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Impact of Soft Contact Lenses for Digital Devices on Visual Performance, Tear Film, Accommodative Response and Dehydration in young adult subjects: A Pilot Study

Dissertação de Mestrado
Mestrado em Optometria Avançada

Trabalho efetuado sob a orientação do
Professor Catedrático José Manuel González-Méijome
e da
Professora Doutora Rute Juliana Ferreira Macedo de Araújo

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Avelino N. F. Mazuze, May 2021

STATEMENT OF INTEGRITY

I hereby declare having conducted this academic work with integrity. I confirm that I have not used plagiarism or any form of undue use of information or falsification of results along the process leading to its elaboration.

I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

ABSTRACT

Impact of Soft Contact Lenses for Digital Devices on Visual Performance, Tear Film, Accommodative Response and Dehydration in young adult subjects: A Pilot Study

The purpose of this study was to investigate the effect of soft contact lenses (CLs) claimed to be beneficial for use of digital devices on visual performance, accommodative response as well as tear film and dehydration in young adult subjects. Seven young-adult myopes with mean age of 25.71±3.40 years wore two designs of CLs for digital devices - Biofinity Energys (Comfilcon A) and Bausch + Lomb ULTRA (Samfilcon A) - for a week each in a randomised single-masked cross-over study. Visual performance was measured with high and low-contrast visual acuity at distance (ETDRS visual charts), optical quality (aberrometry), light disturbance (LD) measured with a Light Disturbance Analyzer, tear film (dynamic cornal topography), accommodative response (badal optometer coupled with an open-field autorrefractometer), quality of vision (Quality of Vision questionnaire) and comfort were evaluted at lens dispensing visit (LDV) and after one week of wear. CLs dehydration was evaluated *in vitro* and *ex vivo* using a gravimetric method. A single vision contact lens was used as control device.

The results showed that no significant differences in the level of visual performance achieved with both types of CLs for digital devices in comparison with Control lens ($p > 0.05$, Friedman test). Concerning optical quality, significant differences were found for coefficients Astig Obli, Horizontal COMA, 4^{th} and 6^{th} order spherical aberration with CLs tested (all $p \leq 0.03$). The irregularity parameter of LD showed significant differences in monocular condition between CLs tested ($p=0.028$). Tear Film Surface Quality (TFSQ) Index and TFSQ Area increase significantly with CLs tested compared to baseline ($p<0.05$, Friedman test). Auto Tear Break-Up Time (BUT) was significant higher at Baseline than CLs tested ($p<0.05$, Friedman test). Accommodative response, comfort and QoV did not change significantly ($p>0.05$, Friedman test). CLs dehydration rates (*vitro* and *ex vivo*) did not change significantly ($p>0.05$, Unpaired T-test and ANOVA).

The findings of this study suggest that soft CLs for digital devices offer similar visual quality outcomes and clinical performance compared to the Control lens. Importantly, change in tear film stability, comfort score and QoV were not statistically significant, but were clinically significant. Thesepreliminary outcomes should be confirmed with a larger sample size.

Keywords: accommodative response and tear film instability; contact lenses; digital devices; visual performance..

RESUMO

Impacto das lentes de contato para dispositivos digitais no desempenho visual, filme lacrimal, resposta acomodativa e desidratação em jovens adultos: um estudo piloto

O presente estudo teve como objectivos investigar o impacto das lentes de contato (LC) destinadas ao uso com dispositivos digitais na performance visual, resposta acomodativa, bem como filme lacrimal e desidratação em adultos jovens. Sete míopes adultos jovens (25,71 ± 3,40 anos) foram adaptados dois desenhos de LC para dispositivos digitais - Biofinity Energys (Comfilcon A) e Bausch + Lomb ULTRA (Samfilcon A) por uma semana, num estudo cruzado aleatório e simples cego. O desempenho visual (cartas visuais de ETDRS), qualidade óptica (aberrometria), distorção luminosa (LD) medida com um analisador de perturbação da luz, filme lacrimal (dynamic cornal topography), resposta acomodativa (badal optometer acoplado a um autorrefractómetro de campo aberto), qualidade de visão (Questionário de Qualidade de Visão) e conforto foram avaliados na visita de dispensa (LDV) e após uma semana de uso. A desidratação das (LC) foi avaliada in vitro e ex vivo, utilizando o método gravimétrico. Uma lente de contacto de visão única foi utilizada como dispositivo de controlo.

Os resultados mostraram que não houve diferenças significativas na performance visual alcançado com ambos os tipos de LC para dispositivos digitais em comparação com as lentes de controlo ($p > 0,05$, teste Friedman). Relativamente à qualidade óptica, foram encontradas diferenças significativas para os coeficientes Astig Obli, Horizontal coma, 4th and 6th ordem de aberração esférica na visita de dispensa e de acompanhamento (todos $p \leq 0,03$). O parâmetro de irregularidade da LD mostrou diferenças significativas em condição monocular entre lentes. Os Índices Tear Film Surface Quality (TFSQ) e TFSQ Área aumentam significativamente da baseline em comparação com as lentes testadas ($p < 0,05$, teste Friedman). O tempo de ruptura do filme foi mais elevado na Baseline do que nas lentes testadas, com diferenças significativas entre a Baseline em comparação com as lentes testadas ($p <0,05$, teste Friedman). A resposta de acomodativa, conforto, QoV e a desidratação (vitro e ex vivo) não foram estaisticamente significativamente ($p > 0,05$).

Os resultados deste estudo sugerem que as LC para dispositivos digitais oferecem resultados de qualidade visual e desempenho clínico semelhantes em comparação com as lentes de controlo. É importante ressaltar que as mudanças na estabilidade do filme lacrimal, conforto e QoV não foram estaticamente significativas, mas foram clinicamente relevantes. Esses resultados preliminares devem ser confirmados com amostras de tamanho maior.

Palavras-chave: desempenho visual; dispositivos digitais; lentes de contato; resposta acomodativa e instabilidade do filme lacrimal..

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GLOSSARY OF TERMS & ABBREVIATIONS

AOA: American Optometric Association

AC - Accommodative Convergence

AC/A: Ratio convergência acomodativa/ acomodação

AP: Associated Phoria

BUT: Break-up Time

BCVA: Best corrected visual acuity

BFCIrreg: Best fit circle irregularity

BFCIrregSD: Best fit circle irregularity standard deviation

BFCRad: Best fit circle radius

BVD: blurred vision looking into the distance;

BVvC: blurred vision while viewing the computer

CEORLab: Clinical and Experimental Optometry Research Laboratory

CVS: Computer Vision Syndrome

CEORLab: Clinical Experimental Optometry Research Laborattory

CL: Contact lens

CRT: Cathode Ray Tube

CVS: Computer Vision Syndrome

CVS-Q: Computer Vision Syndrome Questionnaire

CIC: Conjunctival Impression Cytology

CLs: Contact lenses

DEQ: Dry Eye Questionnaire

DED: Dry Eye Desease

DES: Digital Eyestrain

DE: dry eyes

D: dioptria

ES: eyestrain

ETDRS: Early Treatment of Diabetic Retinopathy Study

ESF: External Symptoms Factor

EWC: equilibrium water content

FHP: Forward Head Position

HA: Headache

HCDVA: High contrast distance visual acuity

HOA: High Order Aberrations

HC: Habitual Correction

IEBI: Inter-eyeblink intervals

ISF: Internal Symptoms Factor

LCDVA: Low contrast distance visual acuity

LCD: Liquid Crystal Display

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

LD: Light disturbance

LDI: The Light disturbanceindex

LE: Left Eye

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

LOA: Low Order Aberrations

MCLs: Multifocal contact lenses

MV: Monovision

MGD: Dysfunction of Meibomian Glands

NIBUT: Non-Invasive Tear Break-up Time

NPA: Near point of accommodation

NPC: Near point of convergence

TE: tired eyes

TFSQ: Tear Film Surface Quality

TBUT: Tear Film Break Up Time

OSDI: Ocular Surface Disease Index

OSHA: The Occupational Safety and Health Administration of the US Governnment

p: Statistical significance

PALs: Progressive Addition Lenses

PRT: Phenol Red Thread

PD: Prism dioptres

QoV: Quality of Vision Questionnaire

RE: Right Eye

RML: relative mass loss

RMS: Root Mean Square

RE: Refractive Error

SD: Standard deviation

SRI: Surface Regularity Index

SAI: Surface Asymmetry Index

Si-Hy: Silicone Hydrogel

SVC: Single Vision Contact Lenses

SECVS: The Ethics Subcommittee for Health and Life Sciences

SVL: Single-Vision Lenses

SEBR: Spontaneous Eyeblink Rate

SBL: Sensitivity to Bright Light

SPSS: Statistical Package for the Social Sciences

TBUT: Tear Break-up Time

VA: Visual Acuity

VDT: Vídeo Display Terminal

VDU - Visual Display Units

URE: Uncorrected Refractive Error

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À minha Mãe!

“The size of your dreams must always exceed your current capacity to achieve them. If your dreams don’t scare you, they aren’t big enough.”

(Ellen Johnson Sirleaf')

“''Development doesn’t happen without transformation, first of people themselves, then of institutions, then of systems.''

(Graça Machel)

Chapter 1

Introduction, Research Rationale and Justification of the study

Avelino Nelson F. Mazuze

1. INTRODUCTION

1.1 Research rationale and justification of study

In the last decade, the use of digital devices has increased significantly and became part of our daily life (Palaiologou, 2014). This exponential growth and expansion of the digital technology and information has led to some consequences and changes in the human eyes (Maducdoc *et al.,* 2017). As a result, the number of people with complaints of vision-related symptoms associated with the use of digital devices such as ocular discomfort, headache, double vision, visual fatigue, irritation, itching, redness, burning, blurred vision, tearing of the eyes and dryness has increased significantly in the consulting room (Talens-Estarelles *et al.,* 2020; Chu, *et al.,* 2011; Parihar *et al.,* 2016; Lin *et al.,* 2019).

Several studies have demonstrated that vision and eye-related symptoms are one of the most common complains among digital devices users, and the overexposure to digital displays can cause changes in binocular vision function (accommodation and vergence system) and tear film, not only in the computer workers but also in the general population that use digital devices. (Portello *et al.,* 2013; Reindel *et al.,* 2018; Moon *et al.,* 2016, Chiemeke *et al.,* 2007).

Currently, different optical strategies to reduce the symptoms commonly associated to the use of digital devices have been projected and are commercially available in order to improve visual performance, ensure wearer's comfort and reduce the accommodative demand and binocular vision stress. One of these options that currently are available and have been gained interest by eye care specialist are soft contact lens (CLs) intended for digital devices (Koh *et al*., 2019; Sha *et al.,* 2018). Despite the existence of a variety of CLs design and the continuous increasing in CLs fittings, the majority of multifocal contact lenses (MCLs) and single vision contact lenses (SVCL) do not change the accommodative response in healthy young adult subjects (Montés-Mico *et al.,* 2011; Pettersson *et al.,* 2011; Kang and Wildsoet, 2015; Gong *et al.,* 2017; Ruiz-Alcocer *et al.,* 2012; Ruiz-Pomeda *et al.,* 2018; Ruiz-Pomeda *et al.,* 2018).

With this in mind, the present dissertation presents a comparative clinical trial of two novel CLs specifically developed for digital devices in young adults subjects. The purpose of this study was to

investigate the impact of different designs of soft CLs for digital devices on visual performance, tear film, accommodative response and dehydration in young adult subjects. In this context, this thesis seeks to answer the following research questions:

1. What is the impact of soft CLs for digital devices on visual performance, accommodative response and tear film in healthy young adult subjects?

2. Do soft CLs for digital devices provide a better visual performance and which is their impact on the higher order aberrations in normal young adult subjects?

3. Do soft CLs for digital devices provide greater comfort and better quality of vision in normal young adult subjects?

This dissertation begins with an introduction and research rationale (chapter#01). In the chapter#02 a literature review is presented; chapter#03 presents the aims and the hypothesis of the study are outlined; In chapter#04 is described in detail the experimental design and methodology of the study; The chapter#05 presents the results obtained for the main variables relevant in this dissertation. Chapter#06 discusses the results with previous studies. Finally, in the last chapter (charpter#07) the conclusions based on the result of the current research, the limitations of the study and future works are presented. An overview of the Thesis organization followed is shown in **Figure 1-1**.

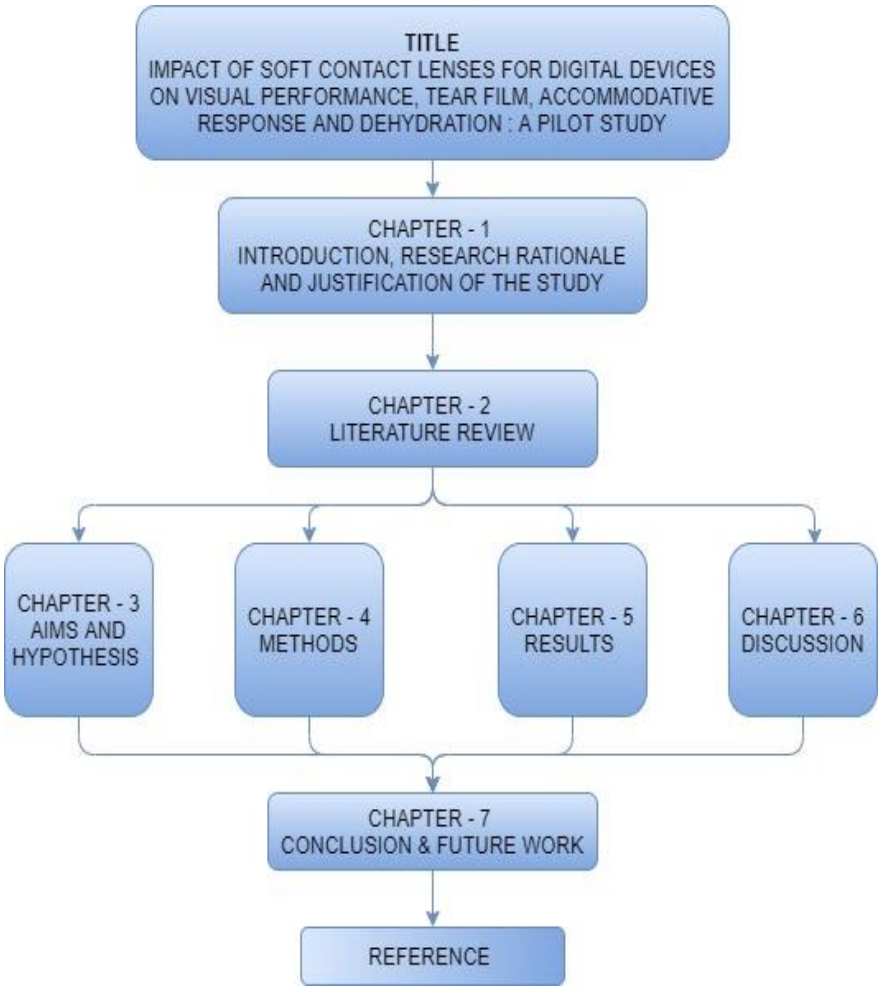


Figure 1-1 - Flowchart showing the organization followed in the current dissertation.

Chapter 2

Literature Review: Effect of Digital Devices on Vision

Avelino Nelson F. Mazuze

2. LITERATURE REVIEW

Nowadays, many people spend hours and hours every day in front of digital devices such as computer screen, mobile phones and tablets. The amount of time that is spent in front of the screen, using different types of digital devices, conducting near-vision tasks, such as reading, writing, and using the internet has increased significantly in over the world in last year's (Randolph, 2017; AOA, 2013). Globally, it is estimated that about 4208 million people use the internet (**Figure 2-1**). In 2019 approximately 91 % of European Union (EU) young people with ages between 16-29 years were internet users on daily basis (Internetworldstats, 2020; Eurostat, 2020).

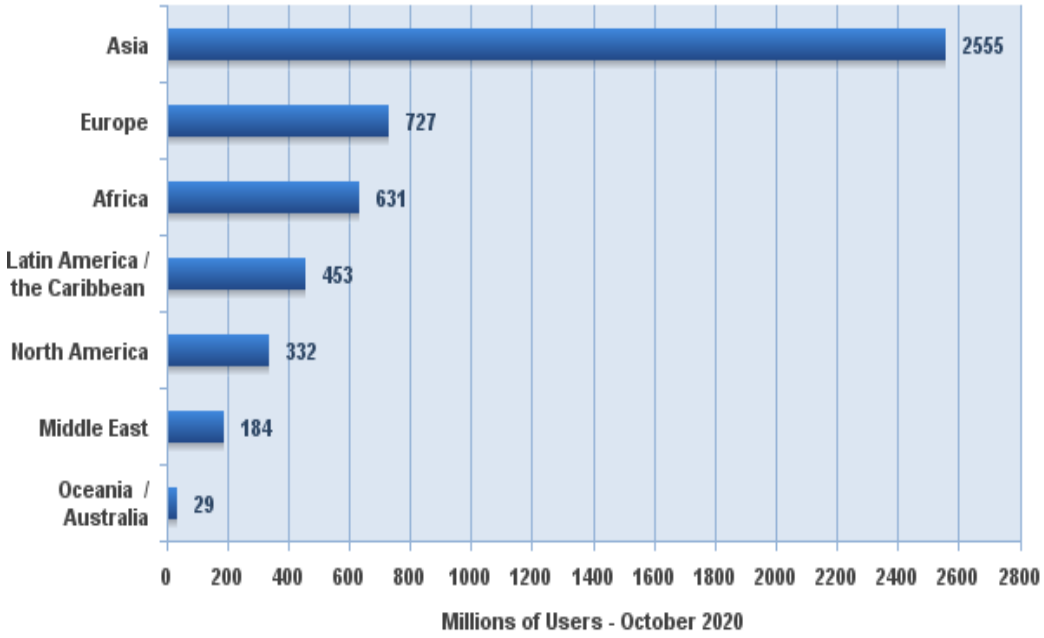


Figure 2-1 – Internet users in the World in 2020. Source: Internet World Stats- **https://www.internetworldstats.com/stats.htm**, accessed in January of 2021.

The aim of the current chapter was to review the scientific literature published to date related to the effect of digital devices on vision. For this purpose, all studies related to digital devices and vision were reviewed and the results obtained were analysed following a sequential scheme**: (i)** symptomatology associated with use of digital devices, **(ii)** symptom-inducing risk factors **(iii)** effect of digital devices on vision, **(iv)** treatment strategy of visual and ocular symptoms associated to digital devices **(v)** impact of contact lenses on ocular surface and use of digital devices; **(vii)** contact lenses

dehydration. Special emphasis will be given to the effect of digital devices on vision system, such as visual performance, accommodation and vergence system and tear film (tear evaporation rate and tear film stability).

2.1 Methods of the bibliographic search

A search of contemporary literature on CVS was carried out in electronic health science databases such as PubMed, Scopus and ScienceDirect, using keywords combined with adjacency and proximity Boolean operators. The search was performed on January of 2020 and was limited to articles written in English language, and it includes different study design (systematic review and meta-analysis articles, epidemiology study and clinical trials). The terms used were: (computer vision syndrome), (digital eyestrain), (computer vision syndrome OR digital eyestrain), (problem related to computer user), (occupational asthenopia), (eye-related discomforts OR visual fatigue), (computer and visual terminal display OR visual display unit). Original articles written in other languages such as Chinese, Japanese, Russian, or Arabic were excluded of this search. Relevant literature related to the effect or impact of digital devices on visual performance, binocular vision (accommodation and convergence) and tears film (dry eye and blinking rate) and dehydration of CLs were also included. Search terms for impact on binocular vision, ocular surface and tear film were: (accommodation OR accommodative function); (convergence OR vergence); (tear film OR blink rate); (tear function OR tear quantity). Classic books, paper from conferences and any form of relevant references were also included in this literature review. Two hundred and sixty-four articles (after exclusion of duplicated and non-related articles) published between 1973 and 2020 were identified using the combination represented by the junction of keywords*: computer vision syndrome OR digital eyestrain*. Only articles published between 1990 and 2020 were included in the literature review of the present work (with the exception of two articles dating from 1988).

In the recent years the interest to investigate the effect of digital devices on the visual system has increased significantly. **Figure 2-2** shows that from 2015 to 2019 the publication rate (yearly) in the field has tripled if we consider that the average number of publications per year was 5 articles from 1973 to 2010. Therefore, a lot of information has been produced recently and needs critical review and reassessment.

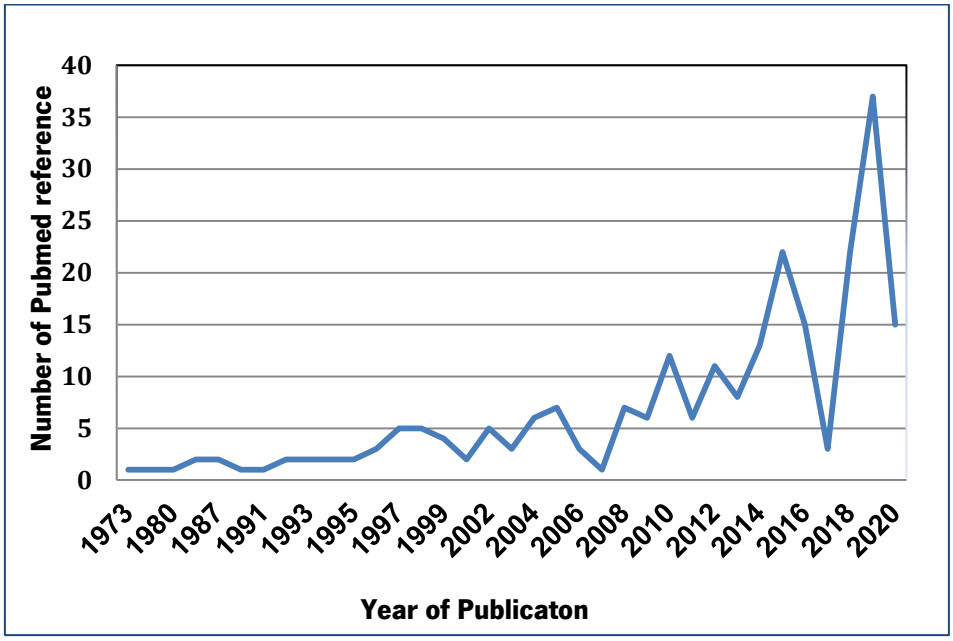


Figure 2-2 - Publication rate (yearly) related to computer vision syndrome or digital eyestrain as retrieved by the National Library of Medicine search engine (PubMed) by January 2020, using keywords: "computer vision syndrome OR digital eyestrain". Source: https://www.ncbi.nlm.nih.gov/pubmed/, accessed in January 2020.

2.2 Symptomatology associated with use of digital devices

Several studies have demonstrated that individuals who spend more than six hours per day using digital devices may experience visual symptoms such as eye strain, eye fatigue, discomfort, burning, irritation, blurred vision, headaches, difficulty focusing, dry eyes and red eye, diplopia, photophobia, blur, itching, tearing, dryness and foreign-body sensation (Yan *et al.,* 2008). The severity of symptoms varies according to the exposure time, and occurs when the visual system cannot perform comfortably the demanding near visual work, such as secretaries, accountants, bookkeepers, etc. (Rosenfeld, 2016; Blehm *et al.,* 2005; Sheedy and Parson, 1990). **Figure 2-3** shows the classification of **s**ymptoms associated with use of digital devices, according to Coles-Brennan *et al.* (2019).

Sheedy *et al.* (2003) categorized the symptoms associated with the use of digital devices in two groups, according to the etiologic factor: external symptoms factor (ESF) and internal symptoms factor (ISF). The symptoms associated with the first group (ocular symptoms) include burning, irritation, ocular dryness and tearing, and the factors related to these symptoms were reading under conditions of

glare, flickering light, small font size and upward gaze. The symptoms related with the second group (visual symptoms) include eyestrain, headache, eye ache, diplopia and blurred vision, and is generally caused by uncorrected refractive error (far or near vision), accommodation problems and binocular alignment problems. In a review of Computer Vision Syndrome (CVS) Bali *et al.* (2016) claim that the symptoms related to ocular surface such as eye dryness, burning and grittiness may result from the environmental factors like dry air-conditioned interiors, draught from ventilation fans, static build-up, airborne paper fragments, and general office dust can have some bearing on the ocular surface symptoms.

Others symptoms associated with the use of digital devices are musculoskeletal symptoms. Many computer workers who maintain the same posture or inadequate posture for extended periods of sitting can report symptoms related to neck aches, shoulder aches, backaches, pain, muscle fatigue, headache, muscle imbalances, a tendency to forward head position (FHP) and augmented spinal loads, tension neck syndrome, venous thrombo-embolism, carpal tunnel syndrome, shoulder tendonitis, elbow epicondylitis and wrist tendonitis (Parihar *et al.,* 2016, Laparra *et al.,* 2019). In a cross sectional study, Hales *et al.* (1994) analyzed the relationship between workplace factors and work-related upper extremity musculosketal disorders in 533 telecommunication employees, and found a prevalence of 22% of musculoskeletal symptoms such as neck, shoulder, elbow and hand/wrists pain in computer users.

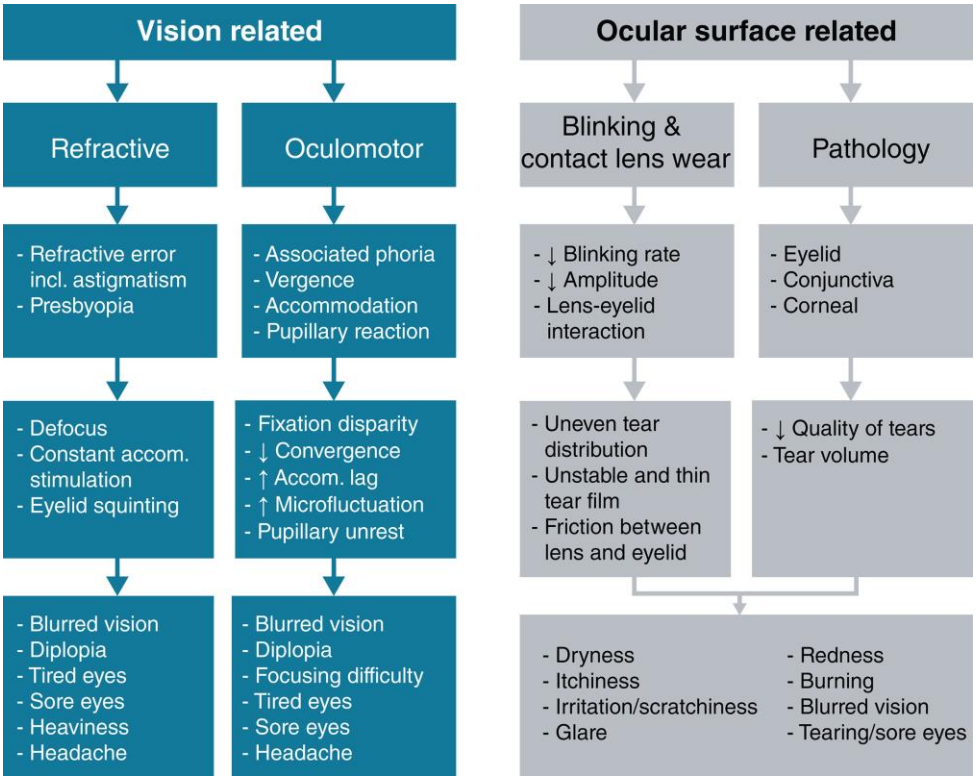


Figure 2-3 – Visual and ocular symptoms associated with use of digital devices. Reproduced from Coles-Brennan *et al.* (2019)

2.3 Symptom-inducing risk factors

Numerous factors such as lighting, display characteristics, screen reflections, dry eye, high concentration, continuous looking at a fixed object, glare, individual visual problems, poor workplace conditions, improper work habits, refresh rates, radiation and positioning of computer monitors and lesser blinking of eyelids, were describe as potential causes and risk factors for developing CVS (Blehm *et al.,* 2005; Bali *et al.,* 2016; Sheedy and Shaw-McMinn, 2003). **Figure 2-4** illustrates the major factors that contribute to symptoms associated with use of digital devices.

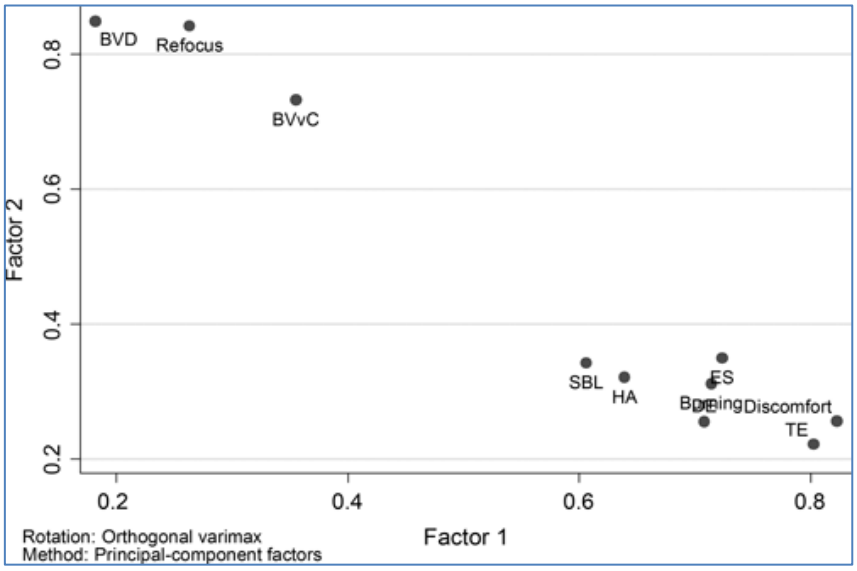


Figure 2-4 - Factor analysis of visual symptoms related to CVS in 520 office worker. *Two dimensions are clearly identified, namely factor 1 (related to dry eye) and factor 2 (associated with ocular accommodation). SBL, sensitivity to bright light; HA, headache; ES, eyestrain; Discomfort, eye discomfort; TE; tired eyes; Burning, burning eyes; DE, dry eyes; BVD, blurred vision looking into the distance; BVvC, blurred vision while viewing the computer; Refocus: slowness in refocusing*. Data from Portello *et al.* (2012).

In a review related to computer and visual display terminal (VDT), Parihar *et al.* (2016) categorized the causes and factor of eye-problem related to the use of digital devices in four groups: (1) environmental and work factors; (2) personal factors; (3) device related factors; (4) ocular surface disorder. The environmental and work factors that mainly contribute to CVS are caused by office air quality, lighting geometry and quality, screen reflections, computer display design such as contrast polarity, resolution flicker and workstation arrangements. Lighting and glare has a significant influence on visual performance when using a computer and digital devices. Research has suggested that the lighting of the workplace must be constant and the room should have the proper types of lighting. Yan *et al.* (2008) suggest the use of natural or artificial lamps such as filament lamps, fluorescent, incandescent, mercury or sodium. Several studies have revealed the effect of glare and lighting on vision. Wolska and Swituta (1999), for instance, analysed different values of surrounding luminance under 3 lighting conditions and found a significant reduction of the accommodation amplitude

(significance level <.05).The authors also observed no statistically significant difference in the value of surrounding luminance on the asthenopic symptoms for either CRT or LCD monitors.

Personal factors were also identified as risk factors for vision problems associated with the use of digital devices. The most frequent causes and risk factors include nicotine use, gender, age and refractive error. Refractive error such as hyperopia, myopia and astigmatism are one of the most significant personal factors that can affect visual performance (reduced visual acuity for both distance and near), the comfort and increase the post-task symptoms such as eye strain, headache and blurred vision in computer users (Yan *et al.,* 2008). These symptoms are generally temporary and get worse at the end of the day or after computer use. However, more investigations are needed to study the effect of uncorrected refractive error on task performance associated to computer users.

Besides personal factors, other cause of symptoms associated with the use of digital devices is the device-related factors. This cathegory includes the height and angle of video display terminal (VDT), flicker frequency screen resolution, background and text color, and 3D stereoscopic display. Macknik *et al.* (1991) studied the effects of flicker on space perception using the displacing a flickering target during saccadic eye movements, and observed that at lower flicker rates it was easier to detect the displacements. This finding suggests that higher frequency flickering target on video display terminals may distort space perception easily during saccadic eye movement and increase risk of complain such as eye fatigue in VDT user.

2.3.1 Dry eye and digital devices

Dry eye (DE) is recognized as one of the major contributor factor to vision problems associated with the use of digital devices (Ahn *et al.,* 2014; Yaginuma *et al.,* 1990; Tsubota, 1993; Rosenfield, 2011). Reduced lacrimal lipid secretion, decreased of blink frequency, inappropriate workplace humidity, larger palpebral aperture, and incomplete blink were reported as main cause of CVS-related to dry eye (Sheedy and Shaw-McMinn, 2003; Munshi *et al.*, 2017). Dryness is experienced by up to 21.5% of VDTs users (Uchino *et al.,* 2008).

Several studies have investigated the prevalence of dry eye among the computer and digital devices users and the evidence from recent studies suggests that the use of visual display terminal for

many hours may cause changes in ocular surface and increase the symptoms (**Figure 2-5**) commonly associated to CVS. For instance, Portello *et al.* (2012) investigated the prevalence of visual symptoms in 520 New York City office workers, using The Ocular Surface Disease Index questionnaire (OSDI) and found a high prevalence of dry eye in office workers (32 % and 31% of the subject reported symptoms of dry eye and eye discomfort). The high prevalence of computer-related visual symptoms has been correlated with the OSDI and DED. Likewise, Uchino *et al.* (2013) investigated prevalence of DED and its risk factors in 672 young and middle-aged Japanese visual VDT users, using dry eye questionnaire (DEQ) and dry eye testing, and found higher prevalence of DED among young to middle-aged Japanese VDT users (the percentage of women with a composite outcome of definite DED or probable DED was higher (76.5%) than men - 60.2%). Decrease in BUT and corneal staining accompanied by normal Schirmer test values were also observed. Equivalent findings were reported by Yokoi *et al.* (2015) and Moon *et al.* (2014*)* in a study where the association between VDT use and DED was evaluated in two-hundred eighty-eight school Children using a self-administered questionnaire. The authors found an association between the daily duration of smartphone use and increased risk of DED. Furthermore, the authors postulate that the use of smartphone is an important risk factor for developing DED in children.

Lastly, Uchino *et al.* (2008) which have investigated the prevalence of DED in 4393 young and middle-aged Japanese office workers, also observed high prevalence of dry eye in females, CL wearers, and prolonged VDT users. Likewise, Yamanish *et al.* (2019) compared the prevalence of DED among VDT users using the revised and previous DED criteria and also found an increased prevalence of dry eye from 11.6% to 58.6%, according to the revised DED diagnostic criteria of the Asia Dry Eye Society.

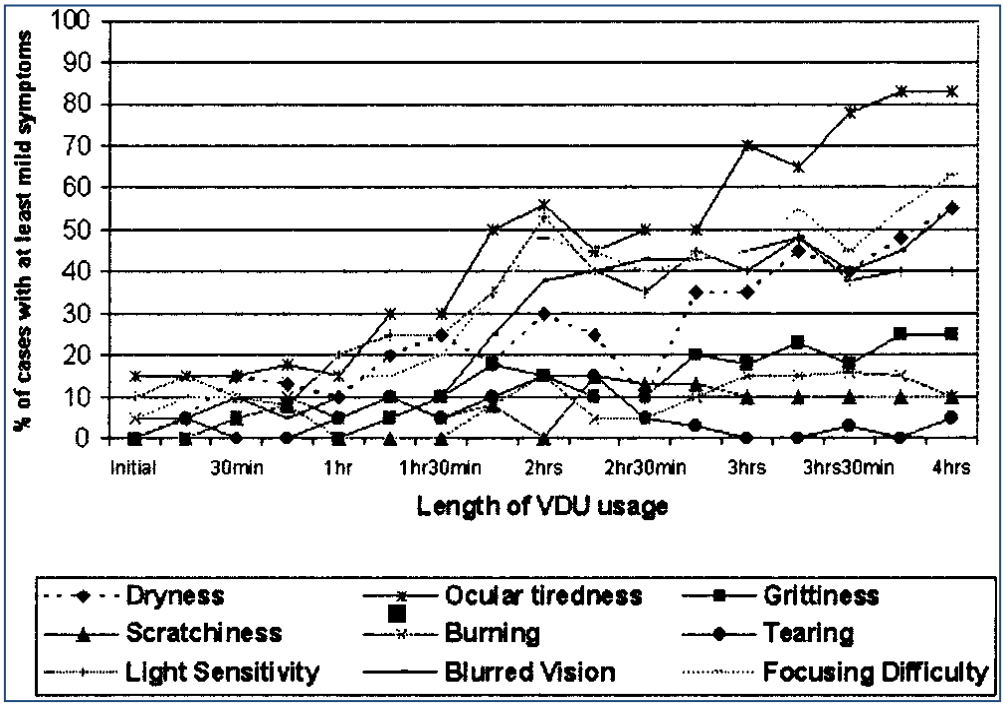


Figure 2-5 - Incidence of the ocular symptoms after 4h of computer task in 20 subjects. Data from Guillon *et al.* (2004).

2.4 Effects of digital devices use on vision

2.4.1 Visual Performance

Visual performance is one of the visual parameter that could be affected by a large number of devices and parameters, such as lightning conditions, flicker frequency screen resolution, background and text color, font size, structure, and style and viewing distance (Bali *et al.,* 2019). A few studies have investigated the impact of digital devices on visual performance among the computer users. For example, Ziefle *et al.* (1998) studied the effect of display resolution on visual performance and observed a strong correlation between visual fatigue and monitor with low-resolution. The authors also concluded that reading performance was significantly better in the paper condition than in the 2 CRT conditions. Lin *et al.* (2008) studied the influence of different illumination colors (red, blue, green and white) on visual performance and fatigue in VDT workstation and observed that visual acuity was significantly affected by the color of light (**Figure 2-6**).

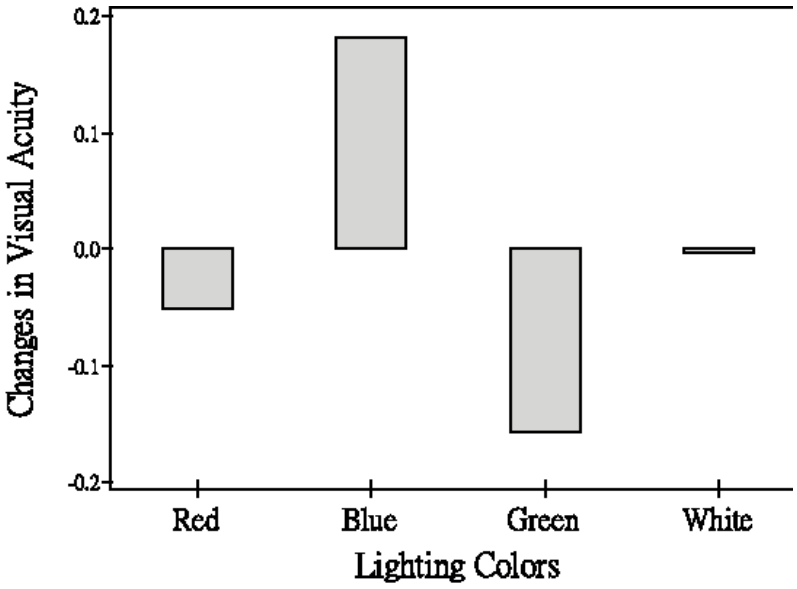


Figure 2-6 - Change in visual acuity at four lighting colors in 10 subjects. Data from Lin *et al.* (2008).

Lin *et al.* (2019) investigated the effect of reflected glare and visual field lighting on CVS, measuring different parameters such as visual function tests, questionnaires, and visual performance tests, and found a statistically significant decreased of critical fusion in all groups study after the performance of the visual task. They did not found statistically significant differences in visual function parameters, such as heterophoria, accommodative convergence (AC) per unit of accommodative (A) response (AC/A ratio), and accommodative facility between the first examination and the second examination. In contrast, Safdar *et al.* (2009) analysed the variation in visual acuity during workday, in forty-eight radiologists, found a statistically significant difference between the visual acuity of radiologists in the morning and visual acuity throughout the day.

Besides the glare discomfort, the size of text can also affect the visual performance. Bababekova *et al.* (2011) analysed the font size and viewing distance of handheld smart phones in 129 subjects with mean age of 23.2 years and concluded that the mean visual acuity required to view comfortably the font size (6/15.1 or 0.8 M letter) is at least 6/5. Sheedy and Shaw-McMinn (2003) suggested that computer monitor or other form of electronic devices should be three times better than the required to read the text on the display. This would help to minimize the visual symptoms such as tired eyes, blur or eye strain.

2.4.2 Accommodation

Perform visual activieties at a short distance from the eye for extended periods of time will increase the accommodative demand of the eye system. The same happens when those activities are performed in electronic screens (Coles-Brennan *et al.*, 2019). Accommodative abnormalities are the major cause of asthenopia, once computer-related activities overload the accommodation mechanism (Amalia *et al.,* 2010). **Figure 2-7** illustrates mean values of accommodative response at a viewing distance after 30 mints of computer task.

Several studies have investigated the effect of different digital devices on several components of the accommodation system: accuracy of accommodation (accommodation lag), flexibility (accommodative facility) and amplitude of accommodation. However, the results reported are not conclusive. Some studies report an increasing in accommodation (accommodation lag) during near task activities in visual display, while others did not report any change in accommodation (Coles-Brennan *et al.*, 2019; Bali *et al.,* 2019). For example, Rosenfield *et al.* (2010) analysed the changes in accommodation system in twenty-two subjects after reading a text from a computer screen during 25 min, and did not found any significant change in monocular accommodative during the computer task. Similarly, in a cross-sectional and observational study where 44 bank employees and 44 people as the control group members were observed, Mahjoob *et al.* (2013) demonstrated that there was no significant differences in some components of accommodative system such as accommodation range (one eye and both eyes), ease of accommodation (one eye, both eyes), and positive and negative related accommodation in none of the groups.

In contrast, a study conducted by Tosha *et al.* (2009) that aimed to evaluate the magnitude of accommodative errors and variability at different viewing distances in college students with low and high visual discomfort using objective measures of accommodation, found a higher accommodative lag at a near viewing distance over time. The authors also concluded that high visual discomfort was characterized by accommodative fatigue, with a higher lag of accommodation developing at a near viewing distance over time. Likewise, Park *et al.* (2014) investigated changes in accommodative system in young adult's subjects, and concluded that the use of smartphones may affect some components of accommodation system such as accommodative amplitude and accommodative facilities (decrease in monocular and binocular, respectively).

Alongside with the accuracy of accommodation, many others components of accommodative system were investigated during the computer tasks: micro fluctuations, accommodative facility and amplitude of accommodation. Gray *et al.* (2000) analysed accommodation micro fluctuations and steady-state accommodation pupil response during the sustained viewing of visual display terminal, in five young visually-normal emmetropic subjects, using a modified Canon Autoref R-1 infra-red objective optometer and a Hamamatsu C3160 Perceptscope Video Area Analyser. The authors did not found a significant variation in the magnitude of the accommodation micro-fluctuations with either display or task duration, nor any significant interaction between these two factors.

Harb *et al.* (2006) studied the behaviour and characteristics of accommodation during the sustained reading in emmmetropes and myopes eyes and found a significant increase in the power of accommodative micro fluctuations with closer demands ($p<0.05$) and with increasing myopia at closest reading demands ($p<0.01$). The authors concluded that the difference in the accommodative behaviour between individuals with different refractive states suggests a possible relationship between variability in accommodation and the development of myopia.

Simmers *et al.* (2001) investigated the influence of tinted lenses on ocular accommodation in four different conditions: prescribed tinted lens, neutral density filter, tinted lens of complementary colour and no absorptive lens. The authors found greater low-frequency micro fluctuations in accommodation in the no lens condition than in the other three lens condition. The authors concluded that this may be related to the reduction in luminance in tinted lenses. Saito *et al.* (1994) examined changes in visual function and accommodative function after a four-hour VDT operation task, and observed that both accommodative facility and amplitude of accommodation decreased significantly after 2h of computer work.

In summary, the use of digital devices may affect the accommodative system, by increasing the accommodation lag and decreasing the amplitude of accommodation. However, it is still unclear how exactly computer tasks may affect the accommodative facility. The presence of accommodative insufficiency, accommodative infacility and lag of accommodation associated to refractive asthenopia constitute the most common conditions related to CVS. (Shrestha *et al.*, 2011). The anomalies of accommodation may be detected by means of the near point of accommodation (NPA).

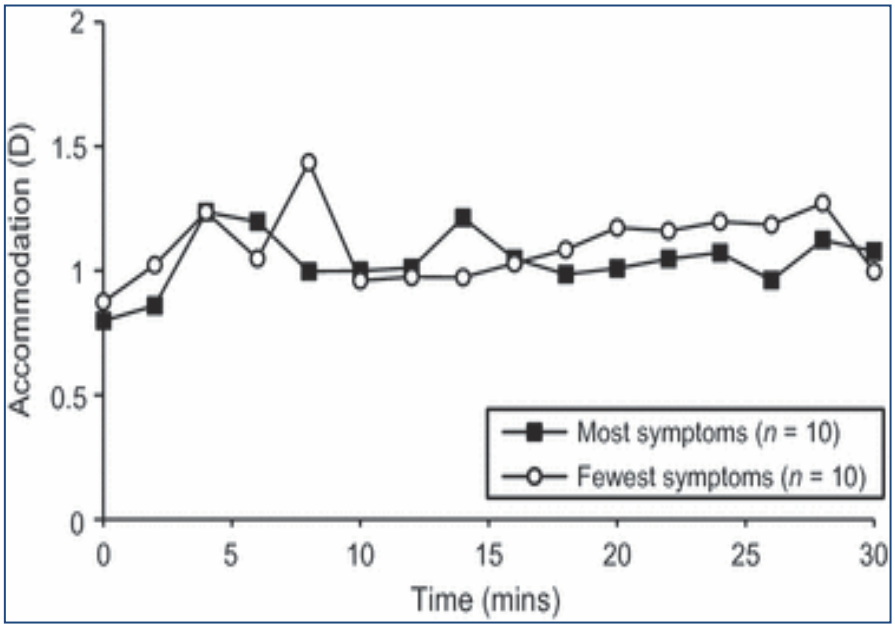


Figure 2-7 - Mean values of accommodative response at a viewing distance after 30 mints of computer task in 20 subjects. Data from Collier and Rosenfield, (2011).

2.4.3 Binocular Vision

Vergence system may also be affected by prolonged use of digital devices. Changes in near point of convergence (NPC), near negative fusional vergence and positive fusional vergence associated to exophoria or esophoria at near and distance, after prologued use of digital devices were reported as main signs of anomalies of binocular vision (Rosenfield *et al.,* 2010; Hall and Coles-Brennan, 2015; Watten *et al.,* 1994; Collier and Rosenfield, 2011).The vergence anomaly most commonly related to CVS is convergence insufficiency, which is characterized by poor convergence ability and fusional insufficiency.

Few studies have linked the use of digital devices and change in vergence system, but the link between these binocular function and ocular and visual discomfort symptoms related to computer use remains inconclusive (Rosenfield, 2011). Gur *et al.* (1994) evaluated the effect of 4 days of video display terminal (VDT) in accommodative and vergence system, in 16 visual display units (VDU) and 13 control workers with age between 24 to 43 years, before work at the beginning of the week (first examination) and again four days later at the end of the work day (second examination), using NPA and the near point of convergence (NPC). The authors found a statistically significant decreased in both

accommodation and convergence range. Watten *et al.* (1994) reported significant reduction in NPC positive and negative relative vergence in office workers after eight hours of computer use. The authors concluded that the use of computer may affect the vergence system with decrease of converge and diverge.

Gratton *et al.* (1990) investigated changes in visual function during work with VDT and also found a decrease in fusional convergence and a smaller decrease in divergence in all subjects. The authors concluded that an increase in viewing distance certainly leads to a lower load on accommodation and convergence system during the computer task in office workers. A recent study conducted by Kwon *et al.* (2016) aimed to investigate the effect of excessive near work activities by using a smartphone on the subjective symptoms, accommodative and convergent function in 40 subjects. The results pointed to a significant decrease of negative fusional vergence.

In contrast, Collier and Rosenfield (2011) examined the vergence response using the associated phoria (AP) and observed non significant changes in accommodation or vergence during the course of the 30-minute test period **(Figure 2-8**). Despite those results, the mean AP for the subjects who reported the greatest discomfort during the task was 1.55D exo and ortho. The authors concluded that a slightly reduced convergence response increases subject comfort during the task, which means that the symptoms related to CVS were significantly worse in subjects who exhibited zero fixation disparity than those who had exo AP. Likewise, a survey study conducted by Phamonvaechavan and Nitiapinyasagul (2017) that aimed to examine the effect of viewing text on computer screen and iPad® on visual symptoms and functions, found a significant change in fusional convergence amplitude at near after sustained reading text in both devices.

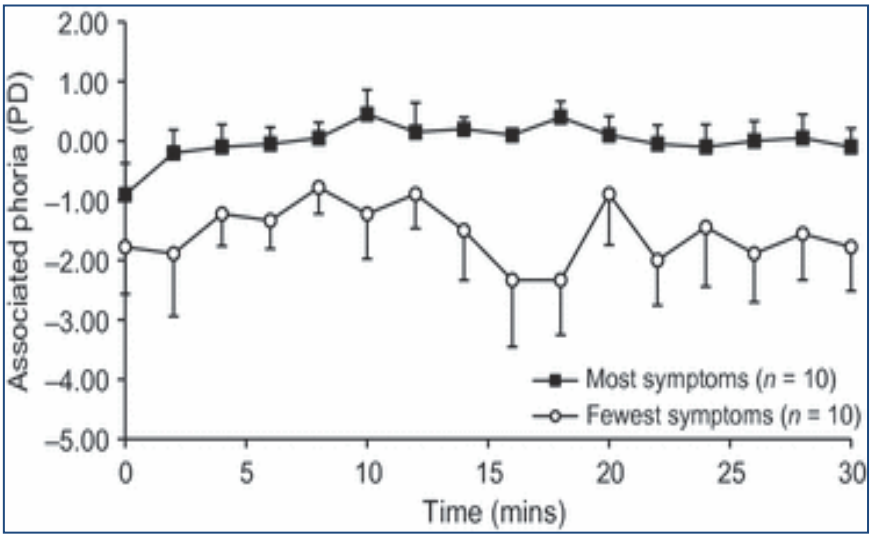


Figure 2-8 - Mean values of associated phoria in prism dioptres (PD) at a viewing distance after 30 mints of computer task in 20 subjects. Data from Collier and Rosenfield, (2011).

2.4.4 Tear film

One of the most important components of the ocular surface which play an important role in quality of vision is the tear film. The tear film is a complex and dynamic liquid layer covering the anterior surface of the human eye and is responsible for maintaining the integrity of the ocular surface as well as provides a proper anterior refractive surface for the human eye (Ramos *et al.,* 2014). Traditionally, the tear film has been described as having three intertwined layers **(Figure 2-9**), with a thickness of approximately 7 - 10 µm. Each of these layers is deriving from different origins and has different functions in the formation and stability of the tear film. The outermost layer of the tear film, the lipid layer, is responsible for delaying evaporation of the aqueous components and reduces surface tension of the tears from the ocular surface (Georgiev *et al.,* 2017). The middle layer, aqueous layer, is secreted continuously by the accessory lacrimal glands of Wolfring and Krause, and is responsible for providing an optically smooth surface for light refraction and lubrication during blinks and eye movements (Kels *et al.,* 2015). The third layer of the tear film is the mucin layer - It has a thickness of approximately of 2.5 to 5 µm, and its main function is to facilitate the retention and even distribution of the aqueous tear film (Conrady *et al.,* 2016; Cwiklik, 2019).

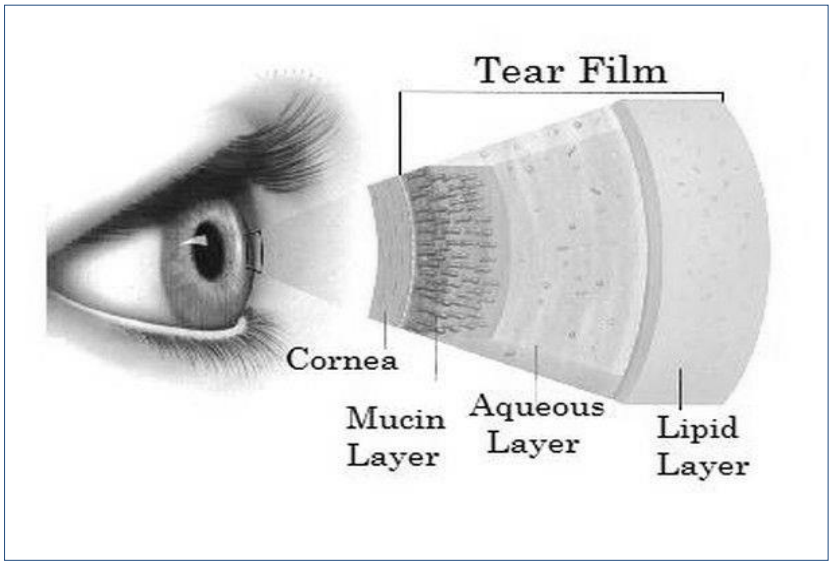


Figure 2-9 - Schematic representation of trilaminar structure of the tear film composed by an outer lipid layer, an intermediate aqueous layer, and an inner mucous layer. Source: https://www.refreshbrand.com/dryeye/dry-item/tear-film, accessed in January 2020.

Several methods have been developed to assess different components/ elements of human tear film such as tear stability, tear volume and tear osmolarity. Many of the developing techniques are non-invasive and are able to give evidence to support diagnosis of some ocular diseases that may affect ocular health, comfort and quality of life of the patient, and monitor the effectiveness of some treatments and interventions (Graig *et al.,* 2017). Clinically, the tear stability is usually measured with BUT and non-invasive break-up time (NIBUT) techniques, interferometry of lipid layer, topographical analysis systems; videokeratoscopy, wavefront aberrometry, confocal microscopy and visual function test (Sweeney *et al.*, 2013; King-Smith *et al.*, 1991). Tear volume measurement methods include Schirmer test (one of the most frequent tests used in the assessment of tear volume), the phenol red thread (PRT) and tear meniscus height. The blink measurement methods include observation of superior eyelid moving downward, video-recording the lid movement and electrophysiological signals to recognise blinks (Sweeney *et al.,* 2013).

2.4.4.1 Effect of digital devices on tear film

Prolonged use of computer screens and other digital devices can lead to and increase in the tear evaporation rate and a decrease in the tear film stability and blink amplitude and frequency. The blink rate is decreased during near work activities including computer and digital device use. Previous studies reported a decrease from 11.6 blinks per minute at rest down to 3.6 blinks per minute during computer use when compared to normal blinking (17–26 blinks/minute) (Coles – Brennan *et al.,* 2019; Abusharha, 2017).

Several studies have documented a relationship between VDT and tear film abnormalities in computer and digital device users. Hirota *et al.* (2013) investigated the relationship between complete and incomplete blinkand tear film stability after 60 min on a personal computer as part of a VDT, in 11 subjects with mean age of 21.3 years, using An RT-7000. The authors found a decrease in the blink rate and short ring breakup time (tear film stability) after 30 min of VDT experiment. Freudenthaler *et al.* (2003) analysed the spontaneous eye blink rate (SEBR) and inter-eyeblink intervals (IEBI) of 51 normal volunteers before and during VDT use, using computer-based video analysis system. The authors found a decrease of the SEBR during VDT work based on the automatic registration of complete eye blinks during 10 min of registration. Himebaugh *et al.* (2009) also observed incomplete blink and reduced tear film break-up during the VDT use. Likewise, a study conducted by Portello *et al.* (2013) found a reduced blink rate and an increased percentage of incomplete blinks in computer users (**Figure 2-10**). The authors also found a significant positive correlation between the total symptom score and the percentage of incomplete blinks during the task ($p = 0.002$).

Nakamura *et al.* (2010) analysed the association between VDT work duration and changes in tear film status (precorneal tear stability, lipid layer and tear secretion), in 1025 Japanese's office workers. They found a relationship between the changes in the tear film stability and the durantion of VDT work and conclude that the lacrimal gland hypofunction in VDT workers could be associated with the increase of its use.

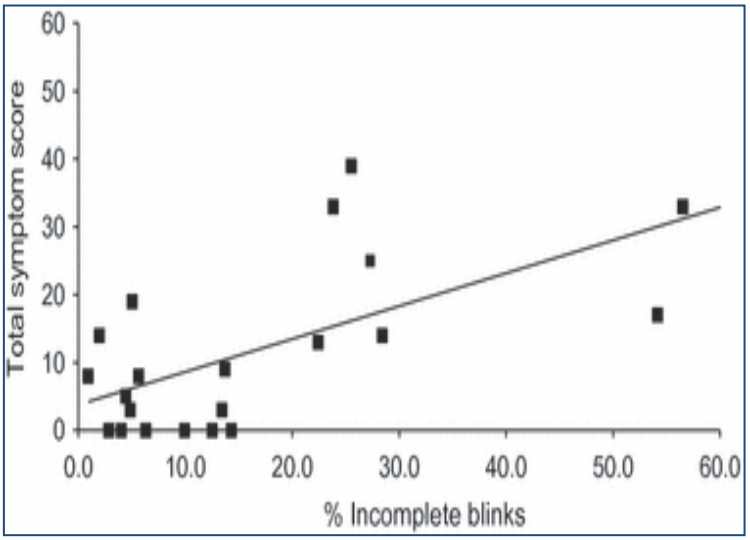


Figure 2-10 - Correlation between the total symptom score plotted and percentage of blinks that were deemed incomplete during the course of a 15min computer task performed at a viewing distance of 50cm in 21 subjects. Data from Portello *et al.* (2013).

Several studies have shown that tear volume and blink amplitude is reduced during computer use. For example, Cardona *et al.* (2011) analysed the blink rate, blink amplitude and tear film integrity in 25 healthy young who use VDT, and found statistically significant differences in blink rate ($F = 595.85$, $p < 0.001$) and blink amplitude ($\chi 2 = 34.00$, $p < 0.001$) during fast-and slow-paced game play. Yazici *et al.* (2015) evaluated changes in symptoms and tear film characteristics in 51 young computer users and found a statistically significant reduction in Schirmer and TBUT values at the end of the working day, comparing to the control group (26 subjects).

More recently, the concentration a mucin secreted by goblet cells of the conjunctiva - 5AC (MUC5AC) - has been investigated in computer users and digital devices. Several studies have demonstrated decreased levels of MUC54C concentration in DED (Wilcox *et al.*, 2017). Uchino *et al.* (2014) investigated the relationships between between tear MUC5AC concentration in VDT users and the severity of DED, the number of VDT working hours, and the frequency of ocular symptoms in 96 young and middle-aged Japanese office workers. The authors found lower MUC5AC concentration in tears in the group that worked longer hours at VDT than in the group that worked shorter hours ($p = 0.049$; estimated difference, −1.65; 95%CI, −3.12 to 0.00). The authors hypothesize that the decrease in the MUC5AC concentration in tears may be one of the reasons why VDT users develop DED.

Other studies also report a positive correlation between Meibomian glands dysfunction (MGD) and DED in VDT users. Wu *et al*, (2014) evaluated the morphological characteristics and function of meibomian glands in 53 Chinese office workers and found a positive correlation between MGD and DED in VDT workers. Therefore, the authors postulate that longer VDT work may cause change in MGD Likewise, Fenga *et al.* (2008) evaluated if MGD could contribute to the development of signs and symptoms of ocular discomfort related to the use of VDT, using the ocular tests such as tear break-up time, fluorescein corneal stain, and basal tear secretion test, and found high prevalence of MGD among the subjects with symptoms of ocular discomfort. The author's concluded that MGD can contribute to the development of ocular discomfort in VDT operators.

In summary, prolonged use of digital devices is related to a multitude of significant ocular surface complaints. Those include the reduction of tear secretion and frequency of blinking, excess evaporation of tear fluid and hypofunction of lacrimal glands. In turn, these can cause temporary stress to the corneal surface, resulting in symptoms such as dry eye. Therefore, the assessment of ocular surface and tear film before and during the use of digital devices is essential for CVS identification. The stability of the tear film and blinking are indispensable for maintain the ocular surface health and to maintain the excellent corneal refractive state (Doughty, 2001; Schlote *et al.,* 2003).

2.5 Management of visual and ocular symptoms related to digital devices

Treatment strategies of visual and ocular symptoms related to digital devices use requires a multifaceted approach due to the variety of complaints, and must take into account the severity of the symptoms and the environments that eyes are subjected to over a 24-hour period (Coles–Brennan *et al.,* 2019; Yan *et al.,* 2008). Therapeutic interventions may be separated into three big major areas, namely:

1) Visual Ergonomics

2) Management of refractive error

3) Management of binocular vision disorders

4) Management of CVS-Related Dry Eye

2.5.1 Visual Ergonomics

Ergonomic changes such as appropriate lighting, adjusting image parameters (resolution, text size and contrast luminance) and visual hygiene are accepted as the most important interventions to have in subjects who suffer from CVS. (Coles–Brennan *et al.*, 2019; Yan *et al.*, 2008; Mowatt *et al.*, 2017). Several visual ergonomics strategies have been suggested to relief the symptoms related to CVS. Those strategies include:

a) Viewing distance (distance between eye and the screen) should be of at least 20 inches (approximately 50 – 60 cm) and the angle between the monitor and computer user should be around 15^{o} lower than horizontal level of view. Reddy et al. (2013) investigated the effect of the level of the monitor on the symptoms of CVS, and found a significant reduction in symptoms in students who viewed the computer screen below eye level than those who viewed the screen at or above the eye level ($p=0.0001$). Likewise, Burgess-Limerick *et al.* (1999) investigated the influence of "eye level" and "low" monitor locations on the head and neck posture and concluded that lowering the monitor to a position 18° below eye level did not cause changes in the posture of the neck relative to the trunk, but increase the flexion of the head relative to the neck. The authors conclude that view the computer screen below the eyes may be beneficial in computer users. In contrast, Jaschinski *et al.* (1998) examined the preferred position of visual displays relative to the eye, at two levels of screen height in computer workers; the authors found that the participants who viewed the computer screen below eye level had more eyestrain than those who viewed the screen at or above the eye level;

b) Variation in posture such as small head rotations to limit neck and shoulder flexion can improve the corporal symptoms related to CVS. Many studies have demonstrated that changes in the temporal pattern during the work tasks could help prevent and relief some symptoms related to musculoskeletal disorder, such as neck aches, shoulder aches, backaches and tension neck syndrome. For example, Laparra *et al.* (2019) and De Vera and Mahon (2007) concluded that frequent microbreaks and regular small head movements can reduce the symptoms related to musculoskeletal disorders during computer use;

c) Ambient light should also be adjusted in order to prevent direct light from the back of the monitor and light sources behind the reader. Several studies have demonstrated that improper light is probably the major environmental factor that contributes to visual discomfort in computer users (Yan *et al.* 2008; Coles-Brennan *et al.* 2019). Therefore, is recommend that the source of light in a computer room should be half as bright as that normally found in a work place (recommended lighting levels are 40–50 Fc for ambient light). A study carried out by Sheedy *et al.* (2005) concluded that the screen lighting should be adjusted to the optimum and the luminance of the room should not exceed three times than the mean luminance on the screen.

2.5.2 Management of refractive error

Uncorrected refractive errors and presbyopia in computer users or other digital devices users may result in complaints such as blurred vision, slow focusing, headache, double vision or difficulty focusing for close work (presbyopia). Therefore, the correction of refractive errors is important to minimize the symptoms associated with use of digital devices and computers by improving the visual performance and comfort during these tasks (Coles-Brennan *et al.,* 2019). The examination and correction of refractive errors should be performed taking into account the patient's working distance. The final prescription should be done taking into account the current visual demands and the design of lenses, especially in presbyopic subjects. Prescription may include spectacle or contact lenses that have positive refractive power. Wearing bifocal lenses may not be satisfactory because it will require fatiguing head postures due to the position and narrow width of the intermediate and near vision zones. Trifocal lenses that contain three focal points: distance, intermediate and near vision (recommended in case of advanced presbyopic patient who require clear distance vision at computer) and progressive addition lenses (PALs) have been suggested as the optimal correction for presbyopia and hypermetropia, and offer excellent vision correction for people who has high accommodative demand (Sheedy and Shaw-McMinn, 2003; Heus *et al.,* 2012).

Several studies have been conducted to test the effect of computer glasses (glasses with special design recommended by American Academy of Optometry (AAO) for patient with CVS) in the relief of symptoms. For instance, Wallin *et al.* (1994) investigated the effects of computer glasses (term used for AOA to describe the eyeglasses designed to eliminate and/or significantly reduce the visual-

ocular problems associated with VDT use) in 79 symptomatic VDT usersand observed that the VDT-related symptoms were reduced through the use of the computer glasses. Kee *et al.* (2018) analysed the effects of wearing conventional single-vision lenses (SVL) versus progressive addition lenses (PALs) on the working distance and refractive status, in sixty-four healthy computer users (young and pre-presbiopic) and observed that the PALs caused less "increased sensitivity to light" compared with SVL.

Specific occupational lenses for computer work have been designed. They have an intermediate vision zone at eye level and specific focal length designed for computer work. It can be more effective and provide better high-quality intermediate and near vision in symptomatic subjects than other eyeglasses such as bifocal lenses and single vision lenses. For example, Hayes *et al.* (2007) analysed the symptoms and quality of life in computer users and concluded that subjects wearing computer spectacles had lower pain response scores. However, those differences were small and there were no statistically significant differences between them and bifocal wearers in terms of neck, upper back, lower back, and shoulder areas.

Jaschinkis *et al.* (2015) investigated the effects of different types of spectacle lenses (single far-vision lenses; single near-vision lenses; and PALs) habitually worn by computer users (**Figure 2-11**). The authors found a significant correlation between ocular strain, musculoskeletal strain and headache and the daily duration of computer work for the wearers of single far-vision lenses (r= 0.66, n=25; p_{cor}=0.0072) than single near-vision lenses (r= 0.16, n=26; not significant) and PALs (r= 0.13, n=63; not significant). Likewise, in a comparative study of two PALs for general purpose, PALs and computer vision PALs with continuous clear vision between infinity and near, Jaschinkis *et al.* (2015) found significantly lower head inclination when looking at the monitor in computer vision PALs than with the general purpose PALs. The authors also observed that 44 per cent of the participants preferred the computer vision PALs.

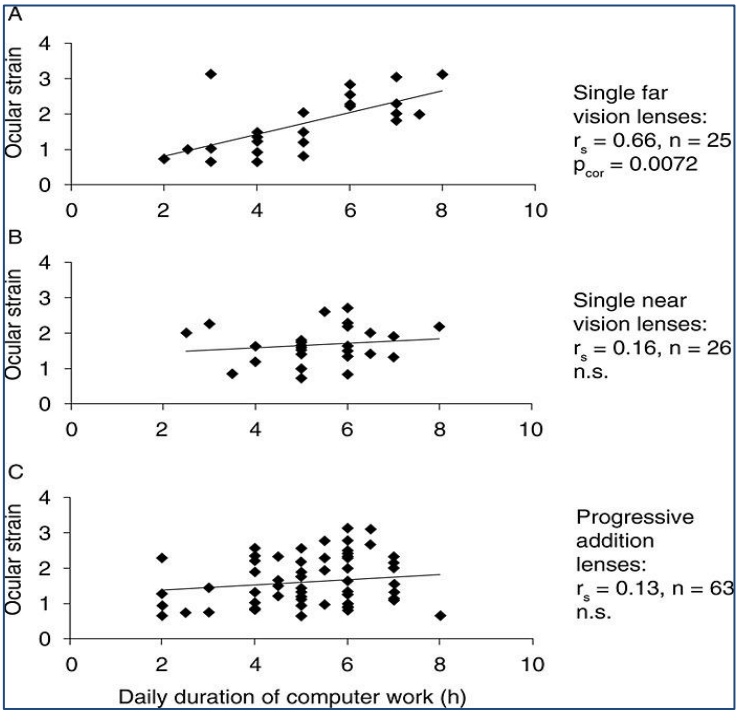


Figure 2-11 - Correlation between ocular strain and the daily duration of computer work for the users of single far-vision lenses, single near-vision lenses and PALs. Data from Jaschinski *et al.* (2015).

Contact lens prescription should also be considered, however, in cases of severe symptoms associated with dry eye, its prescription should be considered with caution. MCLs and SVC are generally prescribed to young adult patients, and a small amount of plus lens should be considered in presence of symptomatic patients. Several aspects should be consideridend during contact lens prescription, especially in computer workers, which are more prone to develop dry eye and consequently CVS. Along with the patients' activity, the characteristics of the ocular surface of the patient and the characteristics of the lens (type, design, material, permeability, water content and replacement) should be carefully analysed. Some of the most popular daily disposables for CVS are: Acuvue Oasys, Proclear, Biofinity Energys® (Coopervision) and Bausch + Lomb ULTRA® with claimed especial design for digital devices. Details of designs and caracteritic of theses lenses will be discussed in chapter r 3.

2.5.3 Management of binocular vision anomalies

Patients with convergence dysfunctions and/or accommodation dysfuntions associated to CVS must be treated with vision therapy or glasses. The prescription of glasses should be indicated in case of blurred vision at all distances.

Visual therapy designed for accommodative and vergence anomalies aims to improve the accuracy and dynamics of the accommodation system (accommodative response) and help the patient to achieve better visual performance during the computer task and digital devices and relief ocular symptoms associated with vergence disorders. Visual therapy should be applied in cases where the treatment with the glasses does not improve the symptomatology, and it only has effect when an improvement of both accommodative and vergence systems is achieved. The prescription of low plus-power spectacles (addition power ranging from +0.41 D to +1.25D over the distance prescription) should be effective in case of accommodative disorders in the pre-pesbyopic patient.

Patients with poor convergence ability should be treated with vision training with Push-up (high sustained, far-near rock and combination), prism jump, prism reading, lens flippers and flippers reading. In case of vertical phoria problems it is recommended the prescriptions of prism. Plus lenses for near (can be in single vision pair of glasses or a multifocal) should be recommended in case of esophoria.

2.5.4 Management of CVS-Related Dry Eye

Treatment followed by patients suffering from CVS-related DED must be multifaceted (Matossian *et al.,* 2019). The treatment should include the use of artificial tears (in case of mild and severity dry eye symptoms), dietary supplement of either omega-3 fatty acids or blueberry extract, changes in ambient humidity, hydration (drinking more water) and frequent breaks - whose benefit is not yet scientifically proven (following the 20-20-20 rule to give your eyes a break: look 20 feet away for 20 seconds, every 20 minutes). All these activities are recommended to moisturise the ocular surface, reduce damage to the corneal epithelium, increase comfort, relax the accommodative system and prevent dryness, irritation, tiredness and difficulty of focusing.

Several medicine options have been used to relieve the symptoms of DED and DED related to CVS. For instance, in experimental investigation with an omega 3 fatty acid (O3FA) oral supplement (2,400 mg/day) conducted by Bhargava *et al.* (2016) in 256 young and middle eyes of VDT users, with ages ranging from 19 to 26 years, they observed significant improvement in symptoms, tear stability, and conjunctival cytology but not tear production in symptomatic VDT users. The authors suggested that the consumption of 2,400 mg/day of O3FA supplement may help to relief the symptoms commonly associated to CVS in symptomatic VDT users. Morita *et al.* (2018) evaluated the effects of heat-killed *Lactobacillus paracasei* KW 3110-containing supplements for eight weeks, on improving ocular disorders and symptoms of eye fatigue, in 62 healthy Japanese volunteers of 35 to 45 years of age, who had experienced eye fatigue, and observed a decrease of critical flicker frequency in the *Lactobacillus paracasei* KW3110 group when compared with the placebo group during the fourth week. The authors suggested that ingestion of *Lactobacillus paracasei* KW3110 had the potential to relief the symptoms commonly associated to VDT such as eye fatigue, especially high levels of eye fatigue.

Others treatment option for relieving the symptoms of CVS-related DED includes: consumption of omega-3 fatty acids (O3FAs); preservative-free eyedrops; and consumption of *Vaccinium uliginosum* extract (DA9301oral pill (1000 mg/day). For example, Bhargava *et al.* (2015) investigated the efficacy of dietary consumption of omega-3 fatty acids (O3FAs) on DED symptoms, in 478 symptomatic patients using computers for more than 3 h per day, for minimum 1 year, and demonstrated a significant improvement in computer vision syndrome symptoms related DED, with decreases tear evaporation rate, increase goblet cell density and improved epithelial cellular morphology. Guillon *et al.* (2004) investigated the effect of povidone 2% preservative-free eyedrops on CL wearers with CVS and found statistically and clinically significant decrease in symptoms of CVS **(Figure 2-12**). However, the symptoms were not fully eliminated by the use of the test eye drop. Park *et al.* (2016) investigated the effect of consumption of *Vaccinium uliginosum* extract (DA9301oral pill (1000 mg/day) during 4 weeks, on tablet computer-induced asthenopia, and observed that oral intake of DA9301 (1000 mg/day for 4 weeks) was effective in the relief of symptoms associated to asthenopia induced by digital devices.

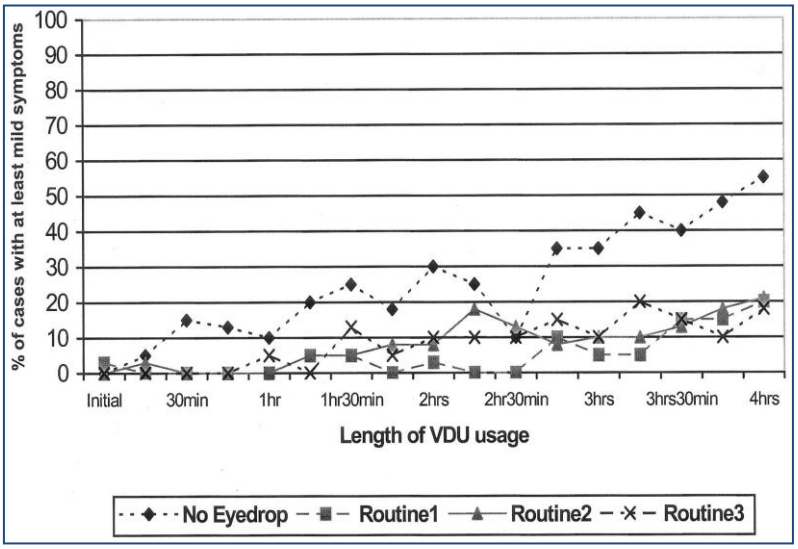


Figure 2-12- Effect of eye drop use and installation routines on the incidence of dryness during the course of a 4h computer task performed in 20 subjects. Data from Guillon *et al.* (2004).

2.6 Contact lenses and use of digital devices

2.6.1 Impact of contact lens on ocular surface and use of digital devices

The presence of CL on the eye alters the distributions and physiology of the tear film **(Figure 2-13**), which increases the risk to presenting symptoms commonly associated with DED such as tired eyes, dryness, burning sensation, grittiness and discomfort, due the unstable of tear film and reduced tear film thickness (Coles-Brennan *et al.,* 2019; Kojima, 2018; Kaido *et al.,* 2019). Reddy *et al.* (2016) investigated the prevalence of DED symptoms among CLs wearers and non-contact lens wearers, and observed that DED symptoms were significantly more prevalent in CL wearers when compared to non-contact lens wearers. Eye dryness (73.5%) was reported as the most frequent symptom in CL wearers while tired eyes (77%) as most frequent symptoms in non-contact lens wearers. There was an increasing trend of their frequency and intensity at the end of the day.

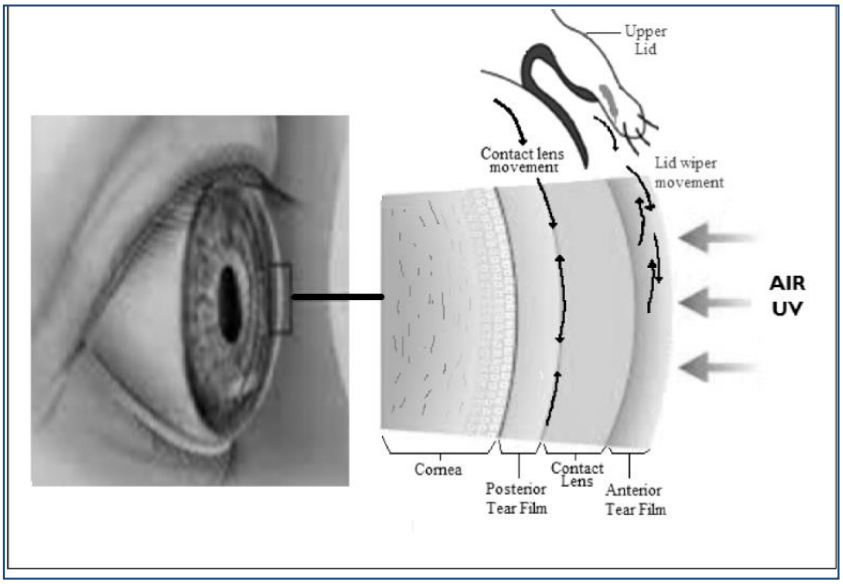


Figure 2-13 - Schematic representation of contact lens interactions with the tear film. Reproduced from Mann and Tighe, (2013).

CL wear while using VDT at work has been reported to increase the risk to develop CVS related DED, due to the instability of the tear film, associated with increased tear evaporation rate and decreased blink frequency and amplitude. (Tauste *et al.,* 2016; Tauste *et al.,* 2017; Tuaste *et al.,* 2014; Kojima, 2017). Few studies have investigated the impact of CLs on the ocular surface that attempted to link these interactions with the use of VDT and the risk of CVS development. For instance, González-Méijome *et al.* (2007) evaluated the ocular symptoms among CLs wearers and non CLs wearers in 334 subjects (university population) who use VDT for different periods of time. The group of CL wearers had a higher prevalence of symptoms of red eye, itching and scratchiness, being statistically significant for red eye ($p<0.009$, $\chi 2$), and scratchiness ($p<0.001$, $\chi 2$). The authors concluded that soft CL wearers who use VDTs for longer periods of time are more likely to develop symptoms like eye burning and scratchiness than non-CL wearers. Tauste *et al.* (2016) analysed the effect of contact lens in 426 computer workers, using Computer Vision Syndrome Questionnaire (CVS-Q), and found a higher prevalence of symptoms related to CVS in CL wearers (65%) than non-CL wearers (50%).

Kojima *et al.* (2018) evaluated the impact of CL wear and VDT work on the ocular surface and tear functions through clinical tests and DEQ, and found lower tear meniscus volume, and lower visual and environmental symptom scores between the two groups. The authors concluded that these symptoms increased with duration of computer work, and scores were significantly higher among

contact lens wearers. Similarly, Tauste *et al.* (2017) analysed the effect of CLs of different materials on tear film and ocular surface in 236 office workers, and found higher risk of ocular surface abnormalities in conventional hydrogel wearers, followed by silicone hydrogel wearers when compared to non-wearers. The authors concluded that the CLs wear during VDT at work increased the risk of anterior eye surface changes such as bulbar, limbal and lid redness, and lid roughness, especially in soft contact lens wearers.

2.6.2 Contact lenses and dehydration process

One of the most important factors to consider in symptomatic CL wearers is lens dehydration. The dehydration of soft contact - which is a significant cause of CL discontinuation - is related with physical properties of the lens. It is a natural process which consists of water content loss as soon as the lens is placed on the eye Gonzalez-Meijome *et al.*, 2007). CL dehydration plays an important role on clinical performance of CLs and it is influenced by several factors such as property of the contact lens material, thickness, palpebral aperture, blink rate, tear film quality and environmental conditions (Jones *et al.,* 2013; Pritchard and Fonn, 1995; Tranoudis and Efron, 2004).

Little and Bruce (1995) demonstrated that lens dehydration can be influenced by environmental conditions (ambient air flow). The authors concluded that the changes in the CL fitting during wear could be related with lens dehydration. Likewise, Tranoudis and Efron (2004) analyzed the material properties of soft contact lenses made from different materials, and found a statistically significant reduction in water content after increasing the temperature from 20 to 35 ^{o}C. The authors further concluded that soft contact lens dehydration leads to a decrease in oxygen transmissibility and total diameter, following a 6 hours open eye wearing period.

Currently, numerous techniques are available to measure soft CL dehydration. These include manual or automatic commercial refractometers, gravimetric techniques, thermal analysis technique, thermogravimetric, spectroscopy, nuclear magnetic resonance imaging, and refractometry techniques (Varikooty *et al.*, 2010). In clinical practice, the gravimetric method - an *ex vivo* method of estimating lens water content - is more precise than *in vitro* studies to determinate the water content of hydrogel CL (Gonzalez-Meijome *et al.,* 2006). The automated lens refractometer obtained the water content from the refractive index values.

Several studies have analyzed the characteristics of dehydration process of different types of CLs. It was reported that silicone hydrogel lens materials are more resistant to water loss than conventional hydrogel materials (**Figure 2-14**) (Sindt and longmuir, 2007; Insua Pereira and Lira, 2017; Jones *et al.*, 2002).

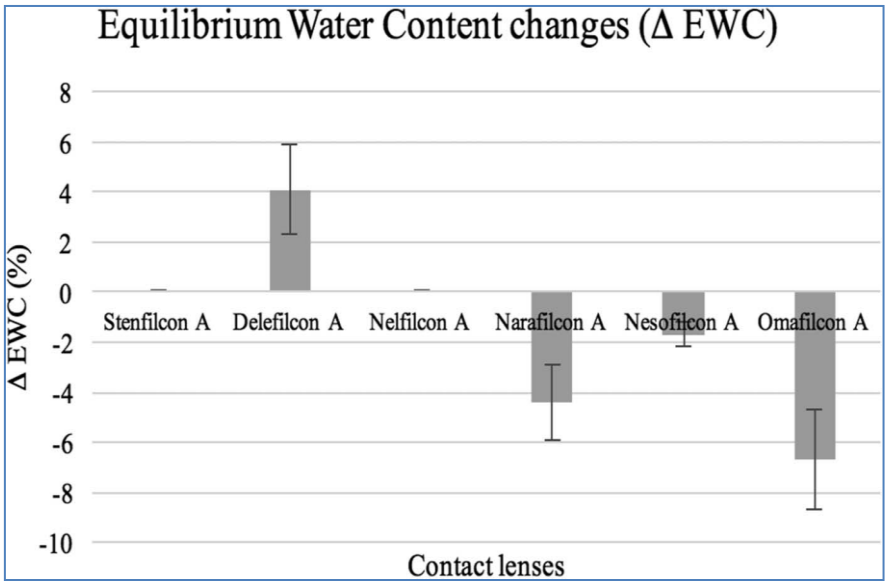


Figure 2-14 - Changes in equilibrium of water content in daily disposable contact lenses. Data from Pereira and Lira, (2017).

Several studied have tried to associate CL dehydration and CL-relared discomfort (including dryness symptoms) in CL wearers (Pereira and Lira, 2017; Dillehay, 2007; González-Méijome et *al.,* 2007). Alhtough some studies concluded that dehydration is one of the major factors contributing to decreased comfort during hydrogel CL wear and that high water content CLs tend to be less comfortable at the end of the day. (Efron et al 1986; Pereira and Lira, 2017), other studies have failed to find an association between lens dehydration and discomfort or dryness (Fonn et al 1999).

In summary, although there are controversies in the relationship between dehydration and eye comfort, contact lens dehydration may have an important role on visual quality and overall comfort of the wearers, particularly in contact lenses wearer who complain of dryness at the end of day.

Chapter 3

Hypothesis and Goals of the Study

Avelino Nelson F. Mazuze

3. AIMS AND HYPOTHESIS OF THE STUDY

This chapter outlines the problem formulation according to previous studies and the aims and hypothesis of the present research.

3.1 Problem formulation

Computer-related vision problems are an emerging global public health challenge worldwide, affecting 90% of individuals who spend much of their daytime handling digital display devices. Several therapeutic alternatives have been proposed to relief the symptoms associated to the use of digital displays, being CLs one of the most effective and safe treatment options currently used. However, there are many inconsistencies between studies regarding the effect of CLs on visual performance, accommodation function and spherical aberrations in different ages due to variability in CLs design and materials. Some works reported that distance single vision CL do not produce significant changes in accommodative functions (Montés-Mico *et al.,* 2011), while other studies reported that multifocal contact lenses (MFCL) can be effective to support the change in accommodative and binocular vision functions in computer users (Pettersson *et al.,* 2011; Kang and Wildsoet, 2015; Gong *et al.,* 2017; Montés-Mico *et al.,* 2011; Ruiz-Alcocer *et al.,* 2012; Ruiz-Pomeda *et al.,* 2019). However, not all multifocal CL can reduce de accommodative demand in normal young adult subjects (Madrid-Costa, *et al.,* 2011; Gong *et al.,* 2017). In addition, some works reported that spherical aberration reduced significantly with accommodation and that conventional hydrogel materials could induce more changes in the ocular surface than silicone hydrogel CL (Tauste *et al.,* 2016; Ruiz- Alcocer *et al.,* 2018). Furthermore, there are already CLs with special designs that promise to improve symptoms associated with the use of digital devices, but these designs can worsen some other tasks done in low light conditions. Based on these fundamentals, the purpose of this study was to evaluate the effect of two different designs of soft CLs for digital devices on visual performance, accommodative response, optical quality, tear film stability, quality of vision, comfort and dehydration (in vitro and ex vivo) after 7 days of lens wear.

3.2 Hypothesis

We hypothesize that:

- Contact lenses (CLs) with different optical design induce different aberrations, affecting level of visual performance and accommodative response.

- CLs with different optical design and power profile induce different levels of light disturbance phenomena in young adult subjects when compared to monofocal lenses with same material.

- CLs with different polymeric composition undergo different dehydration process and are associated with different ocular symptoms.

3.3 Goals

3.3.1 Main Goals

- To assess and compare the visual performance of two types of soft contact lenses (CLs) for digital devices in young adult subjects;

- To investigate the impact of different designs of soft contact lenses (CLs) intended to be prescribed while using digital devices on accommodative response, tear film and dehydration in young adult subjects.

3.3.2 Specific Goals

- To measure and compare the dehydration (*in vitro and ex vivo*) of two types of soft CLs for digital devices in young adult subjects after 7 days of wear;

- To assess and compare optical quality, accommodative response and light disturbance (LD) with two types soft CLs for digital devices in young adult subjects during 7 days of wear;

- To evaluate and compare the quality of vision of two types of CLs for digital devices in young adult subjects after 7 days of wear;

- To assess and compare the ocular discomfort associated with dry eye with the two types of soft CLs for digital devices in young adult subjects after 7 days of wear;

Chapter 4

Methodology: overview

Avelino Nelson F. Mazuze

4. MATERIAL AND METHODS

This chapter outlines in detail the experimental design of the study, the sample size calculation, masking procedure and randomization. It also outlines inclusion and exclusion criteria, contact lenses used, the methods and equipment used to obtain the necessary measures for the work, and the statistical analysis that were adopted.

4.1 Study design

This study was a comparative, prospective, randomized controlled clinical trial, single -masked, crossover study in young adult subjects who binocularly wore three different contact lenses: Biofinity Energys® soft contact lens, Bausch & Lomb ULTRA® soft contact lens and Biofinity® Monofocal, as illustrated in **Figure 4-1**. Each one of the lenses were used for 1 week with wash-out period of two days. The clinical trial was conducted during the span of 6 months, between September 2020 and Febraury 2021 at the Clinical and Experimental Optometry Research Laborattory (CEORLab) at the University of Minho, School of Sciences, Braga, Portugal. The Ethics Subcommittee for Health and Life Sciences (SECVS) of the University of Minho approved the clinical trial. A written informed consent was obtained from all the participants before enrolment in the study.

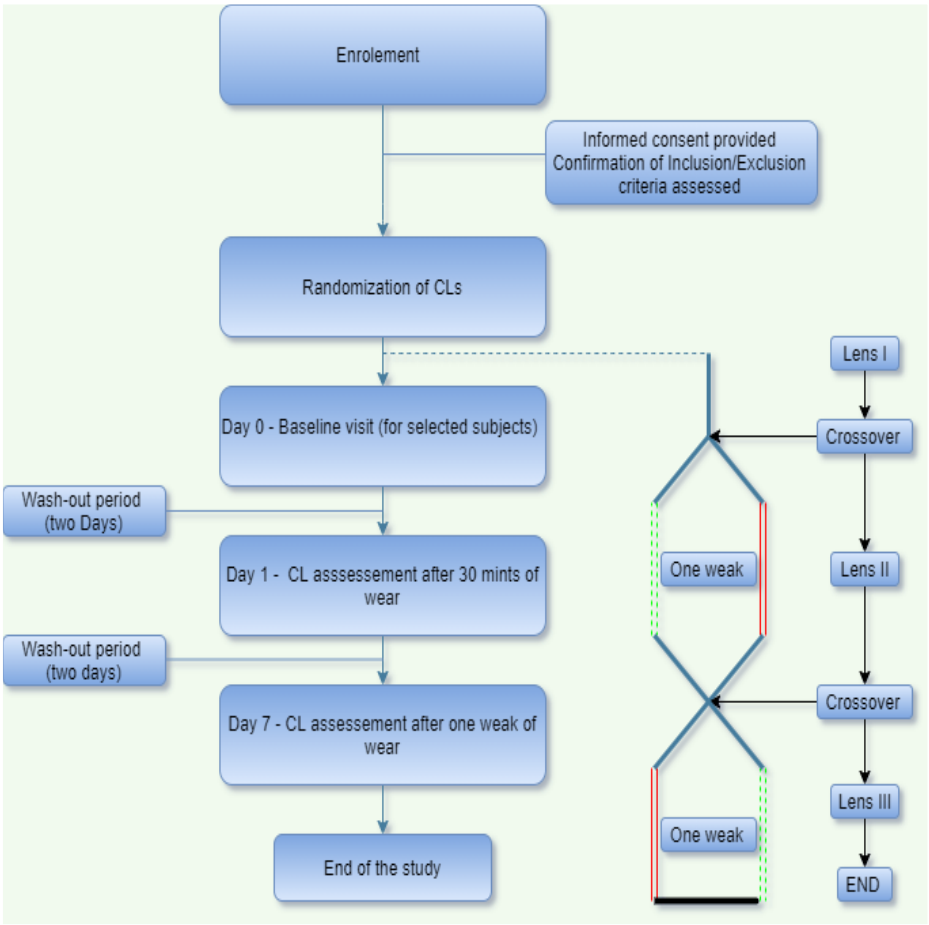


Figure 4-1- Flowchart of study design and visits. Details of visits and procedure are outlined below.

4.2 Sample Size

The Sample size was calculated using online software (http://hedwig.mgh.harvard.edu/sample_size/js/js_crossover_quant.html). Based on data from clinical trial of Koh *et al.* (2019), where a mean difference of 0.5D in the accommodative response with CLs was considered as clinically significant, and assuming a standard deviation of 0.5D in the accommodative response, with statistical power of 80% of the study and level of significance of 0.05%, a minimum sample size of 18 patients were required.

4.3 Recruitment of the participants

The participants were recruited by email to all academic community (students and employees) of the University of Minho. In the email the objective of the research, procedures and the possible

consequences of the study were full explained. All the research procedures were conformed to the principles of the Declaration of Helsinki. The participants could dropout from the study any time without consequences. All the subjects completed the written informed consent (**APPENDIX 1**: Consent Form signed by every participant in this thesis project). To assess the eligibility to participate in the study, subjects underwent a full optometric examination, in which the refractive status, visual acuity and ocular health were evaluated.

4.4 Eligibility Criteria

Thirteen (13) young adult subjects were recruited from University of Minho for this research. Justification of eligibility criteria is summarised in **Table 4-1** and included healthy young subjects with ages between 18 and 30 years, with a best-corrected distance visual acuity (BCVA) of at least 0.00 LogMAR units or better in each eye with the study contact lenses, and with a difference in VA between both eyes less than 0.1 LogMAR units, a spherical refractive error between +3.00 and -3.00D, with astigmatism below 1.00D and less than 1.00D of anysometropia. Subjects must have pupil diameter under mesopic conditions ≥ 6mm on the study. Subjects with severe dry eye, previous refractive surgery, eye infections or irritations, eye diseases or disorders (including history of corneal opacities) that would contraindicate contact lens wear or patients who take ocular or systemic medicines that can affect the visual performance and accommodation response were excluded.

Table 4-1 - Justification of of the eligibility criteria included in this study

Criteria	
Gender	This criteria exist to ensure that changes in visual acuity (VA) and refractive error (RE) related to the pregnancy could not confound our results.
Age	Presbyopic subjects were excluded due to eye changes and inaccurate accommodation. These criteria exist to ensure that changes in ocular structures due to aging could not confound our results.
Refractive Error	These criteria exist to minimize the risk of uncorrected residual astigmatism, which may affect the validity of the results.
Ocular Heath	Some eye diseases may cause a change in visual performance and accommodation responses or could be contraindicated for wear contact lenses.
Visual Acuity	This criterion exists to ensure that changes in visual acuity (VA) due to under correction refractive error (RE) could not affect our results.

4.5 Randomization and masking procedure

The randomization of the CLs wear was carried out using a computer-generated random (http://www.randomization.com/) (**APPENDIX 3**). One investigator (Unmasked clinician) conducted the masking process of the CLs and was responsible to perform the CLs fitting and the evaluation of all examinations all the visits: visual acuity, accommodative response, subjective symptoms and aberrations. All the CLs were delivered in the blister in such a way that the subject did not know which lens was being used.

4.6 Study Lenses

Three different designs of CLs were bilaterally fitted in random order in thirteen (13) young adult subjects. Each pair of CL was used for 1 week, with a wash-out period of two days between lenses. Biofinity® soft contact lens (Coopervision) was used as control lens to obtain Baseline values with contact lens wear and two different designs of contact lenses for digital devices: Biofinity Energys®, (Coopervision) and Bausch & Lomb ULTRA® soft contact lens were used to meet the objectives of the study. Details of study lenses are described below and **Table 4-2** .

1. **Biofinity Energys® soft contact lens** (comfilcon A, 48% water content) is a monthly disposable soft contact lenses, which presents an optical zone, called "digital optical zone" (**Figure 4-2**), with multiple aspherical curves in the anterior surface of the optic zone. These multiple aspherical curves distribute the power evenly by simulating a more positive power in the center of the lens that helps to relieve the accommodative effort when subjects change their focus from the screen to a vision in the distance and near. Launched in 2016, this lens is surface treated with an Aquaform technology, which attracts and retains water throughout the lens thus helping the wearer to feel less ocular dryness. This lens has the same parameters as spherical Biofinity® (www.CooperVision.es/BiofinityEnergys): base curve 8.60 mm, central thickness 0.08 mm (for -3.00), diameter of 14 mm and spherical powers of +8 to -12 and Dk/t (160 units for -3.00).

2.

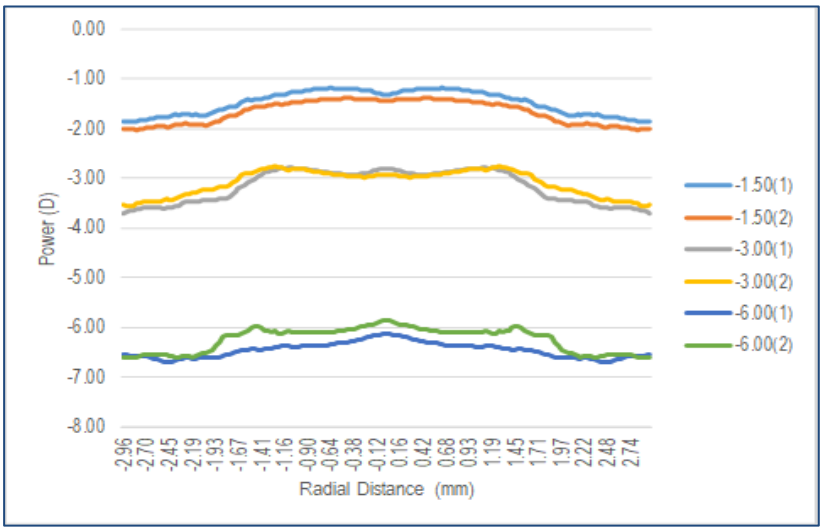


Figure 4-2 - Profile power of contact lenses Biofinity Energy®. (1) and (2) are different samples of the same batch of lenses.

Bausch & Lomb ULTRA® is a monthly disposable silicone hydrogel CL (Samfilcon A) with high oxygen permeability 163 Dk/t. This lens is manufactured with MoistureSeal™ technology (MoistureSeal ® technology) which helps the lenses to maintain 95% of their moisture for the entire day (up to 16h of lens wear), reducing ocular syntoms such as dryness and itching. This lens has a water content of 46% and the design is based on geometry of the aspherical front surface to reduce inherent and induced spherical aberration (http://www.bausch.com).

3. **The Biofinity® (Comfilcon A)** is a monthly disposable silicone hydrogel CL manufactured with Aquaform® Technology. It allows attracting and binding water throughout the lens material to retain moisture even during times of reduced blinking, offering enhanced comfort and vision quality. This lens was designed with an aspheric optical zone to improve vision by minimizing the spherical aberrations of the lens.

Table 4-2 - Lens parameters used in this study

Brand	**Biofinity Energys®**	**Biofinity®**	**Ultra**
Manufacturer	Coopervision	Coopervision	Baush & Lomb
USAN	Comfilcon A	Comfilcon A	Samfilcon A
H_20 content	48.00%	48.00%	46.00%
Material	SiHy	SiHy	SiHy

Lens Technology	Aquaform technology	Aquaform technology	MoistureSeal
Replacement schedule	Monthly	Monthly	Monthly
Oxygen transmissilibilty	160 Dk/t (at -3.00D)	160 Dk/t (at -3.00D)	163 Dk/t (at-3.00D)
Center thickness	0.08 @ -3.00D	0.08 @ -3.00D	0.07 @ -3.00D
Extended wear	Yes	Yes	Yes
Revenue carton size	3 or 6 pack blister	3 or 6 pack blisters	3 or 6 pack blisters
Lens Design	Aspheric Digital Zone® Optics lens design	Aspheric	Aspheric optics
Base curve	8.6 mm	8.6 mm	8.50 mm
Modulus elasticity	0.75 Mpa	0.75 Mpa	0.70 Mpa
Diameter	14.0 mm	14.0 mm	14.20 mm
Sphere power	+8.00D to -12.00D in 0.25Dsteps (0.50D steps after +/-6.00)	+8.00D to -12.00D in 0.25D steps (0.50D steps after +/-6.00D)	+6.00D to -12.00D in 0.25D steps (0.50D steps above -6.00D)
Wearing schedule	Daily or 6 nights / 7 days Extended	Daily or 6 nigths / 7 days Extended	Daily or 6 nights / 7 days Extended

USAN, United State Adopted Names; Si-Hy, Silicone Hydrogel

4.7 Contact Lenses Fitting Procedure

A total of 7 visits were required to complete the study: Baseline visit (Day-0) and 2 visits per CL used (DLV – lens dispensing visit: thirty minutes after lens insertion and follow-up visit: Day 7- one week of lens wear). The summary of visits and procedures are shown in **Figure 4-3**.

Firstly, all the participants recruited had to attend to a full enrollment examination (Baseline visit without contact lens wear), which included anamnesis (medical ocular history) and comprehensive optometric eye examinations, such high and low contrast distance and near LogMAR visual acuity, binocular and accommodative function assessment, objective and subjective refraction, slit-lamp examination and fundus examination. Subsequently, the subjects selected were randomly fitted with a pair of either Biofinity®, Biofinity Energys® or Bausch & Lomb ULTRA® soft contact lens for one week each, with a washout period of two days between lenses wear.

The fitting process of each contact lens was carried out according to the manufacturer's instructions as available in their fitting guides. One visit was required to carry out the fitting process and prescription of each lens. At each visit, lens fit assessment was performed 20 mins after CL insertion, using slit-lamp biomicroscopy. This assessment determined adequate CL position, movement and

centration (horizontal and vertical). Simultaneously, the high (100%) and low (10%) contrast visual acuity with CL were also evaluated with LogMAR chart (Precision Vision, USA). If the fitting was clinically acceptable, the subjects were programmed to start the study. Subjects were dispensed with the CL and care regimen at the end of the Baseline examination. After the pre-fitting assessment, subjects began a 1-week of wearing each contact lens according to the randomization of the contact lenses, and asked to return one week later for a follow-up visit (Day 7). The same protocol was followed for all the contact lens, and was undertaken under the same testing conditions. The study was completed after 3 weeks of wearing the contact lenses with washout of two days between each lens (one week for each lens).

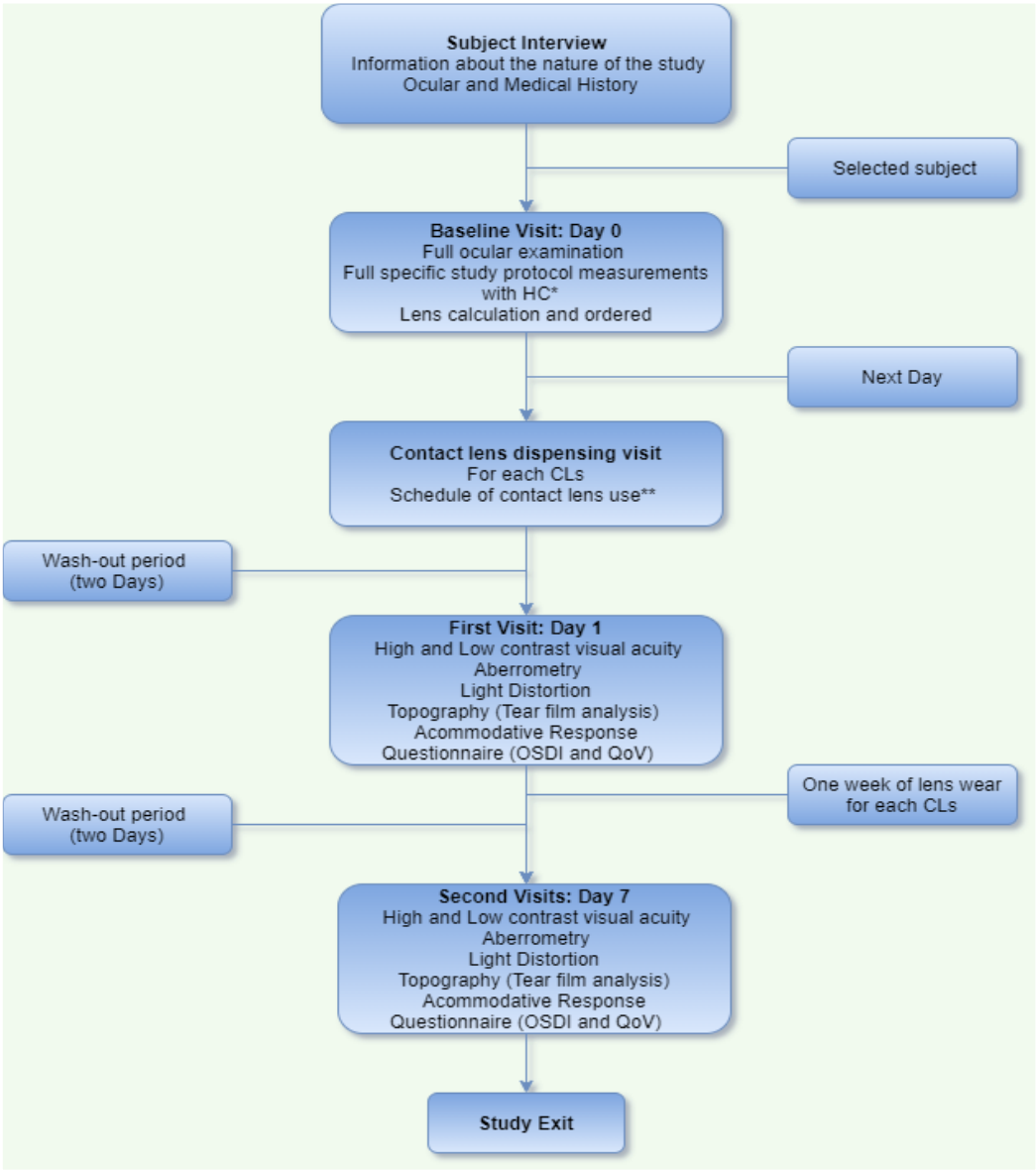


Figure 4-3 - Flowchart of study visits and procedure.** Randomization was performed before lens dispensing visit. Contact Lens assessment was performed at Lens dispensing visit LDV (thirty minutes

after lens insertion) and follow-up visit: Day 7 (one week after lens wear *HC: Habitual correction; CLs: contact lenses.

4.8 Washout period and Lens Care Systems and Solution

The participants were scheduled to have two days without contact lens wear (washout period) between different CLs. During this time, subjects were advised not to wear any kind of CL before returning for the next fitting when the second pair of lenses. We think that the design with two days of washout period was adequate to avoid physiological and optical effects resulting from the use of contact lenses and would not compromising our results (**Figure 4-3**). This wash-out period of 2 days was already mentioned in the literature: A research conducted by Sha *et al.* (2018), which investigated visual performance of myopia control soft contact lenses in non-presbyopic subjects they recommended a washout period of 48 hours in between 7 days of lens wear; Similarly, Bakaraju *et al.* (2017), recommend a minimum of 2-night washout period after 1 week of contact lens wear. Likewise, Fernandes *et al.* (2013), assessing the visual performance with the Biofinity multifocal (MF) and Biofinity single-vision contact lens (SVC), during the 15 days of wearing each lens, also recommended a washout period of 48 hours between each lens type. In other perspective, Pinero *et al.* (2015), recommended a wash period of 1 week between fittings *"to avoid the interference of the potential effect on the cornea and conjunctiva of each contact lens fitting on the next fitting*", however subjects wore hybrid CL and two silicone hydrogel CL.

Additionally, lens care systems, AOSEPT®PLUS with HydraGlyde® Moisture Matrix and Avizor Alvera® Solution, were given to all the participants. Overall, AoSept Plus with HydraGlyde Moisture Matrix ensures a thorough clean and disinfection of any harmful bacteria for any types of contact lens Table 4-3. shows the details of the composition of the lens care systems and solution that was given for all the participants. The subjects were instructed to use the solution following the manufacturer's instructions. All the patients received appropriate instructions regarding the minimum hours of lens wear per day (6 hours) learning and disinfecting procedures and other important reminders (no overnight wear). All subjects were advised to use all three lenses with the same frequency and hours per day – in order to not skew study result. The principal investigator was also responsible to instruct participants about the handling of CLs before contact lens dispensing.

Table 4-3 - Chemical composition of contact lens solution used in this Study

Opti Free® PureMoist ® (Alcon®, Texas, USA)					
Disinfecting agent	Buffer	Chelating agent	Surfactant	Wetting agent	Others
Polyquaternium - 10.001% MAPD (ALDOX)0.0006%	Boricacid; sorbitol	Citrate EDTA 0.05%	Poloxamine (Tetronic 1304)	HydraGlyde (EOBC 41; polyoxyethylene poloxybutylen)	Aminomethyl propanol (AMP-95)

ALDOX, myristamidopropyl dimethylamine; EDTA, ethylenediamine tetra acetic acid; MPDS, multipurpose disinfecting solution; TETRONIC 1304, poloxamine.

4.9 Visits and Assessment

Eligible participants who were qualified for the study at the Baseline (Day-0) examination and which were dispensed lenses had to attend 2 visits for each lens: Visit 1: Lens dispensing visit –LDV- (thirty minutes after lens insertion) and follow-up - visit 2: Day 7 (after at least 60 minutes of lens wear). At the beginning of each follow up visit (Day 7), the examiner asked the participants the number of hours of CL wear per day and the compliance information regarding the frequency and duration were registered in spread sheet. Clinical measurements included visual performance, accommodative response, wavefront aberrometry, light disturbance analysis, tear film analysis and two subjective questionnaires. All the experimental procedures performed were non-invasive and the measurements were carried out by an experienced examiner following the standard protocol for each test.

4.10Clinical Assessments

4.10.1 Visual Performance

Monocular and binocular high and low contrast visual acuity (HCDVA and LCDVA, respectively) were assessed with EDTRS vision charts (Precision Vision. IL) in Logmar scale. This chart has shown good reliability in clinical testing and is peformed at 4 m. The EDTRS chart has an equal number of the letters per line with equal spacing between letters and rows, which the size of the letters increases with a logarithmic progression (Ahmed *et al.* 2018; Dougherty *et al.* 2005). In the EDTRS chart the line of 20/20 (or 1.0 in decimal scale) is equivalent to 0.00 (zero) in LogMAR scale. The HCDVA and LCDVA, was assessed with the best distance visual correction and with CL in each follow up visits.

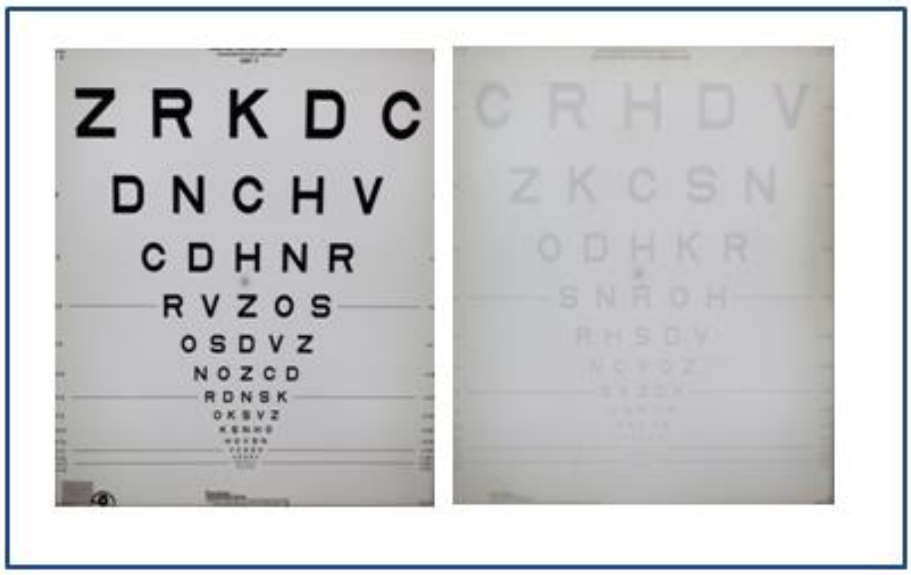


Figure 4-4 - EDTRS chart for HCVA measure (right) and LCVA (left)

4.10.2 Tear Film Analysis

Measurements of tear film stability were performed noninvasively using E300 corneal topography system (E300, Medmont Pty. Ltd., Victoria, Australia). The E300 Medmont corneal topography has software which automatically captures a sequence of images based on specular reflection of a Placido disk on the anterior surface of the cornea or contact lens to analyses the changes

in tear film surface quality and dynamics. The images of the Placido rings provide the Tear Film Surface Quality (TFSQ) (Alonso-Caneiro et al. 2009; Alonso-Caneiro et al. 2009; Kopf et al. 2008; Downie, 2014).

For the measurements, the subjects were instructed to fixate on the green light in the centre of the Placido rings, gently blink twice and then keep their eyes open (not wide, but naturally open), while the video recording and measurements of the tear film image were captured by the examiner. Three repeated measurements were taken on each eye with and without CLs. For the analysis of tear film, values of the following metrics were used:

The Tear Film Surface Quality (TFSQ) Index: represents the index of surface regularity that is only provided by video keratoscopy. The TFSQ value considered normal is less than 0.1. Whenever this value is greater than 0.1 it will be indicative of dry eye (or at least there was a clear disturbanceof the placid discs).

Tear Film Surface Quality Area (TFSQ-Area): represents the area (in percentage) within the 7mm evaluated where the tear film disrupted (area in which tear break-up occurred). The larger the area, the greater the tear film instability.

Auto Tear Break-Up Time (Auto-BUT): which represents time (in seconds) at which the TFSQ-Area (%) is calculated to be at least 5.0% in two consecutive photokeratoscopic images (Alonso-Caneiro et al. 2009; Alonso-Caneiro et al. 2009; Kopf et al. 2008;Downie, 2014).

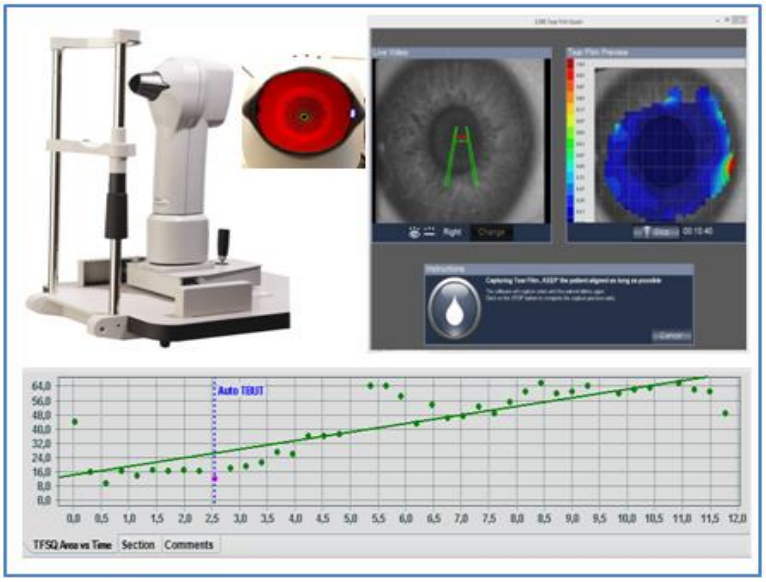


Figure 4-5 - Representation of the video captures process and analysis of the tear film with the topographic and Graph of the variation of the TFS area with time and the NIBUT value presented by the surveyor.

4.10.3 Wavefront Aberrometry

Measurements of ocular aberrations were performed using Hartmann-Shack Aberrometry (Imagine Eyes, IRX-3, Paris). For the measurements, the subjects were instructed to fixate on the "E" letter inside the aberrometer (red light spot) and maintaining the eye wide open. All the procedure was done under mesopic conditions to get maximum pupil size without dilatation. The wavefront was quantified using the Zernike system (Figure 3.6) and the aberrations considered were Total of High Order Aberrations (HOA), HOA Root Mean Square (HOA RMS: from from Z3-3 to Z6-6), Spherical-like HOA RMS (including Z_4^0 and Z_6^0) and Coma-like HOA RMS (including Z_3^{-1}, Z_3^1, Z_5^{-1} and Z_5^1). Three consecutive measures for each lens (in both eyes) were made and the average of the measurements per eye was taken. Measurements were taken for a 5 mm pupil size.

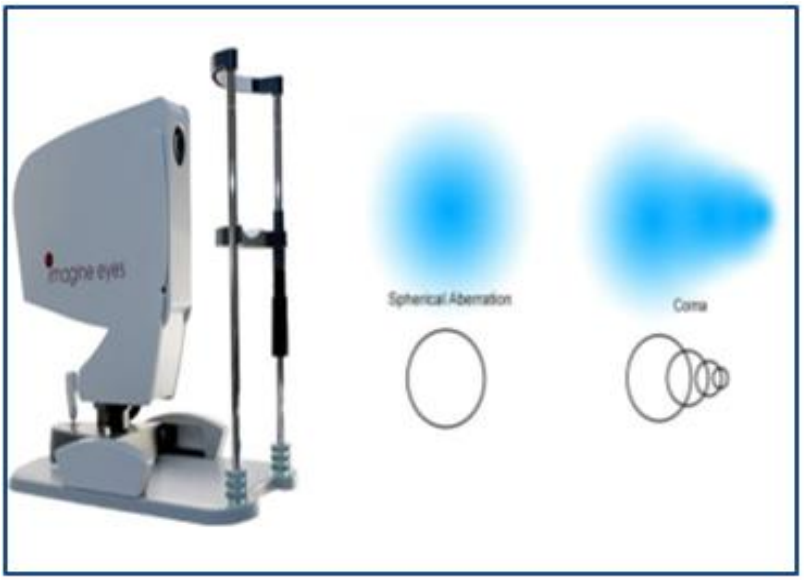


Figure 4-6 - Hartmann-Shack Aberrometry (Imagine Eyes, IRX-3, Paris) and zernike polynomials (spherical and coma aberration). Modified from google.com/images

4.10.4 Accommodative response

A Grand Seiko WAM-5500 open field auto-refractometer (Seiko Co., Ltd., Hiroshima, Japan) with a EDTRS charts (distance and near) to change the vergence was used to assess objectively the refractive state and accommodation. For the measurements, the subjects were instructed to focus a line above the best visual acuity of ETDRS chart at each distance and keep the letters as clear as possible while the refraction were taken under binocular conditions at four different target distance: 400 cm, 100 cm, 50cm and 33cm, giving accommodative demands at 0.25 D, 1.0 D, 2.00 D and 3.00 D, respectively. The size of the letter used was adjusted according the distance at each distance and the luminance was constant in all distance (approximately 85 cd/m2) a calibration of the lighting conditions of the optotypes and room were made to ensure that the luminance of the optotypes was approximately equal across all distances. Three consecutive measurements of refractive state were made for each eye with CLs (right and left) in at each one of the appointments (LDV and Day 7). The conventional spherocylindrical refraction (S: sphere, C: cylinder, and α cylinder axis) collated was transformed to vector components, applying the Fourier analyses by the following equation suggested by Thibos and Douglas (2001):

$$M = S + C/2 \quad \text{(Equation 1)}$$

$$J0 = (-C/2)\cos(2\alpha) \quad \text{(Equation 2)}$$

$$J45 = (-C/2)\sin(2\alpha) \quad \text{(Equation 3)}$$

where M represents the spherical-cylindrical component (Equation 1) and is called the spherical equivalent. J0 and J45 represent the horizontal and oblique astigmatic component, respectively. The J0 describes the differences in the dioptric power between the horizontal and vertical meridian, being positive for astigmatism to the rule and negative for astigmatism against the rule (Equation 2). J45 describes oblique astigmatism, being positive for astigmatisms whose negative axis is 45° and negative for astigmatisms whose negative axis is 135° (Equation 3).

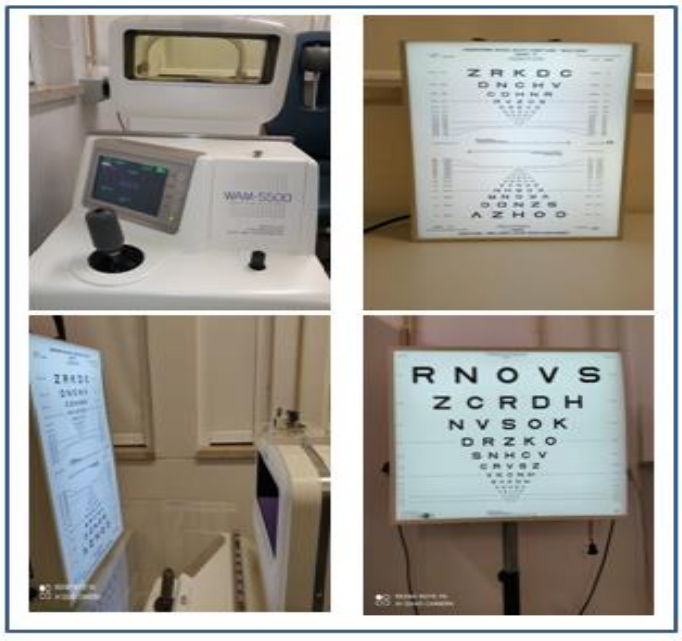


Figure 4-7 - Grand Seiko WAM-5500 open field auto-refractometer (Seiko Co., Ltd., Hiroshima, Japan) with a EDTRS charts (distance and near) used for measurement of accommodative response.

4.10.5 Light Disturbance Analyser

Measurements of light disturbance were performed using Light Disturbance Analyser (LDA), developed by the Clinical and Experimental Optometry Research Laboratory (CEORLab, University of Minho, Gualtar, Braga, Portugal). It consists of an electronic board that has a central LED (**Figure 4-8**) surrounded by others 240 smaller LEDs which are distributed over 24 semimeridians. This electronic

board is connected to a computer with dedicated software (Linhares *et al.* 2013; Brito *et al.* 2015). The details of the LEDs and display characteristics have been described in previous study by Ferreira-Neves *et al.* (2015).

For the measurement, the subjects were seated 2 m from the device. The random continuous in-out routine with an angular separation of 30° (12 semi-meridians analysed) was selected. In this routine, the peripheral LEDs turn-on and off sequentially in the same semi-meridian (randomly choosen) from the center to the periphery of the eletrocnic board. Patients are instructed to fix in central LED (source of glare) that remains on during the entire measurement and press the mouse control button anytime they see the small peripheral LED stimulus. When the peripheral LED tuns on in the center, it could be covered by the source of glare (Central LED) and the patient could not be able to see this peripheral stimulus. The peripheral LEDs of the same meridian will sequentially light up whenever the patient does not press the mouse button (i.e. whenever the patient is not able to see the peripheral LED stimulus). When the peripheral LED is no longer covered by the disturbance caused by the central LED, the patient will be able to see it and will press the mouse button. Then, the system automatically stops the evaluation in this meridian and evaluates the next semi-merdian in a random order. The system repeats 3 measurements for each semi-meridian. The examination was performed monocularly and binocularly in darkened room. The measurements were taken at Baseline (with best spectacle visual correction) and with each one of the CLs at all visits (LDV and Day 7), and the examination routine used was in-out 30º. For the analysis of light distortion, values of the following metrics were used:

The Light disturbance index (LDI) is defined as the percentage of the area (ratio) that is not visible by the subject (disturbance area) considering the total area tested;

Best Fit Circle of the Irregularity (BFCIrreg), expressed in mm, is defined as the sum of the positive and negative deviations from the BFC of the disturbance along the semimeridians tested.

SD of the BFC irregularity (BFCIrregSD) is defined as the sum of the differences squared and divided by the number of semimeridians tested. This parameter is expressed in millimetres (Ferreira-Neves *et al.* 2015; Sanz *et al.* 2014).

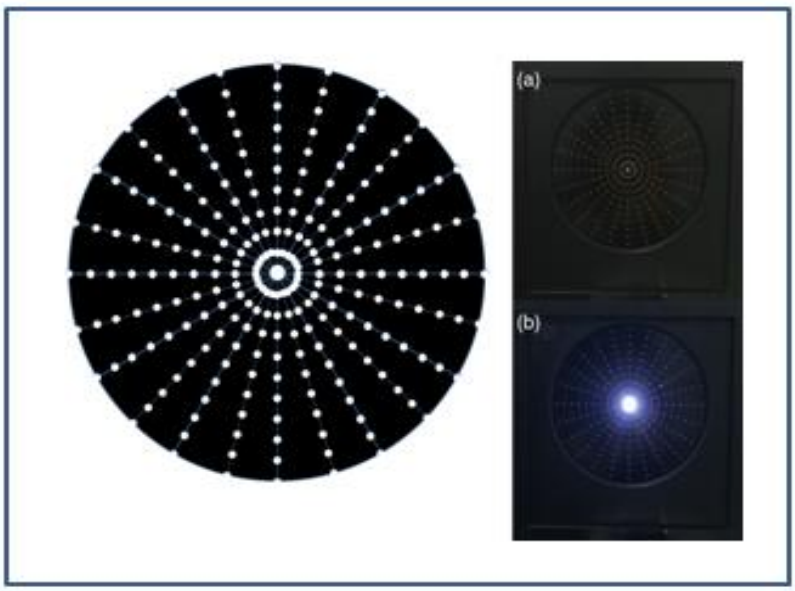


Figure 4-8 - View of a central LED with light turned off (A) and (B) turned on at minimum intensity surrounded by other 240 smaller peripheral stimuli. Reproduced from Ferreira-Neves *et al.* (2015).

4.10.6 Questionnaires

Two questionnaires were administrated in order to assess the symptomatology and the visual quality at Baseline and at each follow-up assessment (LDV and Day 7 for each lens).

4.10.7 Dry eye symptomatology

The Ocular Surface Disease (OSDI) Questionnaire was used to assess the symptoms of ocular discomfort associated with dry eye. The OSDI questionnaire contains 12 items, divided into three subscales, each item has the same five-category response option (All of the time; Most of the time; Half of the time; Some of the time; None of the time). The OSDI is assessed on a scale of 0 to 100, which highest scores represents greater disability (Dougherty *et al.* 2011). The questionnaire was administrated 7 times: at Baseline – to assess symptoms of the subjects with their habitual correction – and at DLV and Day 7 of each one of the three lenses tested. The OSDI final score was calculated using the following formula:

Equation 4 - Equation used to calculate the final OSDI score

$$OSDI = \frac{[(\text{sum of scores for all questions answered})] \times 100}{[(\text{Total number of question answered}) \times 4]}$$

4.10.8 Quality of Vision

The Quality of Vision (QoV) questionnaire was used to evaluate the quality of vision and visual function at Baseline and the differences with each CLs fitted. The QoV questionnaire was designed and validated by McAlinden *et al.* (2010) to measure the quality of vision based in subject's perception. This instrument evaluates 10 symptoms (glare, halos, starbursts, hazy vision, blurred vision, distortion, double or multiple images, fluctuation in vision, focusing difficulties and difficulty in depth perception) rated in each of three scales: frequency, severity, and bothersome (McAlinden *et al.*, 2010). The questionnaires were applied 4 times: before lens wear (Baseline visit) and after the lens wear at every study visit (3 lenses = 6 questionnaires). The QoV score is scaled from 0 to 100, being lower scores considered good quality of vision. The final score of QoV was calculated according the three subscales: subscales: Frequency, Severity and Bothersome of the visual-related symptoms. Subjects with the highest score on the questionnaire are classified as symptomatic (low quality of vision). Questionnaire response categories description is explained in **Table** 4-4.

Table 4-4- Questionnaire response categories and score description (McAlinden et al. 2010)

Question Types	**Response Category**			
Frequency	Never (0)	Occasionally (1)	Quite Often (2)	Very Often (3)
Severity	Not All (0)	Mild (1)	Moderate (2)	Severy (3)
Bothersome	Not All (0)	A little (1)	Quite (2)	Very (3)

4.10.9 Dehydration

Measurements of CLs dehydration (*in vitro and ex vivo*) were performed by gravimetric method, using digital analytical balance (AT 210, Metler Toledo, and Giessen, Germany). This analytical balance has an accuracy of 0.00001g, a wide range of readability – from 0.005mg to 0.1 mg, and range of measurement up to 520g, respectively. Before the measurements of CL mass, digital analytical balance was calibrated and the excess moisture present was removed with the aid of an absorbent paper so that its value is not overestimated. All CLs were placed on the instrument in a concave side up, in order to simulate the ocular surface and the weight of the lens was registered each 60s with a microgram resolution (61106grs). The readings were first obtained at 1 min intervals during the 10 min and later interval of 5 mints, taking the total time of 30 mins. The measurements were done in the laboratory with an ambient temperature of 24°C and a relative humidity of air 73 in order to guarantee the stability of the measurements. Between one measurements of lens to another, the instrument was cleaned. The measurements were performed following the same procedure for both processes (*in vitro and ex vivo*). For the analysis of CL dehydration, values of CL mass loss were collected and considered as CL water loss and, therefore, CL dehydration.

Figure 4-9 - Analytical balance used for lens weight measures.

4.10.10 Dehydration *in vitro*

Measurements of the *in vitro* dehydration process of CLs were done immediately after open the blister of each lens and after 24 hours and 72 hours after soaking them in the packing solution. To minimize dehydration before obtaining the first reading, the time between taking away the CL from the blister packs and the remove of the excess of moisture was 15 seconds. Two different refractive power [-1.50 diopters (D) and -3.00 diopters (D)] of each one of the CL designs used in the present work (Biofinity Energys ®, Biofinity ® and Baush+Lomb Ultra ®) were measured. Three consecutive measurements of each lens power were made, and the mean of the 6 measurements was calculated. Data value of dehydration rate *in vitro* were calculated by the following equation based on previous studies (González-Méijome; Lopez-Alemany; Parafita, 2008; González-Méijome; Lopez-Alemany; Almeida; Parafita; Rejofo; 2007).

$$Water\ Loss = \frac{\text{Weight 1} - \text{Weight 2}}{\text{Weight 1}} \text{ X } 100$$

4.10.11 Dehydration *ex vivo*

Measurements of the *ex vivo* dehydration process of CLs were performed immediately after CL removal (after one week of lens wear) and 24 h after immersing them in the packing solution. To avoid potential lens contamination during the removal of the lens off the eye, medical gloves were used. The measurements were performed following the same procedure *in vitro* dehydration. Data value of dehydration *in vitro* and *ex vivo* dehydration (dehydration rates) were calculated by the following equation based on previous studies (González-Méijome; Lopez-Alemany; Parafita, 2008; González-Méijome; Lopez-Alemany; Almeida; Parafita; Rejofo; 2007).

4.11 Statistical Analysis

Statistical Analysis was conducted using SPSS Statistic software version 23.0 (IBM Inc, IL) and Microsoft Excel version Office 2007. To determine the differences between Baseline (with habitual correction) and CLs modalities in the outcome measured at lens despising visits (LDV) and follow-up

visit (Day 7), a series of Friedman two-way analysis of variance and Post-hoc testing with Bonferroni corrections for multiple comparisons were used to analyse the statistically significant. For pairwise comparisons, Wilcoxon signed-rank test was used to analyse the statistically significant difference between visits for each CL modality.

To determine differences between consecutive measures obtained for *in vitro* dehydration, a series of The Independent sample T-test was used to analyse the statistically significancy, whereas Repeated measures analysis of variance (ANOVA) and Post-hoc testing with Bonferroni corrections for multiple comparisons was used to analyse the statistical significance of differences between lenses in *ex-vivo* dehydration and rehydration.

Furthermore, bivariate correlations were performed using Spearman coefficient correlation to determine the relationships between all variable measured. The correlations were considered strong if they were greater than 0.800, moderately strong if they were between 0.500 and 0.800, reasonable if they were between 0.300 and 0.500 and weak if they were less than 0.300 (Chan, 2003).

The level of statistical significance was set at α=0.05, and p-values less than 0.05 were considered statistically significant..

Chapter 5

Results

Avelino Nelson F. Mazuze

5. RESULTS

This chapter presents in detail the the results obtained for each variable measured at lens despising visits (LDV) and after seven days of CL wear for each one of the CL tested, as well as the comparative analysis between them. For statistic analysis, data from 1 eye of all 7 subjects who completed the follow-up visits were considered. The results presented in tables and figures were expressed as the mean ± standard deviation (SD) and only one eye (right eye) was considered for the statistical analysis since both eyes were strongly correlated.

5.1 Outcome variable

5.1.1 Main outcome measures

Four main outcome variables were investigated in this clinical trial, namely:

1) High and low contrast visual acuity (HCDVA and LCDVA)
2) Accommodative response
3) Tear Film stability
4) Dehydration

The four secondary variables investigated in this trial were:

1) Optical quality
2) Light Disturbance Analyzer
3) Quality of Vision of the contact lenses (QoV)
4) Ocular Surface Disease Index Questionnaire (OSDI)

5.2 Sample Characteristics

Of the total of 13 eligible participants who qualified for the study at the Baseline examination and dispensed lenses, 7 subjects completed all the follow-up visits required. Six (6) subjects were lost to follow-up and did not complete the study protocol due to lack of availability during mobility restrictions related with SARS-Covid-19 pandemic situation. The mean age of the participants was 25.71±3.40 years (range from 22 to 30 years), with 100 % being female. Mean of spherical equivalent (M) was −1.58±0.73 diopters (D) (range from −3.55 to 0.75D). The average of best-corrected visual acuity (BCVA) was - 0.08±0.06 LogMar (range from −0.20 to 0.00 LogMar). **Table 5-1** summarizes the demographics and ocular characteristics of all the participants enrolled at Baseline (including drop-outs) and the seven subjects that completed the study.

Table 5-1- Characteristics of the patients enrolled in the study.

Parameter	Subjects (n=13)	Subjects (n=7)
Ages (years)		
Mean ± SD	24.92±3.22	25.71±3.40
Median (Range)	23 (22 to 30)	26 (22 to 30)
Sex n (%)		
Male	3 (23.1%)	0 (0%)
Female	10 (76.9 %)	7 (100%)
M (D)		
Mean ± SD	-1.76±1.45	-1.58±0.73
Median (range)	-1.50 (-4.88 to 1.13)	-1.50 (-3.55 to 0.75)
J0 (D)		
Mean ± SD	-0.01±0.20	0.09±0.15
Median (range)	0 (-0.36 to 0.43)	0 (0.00 to 0.43)
J45 (D)		
Mean ± SD	- 0.04±0.14	- 0.04±0.14
Median (range)	-0.00 (-0.25 – 0.32)	-0.00 (-0.25 – 0.22)
BCVA (LogMar scale)		
Mean ± SD	-0.07±0.06	-0.08±0.06
Median (range)	0 (-0.20 to 0.00)	-0.1 (-0.20 to 0.00)

M - Spherical equivalent; J0 - Difference in diopter power between the horizontal and vertical meridian; J45 - expresses the value of oblique astigmatism (45° and 135°); BCVA - Best-corrected
Visual acuity.

5.3 Visual Performance

Figure 5-1 shows the changes over time of Monocular High and Low Contrast Visual Acuity in LogMAR scale (HCVA and LCVA) with three types of contact lenses fitted for 7 eyes of the 7 subjetcs that completed the study. There were no differences in the mean HCVA between Baseline (with habitual correction) and follow-up visits with all the lenses tested (all $p > 0.05$, Friedman test). There was a slight better performance at LDV with the CLs tested for LCVA comparing to Baseline, but without statistically significant differences (all $p > 0.05$, Friedman test). Comparisons between CLs designs revealed no statistically significant differences between the three lenses in HCVA (all $p > 0.05$, Friedman test) neither between visits for each lens (all $p > 0.05$, Wilcoxon). Likewise, there were no statistically significant differences between contact lenses in LCVA (all $p > 0.05$, Friedman test) neither between visits for each lens (all $p > 0.05$, Wilcoxon).

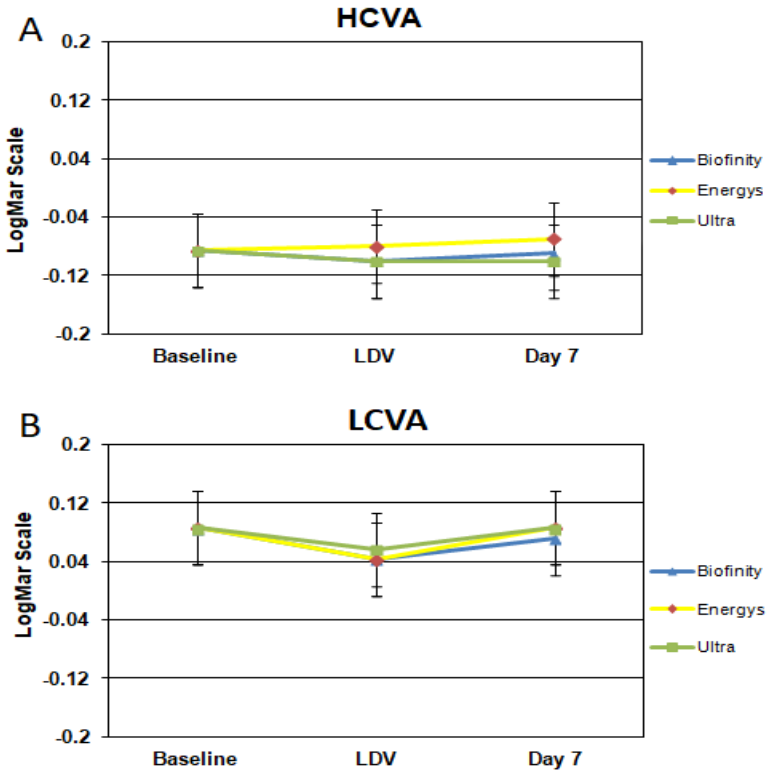
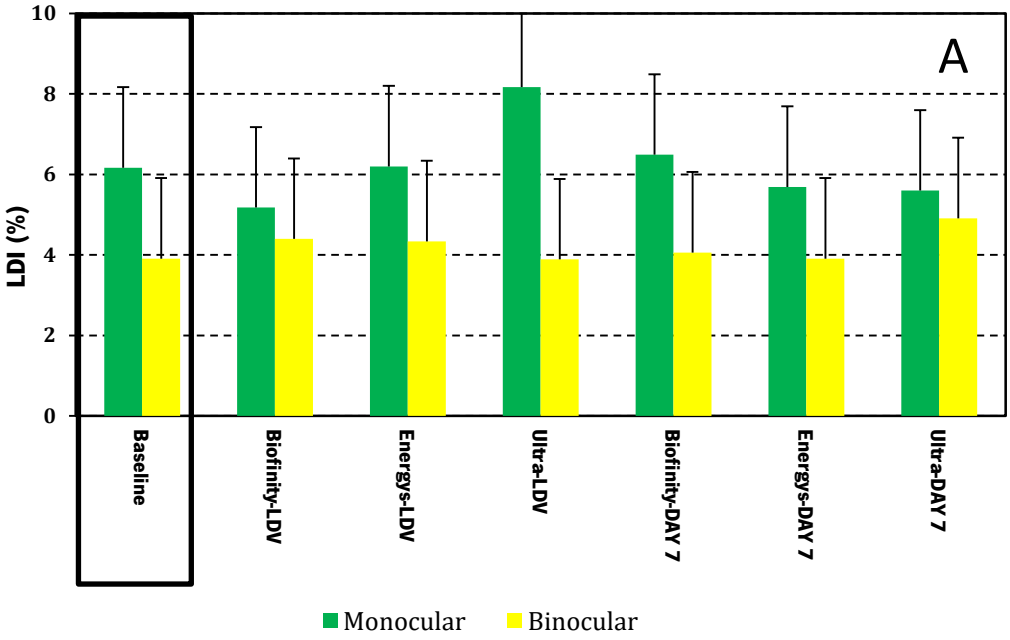


Figure 5-1- Change in HCVA (A) and LCVA (B) at Baseline with habitual correction (HB) and with each contact lens modality at the 1st day (LDV: lens dispensing visit) and 7th day visit. Error bars represent standard deviation.

5.4 Light Disturbance Analysis

Figure 5-2 shows the changes over time of light disturbance (LD) parameters: Light disturbance Index (LDI), Standard Deviation of the Irregularity of Best Fit Circle (BFCIrregSD) and Best Fit Circle Irregularity (BFCIrreg) for each contact lens modality. There were no statistically significant differences in LD parameters between Baseline (with habitual correction) and follow-up visits with all CLs tested (all $p > 0.05$, Friedman test) in both monocular and binocular (all $p > 0.05$, Friedman test). Comparisons between CLs designs in monocular conditions revealed no statistically significant differences in LDI (%) and BFCIrreg (mm)($p > 0.05$, Friedman test). There were statistically significant differences in BFCIrregSD only in follow-up visit (Day 7) between Biofinity vs Biofinity Energys and Biofinity vs Bausch + Lomb ($p = 0.028$, Friedman test and Bonferroni post hoc test), with Biofinity lens showing less irregularity. Relatively to binocular condition, there were no statistically significant differences for any LD parameter between contact lenses modalities ($p > 0.05$, Friedman test) and between visits for each lenses (all $p > 0.05$, Wilcoxon).



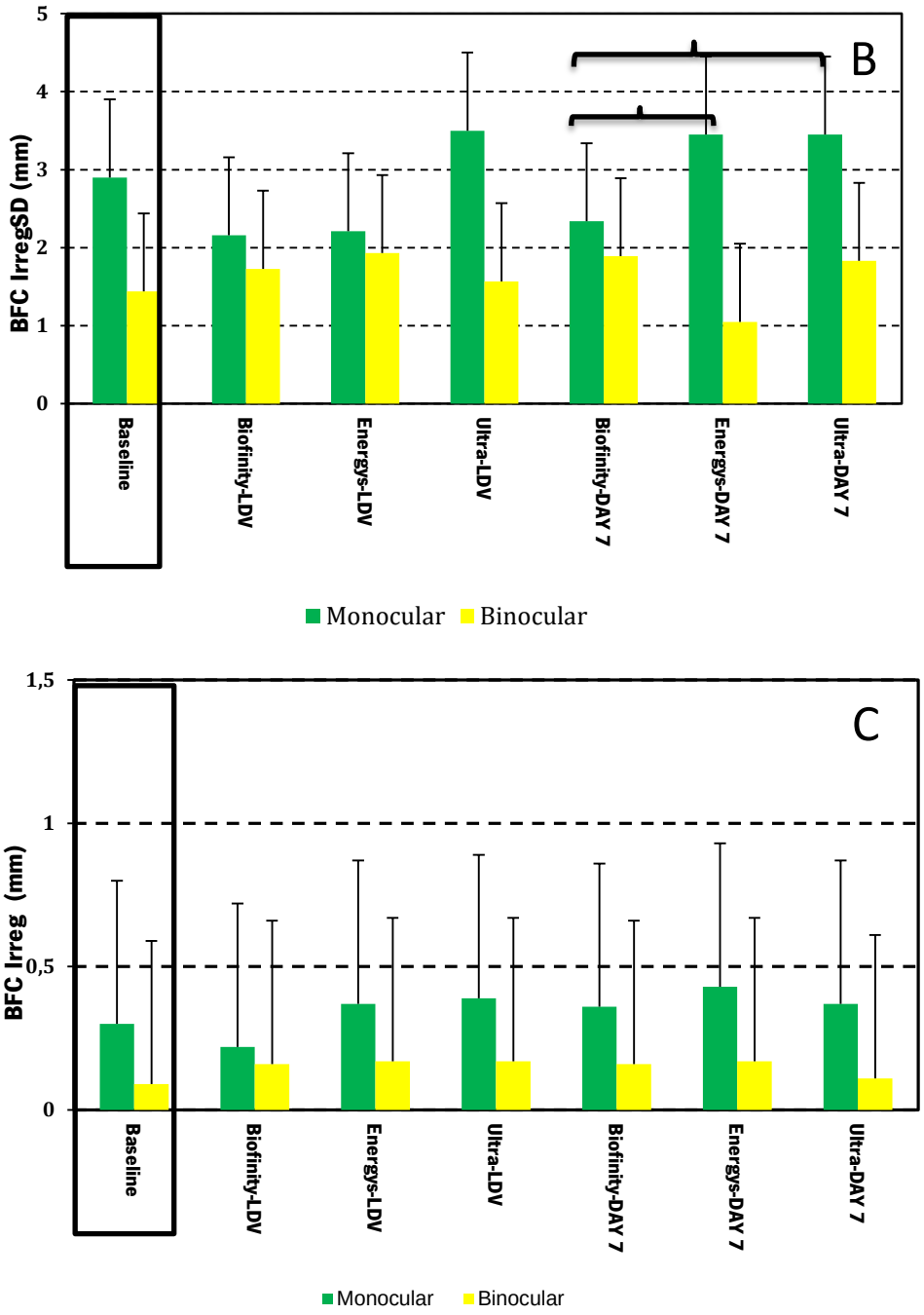


Figure 5-2 - Monocular and binocular LDI (A), BFCIrregSD (B) and BFCIrreg (C) at Baseline with habitual correction (HB) and with each contact lens modality at the 1st day (LDV: lens dispensing visit) and 7th day visit. Error bars represent standard deviation. (⑃) Statistically significant differences.

5.5 Ocular Aberration

Figure 5-3 shows the changes over time of Zernike coefficients expressed as oblique astigmatism, defocus, high-order comatic aberrations (3rd order), spherical aberration (4th and 6th order), as well as the root mean square (RMS) up to 8th order of spherical aberration (RMS_SA), secondary astigmatism (RMS_SecAstig) and high order aberrations (RMS_HOA), calculated for a pupil size of 5 mm.

There was an increase in Oblique Astigmatism with all CL tested compared to Baseline (all $p > 0.05$, Friedman test). This increase was more pronounced for Ultra Bausch+Lomb CL. There was a decrease with all CL tested compared to Baseline. This increase was more pronounced for Biofinity Energys and Bausch + Lomb CL. Although there was no significant changes between Baseline and Follow-up Visits in the Horizontal Coma with the Control Lens (Biofinity), there was an augment/ a shift from positive to negative with both lenses tested (Energys and Ultra). The 4^{th} order spherical aberration changed from slighty positive in the Baseline (without lens) to negative in the follow-up visits, being this difference more noticible for the lens tested (Energys and Ultra). There was also an augment (with a shift from positive to negative) in the 6^{th} order spherical aberration from Baseline to Day-7 with the lens tested (Energys and Ultra), but also with the Control Lens (Biofinity). Those augments are decipected in **Figure 5-3 F** (RMS_SA). Along with the decrease in Defocus with all lenses, there was also a statistically significant decrease in Total RMS with all CLs tested compared to Baseline. Relatively to comparisons between CLs, statistically significant differences were found for coefficients Astig Obli in LDV (Biofinity vs Energys), Horizontal COMA also in LDV (Biofinity vs Ultra; Biofinity vs Energys), SH_4th (Biofinity vs Ultra) and SH_6^{th} in Day 7 (Ultra vs Biofinity; Ultra vs Energys) (all $p < 0.03$, Friedman test and Bonferroni post hoc test). In contrast, the coefficients Defocus, Vertical Astig, Vertical_COMA, RMS_SA, RMS_COMA, RMS_Astig Sec, RMS_Trefoil , RMS_HOA , RMS_Total did not differ significantly between contact lenses ($p > 0.05$, Friedman test) and between each lenses modalities (all $p > 0.05$, Wilcoxon).

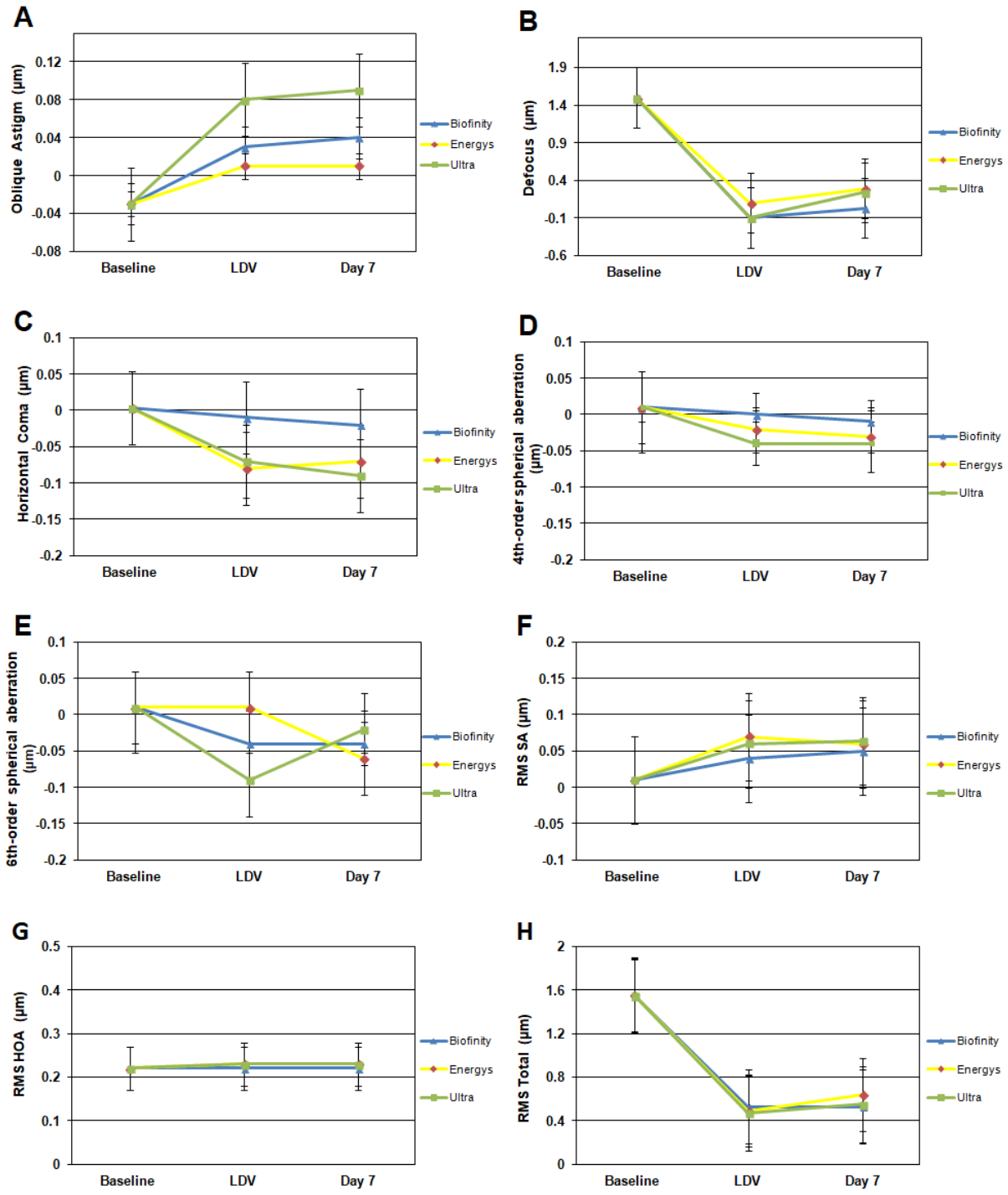


Figure 5-3 - Changes in Zernike coefficients at Baseline (with HB) and with each contact lens modality at the 1st day (LDV: lens dispensing visit) and 7th day visit. Error bars represent standard deviation.

5.6 Accommodative Response

Table 5-2 presents the results of accommodative response for the spherical equivalent (M) for each target vergence with the three types of CLs fitted. The values of accommodative response were calculated from the refraction measured with Grand Seiko WAM-5500 open field auto-refractometer for each target vergences for each CL. The values presented in **Table 5-2** are illustrated graphically in **Figure 5-4**. There was an increase of 0.25D in accommodative response for the spherical equivalent (M) in both CLs modalities (Biofinity Energys and Bausch + Lomb) compared to Control lens (Biofinity), but without statistically significant differences between CLs neither for any target vergence ($p > 0.050$, Friedman test) and between visits for each lens (all $p > 0.05$, Wilcoxon). This increase was more pronounced for Ultra Bausch+Lomb CL.

Table 5-2 – Mean ± standard deviation of the accommodative response for the spherical equivalent (M) for each target vergence with the three types of contact lenses fitted

Stimulus	Contact Lens	LDV	Day 7	*p-value*[1]
0.25D	Biofinity	0.00±0.26	-0.15± 0.28	*p=0.063**
	Biofinity Energys	-0.23±0.33	-0.25±0.27	*p=1.000**
	Ultra Bausch Lomb	-0.22±0.48	-0.18±0.59	*p=0.310**
p-value[2]		*p=0.102*†	*p=0.867*†	
Post hoc test		X	X	
1.00D	Biofinity	-0.47±0.40	-0.55±0.33	*p=0.499**
	Biofinity Energys	-0.72±0.16	-0.61±0.25	*p=0.176**
	Ultra Bausch Lomb	-0.50±0.74	-0.66±0.20	*p=0.352**
p-value[2]		*p=0.066*†	*p=0.368*†	
Post hoc test		X	X	
2.00D	Biofinity	-1.64±0.20	-1.60±0.26	*p=0.398**
	Biofinity Energys	-1.54±0.39	-1.54±0.29	*p=0.866**
	Ultra Bausch Lomb	-1.28±0.54	-1.40±0.54	*p=0.310**
p-value[2]		*p=0.495*†	*p=0.495*†	
Post hoc test		X	X	
3.00D	Biofinity	-2.19±0.81	-2.41±0.39	*p=0.310**
	Biofinity Energys	-2.30±0.41	-2.40±0.46	*p=0.310**
	Ultra Bausch Lomb	-2.32±0.57	-2.22±0.63	*p=0.866**
p-value[2]		*p=0.867*†	*p=0.895*†	
Post hoc test		X	X	

M - Spherical equivalent; LDV– lens dispensing visit after more than 15 minutes of lens wear; *p-value*[1] – differences between visits for each lens; *p-value*[2]; (†) Friedman test and Bonferroni post hoc test; (*) Wilcoxon; statistically

significant differences between contact lenses modalities highlighted in bold. X—non-statistically significant differences with a pair-by-pair comparison.

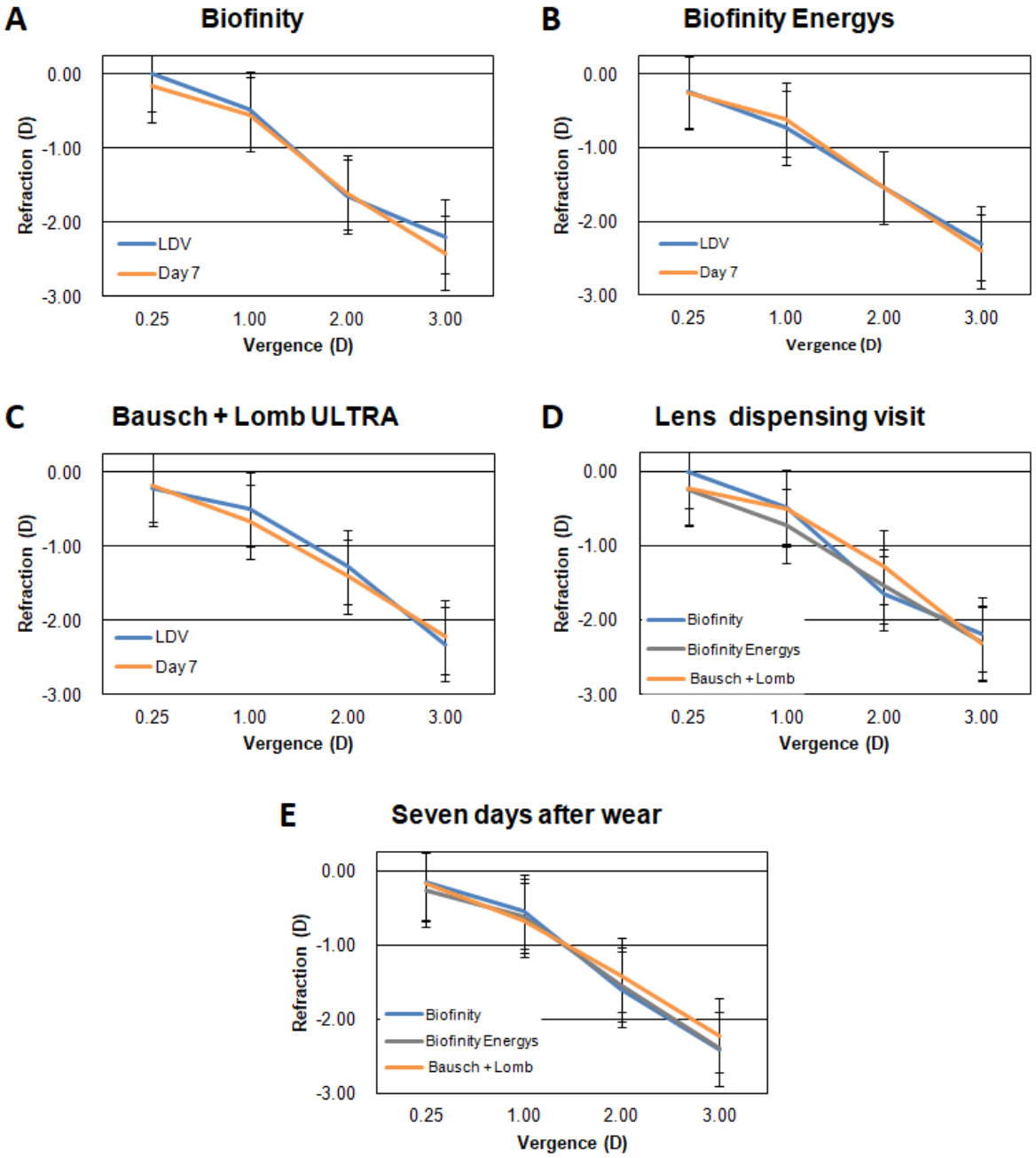


Figure 5-4 - Profile of accommodative response for the spherical equivalent (M) for each target vergence at the 1st day (LDV: lens dispensing visit) (a) and 7th day visit (b) for three types of contact lenses fitted. Vergence (Stimulus) and Refraction (Response): normalized refraction according to the long-distance refraction

5.7 Tear Film Analysis

Table 11-4 shows the changes over time of tear film parameters: Tear Film Surface Quality (TFSQ) Index, Tear Film Surface Quality Area (TFSQ Area) and auto Tear Break-Up Time (Auto BUT) for each contact lens modality. CL wear increased the tear film instability, as there were statistically significant increases ($p < 0.05$, Friedman test) in TFSQ Index and TFSQ Area and a decrease in Auto BUT ($p < 0.05$, Friedman test) between Baseline (without lens) and follow-up visits (with CLs). Regarding comparisons between CLs designs, there were no statistically significant differences in any tear film parameters between contact lenses modalities ($p > 0.05$, Friedman test) and between visits for each lenses (all $p > 0.05$, Wilcoxon). However, the Biofinity (Control lens) showed a better performance than Ultra and Energys in TFSQ and TFSQ area, but not for Auto BUT.

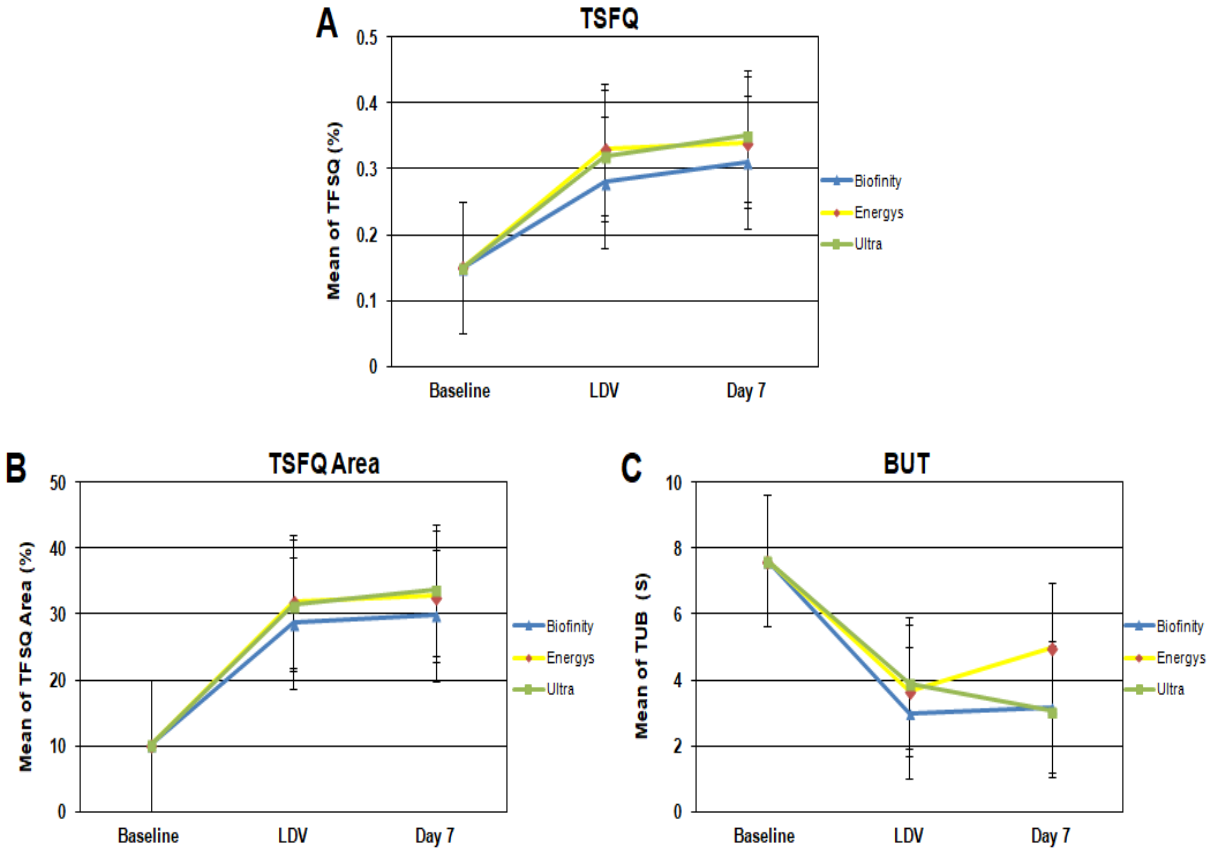


Figure 5-5 - Changes in Tear film parameters at Baseline and with each contact lens modality at the 1st day (LDV: lens dispensing visit) and 7th day visit. Error bars represent standard deviation.

5.8 Questionnaires

5.8.1 Quality of Vision Questionnaire (QoV)

Figure 5-6 compares the results of the QoV questionnaire at Baseline with LDV and Day-7. The increases in the subscales of QoV score (frequency, severity and bothersome of vision-related symptoms) were not statistically significant compared to Baseline (all $p > 0.05$, Friedman test), nor significantly different between contact lenses modalities ($p > 0.05$, Friedman test) and between visits for each lenses (all $p > 0.05$, Wilcoxon).

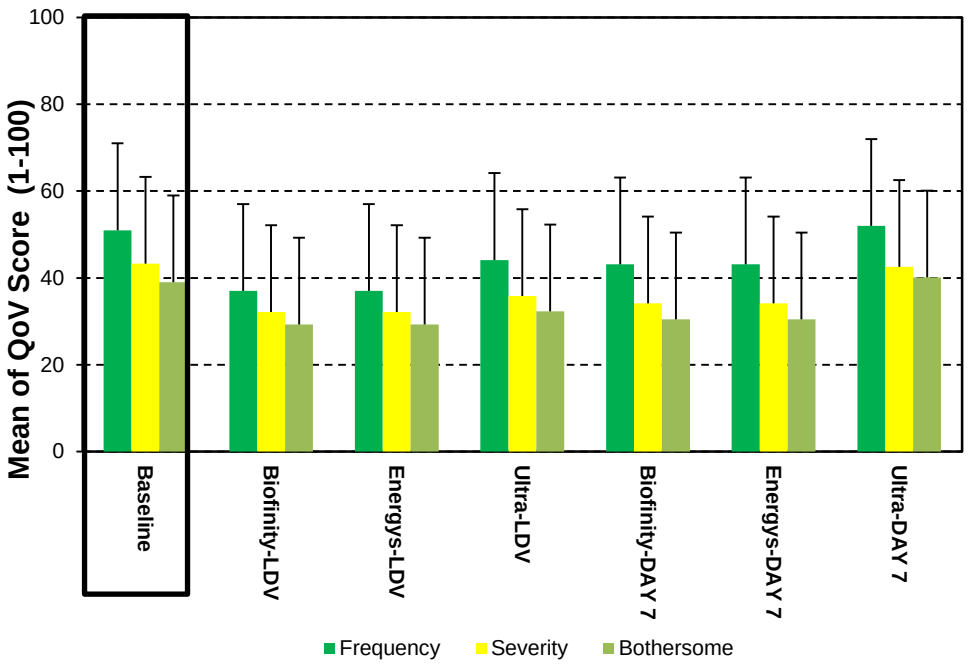


Figure 5-6 – Overtime changes in the frequency, severity and bothersome of vision-related symptoms (QoV questionnaire). Baseline (without lens); 1st day of lens wear (LDV lens dispensing visit); 7th day of lens wear (Day 7). The scale ranges from 1 to 100, with higher scores indicating worse quality of vision. Error bars represent standard deviation.

5.9 The OSDI Questionnaire

Figure 5-7 shows the changes over time of OSDI questionnaire. Although there was an increase in OSDI Scores from LDV to Day-7 for CL tested (Biofinity Energys and Bausch + Lomb), there were no statistically significant differences in the mean OSDI score between Baseline (with habitual correction) and follow-up visits (all $p > 0.05$, Friedman test). Although there were no statistically significant differences, this increase is considered clinically relevant: it was more pronounced for Bausch+Lomb CL (an increase of more than 30 OSDI units) and for Biofinity Energys (an increase of 20 OSDI units). There was a slight decrease in OSDI scores with Control lens in comparison to Baseline.

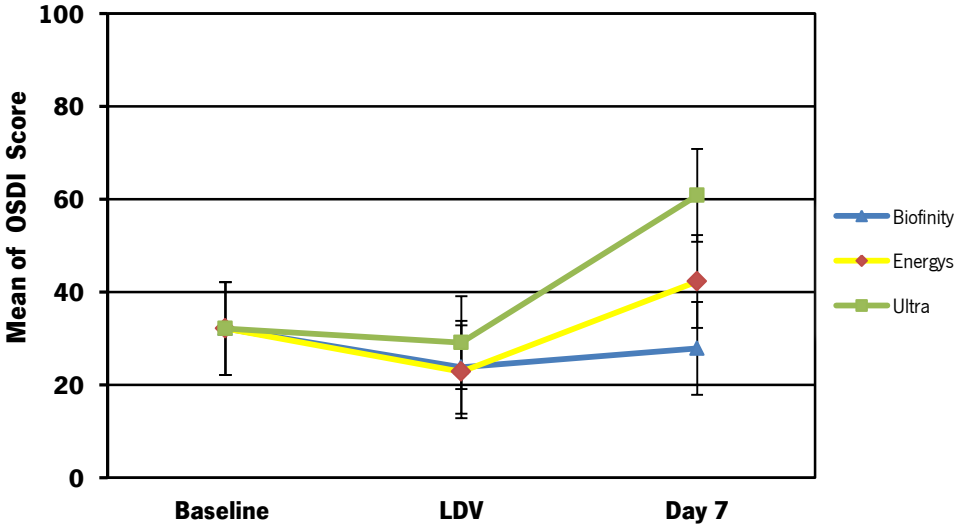


Figure 5-7 - Changes in OSDI scores thourgh time for all contact lens tested. Baseline (without lens); 1st day of lens wear (LDV lens dispensing visit); 7th day of lens wear (Day 7). The scale ranges from 1 to 100, with higher scores indicating more symptoms. Error bars represent standard deviation.

5.10 Dehydration

5.10.1 *In vitro* dehydration

Results of *in vitro* dehydration were described in percentages, by means of relative mass lost, which represent the water loss. The measurements were performed 15 seconds after taking the lens from the blister, and after 24 hours and 72 hours after soaking them in saline solution. After removing the lens from the blister and placing it on the scale, a 30 minutes' continuous evaluation of mass loss was done: measurements were performed in 1 min intervals in the first 10 min (0 to 10 min after opening the blister) and in 5 min intervals in the last 20 min (from 10 to 30 min after opening the blister). Then the lens was placed in the lens case with saline solution and the same measurements were repeated after 24 hours and after 72 hours. Each data point on the graph is a mean of 6 measurements. Two refractive power (-1.50D and -3.00D) for each lens studied were analyzed**.**

Figure 5-9 shows the avarege change in water loss over the time for Biofinity Energys (Comfilcon A) and Bausch + Lomb plotted over the three day period. The representation of profile of *in vitro* dehydration curve over the time of each lens modality is ilustretd in **Figure 5-9** .The mean of dehydration rate for Biofinity Energys (Comfilcon A) with power of -3.00D and -1.50D was -11.85%±2.71 and -11.77% ±2.55, respectively, with no statistically significant (p=0.984, Unpaired T-Test). For Bausch + Lomb the mean obtained for *in vitro* dehydration for power of -3.00D over three days was -11.54%±2.46 and -11.31%±2.54 respectively. Likewise, no statistically significant differences were found in the dehydration rate between Ultra Bausch & Lomb with power of -3.00D when compared with -1.50D (p=0.949, Unpaired T-test.).

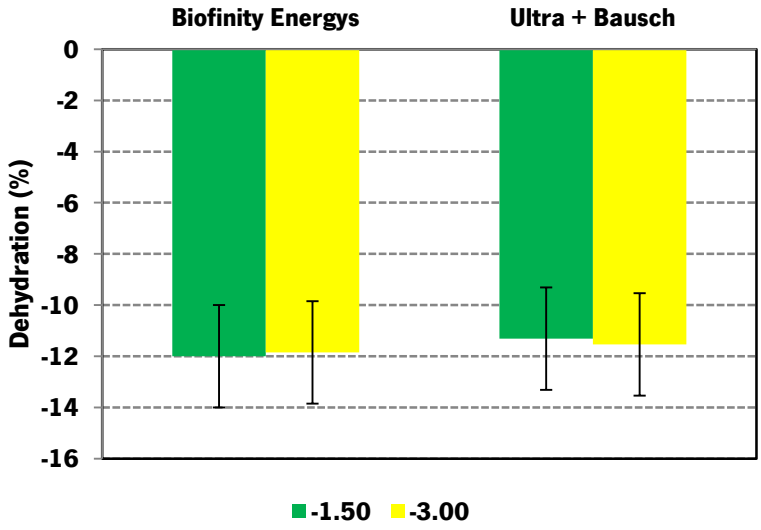


Figure 5-8 – Mean of *In vitro* Dehydration value for Biofinity Energys compared to Bausch + Lomb for two power refraction. Error bars represent standard deviation.

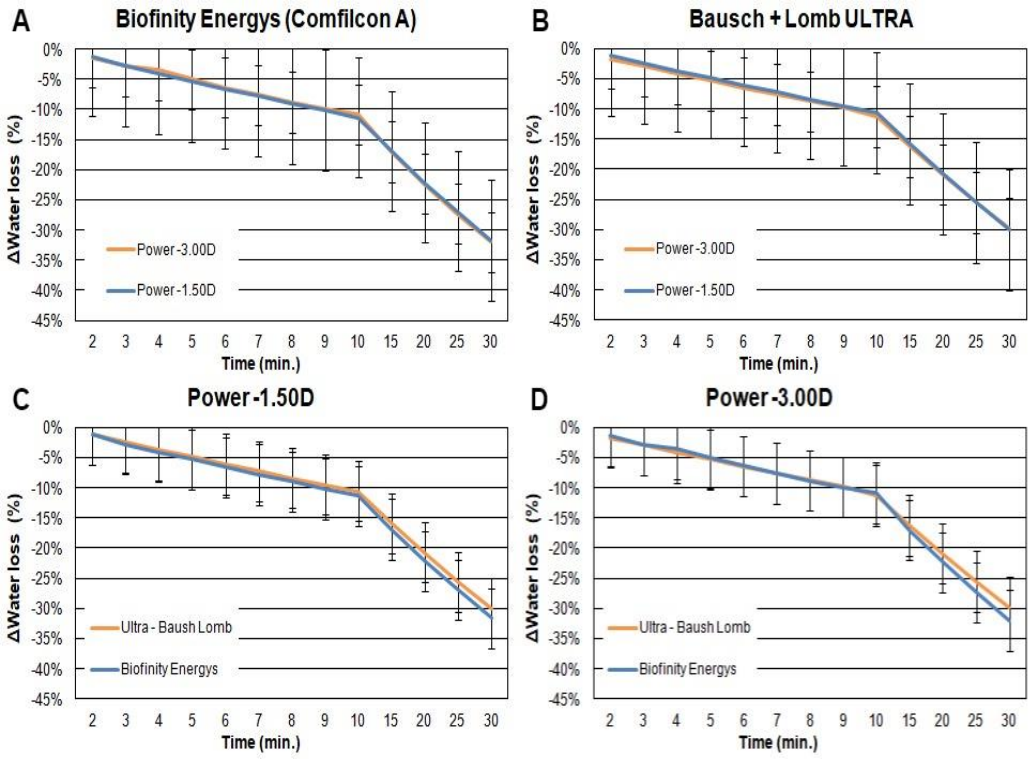


Figure 5-9 - Change in water loss over the time for Biofinity Energys (Comfilcon A) and Bausch + Lomb plotted over the three days period. Each data point represents a mean of six measurements. Error bars represent standard deviation.

5.10.2 *Ex vivo* dehydration

Results of *ex vivo* dehydration were described in percentages, by means of relative mass lost, which represent the water loss. For each lens modality, an average lens weight of all 7 subjects who completed the study was calculated.

Figure 5-10 illustrated the mean of *ex-vivo* dehydration of Biofinity (Control lens), Biofinity Energys (Comfilcon A) and Bausch + Lomb after one week of lens wear and after 24 hours of rehydration**.** The representation of profile of *ex vivo* dehydration curve over the time of each lens modality is ilustretd in **Figure 5-11**. The mean of *ex vivo* dehydration rate for Biofinity was -10.56%±2.40; -13.22%±2.83 for Biofinity Energys; and -13.97% ±2.91 for Bausch + Lomb**.** There were no statistically significant differences in the ex *vivo* dehydration rates between CLs after one week of wear (p=0.652, ANOVA).

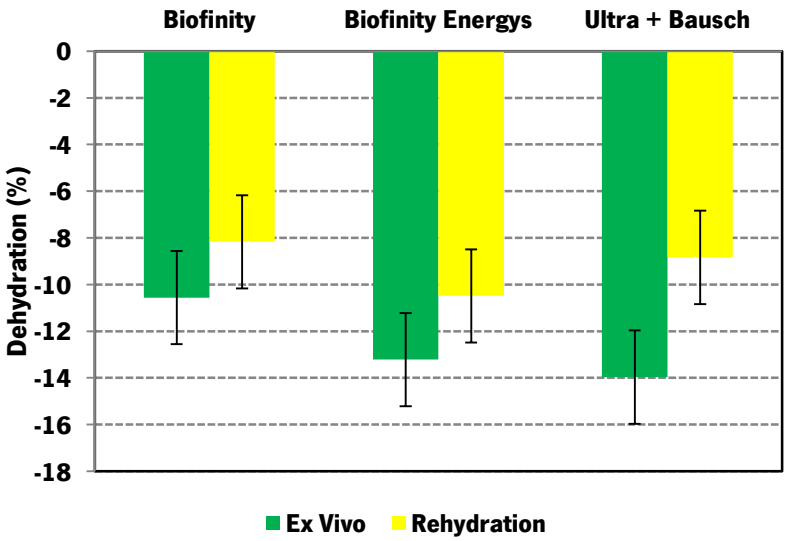


Figure 5-10- Mean of *Ex vivo* Dehydration (%) and Rehydration of each CL tested after one week of lens wear (green bar) and after rehydrating them in saline solution for 24h (yellow bars).

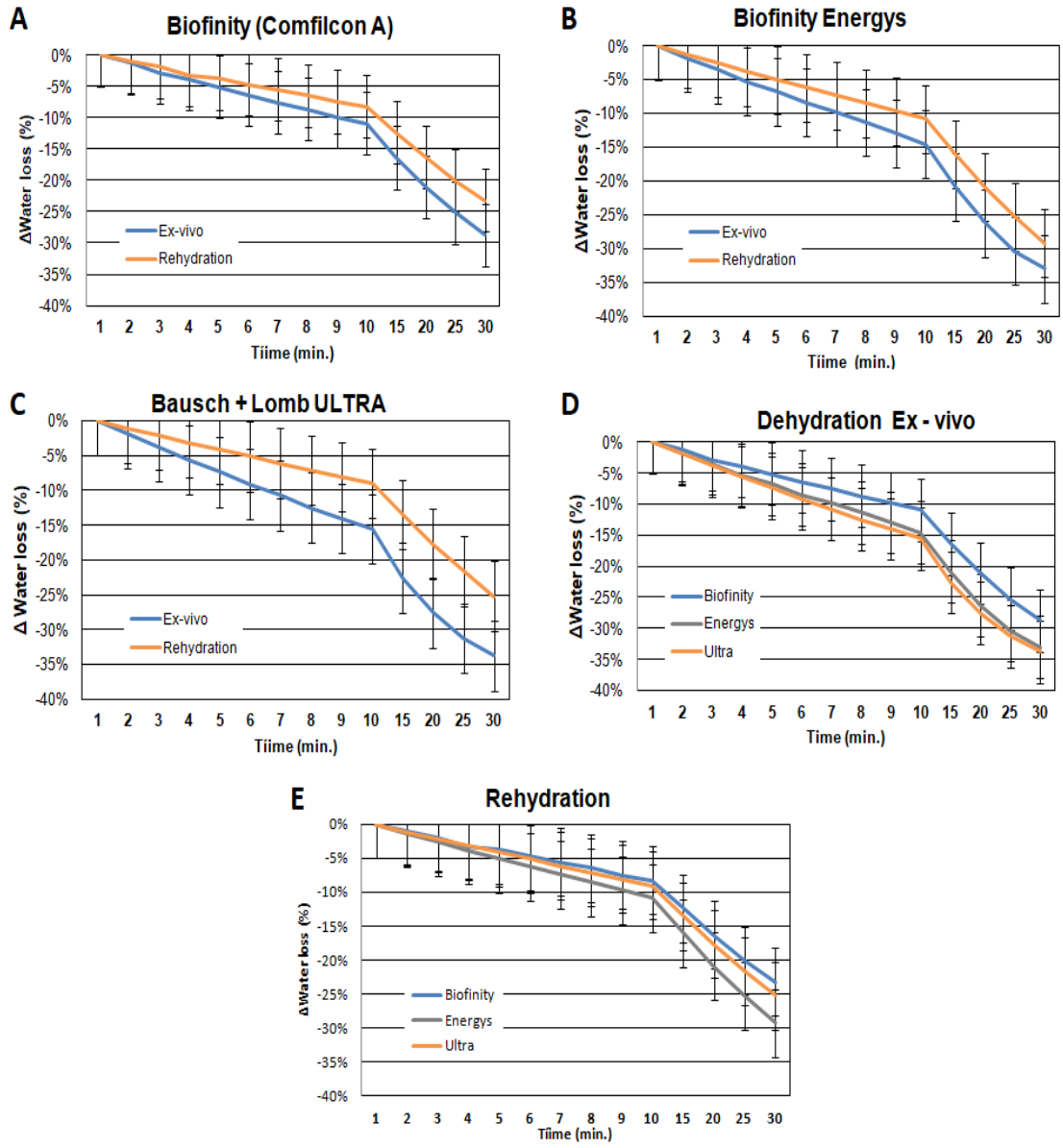


Figure 5-11 - Change in water loss (for both eye, all subjcets) over the time for each lens types after seven of wear and after rehydrating them in saline solution for 24h. Each data point represents a mean (of water loss) of seven subjects for each lens. Errors bars represent standard deviation

5.11 Correlation analysis

5.11.1 Correlation between Zernike polynomials with other variables

Table 5-3 presents the results of correlations between Zernike polynomials and HCVA, LCVA, LDI, BFCIrregSD and QoV outcomes (frequency, severity and bothersome of the symptoms) for all contact lenses studied after one week of wear. The subsequent analyses were performed in all contact lenses separately after seven days.

There were strong significant and inverse correlations between Defocus and BCFIrreg for Ultra Bausch Lomb (r= -0.964, p < 0.001), Vertical_Astig and HCVA for Energys (r= -0.791, $p < 0.05$), Vertical_COMA and HCVA for Energys (r= -0.791, $p < 0.05$), Horizontal_COMA and QoV (Severity and Bothersome) for Ultra Bausch Lomb (r= -0.906, $p < 0.001$; and r= -0.883, $p < 0.001$). A positive strong significant correlation was observed between RMS_Astig Sec and Qov (Freq) with Energys (r= 0.764, $p < 0.05$). For the remaining variables, the Spearman Rho values were not statistically significant ($p > 0.05$) and vary between weak to strong, for all CLs tested.

Table 5-3 - Correlations (Spearman) between Zernike polynomials and some variables after one week of wear

		HCVA	LCVA	LDI	IrregSD	Irreg	Freq	Sev	Both
Astig Obli	Biofinity	-0.611	-0.231	-0.414	-0.532	-0.727	0.514	0.185	-0.018
	Energys	0.316	0.107	0.255	-0.505	-0.218	0.079	0.079	0.360
	Ultra	-	0.538	-0.532	0.607	-0.500	0.255	0.473	0.739
Defocus	Biofinity	-0.217	0.000	-0.559	-0.126	-0.364	0.110	-0.259	0.091
	Energys	0.474	0.060	-0.179	0.491	-0.685	-0.036	0.079	0.198
	Ultra	-	0.179	0.018	0.321	**-0.964†**	-0.073	0.020	0.054
Vertical Astig	Biofinity	0.611	0.347	-0.054	-0.126	0.128	-0.565	-0.148	0.218
	Energys	**-0.791‡**	0.139	-0.107	-0.236	0.613	0.218	0.118	-0.108
	Ultra	-	-0.020	0.162	-0.679	0.179	0.109	0.020	0.054
Vertical_COMA	Biofinity	-0.315	-0.694	0.559	0.036	0.145	0.128	0.334	0.273
	Energys	**-0.791‡**	-0.558	0.500	0.018	-0.342	-0.327	-0.118	-0.108
	Ultra	-	-0.219	0.000	0.464	-0.107	0.000	0.335	0.613
Horizontal_COMA	Biofinity	0.808†	0.579†	-0.090	0.685	0.746	-0.606	-0.593	0.200
	Energys	0.632	0.020	0.250	-0.109	-0.126	0.109	-0.158	-0.036
	Ultra	-	0.000	-0.126	-0.500	0.071	-0.665	**-0.906†**	**-0.883†**
SH_4th	Biofinity	0.512	0.463	-0.450	-0.054	0.073	-0.532	-0.148	0.091
	Energys	-0.632	0.359	-0.071	-0.164	0.234	0.491	0.355	0.378
	Ultra	-	0.558	-0.450	-0.321	0.357	0.346	0.236	0.432
SH_6th	Biofinity	0.059	0.386	-0.847†	-0.144	-0.418	-0.257	-0.408	-0.327
	Energys	-0.399	0.000	0.126	-0.505	0.536	0.156	-0.030	-0.127
	Ultra	-	-0.080	0.300	-0.126	-0.306	0.193	0.268	0.355
RMS_SA	Biofinity	0.315	0.347	0.198	0.054	0.182	-0.110	-0.111	-0.218
	Energys	0.474	-0.339	0.036	0.055	0.360	-0.436	-0.591	-0.739
	Ultra	-	-0.418	0.577	0.143	0.000	-0.073	-0.236	-0.595
RMS_COMA	Biofinity	-0.099	-0.347	0.396	-0.342	-0.037	-0.037	0.408	0.055
	Energys	0.316	-0.219	0.393	-0.327	0.072	-0.727	-0.394	-0.252
	Ultra	-	-0.239	0.036	0.321	-0.107	0.182	0.571	0.703
RMS_Astig Sec	Biofinity	0.315	0.0579	-0.198	-0.144	-0.127	-0.184	-0.259	-0.491
	Energys	0.000	-0.020	0.179	0.546	-0.306	**0.764‡**	0.709	0.685
	Ultra	-	0.100	0.378	-0.250	-0.179	0.346	0.059	0.703
RMS_Trefoil	Biofinity	-0.375	-0.617	0.378	0.198	0.127	0.073	0.0482	-0.055
	Energys	0.632	-0.299	0.750	-0.491	-0.162	-0.382	-0.158	0.054
	Ultra	-	-0.100	-0.450	-0.143	0.607	-0.255	-0.020	0.360
RMS_HOA	Biofinity	0.177	0.039	0.000	-0.054	0.036	-0.441	0.259	-0.346
	Energys	0.632	-0.418	0.714	-0.400	-0.036	-0.491	-0.256	-0.126
	Ultra	-	-0.485	0.360	0.321	-0.179	0.182	0.532	0.541
RMS_Total	Biofinity	0.374	0.733	**-0.901†**	-0.378	-0.418	-0.330	-0.445	-0.145
	Energys	0.316	0.418	0.107	0.218	-0.288	0.109	0.079	0.396
	Ultra	-	0.657	-0.180	0.143	-0.321	0.600	0.493	0.577

† $P < 0.001$
‡ $P < 0.05$

5.11.2 Correlation between OSDI and tear film parameters

Figure 5-12 shows the correlation between OSDI and tear film parameters after one week of lens wear. Although without statistical significance (all p>0.05), there were strong correlationns between OSDI Score and TFSQ and TFSQ Area for Biofinity Energys (r=0.714; r=0.786) and between OSDI Score and TFSQ for Ultra CL(r=0.714), whereas moderated but inverse correlations for Biofinity between OSDI Score and TFSQ and TFSQ Area (r=-0.631; r=-0.667).

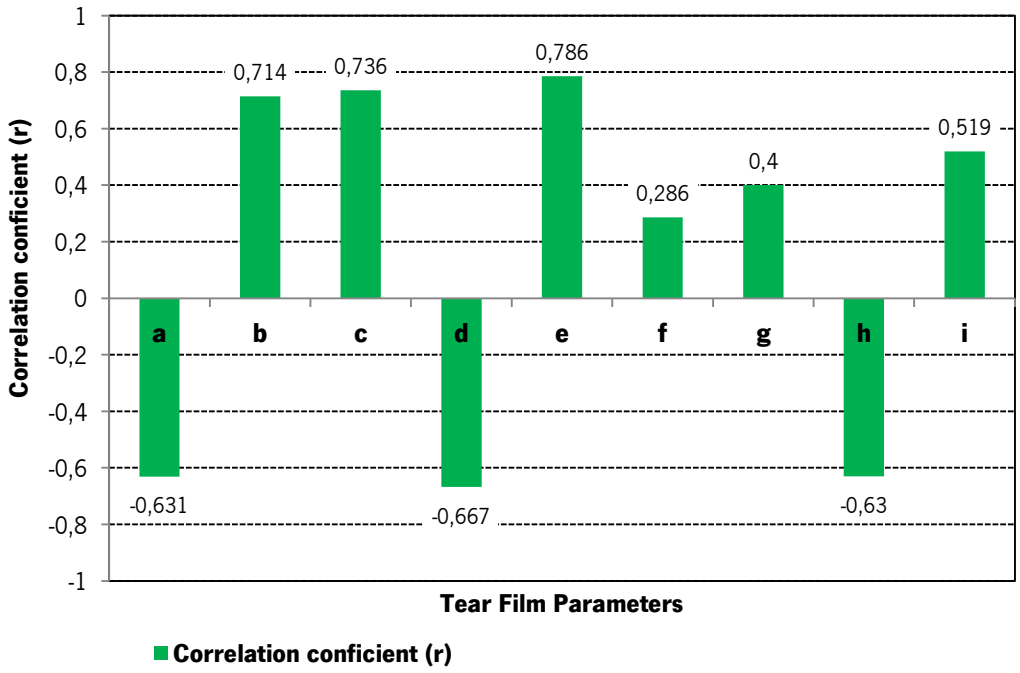


Figure 5-12 - Correlation coefficient (r) between OSDI score and tear film analyses. Note. The abscissa axis represents: a: Biofinity-TFSQ, b: Biofinity Energys-TFSQ, c: Ultra Bausch Lomb-TFSQ, d: Biofinity–TFSQ Area, e: Biofinity Energys–TFSQ Area, f: Ultra Bausch Lomb – TFSQ Area, g: Biofinity-BUT, h: Biofinity Energys-BUT, i: Ultra Bausch Lomb-BUT; vertical axis: correlation coefficient.

Chapter 6

Discussion

Avelino Nelson F. Mazuze

6. DISCUSSION

In this chapter, the results obtained will be discussed. Following the structure of the presentation of the results and the relationship between some variables, in the next pages, the results of the present study will be discussed and compared with the results of other studies that evaluated the same lens materials or other, or which used the same devices that were used in the present research.

The potential effects of the use of digital devices in CL wearers and non-CLs wearers on the visual performance, accomodative response and ocular surface are well documented. However, few clinical trials have investigated the effect of novel soft CLs specially designed for those young adults who spent many hours working with digital devices (Yuan *et al.* 2020; Talens-Estarelles *et al.* 2020; Talens-Estarelles *et al.* 2021; Tuaste *et al.* 2016). In the present study, we compared the effect of two novel CLs modalities specially designed with new tehcnologies for maintaining moisture or optical properties to minimize the effects of the use of digital device on visual performance, optical quality, accommodative response, tear film stability during the computers tasks: Biofinity Energys ™ lenses, a lens with the same mechanical characteristics as Biofinity ®, but designed with a new optic zone called Digital Zone Optics ™, which promise to reduce eye strain caused by the need to focus close up when using digital devices. Bausch + Lomb ULTRA® with highest oxygen transmissibility (Dk/t 163) and lowest modulus (70 g/mm2), offering moisture retention for a full 16 hours, better end of day vision for digital device users and a new technology (MoistureSeal ® technology) which helps the lenses prevent dehydration blur and maintain 95% of their moisture for the entire day (up to 16h of lens wear), reducing ocular syntoms such as dryness and itching.

In terms of visual performance, there was improvement in HCVA and LCVA with both CLs for digital devices (Bausch + Lomb and Biofinity Energys) without significant differences between designs. Notably, in present study, there was a trend of the Bausch + Lomb CL to provide better distance HCVA and worse LCVA comparatively to Control lens (Biofinity) and Biofinity Energys after one week of wear, while the Biofinity Energys remained stable over the follow-up period. Fedtke *et al.* (2016) evaluated the visual performance of single vision and multifocal contact lenses in non-presbyopic myopic eyes. Similar to our results, they found an average of HCVA of −0.06 to −0.10 logMAR for different lenses. Sha et *al.* (2020) evaluated the visual performance of soft contact for myopia control in non-presbyopic: MiSight™,

center-distance Proclear® Multifocal (+2.00 D add), and two prototype lenses. Similar to our results, they found an avarege of HCVA and LCVA of -0.01±0.08 and 0.18±0.12, respectively.

Concerning the aberrometry outcomes - analyzed for a 5-mm pupil size –, the present study found some significant changes in some aberration terms with CLs tested, as seen in **Figure 5-3**. Those changes were found in the coefficients: Astig Oblique, Horizontal COMA, 4th and 6th order spherical aberration. The Total HOA decreased with CLs tested compare to baseline, while the HOA RMS Total remained the same with CLs tested compare to baseline over seven days, but without statistically significant differences. Despite the increase observed in some coefficient such as 4th and 6th order spherical aberration (the higher order aberration with largest influence on visual acuity) there were no statistically significant correlations between them and HCVA or LCVA. Wagner *et al.* (2015) studied the profile power of single vision and multifocal soft contact lenses. Regarding single vision contact lenses, the authors observed a greater presence of negative spherical aberration in most of single vision evaluated, which is in accordance with our results. McAlinden *et al.* (2010) evaluated the effect of aspheric designs of two contact lenses: Balafilcon A (PureVision) and Comfilcon A (Biofinity). Differently to our results, the authors found no changes in spherical aberration, but changes in other HOA. Likewise, Roberts *et al.* (2006) quantified the aberrations induced by soft CLs in normal eyes with myopia. Differently to our results, the authors found increased levels of total HOA. However, despite there were no statistically significant differences between measurements with and without CLs, there was an increase in total coma, trefoil and spherical aberrations.

The sign of spherical aberration induced by different CLs designs can be important, particularly under low light conditions (Santolaria Sanz et *al.,* 2015). Our light disturbance results showed a significant increase (deterioration in the sensation) only for BFCIrregSD with CLs for digital devices compared to control, while size (LDI) and irregularity (BFCIrreg) underwent a decrease with CL tested, but without statistical difference, as showed in **Figure 5-2**. Martins *et al.* (2020) evalueted light disturbance of different contact lens prototypes with potential for myopia control using as control lens (Biofinity) and the same testing device used in the present study. The authors found a significant increase in size of disturbance (LDI) with the lenses tested compared to the control lens. In this same study, the mean values of in LD parameters for Control lens (Biofinity) was sligh lower than the values reported in the present study - the mean LDI value was 4.65±2.25, 0.42±0.35 for irregularity (BFCIrregSD) and irregularity (BFCIrregSD) 2.83±1.57- and similar with Test lenses. Fernandes *et al.*

(2018) assessed the light disturbance on two different presbyopic contact lens corrections: multifocal contact lens (Biofinity Multifocal) and monovision (Biofinity Monofocal) using the same testing device. The authors found a significant increase in LDI and BFCRadius parameters for monovision (Biofinity Monofocal), comparatively to baseline. Considering the power profile and lens material of the CLs studied some statistically significant differences between contact lenses modalities in the LD outcomes were expected in the current study. García-Marqués *et al.* (2021) compared the light disturbance for myopia control contact lens and a single vision contact lens (Biofinity, Comfilcon A, USA) using the same testing device. They found higher light disturbance with multifocal contact lenses design than single vision contact lens. The authors concluded that the design of contact lens (dual-focus) may have affected the light disturbance. Since Biofinity Energys has a different design (Digital Zone Optics ™) to help near vision activities, it should be expected that this lens design could somewhat deteriorate the quality of vision under dim light conditions. However, although without statistically significant differences, the Bausch + Lomb CL showed a worse monocular performance for both size and irregularity of light disturbance (LDI and BFCIrregSD), when compared to both Biofinity (Control lens) and Biofinity Energys. Because of that, differences between lenses could be explained with the sign of spherical aberration. The impact of CLs for digital devices in night visual disturbances could be more explored in future stuideis, due to the effect of the illumination of the digital devices on near task.

The impact of soft CLs on night vision disturbances is also an important factor to analyze the clinical performance of soft CLs for digital devices. The subjective sensation of vision-related phenomena improved - both frequency, severity and bothersome - for Biofinity (Control lens) and Biofinity Energys contact lenses, while Bausch + Lomb underwent a increased when we compared to Baseline over a short-term, but without statistical significance (**Figure 5-6**). Several studies have assessed the Qov with different designs of CLs. Fernandes *et al.* (2018) evaluated the QoV for multifocal CL for presbyopia correctionand compared it with a monofocal CL (Biofinity Monofocal). Similarly to our study, they did not find significant changes in quality of vision questionnaire between CLs. Recently, Garcia - Marques *et al.* (2021) compared the optical and visual performance of a dual-focus contact lens used for myopia control with a single-vision contact lens of the same material and found a statistically significant difference between contact lens designs in QoV.

The accommodative response analysis showed a transient increase at LDV for Bionity (Control lens) and Bausch + Lomb CL followed by a similar reduction at day 7 (**Figure 5-4**). These changes

did not varied significantly across different target stimuli and distances between both lenses for digital devices compared the Control lens (biofinity). Logically, it would be expected to find significant differences between the lenses in the accommodative response, because the Biofinity Energys lens has been specially designed with Digital Zone Optics ™, which helps to reduce eye strain caused by the need to focus close up when using digital devices. However, in the present study this was not observed. One of the possible explanation of theses finding may be f the limited sample size, which was not powered enough to detected the statically difference between lenses. In addition to this, the limited add power in the optical zone (approximately 0.25D) of the Biofinity Energys and its induced spherical aberration (we found similar amounts of negative spherical aberrations for both contact lenses studied) may partly explain these findings. Several studies have assessed the accommodative response in young adults with different designs of CLs using different devices. Shen *et al.* (2019) evaluated accommodative response of different design of contact lenses using the same device. Similarly, the authors did not found any significant differences in the accommodation responses between single vision and multifocal contact lenses. Likewise, Ruiz-Alcocer *et al.* (2012) did not found significant differences in the accommodation responses between single vision and multifocal contact lenses. In contrast, Koh *et al.* (2019) assessed the accommodative response in nonpresbyopes wearing low-add contact lenses using an open-field autorefractor. They found significant differences in accommodative response between lenses, but only at 40 cm (2.5 D of stimulus) and 25 cm (4.0 D of stimulus).

Beside the accommodative response, the present work also investigated the impact of soft CLs for digital devices on the tear film and comfort. Considering tear film analysis it was seen that both CLs tested showed a significant worsening in tear film parameter compared to basilene, as both TFSQ and TFSQ Area underwent an increase with CLs (larger TFSQ and_TFSQ area values). The Auto But showed in decrease **(Figure 5-5**). The Control lens (Biofinity) showed a better performance in TFSQ Index and TFSQ area and a lower Auto Tear Break-Up Time. Interestingly, in the present study we expected that there would be differences between CLs due the difference in the designs evaluated, which could lead to differences in the tear destabilization pattern that would have consequences on the tear quality measured on the lens. Nevertheless, no statistically significant differences in the tear film parameters were found between CLs modalities at both visits. Several studies have evaluated the tear film stability with CLs using different methodologies. García-Marqués *et al.* (2021) assessed the tear film stability of two different CL with the same lens material – one dual-focus lens (MiSight) and one monofocal lens (Proclear 1-Day). Using the same metholodogy as the present study, the authors found a statistically

significant reduction in the stability of the pre-lens tear film with the dual-focus CL compared to a monofocal lens (higher TFSQ and TFSQ_area with dual-focus). There were no differences in auto TBUT between both lenses. Kopf *et al.* (2008) evaluated the tear film surface quality (TSQ) of hydrogel and the silicone hydrogel contact lenses using dynamic videokeratoscopy. The author found a significant worsening of TSQ in CLs wear compared to bare eye measurements. The study also reported no significant differences between the lens types and materials. These data and our findings suggested that the the pre-lens tear film stability may be affected by material properties of a CL.

The increase in tear instablity mentioned was accompanied by an increase in the symptomatology associetd with discomfort with CLs tested compared to baseline, but without statistically significant differeneces. This increase was approximately 30 OSDI units for Bausch+Lomb CL and 20 OSDI units for Biofinity Energys when compared to baseline score and control lens (Biofinity) across seven days of lens wear, as can see in **Figure 5-7**. Surprisingly, although there has been a considerable increase (wich it is consiedered clinically significant) in the OSDI score over seven days, no statistically significant differences were observed between lenses. Considering that Biofinity and Biofinity Energys have the same material characteristics, differences would not be expected between these lenses. However, there was a difference of 14 OSDI units between them at Day 7, which could mean that the optical design of the lenses could have a considerable impact in the physical comfort of the lens. Martínez-Alberquilla *et al.* (2020) evaluated the surface integrity and dry eye symptoms of the extended depth-offocus (EDOF) design and a conventional multifocal (MF) contact lens (CL) after 15 days of wear and did not found significance change in OSDI score between the different CLs. Likewise, Tasci *et al.* (2016) also did not found changes in the symptomatology measured with OSDI questionnaire.

Previous works have already confirmed that hydrogel CLs can suffer *in vitro* dehydration, causing a modification in lens paramaters, and consequently affect the clinical performance of CLs during wear (Efron and Brennan, 1987; Jones *et al*. 2002; González-Méijome *et al.* 2007: Nichols *et al*.2006). It has been demonstrated that materials with high level of dehydration tend to become more uncomfortable (Fonn *et al.* 1999; Pereira and Lira 2018). The present study showed that although CLs tested has differences in water content, lens designs and in surface properties of the 2 silicone-hydrogel for digital devices analyzed, both CLs showed similar profile in both *in vitro* and *ex vivo* dehydration measurements. This fact could be justified because both contact lenses are silicone hydrogel. Previous

studies have demonstrated that silicone-hydrogel CLs suffer less dehydration that others and that materials with high hydration may not have a higher rate of dehydration (González-Méijome *et al.* 2007: Nichols *et al.*2006).

This study has several limitations that need to be acknowledged. One of the main limitations is the small sample size, associated with a significant drop-out rate during the follow-up visits (approximately 50% of subjects enrolled droped out at visit 2), and thus should may interfere with the power and effect size of the findings or cause an error type 1 or 2. This means that our results should be considered as a pilot study. Nevertheless, we believe that the findings of current study enhance current knowledge by providing reasonable estimates of some possible trends which must be confirmed with larger samples.

The nature of study design (comparative clinical trial, single blinded, crossover, and prospective design and with scheduled follow-up appointment) is one of the strengths of the study. To the best of our knowledge, this is the first comparative study addressing the long-term changesof two novel CL for digital devices in the objective measurements - visual performance, accommodative response, ocular aberrations, as well as tear film parameters, dehydration (in vitro and ex vivo) - and subjective measurements - LD, QoV and OSDI at the same time over seven days of wear.

Chapter 7

Conclusion and Future Work

Avelino Nelson F. Mazuze

7. CONCLUSIONS

The present work addressed the impact of different designs of CLs for digital device on visual performance, accommodative response, tear film and dehydration in normal youg adult subjects. The main conclusions of this pilot study can be summarized as follow:

- Contact lenses tested did not show significant differences compared to the Control lens in parameters of HCVA and LCVA.

- Aaccommodative response did not varied significantly across different target stimuli and distances for both contact lenses tested compared the Control lens.

- Both CLs tested can change the tear film parameters (comparing to the Control lens), as both test CLs had higher TFSQ scores.

- All the three CLs evaluated induced a small amount of negative spherical aberration (specialy the two lenses intended for use with digital devices) which could be attributed to lens design (aspheric optics);

- Both CLs intended to be prescribed for use with digital devices induced small changes in different indices (size and regularity) of the light disturbance in both monocular and binocular condition compared to Control lens;

- The comfort rate score showed clinically significantly increase for both CLs for digital devices when compared to control lens (Biofinity). However, this increase was not statistically significant. This possible decrease in comfort ratings (higher OSDI Scores) with the CLS tested after 7 days of lens wear observed in the present study should be considered before fitting those CLs.

8. FUTURE WORK

From the results and conclusions obtained in this study, the following topics could be further studied:

- Conduct studies involving this type of lenses and the same methodology with a larger sample in order to confirm the possible changes on visual performance, accommodative response, tear film and dehydration.

- To carry ot studies involving subjects with CVS using the same parameters already evaluated in this thesis, to determine the efficacy of these CLs in the relief of the symptoms commonly associated with CVS in visual performance and accommodative response;

- To evaluate the contrast sensitivity function (CSF) in order to analyze effect of soft contact lenses for CVS on visual performance in young adult subjects;

- To evaluate the accommodative response with another type of accommodation test, such as Badal system in both monocular as well as binocular conditions;

- To evaluate the electrophysiological activity of the retina and visual cortex in subjects with CVS and other forms of visual discomfort and investigate the potential relationship with the visual symptoms.

"The future for contact lenses remains bright"

Lyndon W Jones. In Superficie Ocular y Lentes de Contacto.

Preface

9. BIBLIOGRAPHY

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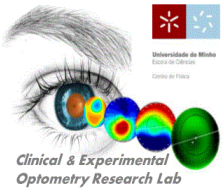
10.APPENDIX 1: Consent Form signed by every participant in this thesis project



Voluntário _____

2020

DOCUMENTO DE CONSENTIMENTO INFORMADO

No âmbito da Tese de Mestrado em Optometria Avançada, na Universidade do Minho, com o tema "**Visual Performance, Accommodative Response and Dehydration of Soft Contact Lenses for Computer Vision Syndrome and Digital Eyestrain in young adult subjects"**, a decorrer no Laboratório de Investigação de Optometria Clínica e Experimental (CEORLab) da Universidade do Minho, o presente documento tem como objetivo informá-lo sobre o procedimento, exames que serão realizados, riscos e benefícios inerentes ao estudo para o qual irá participar, bem como sobre os obter o seu consentimento para a realização do estudo em causa.

O presente documento e os procedimentos a que dizem respeito enquadram-se na "Declaração de Helsínquia" da Associação Médica Mundial (Helsínquia 1964; Tóquio 1975; Veneza 1983; Hong Kong 1989; Somerset West 1996 e Edimburgo 2000, Seul 2008).

Hoje em dia, muitas pessoas passam horas e horas todos os dias na frente da tela do computador, telemóveis e tabletes. O esforço que os nossos olhos fazem ao se concentrarem por muito tempo na frente da tela e o tipo de luz que estes dispositivos emitem pode afetar a saúde dos olhos. Os tipos de efeitos decorrentes do uso prolongado incluem redução da taxa de pestanejo, secura, irritação, vermelhidão, fadiga ocular e visão desfocada, entre outros. Para pessoas que usam lentes de contato, esse efeito pode ser ainda mais significativo. Para minimizar esses efeitos, existem atualmente lentes de contato com propriedades mecânicas e ópticas que pretendem proporcionar o alívio dos sintomas associados ao uso destes dispositivos.

A presente investigação tem o objetivo de avaliar a eficácia destas lentes de contacto no alívio dos sintomas associados com a Síndrome Visual de Computadores. Portanto, pretende-se avaliar a

performance visual, resposta acomodativa, desidratação e a qualidade ótica de duas novas lentes de contacto (Biofinity Energys; Ultra Baush Lomb e Biofinity Monofocal – como lente de controlo) para Síndrome Visual do Computador em sujeitos jovens adultos expostos a esforço visual intenso nas condições descritas.

O estudo terá duração de aproximadamente 3 semanas e o procedimento experimental será realizado no Laboratório de Investigação em Optometria Clínica e Experimental (CEORLab), do Centro de Física da Universidade do Minho e, consistirá na avaliação da acuidade visual, acomodação, estabilidade lacrimal medida com um topógrafo corneal e desidratação com 3 lentes de contacto de diferentes desenhos em ambos os olhos. Cada procedimento terá uma duração no máximo de 20 minutos e será feito nos dois olhos (monocular e binocular). Para tal usar-se-ão os seguintes instrumentos:

- **Acuidade Visual:** é um exame não invasivo que expressa a capacidade de descriminar formas (pequenos detalhes), ou seja, letras com alto e baixo contraste. É um teste monocular, onde o paciente fica sentado, com o olho esquerdo tapado e pede-se para que olhe para a tabela e leia as letras até onde consegue ver. Serão realizadas medidas com escalas de alto e baixo contrastee contraste inverso. As medidas serão feitas a cada olho separadamente e a ambos os olhos simultaneamente (condições binoculares)

- **Aberrometria**: é um exame monocular, não invasivo em que o paciente permanece sentado fixando um alvo de luz de cor vermelha (letra E) que mede as aberrações óticas do olho, a partir de um feixe de laser infravermelho, focado na retina. O exame tem uma duração de 5 mints e serão feitas duas medidas para cada olho.

- **Distorção luminosa**: medida do espalhamento de uma fonte de luz brilhante contra um fundo escuro realizado a cada um dos olhos, e ambos os olhos (binocularmente).

- **Topografia**: medida da curvatura da superfície anterior da lente de contacto durante 30 segundos pra avaliar a estabilidade do filme lacrimal disposto à frente da lente.

- **Auto refratómetro:** é uma técnica não invasiva que permite determinar a resposta acomadativa quando se afasta ou se aproxima um objeto do paciente em condições monoculares e binoculares. As medidas serão realizadas em ambos os olhos (direito e esquerdo). Após o registo dos valores iniciais com a correção habitual do paciente, serão realizadas novamente medições após duas

situações distintas na seguinte ordem: Paciente com lentes de +2,50D durante 3 minutos, a utilizar o seu telemóvel a uma distância de trabalho de 20cm; Paciente com lentes de -2,50D

Cada voluntário utilizará as 3 lentes descritas no estudo em ordem aleatória, durante uma semana. Por questões metodológicas não sendo informado de qual será a lente a usar em cada momento pelo que se por algum motivo for preciso identificar a lente, deverá contatar a equipa de investigação. As medidas supramencionadas serão obtidas antes de iniciar a participação no estudo para caraterizar o estado refrativo e de saúde ocular de cada voluntário, e no final de um período de 5 a 7 dias tendo usado a lente.

Reações adversas

As reações adversas resultantes do uso de lentes de contacto para Síndrome Visual de Computador serão as mesmas do uso de lentes normais, e incluem: ardor, prurido e/ ou sensação de picada nos olhos, desconforto, sensação de corpo estranho nos olhos, vermelhidão do olho, aumento do lacrimejar, secreções oculares anormais, deficiência visual, visão turva halos à volta dos objetos, sensibilidade à luz (fotofobia) e secura ocular. Em casos pouco raros poderá acontecer inflamação ou infeção da superfície do olho o que poderá provocar supuração ocular, dor, sensação de corpo estranho no olho, fotofobia, perda da visão entre outras.

Em casos de verificar um dos sinais acima descritos durante o estudo é importante que informe o investigador.

Condições de confidencialidade e financeiras

Antes e durante todo o processo do referido estudo, o participante poderá entrar em contacto com os investigadores a fim de obter qualquer esclarecimento que possa advir.

Os resultados da investigação poderão ser tratados estatisticamente e publicados com propósitos pedagógicos e científicos, mantendo sempre o anonimato do voluntário.

Não há quaisquer custos envolvidos para o voluntário pela participação neste estudo, nem pagamentos ou gratificações que lhe sejam devidas pela mesma participação.

A participação no estudo é voluntária podendo desistir a qualquer momento, sem que essa decisão tenha qualquer tipo de consequência.

Coloque as iniciais do seu 1º e último nome à frente de cada afirmação se concordar com a mesma:

Li e compreendi este documento;

Foi-me prestada a informação necessária, e foi igualmente dada oportunidade de colocar qualquer questão, tendo sida respondida de modo satisfatório; _____

Concordo em que seja realizado o procedimento, que consiste na colocação de 3 tipos de lentes de contacto para Síndrome Visual de Computador, com desenhos distintos, e a posterior execução dos exames descritos anteriormente; _____

Compreendo que posso recusar, a qualquer momento, participar neste estudo sem qualquer tipo de consequências; _____

Concordo em que os dados obtidos sejam utilizados de forma anónima para fins científicos e/ou académicos que a equipa investigadora considerar apropriados. _____

Braga, _____ de _____ de 2020

Assinatura do participante_____

Assinatura do investigador_____

Atenciosamente

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11. APPENDIX 2 - Tables of values described throughout the dissertation project.

Table 11-1 – Comparison of High and Low Contrast Visual Acuity with the three types of contact lenses fitted.

Measurement	Contact Lens	LDV	Day 7	*p-valeu*[1]
HCVA Monocular	Biofinity	-0.10±0.04	-0.09± 0.06	*p=0.285**
	Biofinity Energys	-0.08±0.03	-0.07±0.04	*p=0.317**
	Ultra Bausch Lomb	-0.10±0.04	-0.10±0.00	*p=0.655**
***p-valeu*[2]**		*p=0.779*†	*p=0.549*†	
LCVA Monocular	Biofinity	0.04±0.05	0.07±0.07	*p*=0.157 *
	Biofinity Energys	0.04±0.05	0.08±0.06	*p*= 0.083 *
	Ultra Bausch Lomb	0.05±0.05	0.08±0,06	*p*= 0.157 *
***p-value*[2]**		*p=0.717*†	*p=0.819*†	

LDV – lens dispensing visit after more than 15 minutes of lens wear; *p-valeu*[1] – differences between visits for each lens; *p-valeu*[2] – Differences between lenses for each visit; (†)Friedman test and Bonferroni post hoc test.; (*) Wilcoxon; statistically significant differences between contact lenses modalities highlighted in bold.

Table 11-2 – Comparison of Light disturbance with the three types of contact lenses fitted.

Parameter	Contact Lens	LDV	7 days	*p-value*[i]
LDI Mon (%)	Biofinity	5.18±2.24	6.49±2.76	*p=0.416**
	Biofinity Energys	6.20±3.25	5.69±1.23	*p=0.735**
	Ultra Bausch Lomb	8.17±2.89	5.60±1.40	*p=0.063**
p-valeu[ii]		*p=0.341*[†]	*p=0.964*[#]	
LDI Bin (%)	Biofinity	4.40±1.09	4.06±1.75	*p=0.138**
	Biofinity Energys	4.34±1.68	3.91±0.30	*p=0.599**
	Ultra Bausch Lomb	3.89±0.72	4.96±1.61	*p=0.068**
p- value[ii]		*p= 0.504*[†]	*p=0.084*[#]	
BCF IrregSD Mon (mm)	Biofinity	2.16±2.05	2.34±1.65	*p=0.917**
	Biofinity Energys	2.21±1.65	3.45±1.05	*p= 0.128**
	Ultra Bausch Lomb	3.57±0.74	3.45±1.05	*p= 0.866**
p-value[ii]		*p= 0.135*[#]	***p=0.028***[#]	
Post hoc test		X	Biofinity vs Ultra Biofinity vs Energys	
BCF IrregSD Bin (mm)	Biofinity	1.73±1.64	1.89±1.86	*p=0.500**
	Biofinity Energys	1.93±1.80	1.05±1.34	*p=0.293**
	Ultra Bausch Lomb	1.57±1.55	1.83±1.73	*p=0.465**
p-value[ii]		*p= 0.623*[†]	*p=0.554*[#]	
BCF Irreg Mon (mm)	Biofinity	0.22±0.30	0.36±0.32	*p=0.345**
	Biofinity Energys	0.37±0.27	0.43±0.34	*p= 0.499**
	Ultra Bausch Lomb	0.39±0.21	0.37±0.29	*p= 0.799**
p-value (DBLFV)		*p= 0.341*[†]	*p=0.772*[†]	
BCF Irreg Bin (mm)	Biofinity	0.16±0.22	0.16±0.20	*p=1.00**
	Biofinity Energys	0.17±0.20	0.17±0.22	*p=0.917**
	Ultra Bausch Lomb	0.17±0.17	0.11±0.17	*p=0.461**
p-value[ii]		*p= 0.854*[†]	*p=1.93*[†]	

Mon – Monocular; Bin - binocular; LDV – lens dispensing visit after more than 15 minutes of lens wear; *p-valeu*[i] – differences between visits for each lens; *p-valeu*[ii]; (†) Friedman test and Bonferroni post hoc test.; (*) Wilcoxon; Statistically significant differences between contact lenses modalities highlighted in bold. X—non-statistically significant differences with a pair-by-pair comparison.

Table 11-3 – Comparison of aberrotric data with the three types of contact lenses evaluated.

	Contact Lens	LDV	Day 7	*p-value*[1]
Astig Obli (μm)	Biofinity	0.03±0.20	0.04±0.16	*p=0.063**
	Biofinity Energys	0.01±0.24	0.01±0.18	*p=0.866**
	Ultra Bausch Lomb	0.08±0.19	0.09±0.17	*p=0.063**
p-value[2]		***p=0.012***[3]	*p=0.386*[4]	
Post hoc test		Biofinity vs Energys	X	
Defocus (μm)	Biofinity	-0.09±0.50	0.03±0.53	*p=0.176**
	Biofinity Energys	0.11±0.28	0.29±0.58	*p=0.237**
	Ultra Bausch Lomb	-0.09±0.30	0.24±0.45	*p=0.612**
p- value[2]		*p= 0.102*[3]	*p=0.180*	
Vertical Astig (μm)	Biofinity	0.11±0.15	0.12±0.15	*p=0.865**
	Biofinity Energys	0.16±0.16	0.10±0.19	*p= 0.173**
	Ultra Bausch Lomb	0.101±0.21	0.09±0.18	*p= 0.499**
p-value[2]		*p=0.651*[3]	*p=0.652*[4]	
Vertical_COMA (μm)	Biofinity	0.06±0.09	0.07±0.06	*p=0.612**
	Biofinity Energys	0.05±0.09	0.04±0.07	*p=1.00**
	Ultra Bausch Lomb	0.02±0.07	0.06±0.05	*p=0.091**
p-value[2]		*p=0.651*[3]	*p=0.276*[4]	
Horizontal_COMA (μm)	Biofinity	-0.01±0.07	- 0.02±0.05	*p=0.866**
	Biofinity Energys	-0.08±0.04	-0.07±0.04	*p= 0.612**
	Ultra Bausch Lomb	-0.07±0.04	-0.09±0.04	*p= 0.310**
p-value[2]		***p= 0.034***[3]	*p=0.772*[3]	
Post hoc test		Biofinity vs Ultra Biofinity vs Energys	X	
SH_4th (μm)	Biofinity	0.00±0.51	-0.01±0.05	*p=0.063**
	Biofinity Energys	-0.02±0.06	-0.03±0.05	*p= 0.866**
	Ultra Bausch Lomb	-0.04±0.04	-0.04±0.05	*p= 0.735**
p-value[2]		***p= 0.050***[3]	*p=0.066*[3]	
Post hoc test		Biofinity vs Ultra		
SH_6th (μm)	Biofinity	-0.004±0.01	-0.00±0.01	*p=1.000**
	Biofinity Energys	0.001±0.01	-0.01±0.01	*p=0.063**
	Ultra Bausch Lomb	-0.01±0.17	.-0.01±0.01	*p=0.310**
p-value[2]		*p= 0.156*[3]	***p=0.02***[3]	
Post hoc test		X	Ultra vs Energys Ultra vs Biofinity	
RMS_SA (μm)	Biofinity	0.04±0.02	0.05±0.03	*p=0.083**
	Biofinity Energys	0.06±0.03	0.06±0.03	*p=0.735**
	Ultra Bausch Lomb	0.06±0.03	0.06±0.03	*p=0.866**
p-value[2]		*p= 0.565*[3]	*p=0.368*[4]	
RMS_COMA (μm)	Biofinity	0.12±0.04	0.11±0.03	*p=0.612**
	Biofinity Energys	0.13±0.03	0.12±0.02	*p=0.398**
	Ultra Bausch Lomb	0.12±0.02	0.13±0.04	*p=0.612**
p-value[2]		*p= 0.651*[3]	*p=0.867*[3]	
RMS_Astig Sec (μm)	Biofinity	0.04±0.04	0.05±0.02	*p=0.310**
	Biofinity Energys	0.04±0.03	0.04-±0.03	*p=0.735**
	Ultra Bausch Lomb	0.04±0.02	0.05±0.01	*p=0.128**
p-value[2]		*p= 0.651*[3]	*p=0.368*[3]	
RMS_Trefoil (μm)	Biofinity	0.14±0.06	0.14±0.04	*p=1.000**
	Biofinity Energys	0.13±0.06	0.15±0.06	*p=0.398**
	Ultra Bausch Lomb	0.15±0.08	0.13±0.05	*p=0.398**
p-value[2]		*p= 0.2765*[3]	*p=0.651*[3]	
RMS_HOA (μm)	Biofinity	0.22±0.04	0.22±0.03	*p=0.866**
	Biofinity Energys	0.23±0.04	0.23±0.07	*p=0.735**
	Ultra Bausch Lomb	0.23±0.07	0.23±0.04	*p=0.866**
p-value[2]		*p= 0.867*[3]	*p=0.565*[3]	
RMS_Total (μm)	Biofinity	0.53±0.29	0.53±0.32	*p=0.735**
	Biofinity Energys	0.49±0.13	0.64±0.36	*p=0.237**
	Ultra Bausch Lomb	0.47±0.15	0.55±0.29	*p=0.612**
p-value[2]		*p= 0.867*[3]	*p=0.276*[3]	

LDV– lens dispensing visit after more than 15 minutes of lens wear; *p-valeu*[i] – differences between visits for each lens; *p-valeu*[e]; (†) Friedman test and Bonferroni post hoc test; (*) Wilcoxon; statistically significant differences between contact lenses modalities highlighted in bold. X—non-statistically significant differences with a pair-by-pair comparison.

Table 11-4 - Comparison of tear film analyses with the three types of contact lenses fitted.

Parameters	Contact Lens	LDV	Day 7	*p-value*[e]
TFSQ (%)	Biofinity	0.28±0.08	0.31±0.14	*p=0.612**
	Biofinity Energys	0.33±0.17	0.34±0.18	*p=1.00**
	Ultra Bausch Lomb	0.32±0.11	0.35±0.06	*p=0.612**
p-valeu[i]		*p=0.156*[†]	*p=0.651*[†]	
TFSQ Area (%)	Biofinity	28.67±13.06	29.81±16.80	*p=0.735**
	Biofinity Energys	31.91±15.49	32.77±19.80	*p=0.866**
	Ultra Bausch Lomb	31.40±11.15	33.67±10.62	*p=0.866**
p- value[e]		*p= 0.254* [†]	*p=0.341*[†]	
Auto BUT (s)	Biofinity	3.00±0.58	3.17±0.94	*p=0.446**
	Biofinity Energys	3.67±1.38	4.97±3.02	*p= 0.463**
	Ultra Bausch Lomb	3.91±1.30	3.05±1.10	*p= 0.237**
p-value[e]		*p=0.254*[‡]	*p=0.341*[†]	

LDV– lens dispensing visit after more than 15 minutes of lens wear; *p-valeu*[i] – differences between visits for each lens; *p-valeu*[e]; Statistically significant differences are presented in bold; (†)Friedman test and Bonferroni post hoc test.; (*) Wilcoxon.

Table 11-5 –Comparison of QoV with three types of contact lenses fitted.

Subscales	Contact Lens	LDV	Day 7	*p-value*[j]
Frequency	Biofinity	37.00±13.94	43.14±6.54	*p=0.293**
	Biofinity Energys	37.00±13.94	43.14±6.54	*p=0.293**
	Ultra Bausch Lomb	44.14±22.37	52.00±7.61	*p=0.345**
p-valeu[g]		*p=0.819*[h]	*p=0.276*[i]	
Severity	Biofinity	32.14±10.55	34.14±5.01	*p=0.735**
	Biofinity Energys	32.14±10.55	34.14±5.01	*p=0.735**
	Ultra Bausch Lomb	35.86±17.32	42.57±6.39	*p=0.352**
p- value[e]		*p= 1.00*[†]	*p=0.069*[f]	
Bothersome	Biofinity	29.29±11.42	30.43±9.81	*p=0.833**
	Biofinity Energys	29.29±11.42	30.43±9.81	*p= 0.833**
	Ultra Bausch Lomb	32.29±20.10	40.14±11.62	*p= 0.344**
p-value[e]		*p= 1.00*[d]	*p=0.069*[f]	

LDV– lens dispensing visit after more than 15 minutes of lens wear; *p-valeu*[j] – differences between visits for each lens; *p-valeu*[c]; Statistically significant differences are presented in bold; (†)Friedman test and Bonferroni post hoc test.; (*) Wilcoxon.

Table 11-6 - Comparison of OSDI score with three types of contact lenses fitted.

OSDI	Contact Lens	LDV	Day 7	*p-valeu*
Total Score	Biofinity	23.83±24.07	27.91± 15.43	*p=0.499**
	Biofinity Energys	22.86±21.53	42.33±18.38	*p=0.128**
	Ultra Bausch Lomb	29.15±17.78	60.87±29.94	*p=0.655**
p-valeu		*p= 0.852*[†]	*p=0.180*[†]	

OSDI – the Ocular Surface Disease Index; LDV– lens dispensing visit after more than 15 minutes of lens wear; *p-valeu*[j] – differences between visits for each lens; *p-valeu*[c]; Statistically significant differences are presented in bold; (†)Friedman test and Bonferroni post hoc test.; (*) Wilcoxon.

Table 11-7 - Comparison of in vivo dehydration each lens according to power and day of measurements.

Contact lens	CL power (D)	Days	Mean ± SD	*p*-value*
Biofinity Energys	-1.50D	after three days	-11.77 ± 2.55	0.984
	-3.00D		-11.85 ± 2.71	
Biofinity Energys	-1.50D	Day 1	-11.77 ± 2.55	0.782
	-3.00D		-12.85 ± 2.89	
	-1.50D	Day 2	-11.54 ± 2.58	0.752
	-3.00D		-10.38 ± 2.51	
	-1.50D	Day 3	-12.85 ± 2.87	0.908
	-3.00D		-12.38 ± 2.71	
Ultra Bausch & Lomb	-1.50D	after three days	-11.31 ± 2.54	0.949
	-3.00D		-11.54 ± 2.46	
Ultra Bausch & Lomb	-1.50D	Day 1	-9.77 ± 2.29	0.836
	-3.00D		-10.46 ± 2.37	
	-1.50D	Day 2	-11.92 ± 2.69	0.775
	-3.00D		-13.00 ± 2.57	
	-1.50D	Day 3	-12.08 ± 2.67	0.836
	-3.00D		-11.31 ± 2.52	
Biofinity Energys Ultra Bausch & Lomb	-1.50D	after three days	-11.85 ±2.71 -11.31 ± 2.54	0.633
Biofinity Energys Ultra Bausch & Lomb	-3.00D	after three days	-11.85 ± 2.71 -11.54 ± 2.46	0.886

Data in table are expressed as the mean ± standard deviation; D: dioptrias; CL power: contact lens power refraction.*Statistical significance when the p value was <0.05, Unpaired T-test.

Table 11-8 - Comparison of ex vivo dehydration and rehydration for contact lenses studied.

Parameter	CL	Mean ± SD	*p*-value	*Post hoc test*
Ex-Vivo Dehydration	Biofinity	-10.56 ± 2.40	0.652+	x
	Biofinity Energys	-13.22 ± 2.83		
	Ultra Bausch Lomb	-13.97 ± 2.91		
Rehydration	Biofinity	-8.17 ± 1.92	0.737+	x
	Biofinity Energys	-10.49 ± 2.42		
	Ultra Bausch Lomb	-8.84 ± 2.08		
One Eye Dehydration- RE	Biofinity	-27.81 ± 0.46	**0.001**+	Biofinity vs Energys Biofinity vs Ultra
	Biofinity Energys	-30.58 ± 0.43		
	Ultra Bausch Lomb	-44.34 ± 0.66		
Ex-Vivo Dehydration - LE	Biofinity	-29.55 ± 1.56	**0.001**+	Biofinity vs Energys Biofinity vs Ultra
	Biofinity Energys	-32.29 ± 1.81		
	Ultra Bausch Lomb	-41.01 ± 3.04		

(+) One way ANOVA and Bonferroni post hoc test. Statistically significant differences between contact lenses modalities highlighted in bold. X—non-statistically significant differences with a pair-by-pair comparison.

12. APPENDIX 3: Table of Randomization

Randomization Plan from **http://www.randomization.com**
1. ○ CONTROL ○ ENERGYS ○ ULTRA
2. ○ CONTROL ○ ENERGYS ○ ULTRA
3. ○ ULTRA ○ CONTROL ○ ENERGYS
4. ○ CONTROL ○ ENERGYS ○ ULTRA
5. ○ ULTRA ○ CONTROL ○ ENERGYS
6. ○ ULTRA ○ ENERGYS ○ CONTROL
7. ○ ENERGYS ○ CONTROL ○ ULTRA
8. ○ ULTRA ○ CONTROL

○ ENERGYS
9. ○ ENERGYS ○ CONTROL ○ ULTRA
10. ○ ENERGYS ○ ULTRA ○ CONTROL
11. ○ ULTRA ○ CONTROL ○ ENERGYS
12. ○ ULTRA ○ ENERGYS ○ CONTROL
13. ○ CONTROL ○ ULTRA ○ ENERGYS
14. ○ ENERGYS ○ CONTROL ○ ULTRA
15. ○ ULTRA ○ CONTROL ○ ENERGYS
16. ○ CONTROL ○ ULTRA ○ ENERGYS
17. ○ CONTROL ○ ULTRA

○ ENERGYS
18. ○ ULTRA ○ ENERGYS ○ CONTROL
19. ○ ENERGYS ○ CONTROL ○ ULTRA
20. ○ CONTROL ○ ULTRA ○ ENERGYS
21. ○ ENERGYS ○ ULTRA ○ CONTROL
22. ○ ENERGYS ○ ULTRA ○ CONTROL
23. ○ ENERGYS ○ ULTRA ○ CONTROL
24. ○ ULTRA ○ ENERGYS ○ CONTROL
25. ○ CONTROL ○ ULTRA ○ ENERGYS
26. ○ ENERGYS ○ CONTROL

○ ULTRA
27. ○ ULTRA ○ ENERGYS ○ CONTROL
28. ○ ENERGYS ○ ULTRA ○ CONTROL
29. ○ CONTROL ○ ENERGYS ○ ULTRA
30. ○ CONTROL ○ ENERGYS ○ ULTRA