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Visual function of novel ophthalmic lenses for the control of myopia progression

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Visual function of novel ophthalmic lenses for the control of myopia progression

Dissertação de Mestrado
Mestrado em Optometria Avançada

Trabalho efetuado sob a orientação do
Professor Doutor José Manuel González-Méijome
e do
Professor Doutor Paulo Rodrigues Botelho Fernandes

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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 falsification of results in the process of the dissertation elaboration.

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

Visual function of novel ophthalmic lenses for the control of myopia progression

ABSTRACT

Myopia, also called nearsightedness, is a refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina. Myopia progression has been alerting researchers because children with high myopia (>-6.00D) have more chances to develop ocular diseases such as glaucoma, cataract, retinal detachment, and myopic maculopathy or myopic macular degeneration. Myopia is already a public health problem and is estimated that 50% of the world population will be myopic in 2050, and 10% of those will be high myopic.

Nowadays, there are many available interventions including optical and medical methods that are reviewed in the present dissertation, all with different efficacy and safety profiles. Nevertheless, there are no standardized and 100% effective methods for controlling myopia progression. That is why more research is needed in current and new methods for myopia control to understand their impact on visual function, that will allow optometrists and ophthalmologists to implement it in their daily practice.

The main goal of the present dissertation is to analyse the visual function of a novel ophthalmic method to control myopia, called perifocal spectacle lenses, in order to obtain more knowledge of these new lenses. We analysed peripheral refraction, contrast sensitivity and light disturbance between monofocal lenses (control) and perifocal lenses (test) in seventeen participants. The sample recruited had a mean age of 24 ± 3.52 years and mean spherical equivalent of -2.80 ± 1.75D for the right eye and -2.81 ± 1.82D for the left eye.

We observed that the perifocal lenses induced a significant myopic defocus at 25 degrees of-axis, mainly in the nasal retina (induced by the temporal side of the lens). In the nasal retina of the participants, the peripheral refraction changed, on average, -0.42D in the right eye, and -0.74D in the left eye. In the temporal retina, affected by the nasal side of the lens, the differences between control and test measurements were not statistically significant. We found no statistically significant changes in the visual contrast sensitivity and in the light disturbance when subjects were using the perifocal lenses.

Keywords: Light disturbance, myopia control, ophthalmic lens, peripheral refraction, visual contrast sensitivity.

Avaliação da função visual de novas lentes oftálmicas para o controlo da progressão da miopia

RESUMO

A miopia é um erro refrativo em que os raios de luz que entram no olho paralelamente ao eixo ótico, encontram o seu foco antes da retina. A progressão da miopia tem alertado os investigadores, porque crianças com miopias elevadas (>-6.00D) têm mais probabilidade de desenvolver patologias oculares, tais como, glaucoma, catarata, descolamento da retina, e maculopatia miópica ou degeneração macular miópica. A miopia já é considerada um problema de saúde pública e estima-se que 50% da população mundial será míope em 2050, sendo que 10% destes serão altos míopes.

Atualmente, existem várias intervenções disponíveis, incluindo métodos óticos e terapêuticos, que são revistos na presente dissertação, todos com diferentes perfis de eficácia e segurança. No entanto, não existe um método padronizado e 100% eficaz para controlar a progressão da miopia. Por esta razão, é necessária mais investigação acerca de métodos atuais e novos para controlar a miopia e compreender o seu impacto na função visual, permitindo a optometristas e oftalmologistas que os implementem na sua prática clínica.

O principal objetivo desta dissertação é analisar a função visual de umas novas lentes oftálmicas para o controlo da progressão da miopia, designadas por lentes oftálmicas perifocais, de forma a obter mais conhecimento acerca destas novas lentes. Foi analisada a refração periférica, a sensibilidade visual ao contraste e a distorção luminosa entre lentes monofocais (controlo) e lentes perifocais (teste) em dezassete participantes. A amostra recrutada apresentou uma idade média de 24 ± 3.52 anos e um valor médio de equivalente esférico de -2.80 ± 1.75D para o olho direito e -2.81 ± 1.82D para o olho esquerdo.

Observou-se que as lentes perifocais induziram um desfocado miópico significativo a 25 graus fora-de-eixo, principalmente na retina nasal (induzido pelo lado temporal da lente). Na retina nasal dos participantes, a refração periférica alterou-se, em média, -0.42D no olho direito e -0.74D no olho esquerdo. Na retina temporal, influenciada pelo lado nasal da lente, as diferenças entre as medidas controlo e teste não foram estatisticamente significativas. Não foram encontradas alterações estatisticamente significativas na sensibilidade visual ao contraste e na distorção luminosa durante a utilização das lentes perifocais.

Palavras-Chave: Controlo da miopia, distorção luminosa, lentes oftálmicas, refração periférica, sensibilidade visual ao contraste.

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GLOSSARY OF TERMS & ABBREVIATIONS

7-MX: 7-methylxanthine

Add: Addition

AL: Axial Length

BCVA: Best Corrected Visual Acuity

BE: Both eyes

BFC: Best Fit Circle

$BFC_{Irreg(SD)}$: Standard Deviation of the Best Fit Circle Irregularity

BFC_{Irreg}: Best Fit Circle Irregularity

BFC_{Orient}: Orientation of the Best Fit Circle

BFC_{Rad}: Best Fit Circle Radius

cd/m^2: Candela Per Square Metre

CLs: Contact Lenses

COMET: The Correction of Myopia Evaluation Trial

D: Dioptre

DA: Disturbance Area

DIMS: Defocus Incorporated Multiple Segments

DISC: Defocus Incorporated Soft Contact Lenses

EDOF: Extended Depth Of Focus

ERG: Electroretinogram

FS: Sagittal Focal

FT: Tangential Focal

HAL: Highly Aspherical Lenslets

IOL: Intraocular Lens

J0: Astigmatic Component in the Horizontal Meridian

J45: Oblique Astigmatic Component

LD: Light Disturbance

LDI: Light Disturbance Index

LE: Left Eye

LED: Light Emitting Diode

lux: Luminous Flux Per Unit Area

M: Spherical Equivalent

MK: Microbial Keratitis

mm: Millimetres

Ortho-k: Orthokeratology

PALs: Progressive Addition Lenses

p-value: Value of the Statistical Significance

RCT: Randomized Clinical Trial

RE: Right Eye

RGP: Rigid Gas Permeable

RLRL: Repeated Low-Level Red-Light

SAL: Slightly Aspherical Lenslets

SCL: Soft Contact Lenses

SD: Standard Deviation

SER: Spherical Equivalent Refraction

SVL: Single Vision Lens

VA: Visual Acuity

VCS: Visual Contrast Sensitivity

X_{coord}: Best Fit Circle Coordinate

Y_{Coord}: Best Fit Circle Coordinate

"I never dreamed about success.
I worked for it."
(Estée Lauder)

"If I have seen further, it is by standing
on the shoulders of giants."
(Isaac Newton)

1. RESEARCH BACKGROUND

The present dissertation is divided into nine main chapters, where this first one gives a research background, that includes an introduction about what is myopia, and a literature review on the current methods for myopia control. The second chapter focuses on the aims and hypothesis of the study, while the third explains how this study was performed. The results are presented in the next chapter, followed by the discussion and main conclusions of this work. Chapter seven outlines possible future work in this field. Chapter eight presents the bibliography used in this dissertation and chapter nine contains the informed consent and record sheet employed in the study.

1.1 Introduction

Myopia, also called nearsightedness, is a refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina as shown in Figure 1.1. This can happen when the eyeball is too long from front to back (axial myopia) or when there is an excessively curved cornea and/or a lens with increased optical power (refractive myopia). Besides axial and refractive myopia, there is also a condition called secondary myopia, characterized when myopia is initiated by a specific cause that is not a recognized population risk factor for myopia development such as drug use, corneal disease, or systemic clinical syndrome. (1,2)

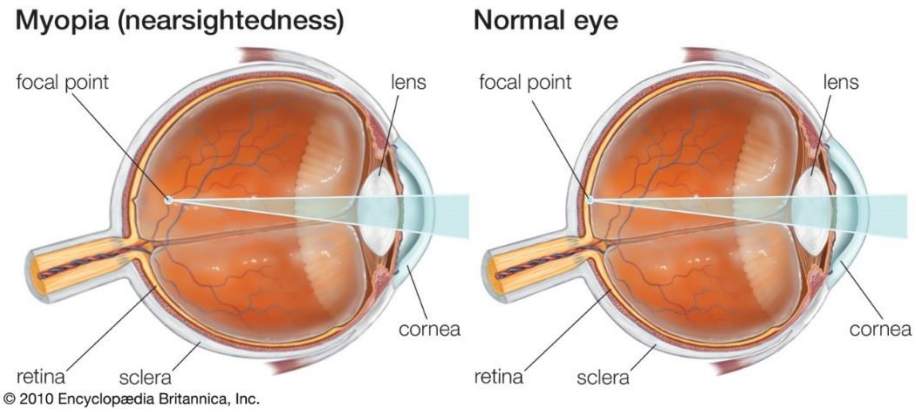

Figure 1.1- Representative image of a myopic eye in the left image where the focal point is in front of the retina, in contrast to a normal eye shown in the right image, where the focal point is in the retina. Adapted from Encyclopaedia Britannica, Inc (2010).

Myopia can be classified as low myopia when the spherical equivalent refractive error of the eye is between -0.50D and -6.00D while accommodation is relaxed, and high myopia when the spherical equivalent refractive error of the eye is higher than -6.00D with relaxed accommodation. (1,2)

In the last few years, a new classification for myopia has emerged, that included "pre-myopia" and it can be applied in the case of a child with a refractive error ≤+0.75D and >-0.50D and other quantifiable risk factors (e.g., myopic parents) that provide a sufficient likelihood of the future development of myopia to merit preventative interventions. (1,2)

Myopia can be divided by age in "school" myopia and late-onset (normally after 15 years of age). It usually progresses more between 7 and 12 years of age and begins to slow in the following years, even though this is not always true because it is influenced by many factors. (3) According to the COMET (The Correction of Myopia Evaluation Trial) study, half of the participants had their myopia stable by age 15 years, although this number increased to 77% by age 18 years and 90% by age 21 years. By age 24, almost every participant had their myopia stabilized. This study also concluded that younger onset of myopia resulted in faster progression, but the stabilization was earlier for this group, even though there was more myopia at stabilization. (4)

Many studies point out that the main risk factors for the development of myopia are education and time spent outdoors. Even though the mechanism involved in education as a risk factor is not completely understood, the visual tasks of reading and writing seem to have a large contribution to myopia progression. (5) Increasing time outdoors by 40 to 80 minutes per day can produce significant reductions in incident myopia, meaning that time outdoors can be an important factor to prevent the onset of myopia, although not to prevent myopia progression. (5) The increase in educational exposure and the decrease in time spent outdoors seems to explain the prevalence of myopia at the end of schooling in children. (6)

Another important risk factor is parental myopia, where some studies show that having one or two biological parents with myopia increases the chances of the child being myopic, with an odds ratio in 6 to 8-year-old patients of 1.4x for one parent with myopia and 2.3x for two myopic parents. (7) Kurtz et al. (2007) reported similar findings in the COMET study, where children with no myopic parents progressed in average -1.81 ± 0.18D, with one myopic parent -2.04 ± 0.13D and with two myopic

parents -2.59 ± 0.19D in the single vision group. This shows that parental refraction, and mainly myopic parents, can be highly associated with the progression of myopia. (8)

Even though these risk factors can help predict myopia onset in children, the cycloplegia spherical equivalent refractive error at a certain age is the best predictor for the onset of myopia in children. (9) In fact, a study showed that the onset of myopia can be somewhat predicted from the refractive error of a child, and if that child has one, two or non-myopic parents. We can see in Figure 1.2 that the probability of remaining not myopic decreases substantially with one or two myopic parents, as well as the refractive error is lower (hight risk was defined as having a refractive error of +0.75D or less). (10)

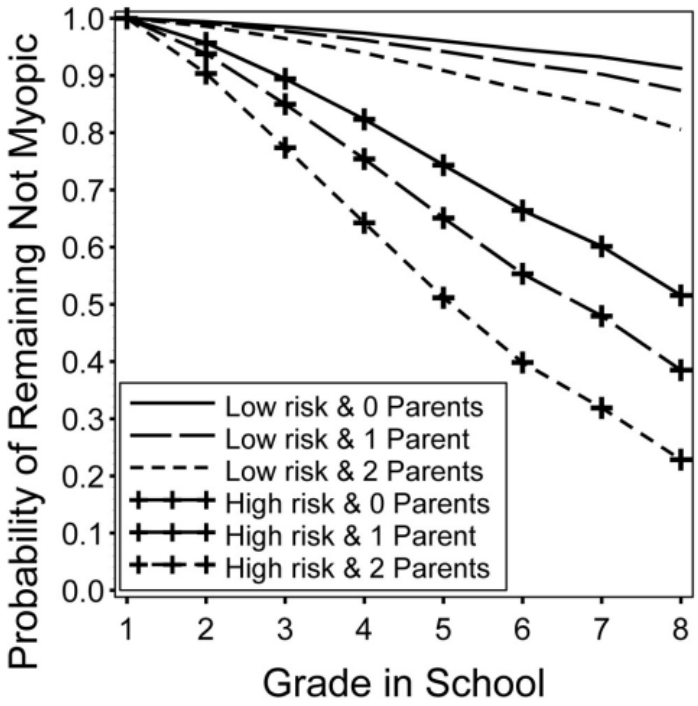

Figure 1.2- Probability of remaining not myopic with low/hight risk children, with zero, one or two myopic parents. Adapted from Jones-Jordan (2010).

The interest to predict and control myopia progression has been present for optometrists, ophthalmologists, and researchers since 1933 when the first article referring to myopia control appeared (11). Since that time, researchers are testing new strategies using optical, pharmaceutical, and environmental approaches to slow myopia progression. But why are researchers so interested in myopia control? Because people with high myopia (>-6.00D) have more chances to develop ocular diseases such as glaucoma, cataract, retinal detachment, and myopic maculopathy or myopic macular

degeneration (12). Besides refractive error, axial length (AL) is also highly associated with pathologies that can lead to visual impairment. Tideman et al. (2016) reported that eyes with an axial length of 28mm or greater, have 11 to 24 times higher risk of visual impairment than eyes with AL inferior to 24mm, for myopic patients with less than 60 years. (13)

Uncorrected myopia can result in visual impairment or blindness and substantially reduce quality of life and productivity. (14) In 2010, a study reported that uncorrected refractive error was the second major cause of blindness and the first major cause of visual impairment worldwide. In the Beijing Eye Study, the second most frequent cause of vision loss was degenerative myopia. (15,16) In fact, the impact on quality of life in high myopic patients (>10D) can be compared to patients with keratoconus. (17) Flitcroft et al. even compared the risks of myopia for the development of ocular pathologies with the increased risks of hypertension and smoking for the development of heart disease. (18)

1.2 Literature review

1.2.1 Treatments for myopia progression control

There are many strategies used for controlling myopia progression, all with different success rates. The main goal of this chapter is to review the scientific literature related to different interventions to control myopia progression. These include bifocals, progressive addition lenses (PALs), multifocal soft contact lenses, orthokeratology (ortho-k), perifocal defocusing lenses, and pharmacological agents. Environmental interventions are also considered, including the influence of indoor lighting, outdoor activities, and ergonomic habits on the onset of myopia in children. A review of innovative methods for myopia control is presented at the end of this chapter.

1.2.1.1 Optical interventions

A few years ago, some optometrists and ophthalmologists considered that under-correction of myopia was an effective option to control its progression, but in 2002 a two-year prospective study proved the contrary. (19) As well as other studies, it showed that undercorrection speeds up myopia development in myopic children, meaning that under-correction increases myopia progression. (19,20)

Evidence shows that single vision lenses (SVLs), single vision soft contact lenses (SCL) and rigid gas permeable (RGP) lenses with conventional geometries do not slow myopia progression, they just allow to maintain a good visual acuity (VA) without any significant effect on myopia progression. (21)

Progressive addition lenses were tested in the COMET study, that was designed to evaluate the differences in myopia progression between a +2.00D PAL and a single vision spectacle lens. This clinical trial demonstrated a 3-year statistically significant difference in the progression of myopia of 0.20 ± 0.08D between the two groups being considered non-clinically relevant. However, this result was considered of low clinical impact and therefore considered not worth of implementation in clinical practice. The results were consistent in terms of axial length, with a 3-year mean difference of 0.11 ± 0.03mm between the PAL and the SVL group. The treatment effect decreased after the first year with the progressive lenses. (22)

Besides progressive addition lenses, bifocal spectacles were one of the first options optometrists and ophthalmologists used to control myopia progression, but nowadays the effect of these lenses is uncertain. (23) A randomized clinical trial (RCT) conducted by Cheng in 2014, using executive bifocals and executive bifocals with a prism, concluded that these lenses were an effective option to slow myopia progression in children with high rates of progression (>0.50D), whereby prismatic bifocals provided better treatment in children with low lags of accommodation. (24) However, Prousali et al. (2019) stated that two RCTs showed no treatment effect on myopia control in 1 year with normal bifocal lenses, and three RCTs showed no treatment effect in 2 years of treatment. (25)

In 2011, Li et al. conducted a meta-analysis on the effect of multifocal lenses on myopia control, where 9 RCTs were included, 3 referring to bifocal lenses and 6 to PALs between +1.50D and +2.00D. This work presented a mean difference in the change of refraction of 0.25D for the PALs and 0.22D for the bifocals, compared to a single vision lens arm, with follow-up between 18 and 36 months depending on each study. In terms of axial length, a statistically significant difference of 0.12 mm was found, where the SVLs groups presented a greater elongation of the eye. (26)

A recent systematic review and meta-analysis conducted by Kaphle et al. (2020) evaluated the effect of multifocal spectacles over time. The results of the meta-analysis are similar to other studies, with a treatment effect of 0.21D in the first year and 0.11 mm less elongation of axial length from control to 24 months. Nevertheless, they concluded that the treatment effect of multifocal spectacles is

reduced over time, so it is not appropriate to estimate the future benefits of this treatment in the first year of use. (27)

After these conventional geometries, new lens designs emerged with myopia control's purpose. One of these was a lens manufactured by Carl Zeiss called MyoVision, designed to reduce peripheral hyperopic defocus. The treatment effect was evaluated in two studies, one in 2010 and another more recent in 2018. Both studies showed no significant treatment effect of these lenses for slowing myopia progression, either in refraction or axial length. (28,29)

Another new technology for spectacle lenses to control myopia progression in children was introduced in the past years, and it is called defocus incorporated multiple segments (DIMS), commercially available as Miyosmart by Hoya Vision Care. This technology consists of a lens with a central clear zone for distance refractive correction and 400 defocus segments surrounding the central zone with +3.5D refractive power to create myopic defocus in the retina. A 2-year double-masked randomized clinical trial was conducted in China to determine the efficacy of this spectacle lens in myopia control. This study included only Chinese children between 8-13 years old, with a spherical equivalent refraction (SER) of -1.00D to -5.00D and astigmatism and anisometropia less than -1.50D. For all 160 subjects that completed the study, DIMS lenses reduced the myopia progression by 59%, with a mean difference of -0.55±0.09D in two years, between DIMS and SVL groups. In terms of AL, DIMS had their axial elongation decreased by 60%, with a mean difference of 0.32±0.04mm in two years, compared to those wearing single vision lenses. They also included visual performance evaluation, which allowed them to conclude that these lenses provided good vision to the users, with no significant differences in visual acuity and accommodation between the control and test arms. (30)

After this 2-year RCT, the children who had worn DIMS lenses continued for another year, and the ones with the single vision lenses switched to DIMS lenses for follow-up evaluation. The treatment effect observed in the first two years of the study was sustained in the third year for DIMS group. The control-to-DIMS group had their myopia progression and axial elongation decreased in the third year compared to the first (mean difference of 0.45D and 0.21mm) and second year (mean difference of 0.34D and 0.12mm). (31)

Recently, new lenses were introduced in the market, designed to decrease myopia progression, called Stellest by Essilor. Bao et al., conducted a double-masked randomized clinical trial to evaluate

the myopia control efficacy with these spectacle lenses for 2 years. This study included 170 children between 8 to 13 years with an SER of -0.75D to -4.75D, where participants were randomized to receive single vision lenses (SVL), highly aspherical lenslets (HAL) or slightly aspherical lenslets (SAL). Compared to the SVL group, HAL slowed myopia progression by 0.80D (55%) and reduced axial length elongation by 0.35mm (51%). Children wearing SAL had their myopia progression slowed by 0.42D and less AL elongation by 0.18 mm compared to the single vision group. This demonstrates that myopia control efficacy increases with higher lenslet asphericity. They also concluded that wearing the HAL at least 12 hours per day increases myopia control efficacy to 0.99D (67%) in terms of SER and 0.41mm (60%) in terms of axial elongation. (32)

Perifocal lenses are a recently introduced ophthalmic lens with the purpose of myopia control. These lenses have a perifocal design, with a central correction zone, surrounded by an increasingly positive treatment zone on the nasal and temporal side to reduce peripheral hyperopia. An article published in 2019, reported a 5-year study with Russian children aged between 7-14 years with SER from -1.00D to -6.00D, examined with the perifocal lens. In terms of refraction, the refractive error of the perifocal group was 0.79D less myopic than the control group after 4 years of follow-up, which means a reduction of 60% in the perifocal group. In terms of peripheral refraction, 15° nasal and temporal points showed myopic defocus as well as the 30° temporal. This study has the limitation of not measuring axial length, only refractive error. (33)

Besides spectacle lenses, other available methods to control myopia progression are implemented in the field of soft contact lenses (SCL). Evidence shows that undercorrection, full correction and overcorrection with single vision SCL cause hyperopic defocus in the peripheral retina, although contact lenses (CLs) can reduce peripheral hyperopic defocus more effectively than spectacle lenses, for eyes with higher myopia. (34)

One of the first CLs used for myopia control was ACUVUE Bifocal (Johnson & Johnson, Jacksonville, FL), a lens with two different powers: one to correct far vision and another for near vision in presbyopes. In myopic children, this type of lens is used to create myopic defocus on the peripheric retina through the positive power rings. The efficacy of these lenses was evaluated in 2006, where a 1-year clinical trial reported a decrease in refractive error of 71% and a reduction in axial elongation of 79% compared to the control group. (35)

Lam et al., presented a different approach to regulate myopia progression with contact lenses, the defocus incorporated soft contact lenses (DISC). According to the authors, this is a custom-made bifocal soft contact lens that has a central correcting zone and 10 to 12 rings of alternating defocusing and correction areas until the periphery, designed to minimize spherical aberration. They did a prospective, randomized, and double-masked study with 128 children. After 2 years of study, the DISC group showed less myopia progression by 25% (mean difference of 0.20D) and had less axial length elongation of 0.11mm (31%) compared to the single vision group, however, the effect of slowing myopia progression increased with daily wearing hours of DISC. (34,35)

Another lens initially used for presbyopia correction is center-distance multifocal CLs. The design of this lens can induce myopic peripheral defocus and thus reduce myopia progression. One example of this lens is Proclear (CooperVision, Pleasanton, CA) dominant D design, that has a spherical central zone to correct distance vision surrounded by an aspheric zone of increasing addition (add) power and a spherical annular zone reaching the maximum add power. Two-year results of The Bifocal Lens Inhibition of Myopia Progression study suggest that Proclear D (add power +2.00D) can regulate up to 50% of the refractive error and 29% of the AL elongation. (36)

A meta-analysis conducted in 2022 evaluated the efficacy and safety of SCL with different add power to slow myopia progression in children. They concluded that higher add power in SCL results in higher efficacy and stabilization of myopia control progression. In addition to this, adverse events or acceptability from the participants are not related to the add power of multifocal lenses. (37)

Li et al (2017) performed a meta-analysis on contact lenses used for myopia control, where they evaluated eight studies: three concerning to concentric ring bifocal soft contact lens, and the others to peripheral addition multifocal SCL, including two concerning to peripheral gradient SCL, two to center-distance multifocal SCL and one to SCL with positive spherical aberration. The eight studies together included 587 myopic children with ages between 6 to 18 years, with a follow-up period of 10 to 24 months. SCLs with concentric ring bifocal showed an effect of 0.31D/year on slowing myopia progression and -0.12mm/year on decreasing axial elongation, compared the control, while peripheral addition multifocal SCLs showed an effect on slowing the myopia progression of 0.22D/year on refractive error and less -0.10mm/year on axial length, presenting slightly less effect than the first lenses. (38)

More recently, Sankaridurg et al., presented novel contact lenses for the control of myopia progression. A peripheral gradient lenses that have the purpose of reducing central and peripheral defocus, and an extended depth of focus (EDOF) contact lenses that aimed to improve retinal image quality for points on, and anterior to the retina, and degrade the image quality for points posterior to the retina. There were 5 groups in this study: a control group with single vision SCL, two types of peripheral lenses and two types of EDOF lenses incorporating higher order aberrations to modulate retinal image quality. The results of this study confirm that all these four contact lenses reduced the progression of myopia, compared to the single vision group, of about 24% to 32% reduction in refractive error and 22% to 32% less axial length elongation. (39)

Different bifocal lenses were used in a clinical trial conducted in 2011, called dual-focus, specifically designed for myopic children. This is a soft contact lens that has a central area to correct distance vision and a series of concentric positive areas around that. Compared to single vision lenses, the mean difference in refractive error was 0.25D and the dual-focus group had 0.11mm less axial elongation. (40)

New contact lenses for controlling myopia progression were developed by CooperVision under the commercial name MiSight. These lenses are SCL with a daily replacement that contains a large central correction area with concentric zones of alternating distance and near powers around the central area. The central area and the other correction zones have the power of the refractive error of the patient and the treatment concentric zones produce 2.00D of simultaneous myopic retinal defocus during both far and near viewing. A double-masked RCT was performed in four countries to evaluate the efficacy of MiSight lenses over 3 years, where the participants were myopic children aged 8 to 12 years old, with SER between -0.75D and -4.00D and astigmatism below 1.00D. Of the 109 subjects that completed the 3-year clinical trial, the Misight group had -0.73D (59%) less change in SER, and 0.32mm (52%) less AL elongation, compared to the control group. There were no serious ocular adverse events reported in any of the study groups. (41,42)

This study was extended for another 3 years, where children who were in the control group also started to use MiSight lenses. Eighty-five participants completed the six-year study and the MiSight lens showed a 71% efficacy in slowing myopia progression for the group that was previously the control group. The results also suggest that the dual-focus lenses continue to slow myopia progression in children who were the lenses for six years. (43)

Other recent contact lenses developed for myopia control are known as Esencia and are manufactured by Tiedra Farmacéutica (Eurolent Servicios Ópticos S.L., Madrid, Spain). These daily disposable SCL have a peripheral progressive addition/treatment of +2.00D on the front of the lens, while the back surface presents a central flattening and peripheral steeping to improve lens centration and enhance peripheral defocus. A longitudinal, double-masked RCT was performed to evaluate the efficacy and safety of the Esencia lens with children aged 7-15 years with SER between -0.50D to -8.75D. A total of 58 participants were analysed for 12 months and the mean difference in cycloplegic autorefraction was 0.29D (51%) compared to the control group, while the mean difference in axial length was 0.09mm (41%), in favour of the Esencia group. These results were obtained with a one-year study, where the effects are usually more visible, therefore these effects should not be extrapolated over the long term. There were no serious adverse events reported in this study. (44)

Other modality of contact lenses used for the control of myopia progression is called orthokeratology (ortho-k). Modern ortho-k applies highly oxygen permeable rigid lenses with reverse geometry to reshape the anterior cornea overnight. This allows patients to be temporarily corrected during the day and to regulate myopia progression in a long term. Although the exact mechanism behind the control of myopia with these lenses is unknown, many authors consider that is the myopic defocus caused on the peripheral retina by ortho-k that slows myopia progression. The effect of induced higher order aberrations has also been reported as potentially related to the therapeutic effect. (45) Because of the reserve geometry design, ortho-k creates an oblate cornea with a flattened central area that causes the image to focus on the central retina and a steeper mid-peripheral cornea that imposes a myopic defocus (the light focuses in front of the peripheral retina, reducing the image quality). (46–48)

Since ortho-k reduces temporarily myopia, axial length measurements are more reliable to evaluate the efficacy of this method. A Cochrane meta-analysis, where two studies with a total of 106 participants were included, concluded that ortho-k reduced axial elongation by 0.28mm compared to the control group. Four meta-analyses published between 2015 and 2016 showed similar results, with a two-year treatment effect between 0.25mm and 0.27mm for ortho-k groups. According to a review published in 2016, 6 different clinical trials evaluated ortho-k method between 2006 and 2012 and showed a reduction of myopia progression by 30% to 50% with ortho-k lenses, in children with ages between 8 to 12 years. (34,46,49)

Since most ortho-k wearers are children, safety is a primary concern. Adverse events related to contact lenses can be divided into serious, namely microbial keratitis (MK), or non-serious, meaning not infectious or sight-threatening, such as red eye or infiltrative keratitis. A few years ago, ortho-k was associated with a few independent cases of microbial keratitis, potentially related to poor compliance from the children. However, according to Lipson et al. (2018), there is an estimated incidence of MK with ortho-k of 7.7 per 10 000 years of wear, compared to 19.5 per 10 000 wearers for overnight use of SCL with conventional hydrogels and 25.4 per 10 000 wearers for overnight use of SCL with silicone hydrogels. Nevertheless, the majority of reported complications during ortho-k lens wear are not serious adverse events and include superficial corneal staining, lens binding, corneal microcysts, papillary conjunctivitis, and others. To guarantee the long-term success of ortho-k treatment it is important to have proper lens fitting, compliance to lens care regimen and routine follow-ups, as well as appropriate treatment of possible complications. In conclusion, ortho-k is considered one of the most effective and safe methods to correct and regulate myopia progression in children. (46,47,50)

1.2.1.2 Pharmaceutical interventions

Atropine is the most known pharmacological method used in myopia control. The efficacy and safety of this medicine have been discussed in many review studies and meta-analyses. Atropine can be administrated in different concentrations, between 1% and 0.01%, and it is a method already used in several countries for myopia control, although its optimal concentration is still unclear. Evidence shows that atropine is one of the most effective methods to control myopia progression, despite some reports of a rebound effect with higher dosage. (51) Two recent meta-analyses showed that the effectiveness of atropine is dose-related, which means that higher doses of atropine are more effective in controlling the progression of myopia than lower doses. In these two studies, 1% atropine showed less refractive error between 0.75D and 0.81D, 0.5% atropine between 0.70D and 0.89D, and 0.05% atropine between 0.54D e 0.62D, compared with the control group. In terms of axial length, 1% atropine showed less axial elongation between 0.34mm and 0.35mm, 0.5% atropine between 0.20mm and 0.23mm, and 0.05% atropine between 0.21mm and 0.25mm, in comparison with the control group, where concentrations below 0.05% (as 0.025%, 0.02% and 0.01%) had even less treatment effect than higher concentrations. (52,53)

Atropine has a few potential adverse events associated with its use, like photophobia, allergy, headache, blushing and gastrointestinal reaction, principally when used in higher concentrations. Some safety outcomes were assessed during a network meta-analysis published by Ha et al. in 2012, and they concluded that higher concentrations of atropine could tend to rise the risk of adverse events. There are some reports of a rebound effect when atropine administration stopped, with myopia progressing faster than the placebo group, mainly in higher doses of atropine, concluding that the rebound effect is closely related to the dose administrated. With all of this in consideration, these studies conclude that 0.05% atropine is likely the optimal concentration, which could slow myopia progression with minimal adverse events and rebound effect after discontinuation. (52–54)

In 2008, Trier et al. published a work referring to a pilot study using a new pharmaceutical called 7-methylxanthine (7-mx), an adenosine receptor antagonist. It was a 12-months placebo-controlled trial with a 36-month follow-up. Seventy-seven children aged between 8 to 13 years completed the 12-month study, but the results were not clinically significant, neither in axial length nor refraction. In the next 12 months of the study, all patients were treated with 7-mx, and the axial elongation was reduced in children who received 7-mx treatment for 24 months compared to those who only received it for 12 months. Even though myopia progression slowed when participants were administrated with 7-mx, it continued as the treatment stopped. These results need to be confirmed in more studies. (55)

Another pharmaceutical tested as a new method for myopia control was crocetin, introduced as dietary supplementation. Some studies showed that this natural compound of saffron could suppress experimental myopia in mice and a murine model of lens-induced myopia. Mori et al. (2019), reported a double-blind RCT with 67 participants aged 6 to 12 years, administrated with crocetin for 6 months. The mean difference between the crocetin group and the control group was 0.08D for refractive error and 0.03mm for axial elongation, in favour of the crocetin group. Even though these results are statistically significant, they are not clinically relevant. No adverse events were reported during the 6 months duration of the clinical trial. (56–58)

1.2.1.3 Environmental interventions

Environmental factors are being studied for several years, where investigators are trying to determine if time spent outdoors, indoor lighting, and near work are influencing myopia onset or

progression. Of these factors listed above, spending more time outdoors is the most effective method to prevent myopia onset in children, but not to slow the progression of existing myopia. A meta-analysis published in 2012 by Sherwin et al. stated that for an additional hour spent outdoors per week, children had a reduction in the risk of myopia by 2%. (59)

The mechanism that is preventive of myopia onset is uncertain. However, researchers hypothesized that this could happen because of the intense lighting outdoors, the decrease in near work tasks, the physical activity undertaken outside or because of the retinal image blur exposure in an outdoor environment. A recent review article stated that physical activity did not have any effect on myopia. This same study, as well as the meta-analysis mentioned above, concluded that time spent outdoors is a protective factor on myopia, with a pooled odds ratio of 0.982 per additional hour spent outdoors per week. Nevertheless, this protective factor is limited to nonmyopic children. They also concluded that excessive near work, such as continuous reading (>30min) and close reading distance (<30cm), increases the risk of having myopia. For example, a child spending four hours a day in near work at 33cm after school has 1.2X more risk of developing myopia. (59,60)

A meta-analysis performed to explore the effect of outdoor time on myopia prevention, also conclude that spending more time outdoors decreased the risk of myopia in terms of refraction and axial elongation shift. They analysed five RCTs with 3 014 participants for 9 to 36 months, and showed the results were in favour of the outdoor group, with smaller changes in SER than the control group by 0.17D in the referred follow-up months, and the axial length was also smaller for the outdoor group by -0.03mm in the same period of time. Also, new cases of myopia were fewer in the group spending more time outdoors than the control group. (61)

Investigators are trying to understand if it is possible to simulate light conditions on outdoor environments, with high indoor ambient lighting, to possible prevention on myopia development. Even though there are only a few studies in this field, one study performed in China found that increasing light in school classrooms reduced the new cases of myopia in the subsequent year. Another China-based study associated LED (Light Emitting Diode) lights with higher levels of myopia in young teenagers compared to incandescent or fluorescence lamps in near work. However, there are not yet conclusive results of these studies. (62)

Torii et al. (2017) published a research paper on the influence of violet light on myopia progression. They performed a retrospective clinical research, comparing a group of children wearing violet light blocking eyeglasses and another group wearing violet light transmitting contact lenses. The mean difference between the two groups in axial elongation was 0.08mm in one year, in favour of the violet light transmitting CLs. They also compared two types of CLs, one blocking partially violet light and another transmitting violet light. The results were also favorable for the transmitting contact lenses, with a mean difference of 0.05mm between the two groups. These results are not clinically significant but can reinforce the importance of outdoor exposure for myopia progression, where violet light is abundant. (63)

After reporting these results in children, Torii et al. (2017) did another retrospective study in adult high myopic patients wearing two types of intraocular lens (IOL), one transmitting violet light and the other blocking violet light. The results were similar to the previous study, showing that patients with the violet light transmitting IOL were less myopic than the other group. (64)

With these favorable results, Torii et al. performed an RCT in 2021, to evaluate the effect of violet light-transmitting spectacle lens on myopia progression in children aged 6-12 years. In the ninety-one children evaluated, the axial length elongation was less 0.03mm for the violet light-transmitting lens, and less refractive error of 0.11D, compared to a single-vision spectacle lens, in two years. These differences were statistically significant, only in children who never used eyeglasses before and spent less than 180min in near work. There were no adverse events reported in relation to the violet light-transmitting lens, in the course of the study. (65)

1.2.1.4 Innovative interventions

In the past few years, investigators, optometrists, and ophthalmologists are trying innovative methods to control myopia progression or prevent its onset in children. In this field, Thakur et al. (2021) investigated the potential effect of short-term exposure to different light, including blue (460nm), green (521nm) and red light (623nm) on axial length and choroidal thickness in twenty-five young adults. The results suggested an increase in axial length after red and green exposure and a decrease in choroidal thickness. In contrast, after blue light exposure, a reduction in axial length was observed, with no changes in the choroidal thickness. This work suggests that blue light can slow myopia progression by decreasing axial length, but it needs to be confirmed in larger studies. (66)

Amorim-de-Sousa et al. (2021) published another work using blue light in myopes. Dopamine effect on myopia progression has been extensively studied in the last years, therefore, in this work, blue light was used to stimulate blind-spot in order to upregulate retinal dopaminergic activity. This study was divided into three experiments. The purpose of the first was to observe the effect of blue light stimulation on the b-wave recorded in the electroretinogram (ERG) in myopic adults. The second experiment aimed to test if the previous effect was also present in the ganglionic layer recorded by pattern ERG responses, in myopic participants. The third experiment compared the retinal response after blind-spot blue light stimulation between myopes and non-myopes. The first experiment showed that the amplitude of the b-wave was larger after 20 minutes of stimulation compared to the control. The second experiment confirmed that this previous effect was also observed in the pattern ERG. The results from the last experiment indicate that the increase in both b-wave and pattern ERG was observed in myopes, but not in non-myopes participants. These findings show that is possible to induce changes in retinal electrical activity by stimulating the optic nerve with blue light. Nevertheless, future work is needed in this field to verify the influence of this effect on the dopaminergic system. (67)

Another innovative and recent work in the field of methods to control myopia progression in children is the application of repeated low-level red-light (RLRL) therapy on myopic children. A multicenter randomized controlled trial was performed between 2019 and 2020 to evaluate the efficacy and safety of this therapy, that was administrated on children between 8 to 13 years, who did two sessions per day, 5 days per week, for a total of 3 minutes per session. 246 children were evaluated, and they concluded that in one year, RLRL therapy induced differences of -0.59D for refractive error and 0.26mm for axial length, in favour of the treatment group, when comparing to a control group. There were no serious adverse events or functional visual loss reported in the one-year RCT. (68)

1.3 Research rationale and justification of the study

As mentioned in the first part of the present dissertation, myopia can lead to visual impairment and other pathologies, especially high myopias (>-6.00D). Myopia is already a public health problem, and researchers estimate that 50% of the world population will be myopic in 2050, and 10% will be high myopic of -5.00D or less. (69) Because of this, it is important for every eye care professional to implement methods to control myopia progression in their patients, mainly in children.

There are many available interventions nowadays, with different efficacy and safety profiles, but there is not a standardized and 100% effective method for controlling myopia progression. That is why more research is necessary to explore interventions for myopia control, to allow optometrists and ophthalmologists to implement it daily in their practice, also understanding their impact on visual function.

The purpose of this study is to analyse the visual function of a novel method to control myopia, called perifocal spectacle lenses, to obtain more knowledge on these lenses. We analyse peripheral refraction, contrast sensitivity and light disturbance between monofocal lenses and perifocal lenses. In this context, this dissertation seeks to answer the following research questions:

1. Do perifocal lenses induce myopic defocus in the peripheral retina of myopic eyes?
2. Do perifocal lenses decrease contrast sensitivity compared to monofocal lenses?
3. Do perifocal lenses induce light disturbance compared to monofocal lenses?

The investigation of these parameters of visual function can also provide input for future optimization of this and other devices, assessing the consequences of changing optical designs to improve their efficacy, without adverse side effects on visual function.

2. AIMS AND HYPOTHESIS OF THE STUDY

2.1 Problem formulation

Even though there is a lot more information today about what is myopia, why it progresses and how to manage that progression, as said before, there isn't a standardized clinical approach for controlling or minimizing its progression. Nevertheless, ophthalmic lenses with specific designs to control myopia progression are one of the most used methods, including the perifocal lenses used in this study. The efficacy of these lenses is already described in the literature (33) but the visual function has not been comprehensively investigated.

This work is intended to study the visual function of these lenses, in terms of how these lenses affect peripheral refraction, contrast sensitivity and light disturbance.

2.2 Hypothesis

H0: The perifocal lenses do not induce significant changes in peripheral refraction, contrast sensitivity and light disturbance.

H1: The perifocal lenses induce significant changes in peripheral refraction, contrast sensitivity and light disturbance.

2.3 Goals

The main goal of this study is to evaluate possible changes in the peripheral vision during the use of these novel lenses with a perifocal defocus design to control myopia progression.

The specific aims are the following:

- Evaluate the changes in peripheral refraction with perifocal lenses.
- Evaluate the changes in contrast sensitivity with perifocal lenses.
- Evaluate the changes in light disturbance with perifocal lenses.

3. MATERIAL AND METHODS

This chapter describes the experimental design of the study, the sample size calculation, and the sample characterization. It also summarizes the inclusion and exclusion criteria, the randomization and masking method, the lenses used in this study, the clinical methods used to obtain the measurements and the statistical analysis used in this work.

3.1 Study design

This study was an experimental, crossover study where young adult myopes wore perifocal lenses for the analysis of peripheral refraction, visual contrast sensitivity (VCS) and light disturbance (LD). These measurements were made in two different sessions, the first moment was the control measurements with monofocal lenses from the trial lens set, where immediately afterwards the patients did the same examinations with the perifocal lenses. The study was non-randomized and non-blinded.

This study was conducted at the Clinical and Experimental Optometry Research Laboratory (CEORLab) at University of Minho, School of Sciences, Braga, Portugal, between July 2022 and September 2022. Written informed consent was obtained from all the participants before enrolment and the study was performed according to the principles of the Declaration of Helsinki. This study was approved by the ethics committee of the University of Minho (CEICVS) that analysed ethics aspects about this study to help protect the rights and well-being of the participants (CEICVS number 113/2022).

3.2 Sample Size

The sample size needed to perform this study was calculated using an online calculator (http://hedwig.mgh.harvard.edu/sample_size/js/js_crossover_quant.html). Considering a statistical power of 80% of the study with a 0.05% level of significance, with a 5 minimal detectable difference in means for the less repeatable variable (light disturbance index) and a 5 units standard deviation within patients, we should have a total of 18 patients in this crossover study.

3.3 Eligibility criteria

All the participants included in this study complied with the following eligibility criteria.

3.3.1 Inclusion criteria

- Age between 18-35 years.
- Spherical refractive error <6.0D.
- Astigmatism <3.00D.

3.3.2 Exclusion criteria

- Systemic illness affecting eye health.
- Eye illness (e.g., keratoconus).
- History of previous eye surgeries.
- Anisometropia ≥1.5D.

3.4 Study lenses

The perifocal lenses used in this study have a perifocal design, meaning that they are monofocal in the center (≈10mm) to correct myopic refraction and allow a satisfactory vision to the patient, whereby have a treatment area around that, in the horizontal plane, to control myopia progression, with positive addition. As shown in Figure 3.1, the temporal side of the lenses has more positive power than the nasal side, which the manufacturer explains that happens because of the differences in profiles between the nasal and temporal peripheral retina. (70)

The lenses were delivered in the raw state by the manufacturer, so they were cut to fit a trial frame, used for the measurements. Five perifocal lenses with different power profiles were available to conduct this study: 0.00D, -1.50D, -3.50D, -5.50D and -7.50D, whereby, after the subjective refraction test, the lens with the closest correction to the refractive error of the patient refractive error was selected between the five lenses mentioned. After this, three lenses were placed in the trial frame, both in control and test measurements. The first, closer to the eye, was the spherical lens selected from the five mentioned before, the second one, in the middle, was the remaining spherical correction and the third was the astigmatic lens, to allow the total correction of the refractive error of the participant.

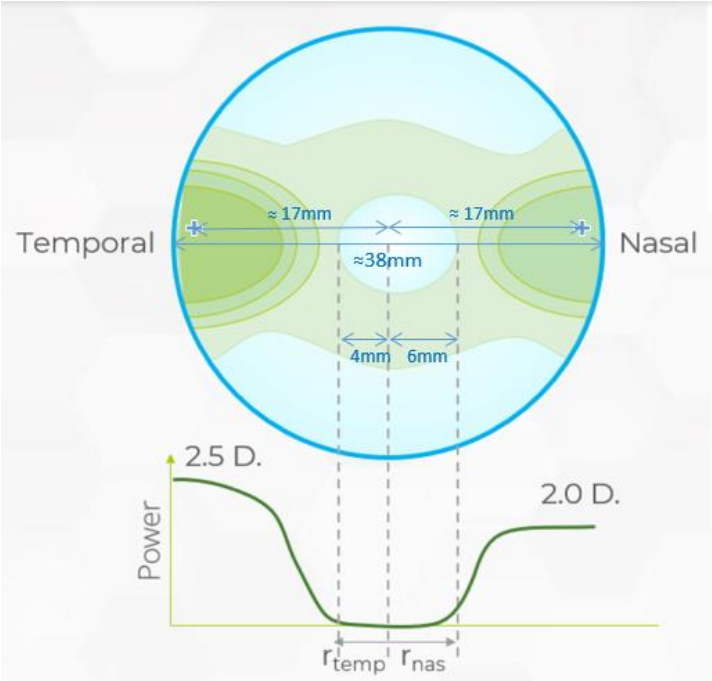

Figure 3.1- Lens design obtained from the manufacturer information brochure. This represents the lens for the right eye of the patient.

Was performed a characterization for each lens with an auto focimeter or lensmeter, in the central area, and 17mm on each side, as well as 15 mm up and down. Results are presented in Table 3.1.

Table 3.1- Characterization of the perifocal lens. Values in brackets represent the difference in spherical power (Δsphere) compared to the central measurement.

	Central	Nasal (@17mm) (Δsphere)	Temporal (@17mm)	Superior (@15mm)	Inferior (@15mm)
Plan	0	+1.25 -0.25x20° (+1.25)	+2.25 -0.50x160 (+2.25)	+0.50 -0.25x160° (+0.50)	+0.50 -0.25x40° (+0.50)
-1.50	-1.50	-0.25 -0.25x165° (+1.25)	+0.50 -0.25x175° (+2.00)	-1.25 -0.25x160° (+0.25)	-1.25 -0.25x20° (+0.25)
-3.50	-3.50	-2.25 -0.25x130° (+1.25)	-1.50 -0.25x180° (+2.00)	-3.25 -0.25x180° (+0.25)	-3.25 -0.25x150° (+0.25)

-5.50	-5.50	-4.50 -0.50x40° (+1.00)	-3.75 -0.25x150° (+1.75)	-5.25 -0.50x170° (+0.25)	-5.25 -0.50x15° (+0.25)
-7.50	-7.50	-6.50 -0.75x70° (+1.00)	-6.00 -0.50x120° (+1.50)	-7.25 -0.50x170° (+0.25)	-7.25 -0.50x10° (+0.25)

3.5 Clinical Assessments

Before any participant was submitted to the clinical exams, an informed consent form (appendix 1) was delivered and signed by each one of them. The study consisted of an hour visit for each participant, where the eligibility criteria was considered to include or not the participants. Axial length was measured with an IOL Master (Carl Zeiss Meditec, Inc, Dublin, CA), topography measured with E300 corneal topographer (Medmont International Pty Ltd., Victoria, Australia) and aberrometry measured with IRX3 wavefront aberrometer (Imagine Eyes, Orsay, France). These measurements were performed under no correction, for descriptive data of the sample. After that, it was determined the refractive error of the participant through autorefractometer and subjective measures, as well as the best corrected visual acuity (BCVA) with ETDRS chart. The control measures were obtained with the patient fully corrected. These measures included peripheral refraction, contrast sensitivity and light disturbance analyses. Thereafter, these measures were repeated with the lenses for myopia control, the test lenses.

3.5.1 Peripheral refraction

To measure the peripheral refractive error was employed an open-field autorefractor (WAM-5500, Grand Seiko Co, Lda, Hiroshima, Japan) at 2 meters from the target point. The target point was a star in the wall that allows us to measure the peripheral refractive error at 25° nasal (25N) and 25° temporal (25T), as showed in Figure 3.2. As we can see in the right image, that illustrate how the measures were obtained, when the patient was rotating his head to look at the target point at 25° of his temporal side of the left eye, the peripheral refraction of the temporal retina was measured through the nasal side of the lens. The measures were obtained monocularly, with the contralateral eye occluded and ambient light.

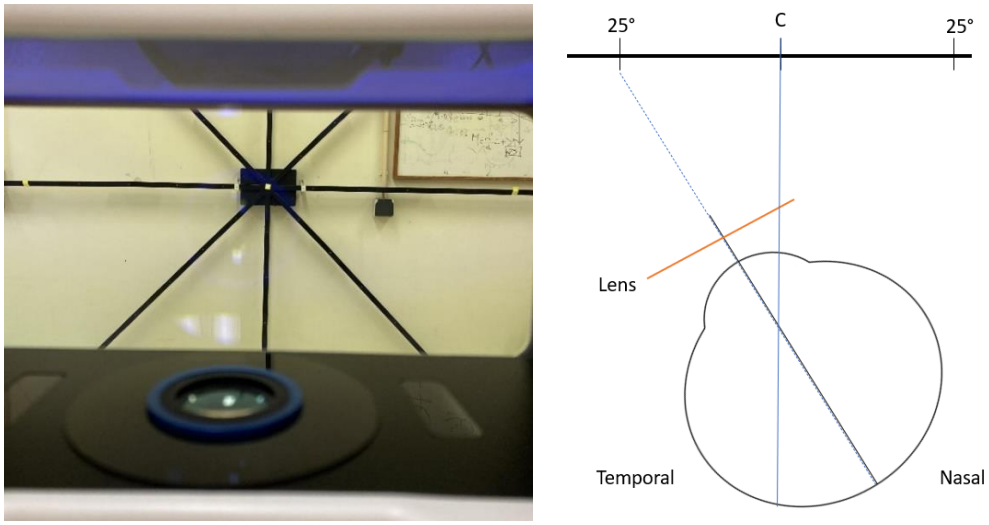

Figure 3.2- In the left there is a picture of the target point seen inside the open-field autorefractometer used in this study; in the right is represented a schematic figure of the left eye to illustrate how the peripheral refraction measurements were obtained.

Some studies showed that there were no significant differences when peripheral refractive measurements are made with eye rotation or with head rotation, so the patients were told to rotate the head to focus on the target point at 25° on each side, which allowed us to measure the peripheral refraction through the sides of the ophthalmic lenses. (71,72) The participants used a hair bow with a laser fixed in it, to aim at the three measured points while turning their heads, to make sure that the measurements were being made at 25 degrees.

To statistically analyse the refraction data, which was obtained from the autorefractor under the form Sphere Cylinder and Axis, we transformed the data into spherical equivalent (M), astigmatic component in the horizontal meridian (J0) and oblique astigmatic component (J45) according to Thibos et al (1997) (73). The first value, M, is calculated by adding half of the cylinder to the sphere (Equation 1). The second value, J0 expresses the differences between the horizontal and vertical meridian in terms of diopters, being this value negative to against-the-rule astigmatism and positive to with-the-rule astigmatism (Equation 2). The J45 describes the value from oblique astigmatism, being negative to astigmatisms whereby the negative axis is at 135° or positive to astigmatisms whereby the positive axis is at 45° (Equation 3). Below is represented in the form of an equation of how we obtained each vectorial component.

$$M = sphere\ + \frac{cylinder}{2}$$ (Equation 1)

$$J0 = -\frac{cylinder}{2} \times \cos(2\ \times axis)$$ (Equation 2)

$$J45 = -\frac{cylinder}{2} \times \sin(2 \times axis)$$ (Equation 3)

The values presented in this work for peripheral refraction are relative values, which means that the central value was subtracted for each value, M, J0 and J45. After this, the tangential and sagittal focals (F_T and F_S, respectively) were calculated using the Equations 4 and 5 represented bellow.

$$FT = M + J0$$ (Equation 4)

$$FS = M - J0$$ (Equation 5)

3.5.2 Contrast sensitivity

The contrast sensitivity was measured at three meters from Vistech system VCTS 6500 (Vistech Consultants. Dayton, Ohio, USA). We measured VCS in low lightning conditions. The luminance of the test was 15cd/m^2 determined with the Luminance Meter LS110 (Konica Minolta Sensing, Inc, Osaka, Japan) and the illuminance of the room was 29lux determined with the Illuminance Meter T10 (Konica Minolta Sensing, Inc, Osaka, Japan) to simulate the visualization under challenging conditions. This test presents different circles, each one with a determined spatial frequency and contrast. The first line, A, presents the same spatial frequency but the contrast is decreasing progressively until number 9, and this is repeated in the other lines. Column 1 has the same contrast until the letter E but the spatial frequency decreases continuously. The bars have a determined orientation as is demonstrated in the bottom of Figure 3.3, as they can be vertical, right-oriented, or left-oriented.

The patients were three meters away from the chart, at first with an occluded eye and then binocularly. It was asked the patient to say the orientation of the bars in line A until they were not seen, following lines B, C, D, and E. We registered the last circle visible to the patient and determined the contrast sensitivity for the five spatial frequencies assessed: 1.5; 3; 6; 12 and 18 cycles/degree.

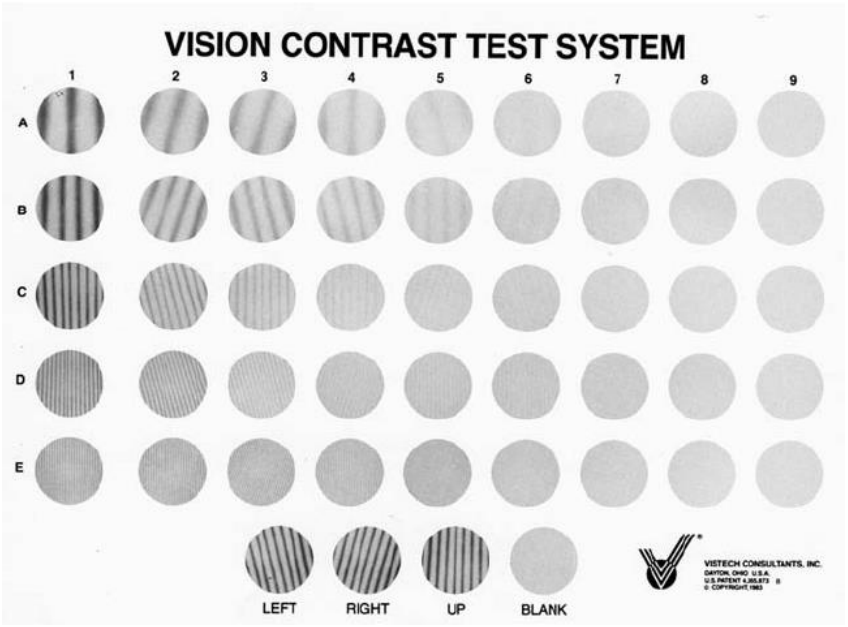

Figure 3.3 - Illustration of the contrast sensitivity chart VCTS 6500. Source: Vistech Consultants (1988)

3.5.3 Light disturbance

In this study, light disturbance was obtained from the *Light Distortion Analyzer* (LDA, CEORLab, University of Minho, Braga, Portugal), a device validated in 2015 by Ferreira-Neves et al. (74) This device has a circular electronic black board with a central light spot with high-intensity light. This central light is a LED that is surrounded by 240 smaller and less intense LEDs distributed over twenty-four semi-meridians with a minimum angular separation of 15 degrees, as demonstrated in Figure 3.4 below. The central LED is responsible for creating the glare condition while the peripheral LEDs are used as limit discriminators of that condition at separate locations in the visual field. These physical LEDs allow to measure some parameters of light disturbance under more realistic conditions. (74)

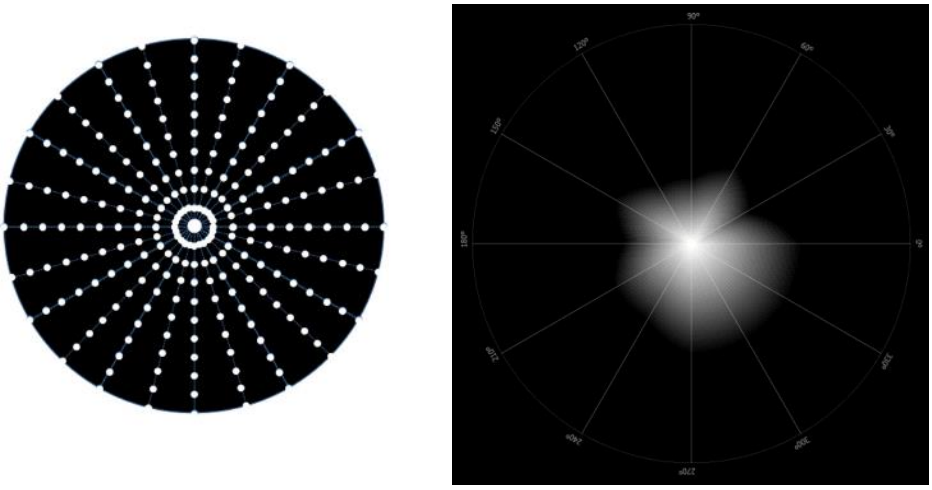

Figure 3.4- In the left there is a representative figure of LDA system, and in the right, there is a simulated image of the light disturbance of one measure, presented by LDA device.

Linhares et al. (2013) described the radiometric characterization of the central and the peripheral LEDs concluding that this device is useful in visual assessments of glare and halos. (75)

The central LED is always on, and the peripheral LEDs light up sequentially throughout the meridians while the patient presses the computer mouse button whenever she/he can identify the light of one of the peripheral LEDs. When that happens, the system presents the next semi-meridian, and the patient repeats the process. The patient is placed two meters away from the electronic board with its visual system aligned with the central LED. The exam was performed under low light conditions, and the measurements were obtained monocularly first and binocularly after, with the best distance visual correction.

This device has four different examination strategies, but in this study, we used the in-out 30° strategy, which means that the peripheral LEDs turn on sequentially from the center to the periphery in random order with an angular separation between the semi meridians of 30 degrees, meaning that are evaluated twelve of the total twenty-four meridians.

In this exam, three evaluations are performed in each meridian with approximately one minute per exam. In case the standard deviation (SD) of the three measurements is 20% above the mean, the system repeats the measurements until it obtains an SD below 20% of the mean value for each meridian. (74)

After the exam is performed, the system presents different metrics of light disturbance that are summarized below:

- Disturbance area (DA): is the sum of the areas of all sectors formed between each pair of semi-meridians under analysis, in mm^2.
- Light disturbance index (LDI): is the percentage of the total tested area that is not visible because of impairment by the light disturbance phenomena. It is estimated by the ratio of the area missed by the patient and the total area explored and is presented in percentage (%). Higher values of LDI are interpreted as the lower ability to discriminate small stimuli surrounding the central source of light.
- Best fit circle radius (BFC_{Rad}): is the radius of a circle that best fits the shape of the DA, whose value is equal to the average length of the disturbance along each semi-meridian under evaluation, and is expressed in mm.
- Best fit circle coordinates (X_{coord} and Y_{Coord}): are the Cartesian coordinates from the center of the display, presented in mm.
- Orientation of the best fit circle center (BFC_{Orient}): is the angle of the BFC center from the origin of coordinates (X_{coord} and Y_{Coord}), which corresponds to the center of the display, and is expressed in degrees.
- BFC irregularity (BFC_{Irreg}): is the sum of the deviations between the actual DA and the BFC outer perimeter along with all the semi-meridians assessed, presented in mm. It is a sum of positive and negative values as the limit of the disturbance is in or out of the BFC perimeter.
- SD of the BFC irregularity ($BFC_{IrregSD}$): is the sum of the differences squared and divided by the number of semi-meridians evaluated (n), expressed in mm. Higher values of $BFC_{IrregSD}$ means a more irregular disturbance. (72)

Figure 3.5 below presents examples of increasing values for the light disturbance index (LDI).

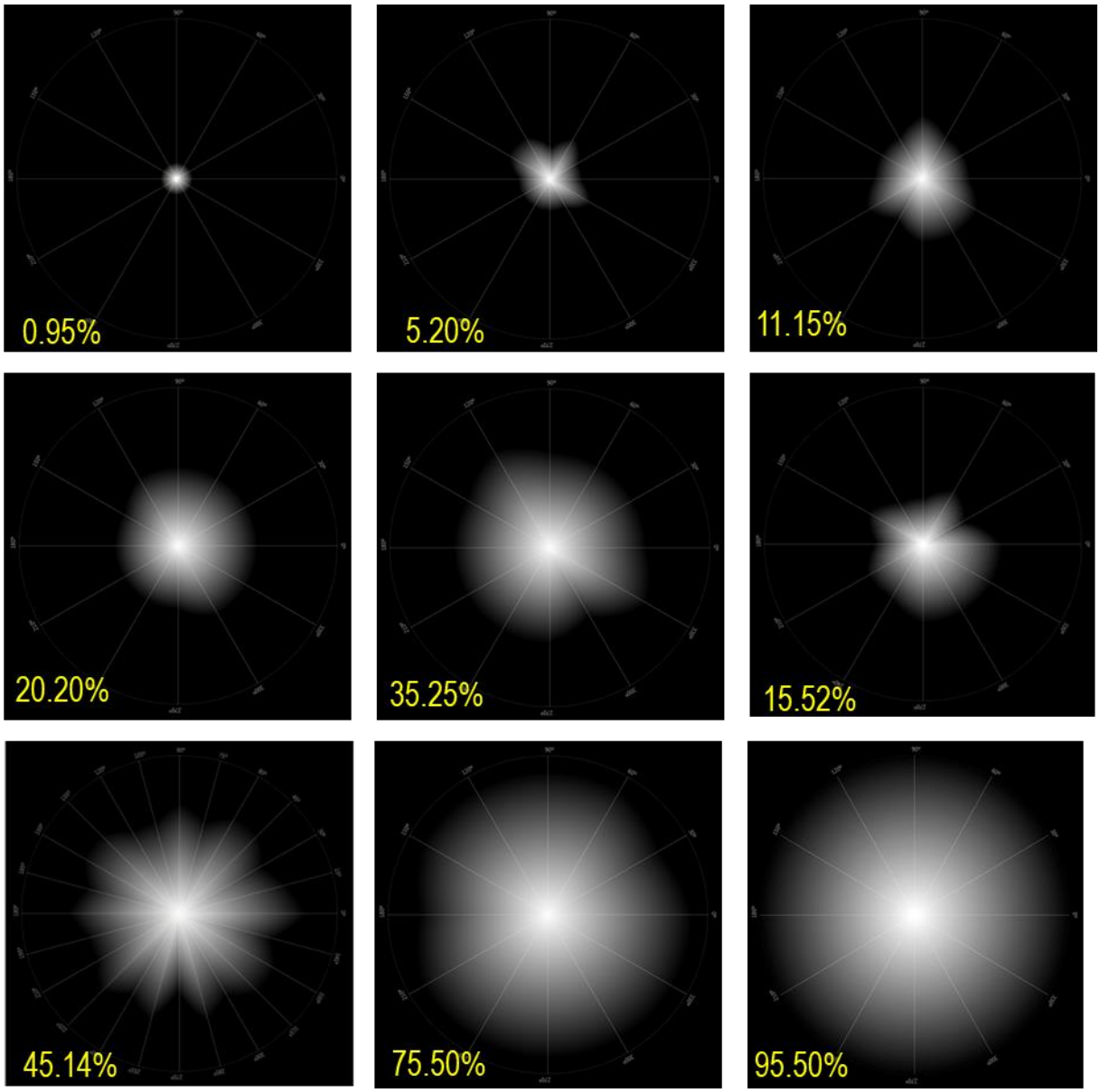

Figure 3.5- Representation of the size of the light disturbance when light disturbance index (LDI) increases from 0.95% to 95.50%.

Figure 3.6 below shows the representation of the best fit circle against the actual shape of the disturbance from which the aforementioned metrics of irregularity are calculated.

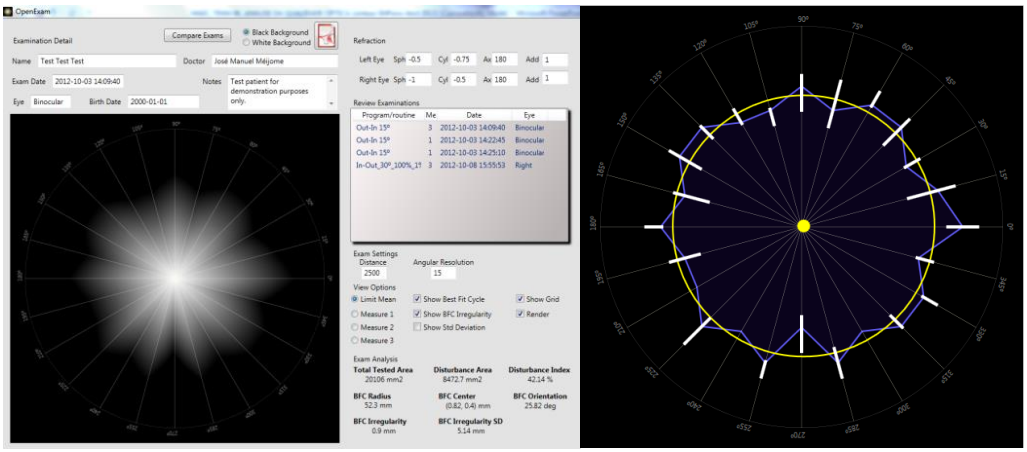

Figure 3.6- In the left there is the image provided by LDA device when measures are obtained. In the right, a representation of the Best Fit Circle against the actual shape of the disturbance measured.

In this study were analysed two metrics that allow to quantify the size of the light disturbance, LDI and BFC_{Rad}, and two metrics that evaluate the irregularity of the distortion, namely the BFC_{Irreg} and the $BFC_{IrregSD}$.

3.6 Statistical Analysis

The data extracted from the measurements were inserted and analysed in Excel, where the statistical analysis was performed with SPSS Statistic software version 29.0 (SPSS Inc, Chicago, IL). The data obtained is presented in the form of mean ± standard deviation, even when the variables did not follow a normal distribution. This choice was made because the results needed to be comparable with each other. Nevertheless, the statistical analyses were made with the parametric or non-parametric tests, according to each variable.

First of all, the normality of variables was evaluated using the Shapiro-Wilk test, since the sample was lower than 30 subjects. For testing the normality of each variable, two hypothesis were tested, the null hypothesis stating that the data follows a normal distribution, while the other stating the contrary. When the value of the statistical significance (p-value) is higher than 0.05, it means that the null hypothesis is accepted, meaning that the data follow a normal distribution, and parametric tests can be applied to perform the various comparisons. When the p-value is lower than 0.05, we reject the null hypothesis and use non-parametric tests to the analysis of this variable. With this p-value, there is the probability of rejecting the null hypothesis, when this hypothesis is correct, which is called Type I error, that is the possible error associated with the results of these work.

For the statical analysis of the differences between the test measurements (when the participants were using the perifocal lens) and the control measurements, a Paired Samples T-Test was used when the two variables followed a normal distribution, and a Wilcoxon test was used when at least one of the variables did not follow a normal distribution. Each time differences between two variables are presented, the values refer to the subtraction of the second condition (with the perifocal lens) minus the first condition (control measures). The majority of the variables were tested with non-parametric tests. When parametric tests were used, they were identified in the tables with an * in each p-value.

For the purpose of statistical analysis, a p-value lower than 0.05 was considered statistically significant.

4. RESULTS

In this chapter, the results obtained from the experimental tests are exposed. First are presented the details about the participants included in this study, in terms of their age and refractive error. After this, the results of peripheral refraction, contrast sensitivity and light disturbance are described.

4.1 Sample characterization

Were recruited to this study seventeen participants, fourteen females and three males, which means a total of 34 eyes were included in the study. To established if just one eye or both eyes of the subjects were going to be analysed for this study, we did a primary statistical analysis and found differences between right eye (RE) and left eye (LE). Therefore, both eyes (BE) of each subject were analysed. This way, we can compare the behaviour of both eyes, to see if there are any differences in the results. The characteristics of the sample in terms of age, gender, refractive error, best corrected visual acuity, axial length, aberrometry and topography parameters is shown in Table 4.1.

Table 4.1- Characteristics of the sample recruited, in terms of age, gender, refractive error, visual acuity, axial length, aberrometry and topography parameters.

Age (years)	24 ± 3.52		
Gender	14 females (82.4%) 3 males (17.6%)		
	RE	LE	BE
M (D)	-2.80 ± 1.75	-2.81 ± 1.82	
J0 (D)	-0.03 ± 0.33	0.04 ± 0.33	
J45 (D)	0.01 ± 0.17	0.05 ± 0.20	
BCVA (LogMar)	-0.03 ± 0.06	-0.03 ± 0.08	-0.12 ± 0.06
AL (mm)	24.61 ± 0.78	24.62 ± 0.89	
Máx. round pupil	6.55 ± 0.71	6.61 ± 0.83	
SA 4th-Order	0.03 ± 0.04	0.04 ± 0.03	
Vertical Coma	0.01 ± 0.15	-0.01 ± 0.11	
Horizontal Coma	0.01 ± 0.06	0.00 ± 0.06	
Spherical-like	0.04 ± 0.03	0.04 ± 0.03	
Coma-like	0.12 ± 0.11	0.11 ± 0.06	
HOA	0.17 ± 0.11	0.16 ± 0.06	
Qmean	-0.17 ± 0.32	-0.18 ± 0.33	
SIM Kmean (mm)	44.24 ± 1.12	44.32 ± 1.19	
IS index (D)	-0.21 ± 0.42	-0.08 ± 0.64	
SRI	0.44 ± 0.10	0.43 ± 0.11	
SAI	0.48 ± 0.13	0.54 ± 0.30	

Figure 4.1 shows the distribution of the sample by age, and Figure 4.2 the distribution of the central refractive error in both eyes. As we can see both, the average age of the seventeen participants is 24 ± 3.52 years, and the mean spherical equivalent (M) is -2.80 ± 1.75D for the right eye and -2.81 ± 1.82D for the left eye, where most of the participants have their refractive error between -1.00 and -2.00D.

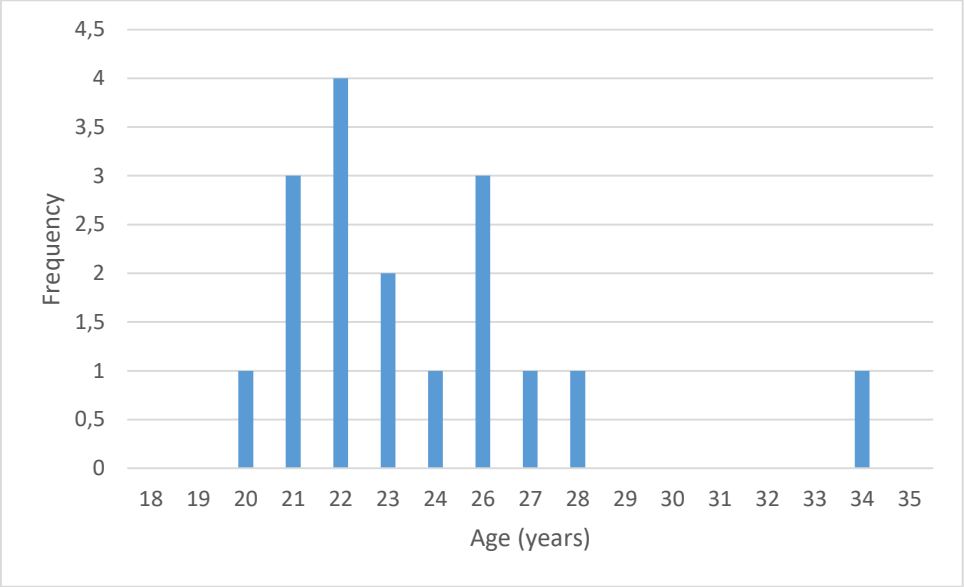

Figure 4.1- Distribution of the sample by age (years).

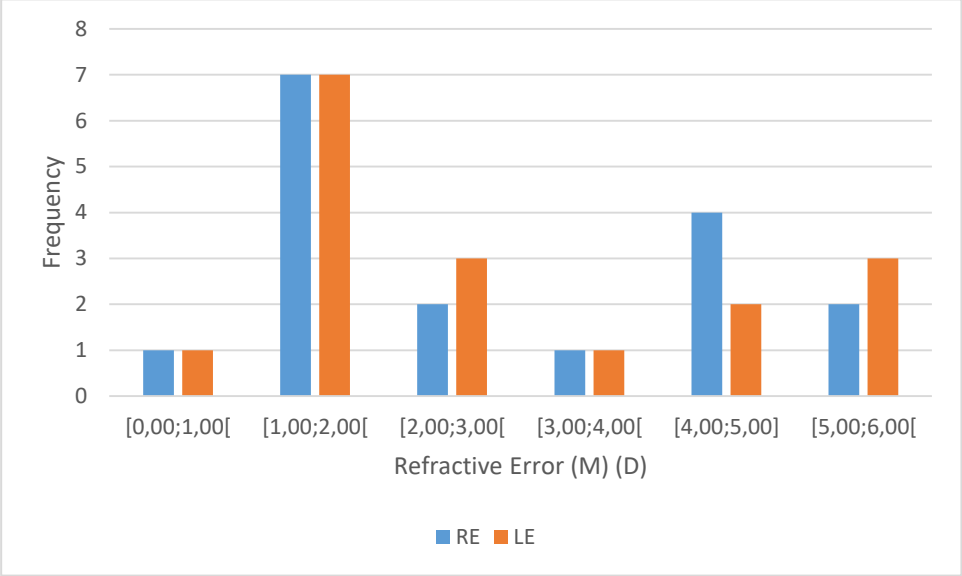

Figure 4.2- Distribution of the sample by refractive error (M) in both eyes.

4.2 Peripheral refraction

Peripheral refraction was measured with an open-field autorefractometer, monocularly, at 25° nasal and 25° temporal for each eye. Figure 4.3 shows the relative peripheral refraction in terms of spherical equivalent (M) of the right and left eyes of the participants, without any correction of the refractive error.

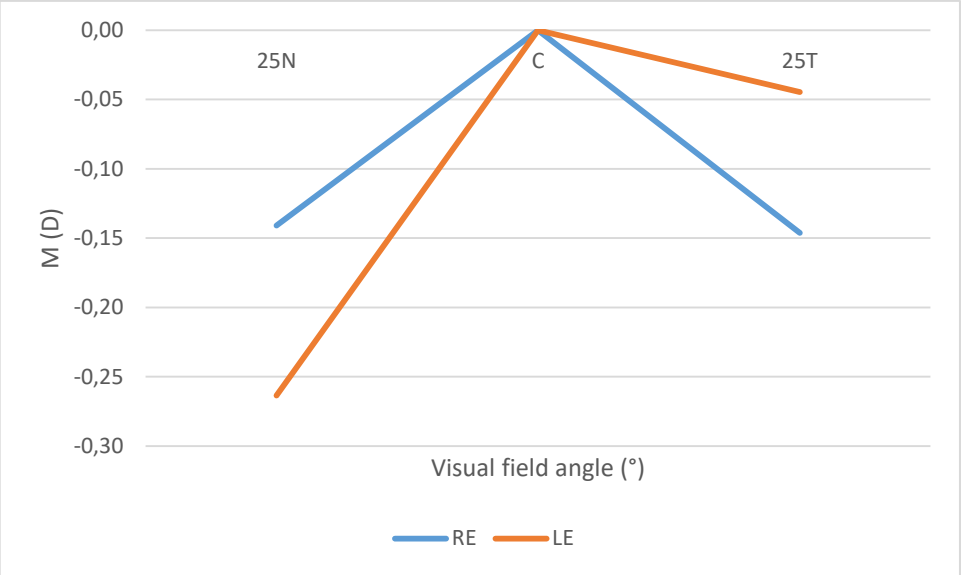

Figure 4.3- Relative mean values of the spherical equivalent M (D) of the right and left eyes of the sample, without any correction.

Table 4.2 describes the relative mean values (which means that the central value was subtracted of the other points) of the spherical equivalent (M) for each eye. The M values measured at 25°N were significantly different (p-value<0.05, Wilcoxon test and Paired Samples T-Test) for both eyes, between control measures and test measures. These values obtained with the perifocal lenses were more negative than with the trial frame lenses, meaning that the perifocal lenses induced a myopic defocus in terms of spherical equivalent in the nasal retina, at 25°.

In Table 4.3 we can see the J0 mean relative values, where the only statistically significant difference (p-value<0.05, Paired Samples T-Test) was in the left eye, where a more negative value of the astigmatic component in the horizontal meridian was induced by the perifocal lenses. The oblique astigmatic component (J45) was reduced in nasal and temporal retina with the perifocal lenses, both in

right and left eyes, as showed in Table 4.4. This reduction was statistically significant (p-value<0.05, Paired Samples T-Test) for the four comparisons.

The mean and standard deviation of the tangential and sagittal foci are described in Table 4.5 and Table 4.6. We can see that the tangential focal suffered a myopic shift in the nasal retina with the perifocal lenses, where the mean values are statistically more negative (p<0.05, Paired Sample T-Test). In the temporal retina of the left eye, the mean values are more positive for the test lenses, but these differences are not statistically significant (p>0.05, Wilcoxon test). In terms of the sagittal focal, the only statistically significant differences were in the nasal retina, where the mean values were less hypermetropic with the test lens than control measures (p<0.05, Paired Sample T-Test).

Table 4.2- Relative mean values (mean ± standard deviation) of the spherical equivalent (M) measure at control and test, for both eyes. The symbol * marks the p-value obtained with parametric tests, contrary to the others obtained with non-parametric tests.

	RE			LE		
M	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
25ºN	0.26 ± 0.97	-0.16 ± 1.01	***0.00**	0.37 ± 0.95	-0.37 ± 0.96	**0.00**
C	0.00 ± 0.00	0.00 ± 0.00	1.00	0.00 ± 0.00	0.00 ± 0.00	1.00
25ºT	0.37 ± 0.87	0.29 ± 0.83	*0.37	0.14 ± 1.09	0.34 ± 1.06	0.08

Table 4.3- Relative mean values (mean ± standard deviation) of the astigmatic component in the horizontal meridian (J0) measure at control and test, for both eyes. The symbol * marks the p-value obtained with parametric tests, contrary to the others obtained with non-parametric tests.

	RE			LE		
J0	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
25ºN	-0.44 ± 0.29	-0.39 ± 0.36	0.98	-0.06 ± 0.38	-0.50 ± 0.43	***0.00**
C	0.00 ± 0.00	0.00 ± 0.00	1.00	0.00 ± 0.00	0.00 ± 0.00	1.00
25ºT	-0.36 ± 0.23	-0.34 ± 0.28	*0.77	-0.65 ± 0.34	-0.50 ± 0.43	*0.08

Table 4.4- Relative mean values (mean ± standard deviation) of the oblique astigmatic component (J45) measure at control and test, for both eyes. The symbol * marks the p-value obtained with parametric tests, contrary to the others obtained with non-parametric tests.

	RE			LE		
J45	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
25ºN	-0.39 ± 0.36	0.08 ± 0.40	***0.00**	0.38 ± 0.37	0.03 ± 0.37	***0.00**
C	0.00 ± 0.00	0.00 ± 0.00	1.00	0.00 ± 0.00	0.00 ± 0.00	1.00
25ºT	0.45 ± 0.44	0.07 ± 0.34	***0.00**	-0.44 ± 0.39	-0.05 ± 0.39	***0.00**

Table 4.5- Relative mean values (mean ± standard deviation) of the tangential focal (FT) measure at control and test, for both eyes. The symbol * marks the p-value obtained with parametric tests, contrary to the others obtained with non-parametric tests.

	RE			LE		
FT	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
25ºN	-0.19 ± 1.11	-0.55 ± 1.19	***0.02**	0.31 ± 1.11	-0.87 ± 1.00	***0.00**
C	0.00 ± 0.00	0.00 ± 0.00	1.00	0.00 ± 0.00	0.00 ± 0.00	1.00
25ºT	0.00 ± 0.96	-0.05 ± 0.93	*0.66	-0.51 ± 1.33	-0.16 ± 1.45	0.06

Table 4.6- Relative mean values (mean ± standard deviation) of the sagittal focal (FS) measure at control and test, for both eyes. The symbol * marks the p-value obtained with parametric tests, contrary to the others obtained with non-parametric tests.

	RE			LE		
FS	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
25ºN	0.70 ± 0.92	0.23 ± 0.94	***0.00**	0.43 ± 0.92	0.13 ± 1.10	*0.09
C	0.00 ± 0.00	0.00 ± 0.00	1.00	0.00 ± 0.00	0.00 ± 0.00	1.00
25ºT	0.73 ± 0.83	0.63 ± 0.81	*0.36	0.79 ± 0.92	0.83 ± 0.73	0.83

The Figure 4.4 graphically displays the relative mean values of the spherical equivalent (M), for the right and left eyes, both in control and test measurements. We can see in this graphic that both eyes suffered a myopic shift with the perifocal lenses in the nasal retina, in contrary to the temporal side. In the following peripheral refraction graphs, the standard deviation of the mean values are omitted for clarity of presentation.

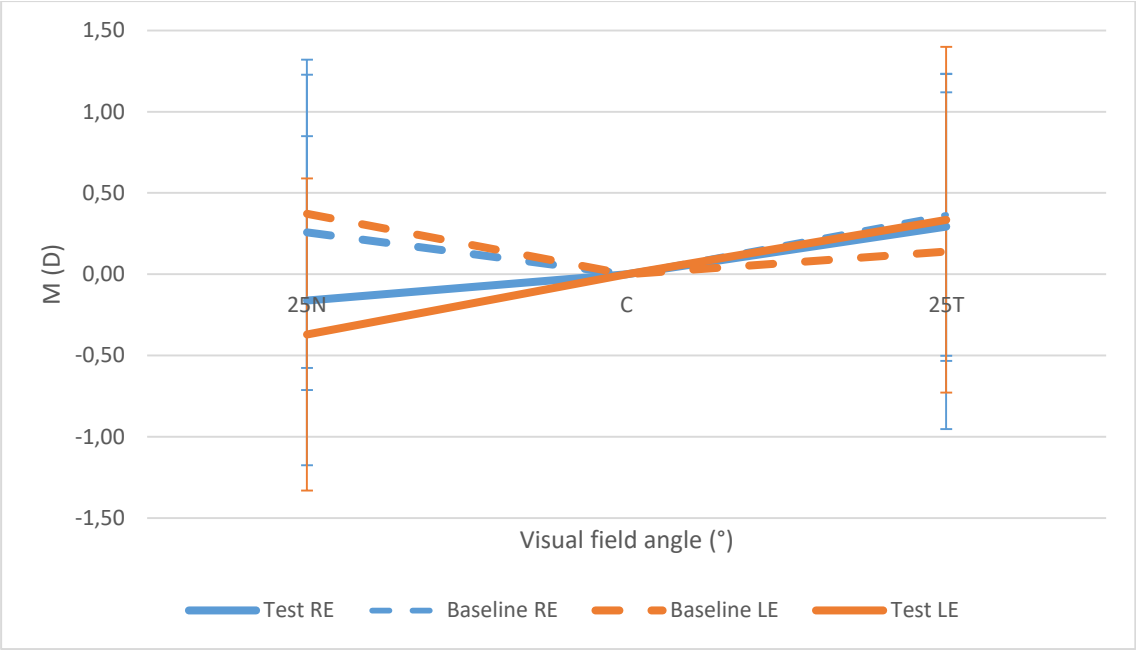

Figure 4.4- Relative mean values of the spherical equivalent M (D) from control (baseline) to test, for both eyes. Error bars indicate 1x standard deviation of each eye.

Table 4.7- Mean differences between test and control (test-control) for M, FT and FS, for right eye and left eye. The numbers highlighted in bold are the differences statistically significant (p-value<0.05).

	M DIFF RE	M DIFF LE	FT DIFF RE	FT DIFF LE	FS DIFF RE	FS DIFF LE
25ºN	**-0.42**	**-0.74**	**-0.36**	**-1.18**	**-0.47**	-0.30
C	0.00	0.00	0.00	0.00	0.00	0.00
25ºT	-0.07	0.19	-0.05	0.35	-0.09	0.04

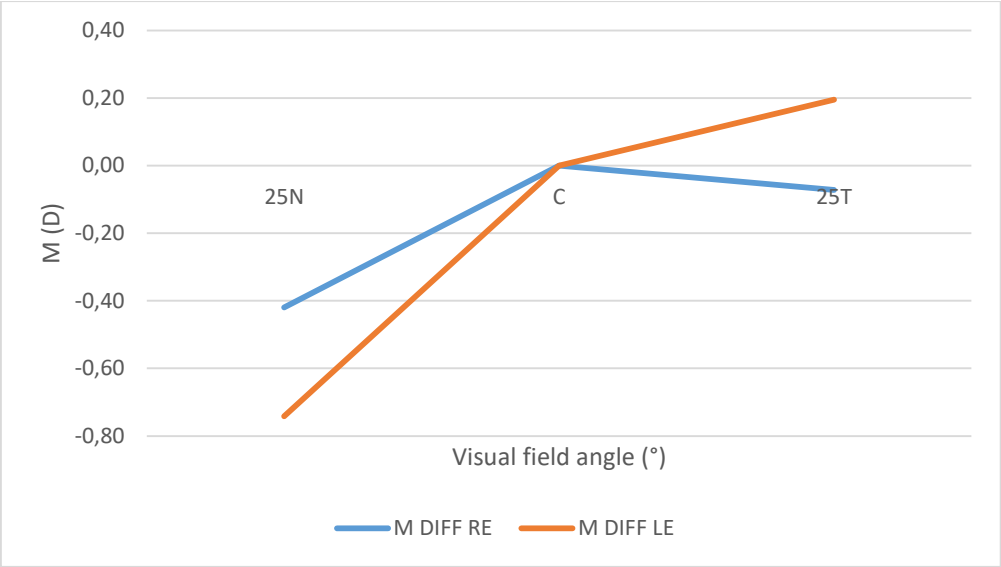

Figure 4.5- Differences in terms of the relative mean value of the spherical equivalent M (D) between test and control measures (test-control) for both eyes.

Table 4.7 shows the mean values of the subtraction of the test condition minus the control condition, for M, FT, and FS in both eyes. The differences in spherical equivalent (M) between control and test (test measures minus control measures) are represented in Figure 4.5. In this image is clearer the myopic defocus that the perifocal lenses induced in the nasal retina for both eyes, especially in the left eye (p-value<0.05). In the temporal side of the retina, this graphic shows a more negative value for right eye, and positive for left eye, even though none of these differences are statistically significant.

Figure 4.6 and Figure 4.7 represents the subtraction of the test values to the control values, in terms of spherical equivalent (M), tangential focal (FT) and sagittal focal (FS) for the right eye and left eye, respectively, as showed above in Table 4.7. For right eye, there are differences only in the nasal side of the retina (p-value<0.05), being the sagittal focal the most myopic. Left eye shows more differences than right eye, mainly in the nasal side, where the values of the tangential focal are more myopic (p-value<0.05), unlike the temporal side where the tangential focal appears more hypermetropic, but these differences are not statistically significant (p-value>0.05).

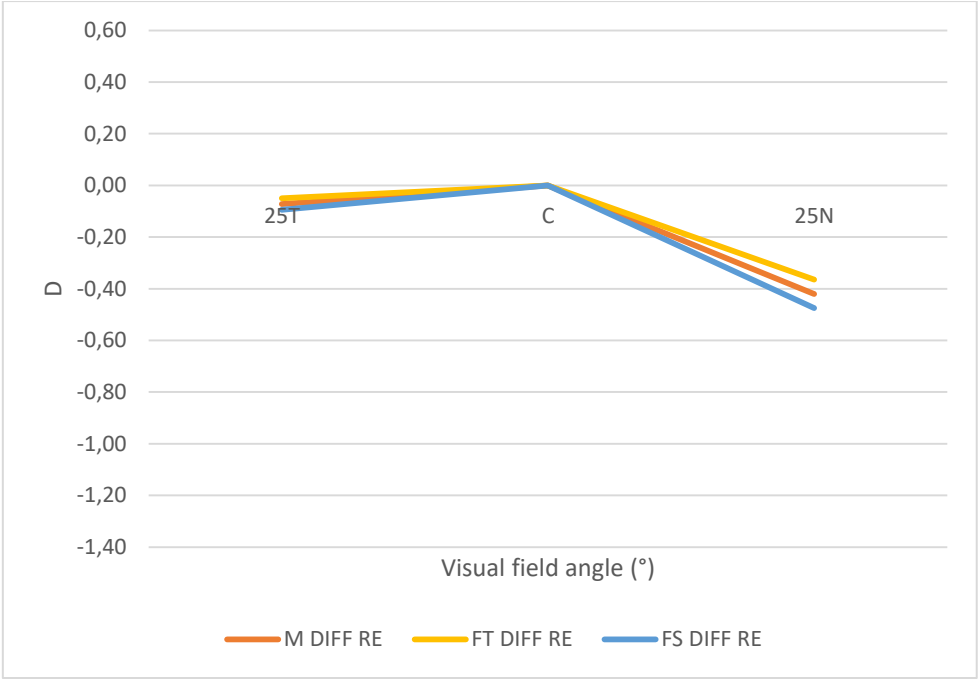

Figure 4.6- Mean values of the differences between test and control (test-control) for M, FT, and FS in the right eye, for the three points measured (25°T, C, 25°N).

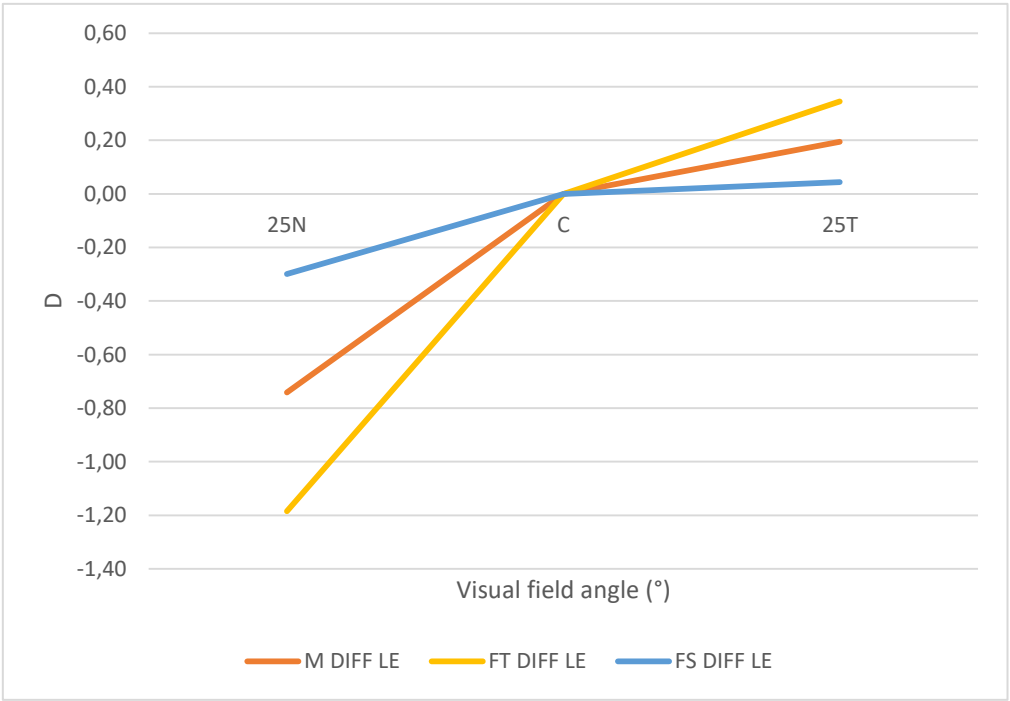

Figure 4.7- Mean values of the differences between test and control (test-control) for M, FT, and FS in the left eye, for the three points measured (25°N, C, 25°T).

4.3 Contrast sensitivity

Contrast sensitivity was measured in low light conditions, three meters away from the VCTS 6500 chart and the measures were obtained monocularly and binocularly. In Table 4.8 is presented the results from contrast sensitivity measurements, for the following spatial frequencies: 1.5, 3, 6, 12 and 18. The results are presented for right eye, left eye and both eyes, with the corresponding p-value for each combination (control-test). As we can see, there were no statistically significant differences between control condition (with normal ophthalmic lenses) and test condition (with the perifocal lenses), in any of the spatial frequencies (p-value>0.05, Wilcoxon Test).

Table 4.8- Mean values ± standard deviation of log contrast sensitivity for five spatial frequencies, for right eye, left eye and both eyes at the same time. All p-values were calculated using a non-parametric test.

	RE			LE			BE		
Spatial Frequency	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
1.5	1.36 ± 0.36	1.38 ± 0.38	0.19	1.34 ± 0.36	1.37 ± 0.37	0.29	1.42 ± 0.37	1.44 ± 0.38	0.83
3	1.61 ± 0.42	1.62 ± 0.43	0.32	1.58 ± 0.42	1.62 ± 0.42	0.14	1.69 ± 0.44	1.68 ± 0.44	0.33
6	1.42 ± 0.40	1.35 ± 0.39	0.19	1.39 ± 0.37	1.4 ± 0.42	0.93	1.48 ± 0.41	1.51 ± 0.41	0.32
12	0.79 ± 0.44	0.77 ± 0.52	0.84	0.81 ± 0.47	0.88 ± 0.43	0.51	1.04 ± 0.31	1.08 ± 0.33	0.09
18	0.13 ± 0.26	0.21 ± 0.31	0.26	0.22 ± 0.37	0.31 ± 0.38	0.32	0.46 ± 0.36	0.40 ± 0.35	0.11

Figure 4.8, Figure 4.9 and Figure 4.10 represent the log contrast sensitivity of the right eye, left eye and both eyes, respectively, in comparison with the normal values of the log contrast sensitivity, represented in the dashed lines. Both in right and left eyes, appears that there is a difference in high spatial frequencies, in favour of the test condition, however, these differences are not statistically significant (p-value>0.05, Wilcoxon Test).

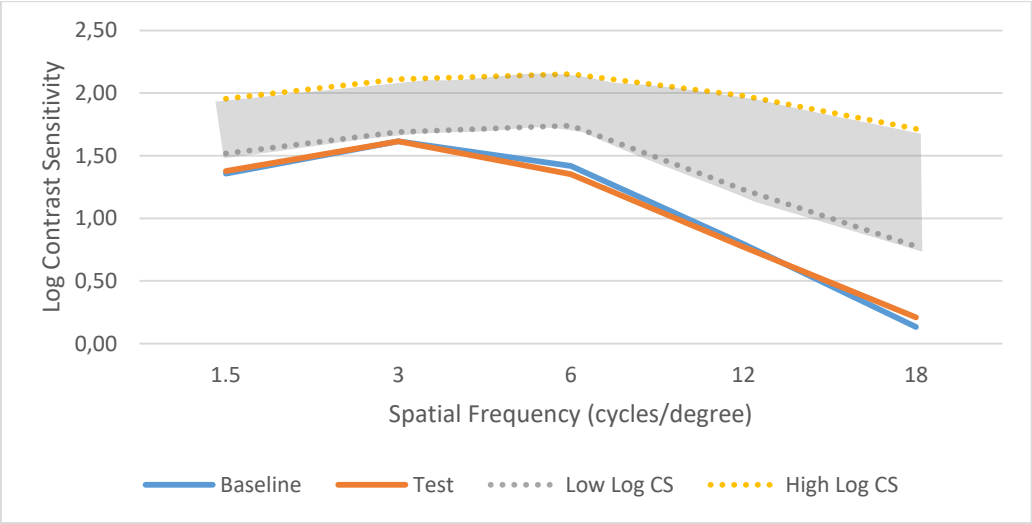

Figure 4.8- Mean ± standard deviation of log contrast sensitivity for control (baseline) and test of the right eye. The shaded area represents the normal ranges under photopic conditions.

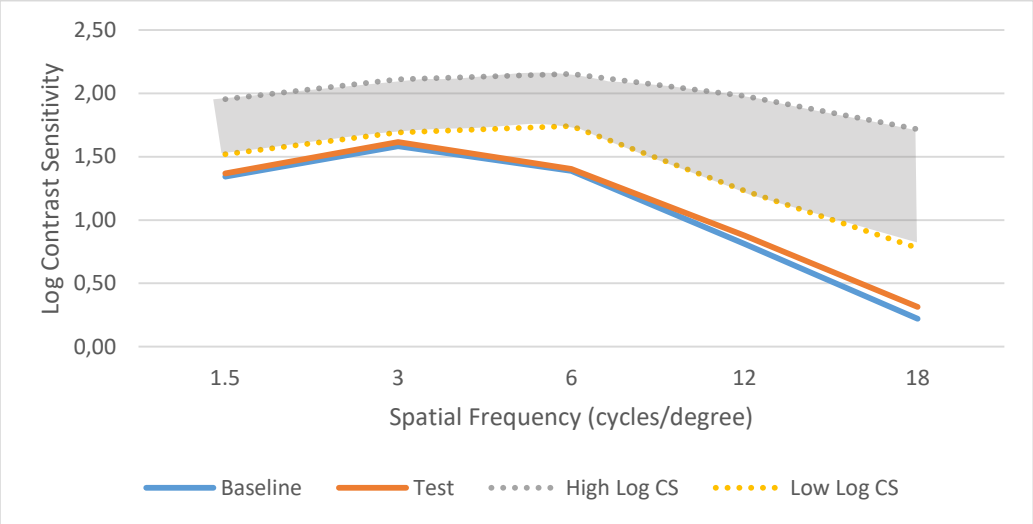

Figure 4.9- Mean ± standard deviation of log contrast sensitivity for control (baseline) and test of the left eye. The shaded area represents the normal ranges under photopic conditions.

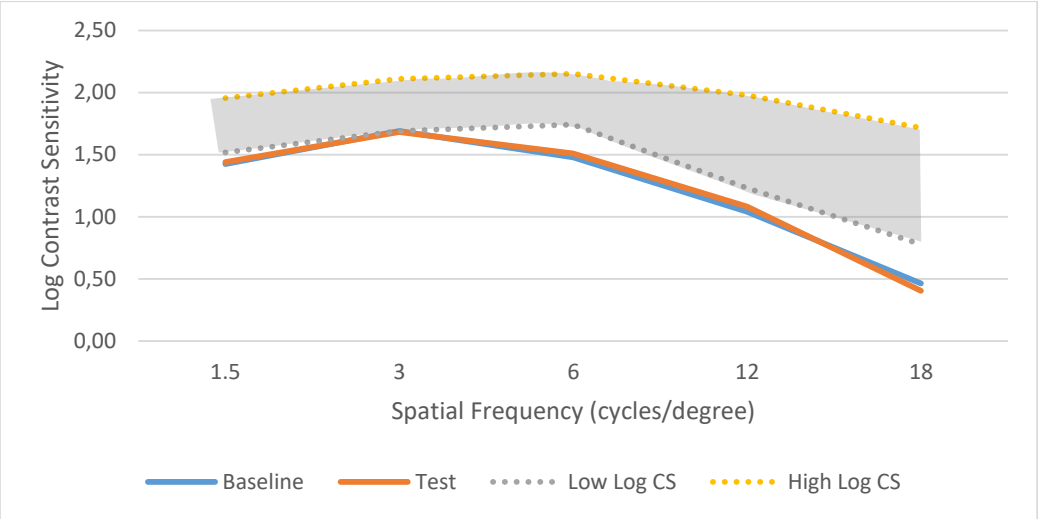

Figure 4.10- Mean ± standard deviation of log contrast sensitivity for control (baseline) and test of both eyes. The shaded area represents the normal ranges under photopic conditions.

4.4 Light disturbance

As mentioned previously, light disturbance analysis was evaluated in low light conditions, two meters away from the LDA device. The measures were obtained both monocular and binocular, with normal correcting lenses (control) and perifocal lenses (test). We analysed four parameters: the LDI, that is the percentage of the total tested area that is not visible because of impairment by the LD phenomena; the BFC_{Rad}, which is the radius of a circle that best fits the shape of the disturbance area; the BFC_{Irreg}, that is the sum of the deviations between the actual disturbance area and the best-fit circle outer perimeter along with all the semi-meridians assessed; and the $BFC_{IrregSD}$, that is the sum of the differences squared and divided by the number of semi-meridians evaluated. The average results from the measurements are presented in Table 4.9, in form of mean ± standard deviation, both for control and test, followed by the corresponding p-value. As we can see, the perifocal lens did not present any statistically significant changes from control measures (p-value>0.05, Wilcoxon test and Paired Samples T-Test) in the four parameters evaluated, both in right eye and left eye, as well as binocular measures.

Table 4.9- Values (mean ± standard deviation) of the four parameters measured for light disturbance analysis, for right eye, left eye and both eyes. The symbol * marks the p-value obtained with parametric tests, contrary to the others obtained with non-parametric tests.

	RE			LE			BE		
LDA Parameters	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**	**Control**	**Test**	**p-value**
LDI (%)	11.60 ± 6.42	10.88 ± 6.10	0.48	10.72 ± 5.02	10.95 ± 5.93	*0.82	6.63 ± 2.60	6.37 ± 2.59	0.53
BFC_{Rad} (mm)	26.85 ± 7.37	26.04 ± 7.02	*0.42	26.08 ± 6.34	26.15 ± 7.35	*0.96	20.66 ± 4.15	20.28 ± 4.03	0.51
BFC_{Irreg} (mm)	0.53 ± 0.48	0.69 ± 0.57	0.25	0.55 ± 0.47	0.33 ± 0.31	0.07	0.27 ± 0.22	0.28 ± 0.24	*0.91
$BFC_{IrregSD}$ (mm)	4.00 ± 1.01	4.07 ± 1.69	0.87	4.03 ± 1.45	4.07 ± 2.59	0.76	2.41 ± 1.48	2.51 ± 1.38	0.83

In the figures presented below, the median and the quartiles of the four parameters are represented to enhance visual representation. In Figure 4.11 is represented the size of the light disturbance in percentage (LDI), for both control and test lenses. The measurements obtained binocularly show less percentage of the size of LD, while wearing the trial frame lenses and the test lenses. The graphic analysis shows no differences between control and test measures, as mentioned before, however, we can see two outliers in right eye test measures.

Figure 4.12 represents the radius of the best fit circle of the light disturbance with trial frame lenses and perifocal lenses. There are no differences between these two conditions, both for right and left eyes, as well as binocular measures.

Figure 4.13 and Figure 4.14 represents the irregularity of the LD. There are a few differences and outliers in both graphics, even though there are no statistically significant differences between normal trial frame lenses and the perifocal lenses tested on this study. All figures show a decrease in glare and halo condition when both eyes are measured at the same time.

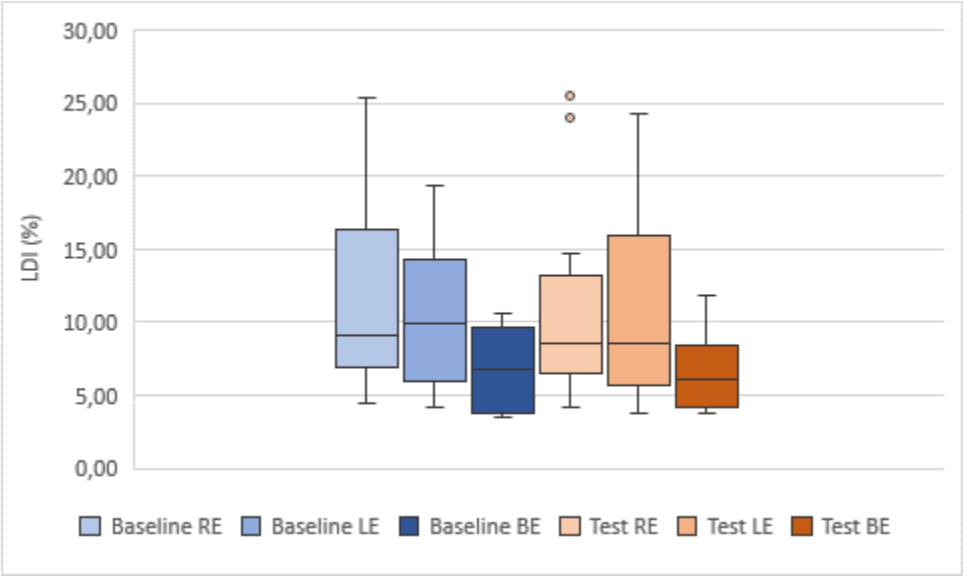

Figure 4.11- Median and quartiles of LDI in percentage, for control (baseline) and test, measured for right eye, left eye and both eyes.

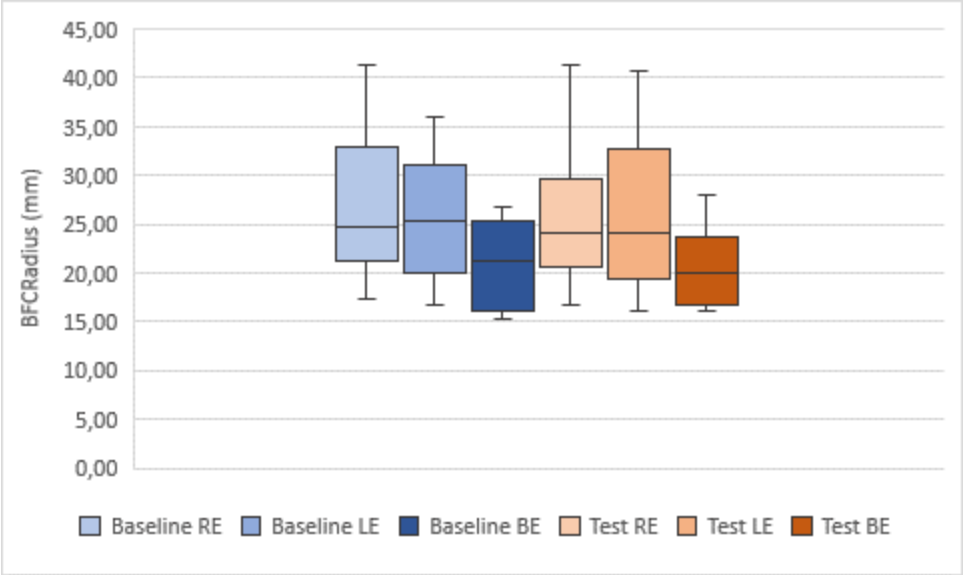

Figure 4.12- Median and quartiles of BFCRadius in mm, for control (baseline) and test, measured for right eye, left eye and both eyes.

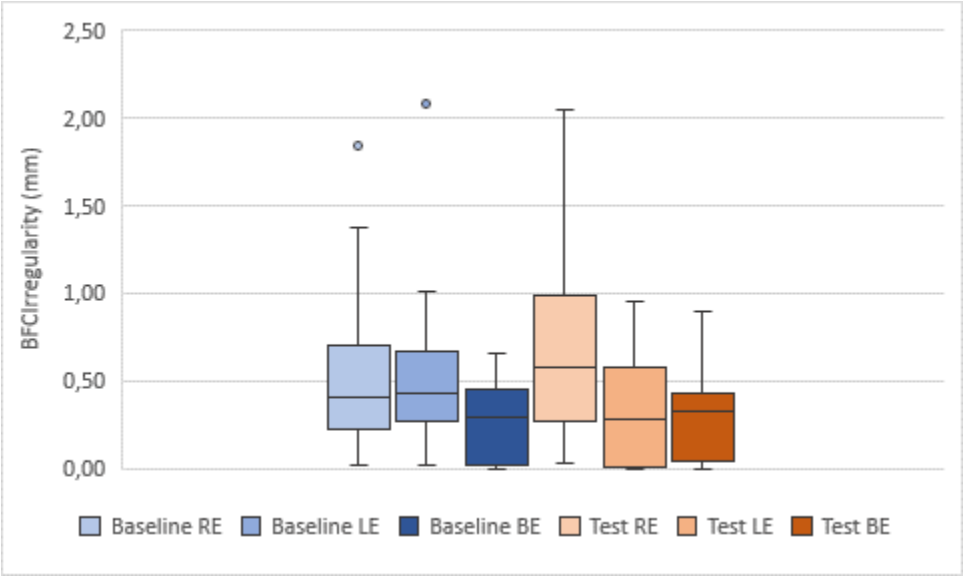

Figure 4.13- Median and quartiles of BFCIrregularity in mm, for control (baseline) and test, measured for right eye, left eye and both eyes.

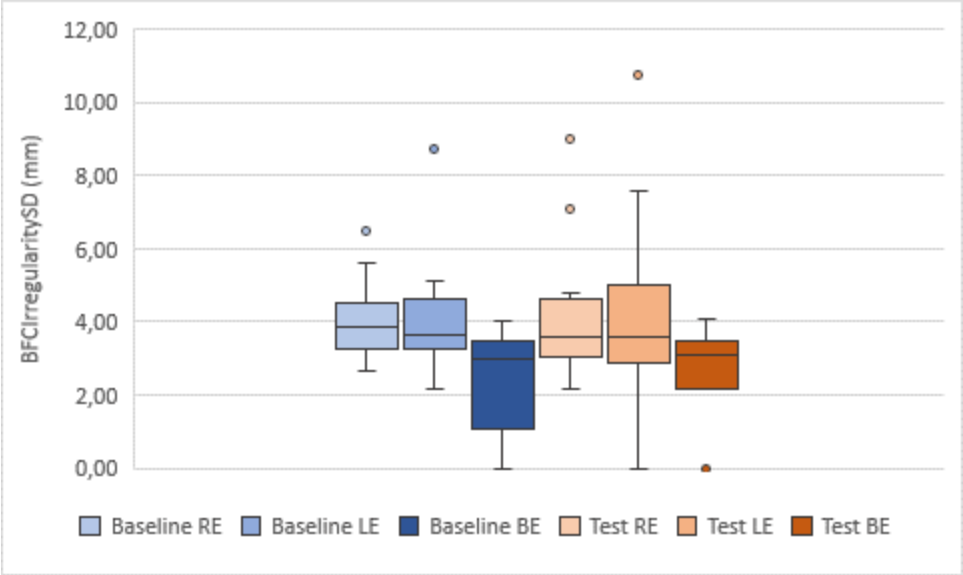

Figure 4.14- Median and quartiles of BFCIrregularity (SD) in mm, for control (baseline) and test, measured for right eye, left eye and both eyes.

5. DISCUSSION

In the present dissertation, the peripheral refraction, the contrast sensitivity, and the light disturbance were analysed with a novel ophthalmic lenses designed for myopia control, a perifocal lenses with a central clear zone for distance vision correction and a treatment zone around this, with positive power of +2.50D in the temporal side of the lens, and +2.00D in the nasal side. This chapter is organized in a similar way to the results section for clarity of presentation and discussion.

5.1 Peripheral refraction

In this work, the perifocal lenses induced a myopic defocus in terms of spherical equivalent (M) in the nasal retina, at 25°. In the nasal retina of the participants, the peripheral refraction changed on average -0.42D in the right eye, and -0.74D in the left eye, as we can see described in Table 4.7. In the temporal retina, affected by the nasal side of the lens, the changes were not statistically significant. These can happen because of the design of the perifocal lenses, that have less positive power by 0.50D in the nasal side of the lenses. In other words, when we measure the peripheral refraction on the temporal retina, we ask the patients to rotate the head to the fixation point, so we can measure through the nasal side of the lens, that has a lower treatment power compared to the temporal lens design. The temporal side of the lens has 0.50D more positive power, that creates more myopic defocus on the nasal retina, and this is confirmed by our results. Some differences between left and right eyes can be explained with the different centering between both eyes with the measuring system.

Tarutta et al. (2019) described long-term results of these perifocal defocus spectacle lenses, in children between 7-14 years old, with progressive myopia. They studied the effect of these lenses on peripheral refraction at 15° and 30° in the nasal and temporal meridians, and it showed that the peripheral refraction was more negative with perifocal lenses, for both nasal and temporal retina, even though in the 30°N the refraction was still positive, but less positive than control. (33) These results coincide with the results obtained in this work just in terms of the nasal retina.

Another work presented in the International Myopia Conference in 2022, studied the peripheral refraction of three spectacle lenses for myopia control, and concluded that these perifocal lenses induced a significant myopic shift in relative peripheral refraction. (76) This work has strong limitations,

because were only analysed three adult patients, one emmetropic and two myopic, and there is no more information about the methods used for the measurements.

Since these perifocal lenses are progressive addition lenses around the central single-vision area, we compare results of peripheral refractive measures from this work to another study where was evaluated on progressive addition lenses for myopia control. Berntsen et al. (2013) determined the effect of progressive addition lens (with +2.00D of addition) on peripheral refraction at 30 degrees in the horizontal meridian and 20 degrees in the vertical meridian, in 84 myopic children. They concluded that superior retina was more myopic with PAL spectacles than with single vision spectacles, because of the inferior near addition of +2.00D of the PAL. They also reported that the defocus on nasal retina was more myopic with PAL than single-vision lens, whereby there were no other significant changes in the other retina locations. These results are consistent with the present study, where nasal retina presented more negative values with perifocal lenses than single vision lenses, and also the myopic shift was higher where the lenses were more positive, like this study. (77)

Queirós et al. (2016) performed a meta-analysis on astigmatic peripheral defocus with eight different contact lenses, including orthokeratology, aspheric rigid gas-permeable lens, experimental RGP and soft contact lens, and three multifocal CLs. The peripheral refraction was obtained from healthy young myopic subjects with all referred lenses. They concluded that only orthokeratology, one peripheral gradient RGP lens and one multifocal soft contact lens with an addition of +3.00D, induced a significant myopic defocus in both nasal and temporal retina, which can be explained by the specific design of each of these lenses. (78)

5.2 Contrast sensitivity

In this study, the VCS did not suffer any changes when patients were using the perifocal lenses. These lenses have a central area designed to correct far distance, so it was expected that the central vision would remain unchanged. As we can see in the figure 7, 8 and 9, the values obtained are below the normal values of contrast sensitivity. This happen because we tested the VCS in low light conditions, to evaluate if there would be any changes under more adverse conditions.

Kaymak et al. also evaluated VCS with a lenses design for myopia control, with the commercial name of Miyosmart, in eight myopic subjects, in photopic and mesopic conditions. They concluded that

this lens did not decrease VCS compared to single vision lens, both in photopic and mesopic conditions. However, the peripheral contrast sensitivity was affected for both nasal and temporal meridians. (79) Other study performed by Gao et al. (2021) also studied peripheral contrast sensitivity with highly aspherical lenslets and slightly aspherical lenslets, although they reported no differences in peripheral VCS with this lens, compared to SVL. (80) In this study we did not measure visual contrast sensitivity when viewing through the peripheral optics of the lens.

A cross-over study published in 2021 by Li et al., evaluated short-term visual performance of three lens for myopia control, highly aspherical lenslets (HAL) and slightly aspherical lenslet (SAL) displayed in concentric rings (namely the Stellest lens by Essilor), and spherical lenslets displayed in honeycomb configuration (namely the Miyosmart lens by Hoya). Contrast sensitivity was evaluated in 36 healthy myopic children, and they have found that HAL and SAL induced smaller impact on contrast sensitivity than spherical lenslets displayed in honeycomb configuration, especially in high spatial frequencies. Like the results reported in the present dissertation, VCS was reduced in mesopic light conditions, especially in high frequencies, in the three lenses (81) and this is in agreement with the results of the present study measured under low lighting (mesopic) conditions.

Mesopic contrast sensitivity is also reported in the literature for MiSight lenses, by García-Marqués et al. (2020). They measure contrast sensitivity between 0.01 cd/m^2 to 3 cd/m^2 with the VCTS 6500, in 28 healthy myopic adults. They reported a statistically significant decrease in mesopic contrast sensitivity with dual-focus contact lenses compared to single vision contact lenses, except for the highest spatial frequency, at 18 cycles per degree. (82) This decrease can happen because of the design of this dual-focus lens, since these results were not similar to the ones reported in the present work.

5.3 Light disturbance

The light disturbance analysis showed that there were no significant changes in the light perception of the patients when they were using these lenses. This can tell us that the central area is possibly large enough that the patients did not notice more subjective glare when using these lenses, comparing to the trial frame lenses.

García-Marqués et al. (2020) reported light disturbance analysis with a dual-focus contact lenses, with the commercial name of MiSight, with Light Distortion Analyser. This study evaluated monocular LD on 28 healthy myopic adults between 18 and 32 years. They concluded that LDI, BFCRadius, BFCIrregularity and BFCIrregularitySD were higher for the dual-focus lenses when compared to a single-vision contact lens of the same material. (82)

Another study made in Spain in 2019 analysing light disturbance perception, in children, with the same dual-focus contact lenses and with LDA device, reported similar results, that this lens increased the perception of light disturbances, but this effect decreased over the 2-year follow up. For the four parameters tested, the results were better for binocular measures, similar to the findings reported in the present work. (83) These differences are expected to happen in a dual-focus contact lens because of the design of this lens but are not expected on a perifocal ophthalmic lens like the one tested on this study.

The fact that the current lens design does not induce changes in LD allow us to hypothesize that subjective complains of glare and haloes might not be reported by these patients and that there is room for future optimization of the lens design, eventually reducing the central clear vision zone and/or increasing the peripheral addition to further induce higher levels of peripheral astigmatic defocus, particularly in the nasal side of the lens compared to the current design.

6. CONCLUSIONS

In this chapter are presented the main conclusions of the present dissertation:

- In terms of peripheral refraction, this work showed that the perifocal lenses induced a significant myopic defocus mainly in the nasal retina (induced by the temporal side of the lens).
- This study showed that the perifocal lenses did not lead to any reduction of the visual contrast sensitivity evaluated in low-light vision.
- There were no statistically significant changes in terms of light disturbance, with the perifocal lenses.

There were a few limitations in the development of the present dissertation, that include:

- The sample size, that is not representative of the target-population in each myopia control techniques are applied.
- The sample age, in the sense that myopia control techniques are usually applied to children.
- All measurements were obtained with three lenses on the trial frame, that can induce dispersion of the light and other phenomena, however, the same exact conditions were applied both in control and test to allow the comparison between these two conditions.

7. FUTURE WORK

In terms of future work, considering the present work, it will be relevant to:

- Evaluate visual acuity both in low and high contrast.
- Evaluate peripheral visual contrast sensitivity with perifocal lens.
- Evaluate peripheral refraction in more meridians to better understanding the power profile obtained in the retina with these lenses.
- Test variations of the present design to evaluate the effect of changing the size of the central clear zone and increasing amounts of peripheral treatment power in visual function and peripheral defocus.

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9. APPENDIX

9.1 Informed Consent

CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

de acordo com a Declaração de Helsínquia[1] e a Convenção de Oviedo[2]

Por favor, leia com atenção a seguinte informação. O presente documento visa informá-lo acerca dos objetivos, métodos e potenciais riscos inerentes ao estudo para o qual se está a voluntariar. Se achar que algo está incorreto ou que não está claro, não hesite em solicitar mais informações. Se concorda com a proposta que lhe foi feita, queira assinar este documento.

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

Título do estudo:

- "Avaliação da função visual de lentes oftálmicas para o controlo da progressão da miopia".

Enquadramento: A miopia afeta cada vez mais pessoas no mundo e, este aumento da prevalência, é preocupante entre os mais jovens, dado que quanto mais cedo aparece a miopia, mais elevado o seu grau pode ser, o que pode conduzir a um maior risco de patologia ocular e consequentemente, cegueira. Atualmente existem diversos métodos para diminuir o aumento da miopia por crescimento excessivo do olho. Entre os tratamentos já implementados encontram-se os óculos e as lentes de contacto com desenhos óticos especiais e algum fármaco como a atropina.

O objetivo do presente trabalho é avaliar possíveis alterações da função visual e influência na visão periférica de umas novas lentes oftálmicas para o controlo da progressão da miopia.

Local: Os estudos serão realizados no âmbito de uma tese de Mestrado de Optometria Avançada, em desenvolvimento no Laboratório de Investigação em Optometria Clínica e Experimental do Centro de

[1] http://portal.arsnorte.min-saude.pt/portal/page/portal/ARSNorte/Comiss%C3%A3o%20de%20%C3%89tica/Ficheiros/Declaracao_Helsinquia_2008.pdf

[2] http://dre.pt/pdf1sdip/2001/01/002A00/00140036.pdf

Física da Universidade do Minho, Campus de Gualtar, 4710-057, Braga, sob a orientação do Professor Doutor José Manuel González-Meijóme e coorientação do Professor Doutor Paulo Fernandes.

Recolha de dados: Cada voluntário que aceite participar no estudo será convidado a participar numa visita para completar o protocolo. Inicialmente serão obtidos valores gerais do estado de saúde ocular e visual, de seguida serão obtidas medidas que incluem a medição da refração objetiva, subjetiva, central e periférica, sensibilidade visual ao contraste, halometria e electroretinograma. Posteriormente vão ser realizados os mesmos exames utilizando umas lentes oftálmicas desenhadas para o controlo da progressão da miopia.

Riscos do estudo: Todo o procedimento tem a duração média de 1 hora e todos os exames são completamente indolores e não invasivos, pelo que não está previsto nenhum malefício inerente aos exames realizados.

Caráter voluntário: A participação neste estudo é de caracter voluntário. Após a leitura desta ficha informativa, terá tempo para ponderar se quer participar neste estudo. Se concordar em participar, receberá uma cópia desta ficha informativa. Também será solicitado que assine o Formulário de Consentimento anexo após ter tido a oportunidade de ler todas as instruções e informações fornecidas, e depois de receber respostas satisfatórias para quaisquer dúvidas que possa ter. Tem o direito a retirar-se do estudo a qualquer momento, sem qualquer penalização, bastando para tal que informe o investigador do estudo. Uma decisão de não participar, ou de se retirar a qualquer momento, não afetará o nível de atendimento que receberá agora ou no futuro.

Condições e financiamento: A participação neste estudo não inclui qualquer remuneração, quer financeira, quer qualquer outra. Porém, todas as avaliações do estudo nas consultas do mesmo serão realizadas gratuitamente, durante a duração do estudo.

Comissão de Ética: Este estudo foi analisado e aprovado por um comité independente de ética. O comité é designado por Comissão de Ética para a Investigação em Ciências da Vida e da Saúde da Universidade do Minho (CEICVS) e analisou os aspetos éticos deste estudo para ajudar a proteger os direitos e o bem-estar dos participantes no estudo.

Utilização dos dados: Quaisquer informações que contenham os teus "Dados Pessoais", recolhidos para os fins descritos neste Formulário de Consentimento Livre e Esclarecido, serão armazenados em

Portugal. Será garantida a confidencialidade e uso exclusivo dos dados recolhidos para o presente estudo. A identificação dos participantes nunca será tornada pública.

Confidencialidade: Os documentos onde constam o seu nome, incluindo os registos do estudo, ou quaisquer formulários que preencha, serão mantidos estritamente confidenciais neste consultório. Os dados serão tratados de forma confidencial e nenhuma informação que identifique os participantes sairá do laboratório Clinical and Experimental Optometry Research Lab (CEORLab) do Centro de Física onde o estudo se desenvolve. A análise dos ficheiros será levada a cabo por uma equipa devidamente qualificada e a sua identidade apenas será rastreável no local do estudo. Para garantir a exatidão dos dados, o patrocinador (ou o seu representante), ou o CEICVS poderão analisar os registos do estudo ficando igualmente comprometidos com os princípios de confidencialidade. Se tiver um problema de saúde associado ao estudo, isto será relatado ao Comité de Ética em Investigação e ao patrocinador do estudo. Os dados provenientes do estudo poderão ser partilhados com o patrocinador do mesmo, ou os seus representantes; porém o nome e morada, serão removidos de qualquer informação utilizada fora deste consultório e não será identificado a partir da mesma.

Se quiser transmitir algum problema ou dúvida relativamente à Proteção dos seus dados, pode fazê-lo através do Serviço de Proteção de Dados da Universidade do Minho, nos seguintes contactos:

E-mail: protecaodados@uminho.pt; Telefone: +351 253 510 006

Proteção de Dados

Universidade do Minho

Edifício 5, Gabinete 1.56

Campus de Gualtar, 4710 - 057 Braga, Portugal

Contacto do Investigador: Dr José Manuel González Méijome (Investigador Principal)

Morada: Universidade do Minho, Largo do Paço, 4704-553 Braga, Portugal

Telefone: (351) 253-604-320; Contacto fora de horário laboral: (351) 934-794-751

Contacto da pessoa que pede o consentimento:

Sara Catarina da Silva Leite (Investigadora)

Morada: Universidade do Minho, Largo do Paço, 4704-553 Braga, Portugal

Email: saracsleite@gmail.com; Telemóvel: (351) 917270355

Assinatura/s: ... ...

O investigador: ... ...

Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pela investigadora responsável, assim como declaro que me foi dada a oportunidade de colocar qualquer questão, tendo sida respondida de modo satisfatório. Foi-me garantida a possibilidade de, em qualquer altura, recusar participar neste estudo sem qualquer tipo de consequências. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando em que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas pela investigadora.

Nome: _____

Assinatura:_____ Data:___/___/_____

9.2 Record sheet

Voluntário nº: _____ Nome: _____

Email: _____ Contacto: _____

Data de Nascimento: _____ Idade: _____ Género: _____

Folha de registo

Data: _____/_____/_____ _____:_____

□**Consentimento informado**

Critérios de inclusão: □Idade entre 18-35 anos

□Erro refrativo <-6.00D

□Astigmatismo <3.00D

Critérios de exclusão: □Doenças sistémicas que afetam a saúde ocular

□Doenças oculares (como queratocone)

□Histórico de cirurgias oculares

Rx habitual: Óculos: Lentes de Contacto/Outro:

OD: _____ OD: _____

OE: _____ OE: _____

1. **IOL MASTER, ABERROMETRIA E TOPOGRAFIA** □
2. **AUTOREFRAÇÃO E SUBJETIVO**

AR: OD: _____ DIP: _____

OE: _____

Sx: OD: _____ AV: _____ AV: _____

OE: _____ AV: _____

Lentes a colocar na armação de prova: OD: _____

OE: _____

Lentes: □0.00D □-1.50D □-3.50D □-5.50D □-7.50D

3. MEDIDAS BASELINE (CORRIGIDOS)

□**SCV central:** OD: OE:

Binocular:

□**Refração periférica:** 25° temporal/nasal, central.

□**LDA:**

OD:

DA: _____ mm^2 LDI: _____ % BFC_{Radius}: _____ mm

BFC_{Center}: _____ mm $BFC_{Orientation}$: _____ deg

$BFC_{Irregularity}$: _____ mm $BFC_{IrregularitySD}$: _____ mm

OE:

DA: _____ mm^2 LDI: _____ % BFC_{Radius}: _____ mm

BFC_{Center}: _____ mm $BFC_{Orientation}$: _____ deg

$BFC_{Irregularity}$: _____ mm $BFC_{IrregularitySD}$: _____ mm

AO:

DA: _____ mm^2 LDI: _____ % BFC_{Radius}: _____ mm

BFC_{Center}: _____ mm $BFC_{Orientation}$: _____ deg

$BFC_{Irregularity}$: _____ mm $BFC_{IrregularitySD}$: _____ mm

4. MEDIDAS COM LENTES

□**SCV central:** OD: OE:

Binocular:

□**Refração periférica:** 25° temporal/nasal, central.

□**LDA:**

OD:

DA: _____ mm^2 LDI: _____ % BFC_{Radius}: _____ mm

BFC_{Center}: _____ mm $BFC_{Orientation}$: _____ deg

$BFC_{Irregularity}$: _____ mm $BFC_{IrregularitySD}$: _____ mm

OE:

DA: _____ mm^2 LDI: _____ % BFC_{Radius}: _____ mm

BFC_{Center}: _____ mm $BFC_{Orientation}$: _____ deg

$BFC_{Irregularity}$: _____ mm $BFC_{IrregularitySD}$: _____ mm

AO:

DA: _____ mm^2 LDI: _____ % BFC_{Radius}: _____ mm

BFC_{Center}: _____ mm $BFC_{Orientation}$: _____ deg

$BFC_{Irregularity}$: _____ mm $BFC_{IrregularitySD}$: _____ mm

9.3 Statement of the ethics committee

Universidade do Minho

Conselho de Ética

Comissão de Ética para a Investigação em Ciências da Vida e da Saúde (CEICVS)

Identificação do documento: CEICVS 113/2022

Título do projeto: *Avaliação da função visual de lentes oftálmicas para o controlo da progressão da miopia*

Equipa de investigação: Sara Catarina da Silva Leite, Optometrista, aluna de Mestrado em Optometria Avançada da Escola de Ciências da Universidade do Minho; José Manuel González-Méijome, Professor Catedrático, Departamento de Física da Escola de Ciências da Universidade do Minho (orientador); Paulo Rodrigues Botelho Fernandes, Professor Doutor do Departamento de Física da Escola de Ciências da Universidade do Minho (co-orientador)

Unidade Orgânica Promotora: Escola de Ciências da Universidade do Minho

Outras Unidades: n/a

PARECER

De acordo com a documentação apresentada, o projeto insere-se no âmbito do projeto de dissertação intitulado "Avaliação da função visual de lentes oftálmicas para o controlo da progressão da miopia" de Mestrado em Optometria Avançada da Escola de Ciências da Universidade do Minho.

Trata-se de um estudo prospetivo, experimental (uso de lentes oftálmicas para o controlo da progressão da miopia), descritivo e analítico, com o apoio institucional do Centro de Física das Universidades do Minho e Porto. É objetivo principal do estudo comparar a função visual de umas novas lentes oftálmicas para o controlo da progressão da miopia com umas lentes oftálmicas monofocais.

Após verificação e análise dos documentos associados ao processo de pedido de emissão de parecer ético sobre o projeto em apreço, a que reporta a respetiva "Análise e justificação do parecer", considera-se que (i) o processo está devidamente instruído, (ii) a análise dos documentos apresentados sobre o estudo a realizar obedecem às regras de conduta ética e requisitos exigidos para as boas práticas na experimentação com humanos e (iii) estão em conformidade com o Guião para submissão de processos a pedido de Parecer Ético na UMinho.

Face ao exposto, a Comissão de Ética para a Investigação em Ciências da Vida e da Saúde (CEICVS) nada tem a opor à realização do projeto, emitindo o seu parecer favorável, que foi aprovado por unanimidade dos seus membros.

Braga, 6 de outubro de 2022

A Presidente da CEICVS

(Maria Cecília Lemos Pinto Estrela Leão)

.....

ANÁLISE E JUSTIFICAÇÃO DO PARECER

Relatora: Nadine Santos

Grelha de verificação e de avaliação ética

(Processo submetido em suporte eletrónico - documentos recebidos assinalados com X e respetiva avaliação ética)

Documentos	**Sim**	**Não**	**Não se aplica**	**Avaliação Técnico-ética**
Pedido de apreciação de projeto enviado à CEICVS «	X			Adequado
Quando aplicável, identificação da Unidade Curricular (UC) no âmbito da qual se insere o projeto (designação do curso, designação da UC e respetivo ano curricular, identificação do/s coordenador/es da UC, nome e número mecanográfico do estudante)	X			Adequado
Carta de Apoio/Autorização da(s) Unidade(s) ou Serviço(s) onde decorrerá o projeto «	X			Adequada
Quando aplicável, informação do Orientador da Tese sobre apoio e/ou enquadramento do projeto	X			Adequado
Protocolo do estudo, incluindo, se aplicável, os instrumentos de recolha de dados e/ou informação para o participante «	X			Protocolo do estudo elaborado de acordo com os requisitos e normas éticas de boas práticas em experimentação com humanos. Deverá ser seguido o Regulamento Geral de Proteção de Dados (RGPD) na colheita e armazenamento de dados.

Curriculum Vitae abreviado do Investigador Responsável e dos membros da equipa e/ou orientadores [a]	X			Presente
Quando aplicável, documento de Consentimento Informado, elaborado e referenciado de acordo com a alínea [c] abaixo indicada	X			
Declaração de Compromisso de Confidencialidade (e/ou Termo de Responsabilidade)	X			Adequada
Quando aplicável, informação sobre financiamento para o cumprimento do projeto, incluindo, se aplicável, cabimento/inscrição no orçamento da Unidade/Serviço em que decorrerá e/ou com fonte de financiamento nacional/internacional	X			
Conforme aplicável, o desenvolvimento de projetos de investigação está associado à emissão de Parecer/Autorização ética e de proteção de dados (DPO) de entidades locais ou nacionais.				

[a] Documentos obrigatórios de acordo com as normas orientadoras para submissão de processos a apreciar pelo Conselho de Ética da UMinho.
[b] Documentos obrigatórios de acordo com o funcionamento da Comissão de Ética para a Saúde do Hospital de Braga (CESHB).
[c] Documento de Consentimento Informado, Livre e Esclarecido para Participação em Investigação de acordo com a Declaração de Helsínquia[i], a Convenção de Oviedo[ii] e o Regulamento Geral de Proteção de Dados (RGPD)[iv]. Guião na elaboração do consentimento informado é disponibilizado pela ARSN[v] e através do "Documento CEIC sobre o Regulamento Geral de Proteção de Dados (RGPD) no contexto da Investigação Clínica"[vi].

Acesso aos documentos da alínea c):
[i] http://portal.arsnorte.minsaude.pt/portal/page/portal/ARSNorte/Comiss%C3%A3o%20de%20%C3%89tica/Ficheiros/Declaracao_Helsinquia_2008.pdf
[ii] http://dre.pt/pdf1sdip/2001/01/002A00/00140036.pdf
[iii] https://eur-lex.europa.eu/legal-content/PT/TXT/?uri=celex%3A32016R0679
[iv] http://www.arsnorte.min-saude.pt/consentimento-informado/
[v] http://www.ceic.pt/documents/20727/0/Documento+CEIC+sobre+o+Regulamento+Geral+de+Prote%C3%A7%C3%A3o+de+Dados+%28RGPD%29_publica%C3%A7%C3%A3o/ced81411-5fe4-46f5-a613-c7c716abbb4b
[vi] https://dre.pt/home/-/dre/123815982/details/maximized

Justificação do Parecer

Trata-se de um projeto efetuado no âmbito do projeto de dissertação intitulado "Avaliação da função visual de lentes oftálmicas para o controlo da progressão da miopia" de Mestrado em Optometria Avançada da Escola de Ciências da Universidade do Minho, com o apoio institucional do Centro de Física das Universidades do Minho e Porto, para a sua realização na(s) Unidade(s), com duração de 10 meses e com início previsto em fevereiro de 2022.

O(a)(s) Investigador(a)(s) Responsável(eis) (IRs), têm formação clínica e/ou académica e/ou técnica e experiência solidificada nas áreas de base do projeto, e/ou o apoio de uma equipa de investigação com experiência.

O objetivo geral do estudo é comparar a função visual de umas novas lentes oftálmicas para o controlo da progressão da miopia com umas lentes oftálmicas monofocais. Esta avaliação é feita através de medidas de refração periférica, sensibilidade visual ao contraste e distorção luminosa. São perguntas específicas do projeto: i) Será que lentes perifocais induzem desfoque miópico na retina periférica de míopes adultos?; ii) Será que lentes perifocais diminuem a sensibilidade visual ao contraste comparando com lentes monofocais?; iii) Será que lentes perifocais induzem distorção da luz?

Trata-se um estudo prospetivo, experimental, descritivo e analítico, não sendo randomizado nem mascarado. Será a população-alvo voluntários de ambos os sexos com idades compreendidas entre os 18 e os 35 anos, com miopia e sem qualquer tipo de patologia ocular. Foram definidos critérios de inclusão e de exclusão. Os participantes vão ser submetidos a um exame refrativo completo no início da consulta, onde seguidamente se realizam medidas de refração periférica, sensibilidade visual ao contraste e distorção da luz. Estas medidas são inicialmente realizadas com lentes monofocais e repetidas logo de seguida com lentes para o controlo da miopia. Os dados recolhidos incluem valores gerais do estado de saúde ocular e visual, de seguida serão obtidas medidas que incluem a medição da refração objetiva, subjetiva, central e periférica, sensibilidade visual ao contraste e halometria. Variável, tipo de variável e/ou categorias da variável e descrição da mesma foram enumeradas/descritas no protocolo de investigação e/ou foi fornecido em anexo o Formulário de Recolha de Dados e/ou Guião da Entrevista e/ou Metodologia Laboratorial.

A recolha de dados será realizada no Laboratório de Investigação em Optometria Clínica e Experimental (CEORLab) do Centro de Física da Universidade do Minho, Campus de Gualtar. Os equipamentos essenciais para esta investigação, produtos e dispositivos a serem utilizados encontram-se disponíveis no CEORLab. Não existem outros recursos de eventuais financiamentos para a realização deste estudo, e a equipa de investigação não possui qualquer interesse ou conflitos de interesses financeiros ou de outra natureza nos dispositivos utilizados.

O projeto envolve a dádiva, e/ou colheita, análise laboratorial e/ou imagiológica e/ou oftalmológico ou afins, e/ou processamento, e/ou preservação, e/ou armazenamento, e/ou distribuição e/ou aplicação de tecidos e/ou células de origem humana.

Será salvaguardado o anonimato e a confidencialidade do participante (não haverá identificação nominal do titular, sendo aposto um código de participante no estudo).

Os participantes serão informados dos procedimentos, da garantia de confidencialidade dos dados e do seu direito de desistir em qualquer momento do estudo sem qualquer prejuízo.

Não estão previstos quaisquer abuso(s) de recursos institucionais, hospitalares e/ou outros, como aplicável, para a realização do projeto.

Não se declaram existirem conflitos de interesse.

Não se declara a investigação envolver diretamente indivíduos privados do exercício de autonomia (crianças, menores, pessoas com incapacidade temporária ou permanente do exercício de autonomia).

Documentos recebidos no órgão institucional de ética da UMinho

Foram recebidos os seguintes documentos:

- Protocolo de investigação e/ou caderno de recolha de dados e/ou guião da entrevista
- Curriculum vitae abreviado do(a) investigador(a) responsável(eis)
- Parecer do(a) diretor(a) do centro de investigação e/ou unidade
- Modelo de documento de consentimento informado
- Cópia do(s) formulário(s) de recolha de dados a utilizar e/ou enumeração dos dados que serão colhidos
- Curriculum vitae abreviado do(a)(s) aluno(a)(s)
- Modelo de declaração de compromisso a utilizar pelo(a) IR e por outros investigadores ou colaboradores na investigação destinado a documentar o seu envolvimento nas garantias de confidencialidade e boas praticas dadas pelo(a) IR (Termo de Responsabilidade)
- Declaração do orientador no compromisso na orientação e/ou Termo de Responsabilidade