and statistical significant correlation was found between NIBUT and comfort with the lens upon insertion (r=0.399, p=0.082 Spearman).

There were no significant correlations between comfort ratings and conjunctival and corneal staining (for none of the comfort questions or local of staining).

Table 4.10 Results of the forced-choice questions of the daily questionnaire.

		Day 1	Day 2	Day 3	p (b)
Have you forgotten that were wearing some of the lens?	Total1	4	8	6	
	MyDay	2	0	1	*0.034* D1vsD3
	Both	12	11	13	
	None	2	1	0	*0.49* D2vsD3
	p (a)	***0.004***	***0.019***	***0.004***	
The lens have stopped being comfortable during the day?	Yes	4	3	5	
	No	16	17	15	
	p (a)	***0.007***	***0.002***	***0.025***	
Which lens do you prefer in terms of comfort?	Total1	6	10	10	
	MyDay	6	7	5	
	Both	7	3	5	*0.005* D1vsD3
	None	1	0	0	
	p (a)	*0.221*	*0.157*	*0.287*	
Which lens do you prefer in terms of vision?	Total1	7	8	10	
	MyDay	5	7	5	*0.008* D1vsD2
	Both	8	5	5	*0.009* D1vsD3
	None	0	0	0	*<0.001* D2vsD3
	p (a)	*0.705*	*0.705*	*0.287*	
In a global evaluation, which lens do you prefer?	Total1	9	10	12	
	MyDay	5	7	5	
	Both	6	3	3	*0.001* D2vsD3
	None	0	0	0	
	p (a)	*0.522*	*0.157*	***0.035***	

p(a), Chi-Square; p(b), Pearson Chi-Square; D1, Day 1; D2, Day 2; D3, Day 3.

Table 4.10 shows the frequencies of patients' answers to the forced choices of the daily questionnaire. For the first question, the majority answered that have forgotten that were wearing both lenses in all the three days. If we focus on the two studied lenses separately, there are more answers in favour of Total1, especially in the second day. There are statistically significant differences between the frequencies of all possible responses in the three days (p=0.004, Chi-Square) and between the frequency of responses given in Day 1 and Day 3 (p=0.034, Pearson Chi-Square) and between Day 2 and Day 3 (p=0.049, Pearson Chi-Square). The next two questions are related to the first one, since both focus on comfort. The high majority stated that the lenses continued being comfortable during the day. The preferred lens in terms of comfort was Total1 that showed an increased preference from day 1 to day 2 and 3. The same can be said for the quality of vision, with the majority of subjects preferring Total1 lenses, namely in day 3. For this question, there was statistically significant differences in the frequency of given answers between all days.

For the last question, in which was asked which lenses the patients have preferred in general, a great number have answered the Total1 lens, having these frequency of answers a statistical difference in the third day comparatively to "MyDay" and "Both" hypothesis (p=0.035, Chi-square).

5. DISCUSSION

Given the extent of the discussion and the large number of results, the discussion of the present thesis will be sub-divided by themes as done in the presentation of results. Some guidelines will be used to uniform all the sub-chapters. First of all, a short summary of the most important findings of each sub-chapter will be done. Then, a discussion comparing the existing literature to our findings will be done. The limitations of each technique (when applied) will be highlighted after each sub-chapter discussions'. Again, each sub-chapter will end with some correlations between them and the anterior results, when applicable: for example, given in section 5.2 the SOQ values, they only will be correlated with NIBUT at the end of section 5.3 (that is the section when NIBUT values will be discussed), and so on.

5.1. Visual Acuity

In the present study we have compared the performance of two new daily disposable soft CLs fitted contralaterally. There are some differences between the two lenses, but with no statically significant differences between them. There is an improvement in LCVA from morning to afternoon in both lenses during the days.

Similarly to other study[183], our results have shown that VA depends on the type of contact lens fitted and it's not constant throughout the day (with the differences being more remarkable for LCVA). Belda-Salmerón *et al*[83] have evaluated the visual performance of several CLs in terms of both HCVA and LCVA at 2h intervals during a 12h of continuous CL wear. In that study, the greater differences across lenses were obtained in LCVA and with increasing wearing time. Among all lenses, Dailies Total1 achieved the better performance both for HCVA and LCVA, with better visual acuity at 4h and 6h, respectively. In the present thesis, Total1 has shown always better performance than MyDay lenses, except for the afternoon visits in LCVA. The referred study may have the answer for it, once Total1 lens suffers a constant degradation after the 4h of lens use.[183] In the same study, the great majority of lenses have its maximum HCVA at 2h of lens wear, starting a visual degradation after it, with worst VA at 12h. In LCVA the performance is most variable, but with similar values up to the 8h, and then start the higher degradation. This can justify the better LCVA found in the afternoon visits in the results of the present thesis, as in the afternoon visit the patients were wearing their lenses for 7 to 8h after the morning visit (where the lenses were re-hydrated). For HCVA, the value found was smaller in the afternoon visits, in accordance to this article that shows visual degradation after the 2h

of CL wear. Other study that intent to compare different lenses has not found statistical differences between the three daily disposable CL used, with values ranging -0.12 and -0.14 for HCVA and 0.13 and 0.19 LCVA.[184]

Our patients were all successful lens fitting, so the variations found in VA may be due to the differences between inherent properties of the two lenses. In fact, one concluded that differences in visual performance between lenses can be due to inherent lens properties, such as material and water content.[183] They also stated that HCVA is not sensitive enough to reveal subtle changes in visual performance during CL wear.

5.2. Subjective Optical Quality

In the present thesis, the time between the last blink and the disappearance of the letters of the line above the highest LCVA were recorded (with EDTRS). The SOQ (or subjective image quality) was measured before by other authors with a slightly different technique. In other studies, subjects were instructed to fixate in the letter group with maximum LCVA (with Pelli-Robson contrast test) and report loss of readability, and then fixate on the letter group with the next higher contrast and recorded the times at each contrast level became invisible (trial finished with the first blink of the subject).[105] One limitation of these pervious techniques is that the trial requires concentration of the patient for longer times and many contact lens wearers are not able to sustain the blink for such period of time. Moreover, the ability of each patient to switch their attention to the next letter may induce differences in the outcome not related with the stability of the tear film. Thus, our technique is simpler and more uniform.

The SOQ values presented in this thesis were very similar in the two lenses, and between morning and afternoon visits, as there were no statistically significant differences between none of the mentioned situations. A study conducted by Tutt *et al*[105] that aimed to examine the optical and visual impact of tear break-up, with objective and psychophysical methods, concluded that tear break-up contributes to the decrease in optical performance. The decline was higher when the subjects were wearing CL. Despite the results, the authors do not know whether these decreases during blinking suppression are due to exposure of irregular tear film during disruption, irregular corneal surface, changes in refractive index of tears or all these factors combined. Other study that aimed to measure

acuity for low-contrast targets with blinking suppression also found a significant loss in acuity in the eyes wearing soft CL, than with RPG or exposed corneas.[185] The results presented in this thesis show a slight and non-statistically significant decrease between morning and afternoon visits with either lens brand, suggesting that the image degradation after a period of blink suppression is little influenced by the time of the day. There are also no differences between the two lenses, with both showing a very similar behavior during the time, being strongly and significantly correlated (p=0.753 for morning visits and p=0.716 for afternoon visits, Pearson). These results may confirm those previously discussed, highlighting that differences may be due to irregularities in tear film and cornea. Although other authors have suggested that psychophysical losses in image quality during blink suppression may be associated to lens parameters secondary to lens dehydration (such as curvature, refractive index and transparency)[185], we concluded that daily disposable Si-Hy lens parameters seem to have no interference in SOQ degradation, when the lenses are used during the same period and under the same circumstances. This might be also a consequence of the similar tear stability at the front surface of both lenses as discussed in the next section.

5.3. Non-Invasive Break-up Time

The pre-lens NIBUT results will be discussed in this section. At the end, a comparison with the anteriorly discussed parameters (SOQ) will be done, as well as the respective correlation.

It is known that adding a lens into the eye unable to form a stable tear film. In the results of the present thesis, there was a reduction in pre-lens NIBUT from morning to afternoon in all the three days. These changes were more pronounced in MyDay lens, once the differences were all statistically significant. In Total1 lens, only a statistically significant difference between morning and afternoon pre-lens NIBUT was found in Day3. Notwithstanding, when the two lenses are compared, there are no statistically significant differences between them, presenting a similar behavior.

Some studies have established a cutoff value of BUT <10 seconds and NIBUT < 10[80] seconds for an abnormal tear film. Notwithstanding, a study that include only subjects with normal tear film, 58% of them have BUT < 10 seconds and 50% NIBUT < 10 seconds, with a mean value of 13.12±2.21 s and 17.50±3.06 s, respectively.[62] In the baseline visit of the present thesis the values were 7.73±2.2 s and 8.3±2.9 s in the different eyes, with just 10% of them having NIBUT values > 10

s and 70% of them having NIBUT < 8 s. Other studies have found NIBUT values of 17.52±6.28s[186] and 14.7±12s[83] for symptomatic CL wearers, which are much higher than the values presented in this thesis. A potential explanation for these differences is that in those two studies the symptomatology was assessed with the McMonnies questionnaire and in the present thesis the OSDI was used, so some differences can be in the "degree" of symptomatology present by the subjects. The variability inter-observer of NIBUT can also justify these differences.

Pre-lens NIBUT was measured over the following six study visits, showing no statistical differences between the measures performed in the three morning visits and between the measures performed in the three afternoon visits, neither for Total1 nor MyDay lenses. Despite this, a reduction in NIBUT from morning to afternoon was seen in all the three days for both lenses. This reduction was previously cited in the literature, even in non-CL wearers. Lira *et al*[51] found a reduction between 6.58±2.62s to 5.38±2.53s in NIBUT (keratometer) for non-CL wearers, with statistical significance. This reduction of 1.2s is higher than the reduction from morning to afternoon encountered in this thesis, which has statistical significance in all the days for MyDay lenses but only in the third day for Total1. Other study[187] that evaluated PLTF has found a small reduction (about 0.1s) after 5h of CL wear in asymptomatic and about 2.55s in symptomatic, with a mean value of 6.2s of pre-lens NIBUT in the afternoon. These values are also slightly higher than the values encountered in this thesis: 4.95±0.63s for Total1 lens and 4.96±0.93s for MyDay. These results show that Total1 seems to affect less the stability of PLTF during the day than MyDay lenses, but no statistically significant differences between the two lenses were detected. In addition, Wolffsohn and colleagues[188] have examined the clinical performance of daily disposables over 16h and found that the pre-lens NIBUT decreased between the 8h and 12h and 12h and 16h. Others concluded that the intolerant CL wearers' tear film changed less than tolerant ones, during 6h of a Group IV hydrogel lens wear. They have justified these findings by the fact that intolerant CL wearers have less volume and poor stability even when they didn't worn the lenses, concluding that these patients are intolerant due to tear film defects prior to lens wear.[189] This may justify the little differences (always < 1s) found in this thesis between morning and afternoon visits in both lenses, as all the patients in our study were symptomatic and although we cannot categorize them as having low tear volume, they certainly have issues related to the tear dynamics at the front ocular surface as shown by our tear stability results.

One of the aims of the present thesis was to know if the time when patients start to loss some image quality (SOQ) was the time when the tear film starts its disruption over the lens (pre-lens

NIBUT). However, the lacrimal disruption over lens surface occurs before the image degradation measured in SOQ (about 4 to 5s for NIBUT and about 7s for SOQ) and there were weak correlations between these two parameters in all the visits and for the two lenses. So, the assumption that the degradation in image quality can be due to tear break-up[105] was not entirely supported by these results. This does not discard a mechanistic relationship between both events. Rather than a coincidental time point, it seems that the subjective image quality perceived by the patients degrades a few seconds after the NIBUT time. This suggests that at the beginning of the tear degradation, the optical quality might not be so much degraded to change the subjective perception of the patient. However, as the process evolves, this seems to be more evident and the patient reports blurring of the image. This result seems to be supported by the dynamic topographic and aberrometric data presented in the next sections, as the topographic indices degrade more significantly after the NIBUT point while the impact in aberrometric terms is less evident over the interblink period of time.

5.3.1. Location of the first tear disruption

As previously described, the location of tear film break up is influenced by CL's presence.[190] In the present thesis, the measures of tear film were always performed by the same observer, as well as the location of the tear disruption. The tear film has disrupted in the inferior zone in the majority of measures and has never disrupted in the superior zone.

In a study conducted by García-Resúa *et al*[62] the superior zone was where the tear film has disrupted with less frequency, with 2.7% in BUT evaluation and 8.9% in NIBUT (with Tearscope). This is in agreement with the present thesis results, where tear film has never disrupted in the superior zone. The most common visible break occurred in the inferior region and was between 65 and 68% of all cases (all visits and two lenses). In that study, the inferior zone is where the tear also disrupts with more frequency, in 45.9% in BUT measures and 35.6% in NIBUT measures. In another study conducted by Guillon an collaborators[83], they found a more frequent tear disruption in the central zone (20% in asymptomatic and 32% in symptomatic CL wearers), and less in the temporal/nasal (6% in asymptomatic and 9% in symptomatic CL wearers), but most frequently the break was not visible (36%), because of patients' reflex blinking. In a recent master thesis (2013) of University of Minho, which aimed to characterize the lacrimal parameters of the Portuguese population, found that the rupture of the tear film in BUT measures were often seen in the inferior zone (50.7%), superior zone

(17.8%) and temporal (13.7%). Less frequently, in the nasal (8.2%) and central (2.7%) zones.[191] Despite this concordance in results, is important to note that all these results are without lenses, and in the present thesis the subjects were wearing their lenses. So, the tear disruption could be attributed to some irregularities in the surface of the lenses caused by lens materials itself or by the manufacturing processes for each lens technology. So, with the results of this thesis, it seems that the position of tear break up is not affected by lens wear (since there aren't great differences between these studies and our results). Despite this, other study compared the BUT zones in PCTF and PLTF and concluded that in PCTF the break-up occur more commonly in parameniscal zone than in central corneal, but the opposite occurred in PLTF.[190]

5.4. Dynamic Topography

The dynamic topography was done to assess the through-time performance of the tear film over each CL. The results were expressed with the SRI and SAI values, and respective TSRI and TSAI values. Considering the average SRI values, the two lenses have a similar behavior with no statistically significant differences between them, but with MyDay showing higher values of SRI in the afternoon visits when compared to Total1. The TSRI values exhibited more instable values for Total1 lens in the morning and for MyDay lens in the afternoon. For SAI values, Total1 revealed a worst performance in the morning and better in the afternoon, when compared to MyDay lens, but with no statistically significant differences between them. The TSAI values showed higher values for Total1 lens in both morning and afternoon visits, but with no statistically significant differences between the two lenses. By a direct observation, it is obvious that SRI is more sensitive to tear film changes through time than SAI values, evidencing more changes through time that could be related to rupture points (as the SRI values change right after a blink and SAI values only change after 7-8 seconds). In the final of this section, correlations between all these parameters and NIBUT values will be performed and discussed, as well as the limitations.

Differences between the two lenses and between throughout day performance has not been found with this technique. The better performance in afternoon visits when compared to morning are consistent with Kopf *et al*[194] findings, that concluded that tear film surface quality (TFSQ) has a systematic improvement during the day, namely in the first day of Si-Hy lens wear. There is a better performance in SAI values when compared to SRI ones, being them very stable up to the 7s and then

begin to increase. In SRI values, the increase begins right after the blink. This is supported by Iskander *et al*[92], that said that the SAI values are more stable and can reach up to a 12s of relative stability period.

A study that intended to compare the tear function of dry eye and normal patients with TSAS[90], showed that dry eye patients have higher SAI, SRI, TSAI and TSRI values than normal subjects. In our findings, the SRI values are between 0.60 and 0.70 in measure 0 and increase up to the 10 seconds, reaching values between 1.00 and 1.09. These values are higher than those found in Kojima *et al*[90] study, with values ranging from approximately 0.6 in the first measure (0s) but never reaching the value 1 during the 10s of measurement. Other study that has examined the eyes of healthy subjects at 5 and 15s of open-eye[193], shows a SRI mean value of 0.18±0.19 at 5s and 0.30±0.19 at 15s, which are significantly lower than those anteriorly mentioned. In the dry eye group of Kojima *et al*[90] study, the values are much higher than those encountered in this thesis, ranging from about 1.5 to almost 2. These findings are reflected in TSRI values, with 0.72±0.3 in normal group and 1.3±0.4 dry eye[90] which are higher than those encountered in our findings, that range from 0.47±0.02 and 0.57±0.1 (depending on the lens and if the measure was taken in the morning or in the afternoon). Conversely, other study show values much lower than those.[193] They found a different behavior, with a 0.42±0.29 for the initial SRI, but with the minimum SRI happening at 7.13±3.87s, with a mean value of 0.41±0.19.[89] They attributed these minimum values between 3 and 10s to the tear build-up time (the time that the tear takes to achieve its most regular state). They have done these measures without CL. So, these results are not supported with the findings present in this thesis; with SRI values experienced an increase up to the 10s, being it's minimum value found in the 1s measurement in both lenses and in both morning and afternoon visits (being this value between 0.60±0.02 and 0.73±0.04, depending on the lens and visit). This might suggest a different tear film behavior when it is measured with or without a CL presence. Other methodological differences might explain the results. Namely, the studies of Iskander *et al*[92], were the first using the methodology of deriving dynamic SRI and SAI from Medmont topography. Meanwhile, the software of the instrument has been updated; we cannot discard also that the preliminary methods used during the technology development are exactly the same that are now available in the commercial versions.

The same study has found an initial SAI of 0.39±0.14 and a minimum SAI of 0.32±0.19 at 5.43±2.72s.[89] In our findings, the minimum SAI was found at the 0s (0.69±0.05) for Total1 and 1s (0.73±0.04) for MyDay in the morning measurements and 1s (0.64±0.06) for Total1 and 2s

(0.65±0.03) for MyDay, in the afternoon visits. So, in similarity to what happened in SRI values, it seems that there is no relation between the two studies and the minimum SAI is always higher in our study. If we compare to the other mentioned study conducted by Kojima *et al*[90], the behavior is also different: in the control group the values are very consistent during the 10s, with values surrounding 0.5 and a TSAI of 1.1±0.9, but are more irregular in dry eye group, with values changing from about 1.5 and 2.6, with a TSAI of 2.1±1.3. In this thesis' results, SAI values have a regular behavior up to the 7-8 seconds, and then began to increase, and TSAI values ranged between 1.02±0.44 and 1.59±0.84 (depending on the lens and the visit). Other study[193] found lower and more stable values in normal and non-CL wearers subjects, with 0.21±0.08 and 0.24±0.10s at 5 and 15s, respectively. These differences can be explained by the fact that all measured done by Németh *et al* [193] were done without CL and in the present thesis the patients were wearing CL. The CL presence alters the tear film behavior. The mean TSRI and TSAI values are always higher in this thesis, supporting that CL wear can have some role in the tear film destabilization.

The explanations provided to the higher values yielded by SAI and SRI values need to be more elucidated. Since the first measure that SAI and SRI yield higher values than the expected normal values for a normal cornea (0.10 to 0.42 and 0.0 to 0.56, respectively).[177] This could be attributed to the CL irregularity by itself or to the irregularities of the tear film disrupted by the CL presence. Another curious fact is that SRI values trend to augment more right after the 2-3s, but the SAI values became more or less stable up to the 7s and then began to increase. As the SAI values are more specific to peripheral changes and SRI to central changes, we can presume that tear film starts its degradation in the central area 2-3s right after a complete blink, but this degradation will only affect the peripheral area later. Nevertheless, this is not in concordance to another result: the position of tear break-up, where the inferior zone was the most common (>60% in both lenses).

In an attempt to correlate the pre-lens NIBUT values with the time that the SRI values start to increase more, no obvious results were found. NIBUT values range between 4.9s and 5.97s for both lenses, and the time that the SRI values start to increase more (after a slightly linear behaviour) are about the 2 and 3s, for both lenses and morning and afternoon visits. In fact, when a correlation between pre-lens NIBUT and the time at SRI reaches its maximum value is done, only a moderately strong correlation (r=0.526, p=0.017, Spearman) appears for morning visits in Total1. Total1's afternoon visits and morning and afternoon visits of MyDay have no correlations between the mentioned parameters. The same comparisons were also done between SAI values and Pre-Lens

NIBUT. For morning visits, it can be seen a mean NIBUT value of 5.59±0.33 seconds for Total1 and 5.69±0.21 seconds for MyDay and of 4.95±0.22 for Total1 and 4.96±0.11 for MyDay in the afternoon (in pre-lens NIBUT). The mean SAI values in the morning visits seem to have a higher increase after the 6 second for Total1 but only for second 8 in MyDay. In the afternoon, the higher increase is shown after 8 seconds for MyDay and seems to augment linearly in Total1. There were no statistically significant differences between the time at SAI value reaches its maximum value and pre-lens NIBUT for none of the lens.

In other approach, the pre-lens NIBUT was also compared to the mean SRI and SAI values. For Total1 lens, there was only a negative and fair correlation between pre-lens NIBUT and mean SAI value (r=-0.448, p=0.047, Spearman) in afternoon. The other correlations are weak and with no significance. For MyDay lens, there are two significant, negative and moderately strong correlations. One is between NIBUT and the mean SRI value in the morning visits (r=-0.503, p=0.024, Pearson) and the other between NIBUT and mean SRI of the afternoon visits (r=-0.512, p=0.021, Spearman). This means that the higher the NIBUT, the lower the SRI values. These values seem to be variable, since there could be some defective measures at any time that can influence these results. So, since the correlations were not systematically found and none of them were strong, they could have no significant interpretation.

There could be some limitations. For example, for the analysis of these results, we need to take into account that in corneal topography the patients must have their eyes wide open and sustain the blink. It is known that tear evaporation could be linked to palpebral fissure width and meaning lower tear film stability,[194] which may alter the dynamic corneal topography measurements[90] and consequently the SAI and SRI values.

5.5. Dynamic Aberrometry

In average, some statistical significant differences were found between morning and afternoon visits for vertical coma in Total1 and horizontal coma in MyDay lenses. Between the two lenses, there are statistical significant differences for vertical coma, horizontal coma and spherical aberration in morning visits, and in horizontal coma and spherical aberration in the afternoon visits.

For instance, Total1 have negative values and MyDay positive values in horizontal coma. These different trends with both lenses are potentially related with lateral deccentration with both lenses, in opposite directions. In our study, the RMS (3rd to 6th order) with the Total1 lens showed a worsening in optical performance after the 8.61s, namely for the afternoon visit. A recent study conducted by Montés-Mico *et al*[102] that aimed to quantify the optical quality of daily disposable CLs during the day, showed that all the lenses used increased the RMS values when compared to the non-contact-lens condition. The increase was right after CL insertion (0h) and continued towards the end of the day. So, our findings are not in concordance with those found by Montes-Mico *et al*[102], where Dailies Total1 was the CL that yielded the lowest RMS values at each point of time (up to 12h), among all the 7 CLs used. Other study that used dynamic aberrometry to quantify ocular aberrations in healthy and dry eye patients, showed that the progression index of HOA and corneal third-order aberrations were significantly higher in dry eye patients.[179] The RMS, 3rd order coma and 4th order spherical aberration values of control group have a most regular behavior in the mentioned study than in the present thesis (during the 10s). Also, the results present in this thesis do not support other study from Montés-Mico *et al*[104], where RMS values seem to be lowest in all patients at approximately 6s after a blink. In coma-like aberrations the scenario is similar, with minimum values at 5-7s after a blink and then a progressive increase up to the 15s. The behavior of spherical aberration was different, with a progressive increase (from 0.012μm to 0.044μm for 3-mm pupil) after a blink and with no minimum value.[104] In our results, the most significant changes in spherical aberration were for morning visit of Total1 lens, with values ranging between 0.001 and 0.015μm. The less stability in our results when compared to other studies could be because the dynamic topography was performed over the CL, and in the other studies in naked-eye. The CLs suffer a movement after the blink, which may affect both horizontal and vertical comatic aberrations. So, the variations in aberrations could also be attributed to lens movements and not only to the tear film destabilization.

When pre-lens NIBUT and the time that the aberrations reach their maximum or minimum value are compared, little correlations are found. For Total1 lenses, the only statistical significant correlations found are just between NIBUT and the time that spherical aberration reaches its maximum value in morning visits (r=-0.766, p=0.016, Pearson); and also between afternoon NIBUT and the time that spherical aberration reach its maximum value in afternoon (r=-0.684, p=0.042, Pearson). This means that the time in which spherical aberration reach its maximum value (in both morning and afternoon visits for Total1 lenses), is higher the less the NIBUT value. So, when the NIBUTs are lower, the maximum value of spherical aberration is encountered latter, meaning that tear

destabilization only affects the central zone (3mm-pupil) more later. The other correlations have no statistical significance, although some are moderately strong, namely: morning NIBUT and the time that spherical aberration reaches its minimum value in Total1 lens (r=0.584, p=0.098, Pearson); morning NIBUT and the time that vertical coma reaches its maximum value in Total1 lens (r=0.639, p=0.064, Pearson).

In MyDay lens there are no significant correlations between these two variables in the morning visit, and in the afternoon visit only a significant correlation is found between afternoon NIBUT and the time that vertical coma reaches its minimum value (p=-0.799, p=0.010, Pearson). The other moderate correlation is found between afternoon NIBUT and the time that the vertical coma reaches its maximum value (r=0.653, p=0.056, Pearson). Despite these two, the other correlations are poor.

Similarly to what happened when we try to found correlations between topographic indices and NIBUT, in aberrometry there also seems to be no consistent and systematic correlations. This could be due to the limitations found in the use of this technique: sometimes, the measures were repeated more than one time due to fixation problems or because the device stopped the measurement before complete all steps; and although there were no significant differences in the pupillary diameter during the measurement, the device assumed a 1-mm pupil at some steps, so that patients could not be included in the results.

5.6. Biomicroscopy

MyDay caused a higher limbal hyperemia than Total1 lens in both morning and afternoon visits, because this lens has lower oxygen transmission, and low oxygen transmission contribute to limbal redness.[165] MyDay eyes seem to improve their behavior up to Day 3 in both times of the day, proving that the eye can suffer a habituation to these lenses. Total1 eyes seem to have a more stable behavior, with no differences between the three mornings or afternoon visits. Despite this, both limbal and bulbar hyperemia have decreased from morning to afternoon in both eyes. This can occur because the morning visits were done 1-2h before CL insertion and some initial reaction to the lens may occur. Contrary to these findings, Glasson *et al*[89] found higher limbal redness after 6h of lens wear, when compared to baseline (no lens wear). In the present thesis, there are no statistical differences between baseline visit and outcome visits neither for limbal nor bulbar hyperemia, which is

in concordance to some studies that have demonstrated that there are no differences between limbal redness during high Dk/t Si-Hy lenses wear when compared to no lens wear.[165] However, a study conducted by Fahmy *et al* [6] found that the subjects refitted with daily disposable CLs have statistically significant improvements in limbal and bulbar redness at both 2 and 4 weeks compared to baseline. A study that evaluated the clinical performance of daily disposables through the day found statistical significant differences in bulbar hyperemia encountered at 8, 12 and 16h of lens wear, with increasing values over time.[188] But we must take into account that they only assessed after 8h of lens use, and we have assessed at 2h too.

Other studies found increases in conjunctival and limbal redness over 18 months of CL wear in neophyte CL wearers.[195] These values increased significantly over the first 6 months and then have stabilized with no differences between materials or regimes of wear, which may justify the fact that there was only one difference between the two lens for limbal redness in V1, and none for bulbar hyperemia. Glasson *et al*[48] found a mean value of limbal redness of 1.5±0.2 in tolerant subjects and 1.6±0.2 in intolerant ones, which are smaller values than those found in this thesis (because we only used the sum of the quadrants and not the mean of them).

In respect of corneal staining, Total1 eyes have a higher value when compared to MyDay, but with no statistical significance. Santodomingo-Rubido *et al*[95] found that increased values of corneal staining are not linked to lens material or regimens of wear. The corneal staining remained roughly equal from morning to afternoon, being slightly higher in Total1. The corneal staining may be caused by vary factors, being one of them abrasions occurring during lens insertion or removal.[162] Since the lenses were removed only about 3 minutes before slit lamp examination, staining could be due to some abrasions during CL removal. Other factors can be due to mechanical effects, as rough edges or foring bodies.[162] Efron *et al*[96] evaluated 150 Acuvue lenses and found that 75% of them were defective, and those defective lenses caused a greater ocular response with higher corneal and conjunctival staining, when compared to the no-defective ones.

Conjunctival staining has increased from morning to afternoon visits in both eyes. The statistically significant differences found in conjunctival staining between the two eyes in V1, V2 and V6 could be attributed to the edge design differences between both lenses. There are differences between the baseline visit and the morning visits of Total1 (p=0.003, Wilcoxon) and MyDay eyes (p=0.003, Wilcoxon), with higher values in the baseline visit. Before the baseline visit the patients must not wear CL and the OSDI score was higher than the final OSDI score. It seems that the lenses

used in this work have decreased the symptoms and the conjunctival staining. There are studies that support the idea that patients with high conjunctival staining have greater symptoms.[197] Other study found that patients re-fitted with a daily disposable CLs have decreased their conjunctival staining after 2 weeks (p=0.035) and after 4 weeks (p=0.008) of lens wear when compared to baseline.[6] This thesis findings show that these improvements can occur right after 3 days of daily disposable CL wear (with both Total1 and MyDay lenses).

The BUT measures were higher in MyDay eyes in both morning and afternoon visits, with decreased values in the afternoon. This reduction is normal, with studies found significant reductions from 6.68±360 to 4.47±1.99 even in non-CL wearers.[51] There were no differences in BUT values between baseline visit and outcome visits, suggesting that the insertion of daily disposable CL does not affect BUT values.

The differences between study protocols and the large variability of techniques used to assess tear film stability could be a limitation, indicating that the comparison between studies must be interpreted with caution.

5.7. Dehydration

The two lenses have dehydrated in both morning and afternoon visits when compared to baseline measures, being this dehydration more pronounced in MyDay lens. These through-day decreases are in concordance with the literature. Hall and colleagues[152] showed a decrease in water content right after 4h of lens wear, that continued up to the 8h and to the 12h. Others used a refractometer method to determine the lens dehydration and have also shown a decrease in water content after 7h of lens wear.[187] This decrease in water content was of -4.6±2.5 in symptomatic wearers and -3.9±2.3 in asymptomatic (Etafilcon A) and -1.6±0.8 in symptomatic and -1.8±1.2 in asymptomatic (Omafilcon A).

Dehydration is negatively correlated to NIBUT values in both lenses and in the morning and afternoon visits, being all the correlations weak and with no significance. When the TSAI and TSRI mean values are compared to the RML values, only a significant and moderate correlation is obtained between morning dehydration and morning TSAI (r=0.513, Spearman) of Total1. Other fair correlations are obtained, but without statistical significance. So, the aim that more instable tear films

(by means of higher TSAI and TSRI and lower NIBUTS) could be related to dehydration were not supported by this study. When dehydration is compared to the time in which each aberration reaches the maximum value, some fair and moderate correlations are found, but with no statistical significant values.

One limitation of these results is that lenses are rehydrated after first removal in the morning visit. However, due to the long period of time until the next visit in the afternoon, we expect that the impact of this rehydration on the end of day actual dehydration would be minimal. Thus, we consider that the afternoon visit dehydration is a fair representation of the actual dehydration over the course of the day. The value found in V3 may be explained by the fact that the "lote" used to do the baseline measures was different from the one used by the patients: this can lead to some differences in central thickness of the lens. Other explanation might be found in lipid deposition that affects particularly silicone hydrogel materials.[198]

5.8. Comfort Assessment

In this section, the OSDI will be discussed first, followed by the patient daily-questionnaire. At the end, some correlations will be shown.

OSDI scores were significantly reduced after this 5-days refitting trial, passing from 32.95±9.82 in baseline to 16.11±11.94 ($p<0.001$, Wilcoxon) and 19.68±12.68 ($p<0.001$, Paired Sample T-test) in the final questionnaire of Total1 and MyDay lenses, respectively. The fact that there were also a statistical significant difference between the two final OSDI scores ($p=0.047$, Wilcoxon), with Total1 showing less symptomatology, emphasizes the effectiveness of this lens in reduction the symptomatology. This reduction in symptomatology after the refitting with daily disposable CL were previously mentioned in the literature, with dailies AquaComfort Plus proven to significantly reduce common CL-related symptoms in symptomatic CL wearers, namely for blurred vision, dryness, tired eyes, deposits, redness, irritated eyes and discomfort.[6]

One patient was Total1 wearer before the study. Its' OSDI baseline value was 39.58 and 14.48 for the final OSDI of Total1 (and 37.5 for MyDay). Because of it, we can consider that the answer to the final OSDI was a little influenced by the assumption that the patients knew that the principal goal of the study was to know if the some of the lenses could decreased the symptoms presented with the

habitual ones. Other explanation could be the compliance. Nonetheless, Dumbleton *et al*[99] showed that patients who complied the recommended replacement frequency had better comfort than non-compliant patients and, once in the study, the patients could have a better compliance than in their habitual days.

The NIBUT values of baseline visits have a wick correlation with the baseline OSDI scores. Other studies have showed no correlations between NIBUT and ocular symptoms, like dryness.[82]

There was also another questionnaire done at the final of each afternoon visit. This questionnaire has 8 questions in a VAS scale and 5 forced-choices. It seems that the ease of handling the two lenses was very similar, with Total1 suffering a significant improvement during the three days. The first impact of handling Total1 lens could be problematic for some subjects because of its' high water content.

A study that has evaluated the comfort with three different daily disposable lenses, show that the comfort after insertion was lesser than after 4 and 8h of lens wear but better when compared to 12h of lens wear in asymptomatic wearers. The scenario was a little different in symptomatic ones, with the comfort after insertion being higher when compared to the 4, 8 and 12h of lens wear.[200] This results are consistent to ours, whit the comfort upon insertion also taking the highest scores, followed by a progressive decrease up to 4 and up to the 8h of CL wear, in both lenses. The level of dryness was better in Total1 lens during the day and after 8h of lens wear when compared to MyDay lenses, although the dryness was felt with more severity after 8h of lens wear, for both lenses. This is in concordance with the literature, with increased dryness the more the wearing time.

For the vision-related questions, the patients also preferred Total1 lenses, with statistical differences in day1 and day2. In the total punctuation (sum of the other punctuations), the Total1 has shown better scores in all the three days, being statistical different from MyDay in Day3.

To better understand the mechanisms that could lead to the differences in comfort, some correlations were done. First, the comfort was compared to dehydration values. For Total1 lens, the relative percent of dehydration in the morning and afternoon was weakly correlated with the values of comfort, vision and ease in handling the lens (questions of daily questionnaire), with all the correlations with no statistical significance. These results are in concordance with the literature, where some studies not consistently show a significant relationship between dehydration and comfort

ratings.[82;151;152;201] For MyDay lens, the scenario is a bit different, with significant and moderate correlations between the morning RML and comfort with the lens after 4h of wear (r=0.462, p=0.40, Pearson), level of dryness throughout the day (r=0.548, p=0.012) and level of dryness after 8h of CL wear (r=0.558, p=0.011). This is a little contradictory and not in accordance with the literature. Few studies have found correlations between dehydration and discomfort, but when is found, is a negative correlation (meaning that more dehydration lead to less symptoms).[152] The correlation between the final score and both morning and afternoon RML was poor and insignificant for both lenses.

Other correlations were done, namely between comfort and pre-lens NIBUT. There are some significant correlations between NIBUT values and the questions of daily questionnaire. For Total1 lens, moderate correlations were found between the morning NIBUT and comfort with the lenses upon insertion (r=0.523, Spearman), comfort with the lenses after 8h of lens wear (r=0.556, Pearson), level of dryness after 8h of lens wear (r=0.513, Pearson), vision with the lenses throughout the day (r=0.626, Pearson), and vision with the lenses after 8h of lens wear (r=0.631, Pearson). There also are statistical significant correlations between afternoon NIBUT and comfort with the lens upon insertion (r=0.523, Spearman), comfort with the lenses after 8h of wear (r=0.556, Pearson), level of dryness after 8h of wear (r=0.513, Pearson), vision with the lenses throughout the day (r=0.626, Pearson), and vision with the lenses after 8h of wear (r=0.631). For MyDay lenses the scenario is the opposite, with only one fair (but not significant) correlation encountered between morning NIBUT and comfort with the lens upon insertion (r=0.399, p=0.082 Spearman). The correlations between the afternoons NIBUT are all fair to poor and without statistical significance. Until nowadays, must authors have found significant associations between decreased pre-lens tear BUT /NIBUT and increased discomfort in soft CL.[82;128;188;195]

In forced-choice, Total1 seems to have conquered patient's preference throughout the days. Most of the patients have answered that have forgotten that were wearing both lenses, but those who have discriminate between them, showed a preference for Total1. The same happened in terms of comfort and in terms of vision, as well as in global terms.

6. CONCLUSIONS

From the current study, the following conclusions:

- The two daily disposable CLs fitted have significantly reduced the symptomatology presented at baseline visit.

- Some comfort issues are moderately correlated to pre-lens NIBUT in Total1 lens, but not in MyDay lens.

- The contralateral fit of the two lenses allows a direct and better comparison between them, since they are exposed to the same conditions. As a result, both lenses showed a very similar performance in HCVA, LCVA, SOQ, pre-lens NIBUT and in dynamic topography and aberrometry values, with minimum differences between them in both morning and afternoon visits.

- The two lenses can be distinguished by their dehydration during the day and by the comfort assessment, with Total1 lens having better performances in these two parameters.

- Dynamic topography and dynamic wavefront aberrometry proved to be sensitive in the assessment of tear film's temporal changes, although the second technique has shown some limitations.

- By direct observation, it is noticeable that SRI is more sensitive to tear film changes through time than SAI values, evidencing more changes through time that could be related to rupture points.

- The SRI and TSRI seem to be similar between the measurements done in the PLTF in symptomatic CL wearers and those taken in PCTF of normal subjects in other studies, and that the lenses used in the present thesis could promote a more stable tear film than normal symptomatic subjects without lenses.

- Both lenses proved that there are no differences in bulbar and limbal hyperemia, BUT and corneal staining parameters between daily disposable lenses wear when compared to no lens wear, since there were no differences in these parameters when compared to baseline visit.

- This thesis findings show that the improvements in conjunctival staining can occur right after 3 days of daily disposable CL re-fit (in both Total1 and MyDay lenses).

7. FUTURE WORK

- Include a larger sample to evaluate the impact of contact lens wear between different symptomatology degrees (non-symptomatic, little symptomatology, and high symptomatology).

- Searching new modes of subjective evaluation that correlate better with gold standard methods measuring tear film break up time.

- Future works can be done with other lens designs, even assessing the contralateral use of monthly CL in one eye and a daily disposable CL in the other eye for better comparisons between the two modalities.

- Both dynamic topography and aberrometry could be integrated in other approaches to compare the tear film behavior of CL wearers and non-wearers.

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9. Appendix 1. Patient Daily Questionnaire

1. Responda às seguintes questões marcando com uma linha horizontal a sua resposta a cada lado da escala vertical, lado direito para a lente direita (🡐) e ao lado esquerdo para a lente esquerda (🡒):

A. *Facilidade de manuseamento das lentes*

B. *Conforto com as lentes logo após a inserção*

C. *Conforto com as lentes às 4 horas de uso*

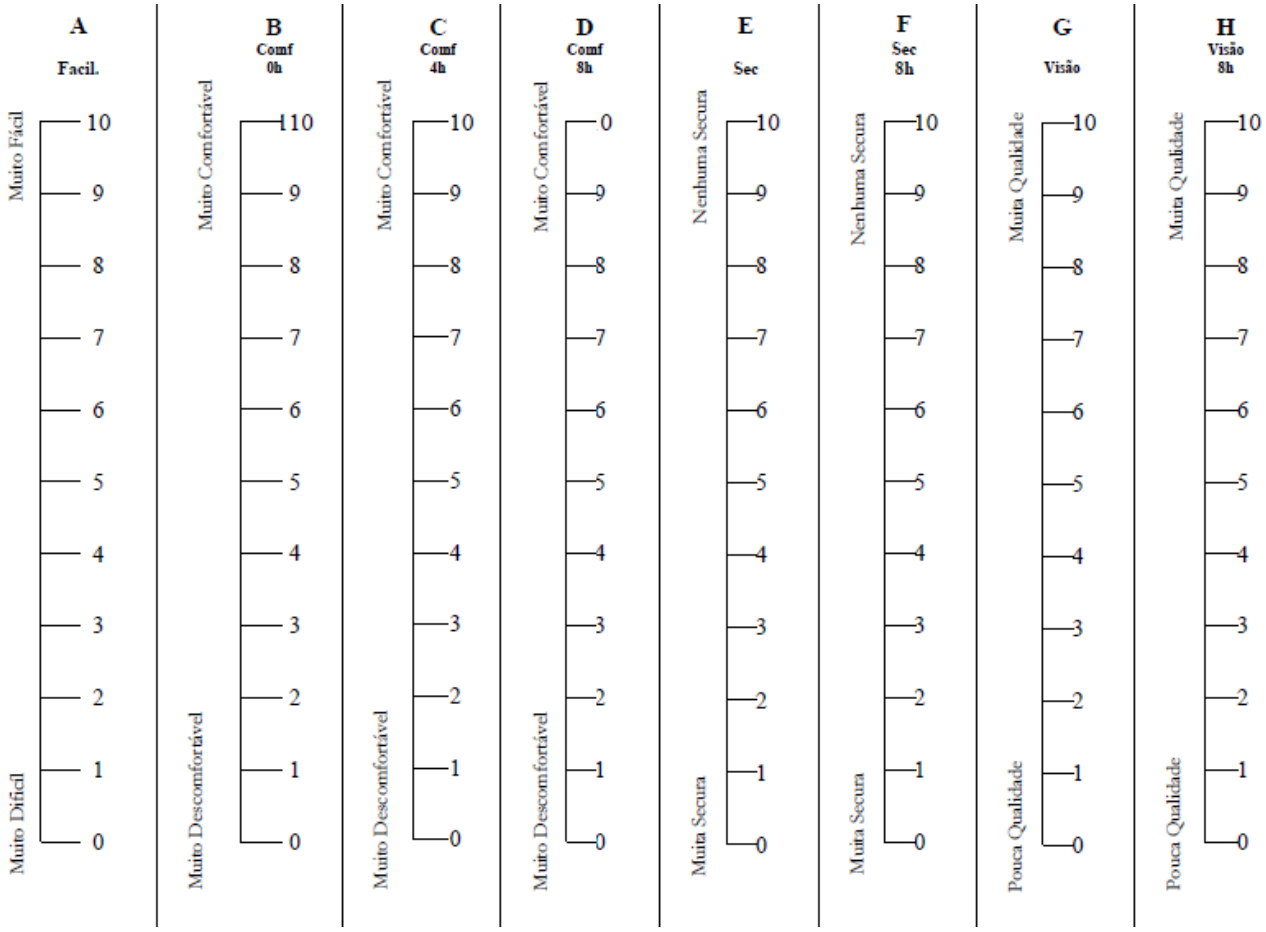
D. *Conforto com as lentes às 8 horas de uso*

E. *Grau de secura durante o dia*

F. *Grau de secura depois de 8 horas de uso*

G. *Visão com as lentes durante o dia*

H. *Visão com as lentes depois e 8 horas de uso*



2. Conseguiu esquecer que estava a usar as lentes?

☐Ambas

☐Lente Direita ☐Lente Esquerda

3. As suas lentes deixaram de ser confortáveis durante o dia?

☐Sim

☐Não

4. Se respondeu sim na pergunta anterior, indique a que horas cada uma delas deixou de ser confortável?

Lente Direita ___:___ Lente Esquerda ___:___

5. Qual a lente que preferiu em termos de conforto?

☐Lente Direita ☐Lente Esquerda

6. Qual a lente que preferiu em termos de visão?

☐Lente Direita ☐Lente Esquerda

7. Em termos globais, qual a lente que preferiu?

☐Lente Direita ☐Lente Esquerda