Universidade do Minho
Escola de Ciências

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Clinical Performance and Biological Interactions During Scleral Contact Lens Wear

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Clinical Performance and Biological Interactions During Scleral Contact Lens Wear

PhD Thesis in Optometry and Vision Sciences

PhD Thesis Under Supervision of:
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January 2019

STATEMENT OF INTEGRITY

I hereby declare having conducted my thesis with integrity. I confirm that I have not used plagiarism or any form of falsification of results in the process of the thesis elaboration.

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

University of Minho, 31st of January of 2019

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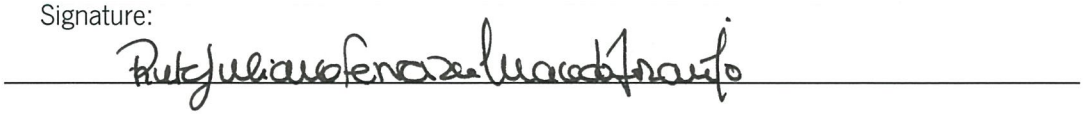

“For long you live and high you fly
And smiles you'll give and tears you'll cry
And all you touch and all you see
Is all your life will ever be.”

Pink Floyd – Breathe (In The Air)

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ABSTRACT

Scleral lenses are among one of the best visual correction options nowadays. Despite the great augment on the peer-review literature related to scleral lenses in last few years, the impact of these lenses on the anterior ocular surface, as well as the comfort and visual enhancements over the long-term lacks to be addressed in both irregular and regular corneal surfaces. The main goal of the present work was to investigate the short-, medium- and long-term interactions of scleral lenses with the ocular surface and quantify the optical enhancement in patients with diseased and non-diseased corneas. We also aimed to evaluate the success rate and the Learning Curve of scleral lens fitting and to develop new measurements to aid during the fitting process and on-eye scleral lens fitting through time. Ninety-five patients were primarily recruited and divided into two groups, according to their corneal condition: irregular cornea or regular cornea. Patients were fitted with scleral lenses from Procornea (Eerbeek, The Netherlands) and were prospectively evaluated over several appoints through a 1-year follow-up time. Clinical measures were obtained at Clinical and Experimental Optometry Research Lab (CEORLab, University of Minho, Portugal).

The results showed that scleral lenses are already adopted as potential devices for visual correction by a significant number of Portuguese and Brazilian specialty contact lens prescribers. Also, that a novel practitioner can reduce significantly the mean number of trial lenses and re-orders after the first fittings. We suggested new approaches that could aid the practitioners during the fitting process and evaluation: first we conclude that scleral topography devices are able to quantify sclero-conjunctival changes after scleral lens wear and therefore aid in the selection of the best landing zone geometry for each eye; second, although the scleral lenses do not touch the corneal surface, some corneal topographic metrics can aid in the selection of the first trial lens to be fitted; and at last, that other devices (such IOLMaster) or techniques (ImageJ) can provide objective values of the central corneal clearance and can be substitutes for the standard subjective measure. The last part of the study showed that scleral lenses promote large gains of visual acuity and quality and that those improvements are stable over a follow-up time. It was also possible to conclude that other measurements – rather than the classic VA measurement – will aid in quantify those changes more precisely (aberrometry and night vision disturbances). The evaluations performed aid to conclude that scleral lenses are safe for both diseased and non-diseased eyes.

RESUMO

As lentes esclerais são uma das melhores opções para correção visual disponíveis nos dias de hoje. Apesar do grande aumento do número de artigos publicados nos últimos anos, o impacto destes dispositivos na superfície ocular anterior, bem como o conforto e melhorias visuais ao longo do tempo ainda não foi profundamente estudado. O principal objetivo deste trabalho foi investigar as interações a curto, médio e longo prazo das lentes esclerais com a superfície ocular e quantificar os ganhos a nível visual e de conforto em pacientes com córneas irregulares e regulares. Outro objetivo foi avaliar a taxa de sucesso e Curva de Aprendizagem da adaptação destas lentes e desenvolver novas medidas que auxiliem o profissional durante o processo de adaptação. Noventa e cinco pacientes foram recrutados e divididos em dois grupos de acordo com a sua condição corneal (córneas irregulares e córneas regulares). Todos os pacientes foram adaptados com lentes da Procornea e avaliados ao longo 1 ano no CEORLab (Universidade do Minho, Portugal).

Os resultados mostraram que estas lentes já foram adotadas como potenciais dispositivos para correção visual por um numero significativo de profissionais em Portugal e no Brasil. Também, que um profissional consegue reduzir significativamente o numero de lentes de teste e novos pedidos de lente após as primeiras adaptações. Sugerimos novas abordagens que podem auxiliar os profissionais durante o processo de adaptação e avaliação das lentes: primeiro concluímos que os novos topógrafos esclerais conseguem quantificar as mudanças que ocorrem na conjuntiva após o uso destas lentes; em segundo, que embora estas lentes não toquem na córnea, alguns dados de topografia corneal conseguem auxiliar na seleção da primeira lente; e, por último, que outros dispositivos (como IOLMaster) e técnicas (como ImageJ) conseguem fornecer valores objetivos da separação córnea-lente e podem substituir as medidas subjetivas. A última parte do presente estudo demonstrou que as lentes esclerais promovem grandes melhorias da qualidade visual e que estas são estáveis ao longo do tempo, e que outras medidas para além da acuidade visual devem ser consideradas para caracterizar os ganhos visuais (aberrometria e avaliação das distorções luminosas). As medidas feitas ao longo dos 12 meses também permitiram concluir que as lentes esclerais são uma modalidade segura (em córneas normais e irregulares).

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GLOSSARY OF TERMS & ABBREVIATIONS

AL	Axial Length
AS	Anterior Segment
AstigObl	Oblique Astigmatism
Barrer:	10·11 (cm2/sec) [ml O2/(ml x mmHg)]
BCR	Base Curve Radius
BFC	Best Fit Circle
BFCIrreg	BFC Irregularity
BFCIrregSD	Standard Deviation (SD) of the BFC Irregularity
BR	Brazil/ Brazilian
BSC	Best Spectacle Correction
BUT	Tear-film Break-up Time
CCC	Central Corneal Clearance
CCLRU	Corneal and Contact Lens Research Unit
CEORLab	Clinical & Experimental Optometry Research Laboratory
CL	Contact lens
CT	Central Thickness
D	Diopter
DC	Cylinder Diopter
Dk/t	Oxygen Transmissibility considering “t” as the local thickness of the lens
Dk	Oxygen Permeability
DEQ	Dry Eye Questionnaire
Dia	Diameter
DK	Oxygen Permeability
ECP	Eye Care Practitioner
EH0-180°	Estimated ocular Height for 0-180° meridian
EH30-210°	Estimated ocular Height for 150-330° meridian
EH30-210°	Estimated ocular Height for 30-210° meridian
ESP	Eye Surface Profiler
ETDRS	Early Treatment Diabetic Retinopathy Study

GCD	Goblet Cell Density
HA.RC	High Astigmatism (from Regular Cornea group)
HC	Habitual Correction
HCVA	High Contrast Visual Acuity
HEMA	Hydroxyethyl Methacrylate
HOA	High-order Aberrations
HVID	Horizontal Visible Iris Diameter
IC	Irregular Cornea
ICRS	Intra-Corneal Ring Segments
IOL	Intraocular Lens
IQR	Interquartile Range
K	Keratometry
KC	Keratoconus
LA.RC	Low Astigmatism (from Regular Cornea group)
LASIK	Laser in situ Keratomileusis
LCM	Laser Confocal Microscopy
LCVA	Low Contrast Visual Acuity
LD	Light Disturbances
LDA	Light Distortion Analyzer
LDI	Light Disturbance Index
LDV	Lens Dispensing Visit
LDV1	Lens Dispensing Visit – right after lens insertion
LDV2	Lens Dispensing Visit – after more than 90 minutes of scleral lens wear
LE	Left Eye
LED	Light Emitting Diode
LOA	Low Order Aberrations
LogMAR	Logarithmic of the Minimum Angle of Resolution
LP	Lens Periphery
LScCL	Axial Length measured with a scleral lens on eye
LT	Lens Thickness
MAX	Maximum
MCA	Mucin Cloud Amplitude

MED	Median
MIN	Minimum
MPS	Multipurpose solution
NIBUT	Non-invasive Tear Break-up Time
NVD	Night Vision Disturbances
OC-SAG	Ocular Sagittal Height
OCT	Optical Coherence Tomography
OSDI	Ocular Surface Disease Index (questionnaire)
PF	Peri Factor
PMD	Pellucid Marginal Degeneration
PMMA	Polymethyl Methacrylate
Prim.IC	Primary Ectasias
PT	Portugal/ Portuguese
Q	Asphericity
QoV	Quality of Vision (questionnaire)
RC	Regular Cornea
RE	Right Eye
RGP	Rigid Gas Permeable
RMS	Root Mean Square
SA	Spherical Aberration
SA_4th	Fourth order Spherical Aberration
SA_6th	Sixth order Spherical Aberration
ScCL	Scleral Lenses (Scleral Contact Lenses)
ScCL-SAG	Scleral Lens Sagittal Height
SCOPE	The Scleral Lenses in Current Ophthalmic Practice: An Evaluation
SD	Standard Deviation
SE	Secondary Ectasia
Sec.IC	Secondary Ectasias (from Irregular Cornea group)
SecAstig	Secondary Astigmatism
Si-Hi	Silicone Hydrogel
SL	Scleral Lens
SL	Slit Lamp

SLS	Scleral Lens Education Society
SPSS	Statistical Package for the Social Sciences
T	Toricity (of the lens haptic zone)
TA	Tangent Angles
T-test	T Student Test
V12m	12-month appointment
V1m	1-month appointment
V3m	3-month appointment
V6m	6-month appointment
VA	Visual Acuity
VertAstig	Vertical Astigmatism
VSOTF	Visual Strehl ratio based on the Optical Transfer Function

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PUBLICATIONS RELATED WITH THIS THESIS

Publications in the following list have been elaborated by the candidate or in collaboration with other authors and co-authors directly related with the contents of the present document. Some of them are fully presented as chapters of the present Thesis.

Articles in Scientific Journals:

1. Macedo-de-Araújo R, Amorim-de-Sousa A, Queirós A, van der Worp E, González-Méijome JM. **Relationship of Placido corneal topography data with scleral lens fitting parameters.** Contact Lens and Anterior Eye. 2019 Feb;42(1):20-27.

2. Macedo-de-Araújo R, van der Worp E, González-Méijome JM. **In vivo assessment of the anterior scleral contour assisted by automatic profilometry and changes in conjunctival shape after mini-scleral contact lens fitting**. Journal of Optometry, 2018 (Epub ahead of print).

3. Macedo-de-Araújo R, Amorim-de-Sousa A, Queirós A, van der Worp E, González-Méijome JM. **Determination of central corneal clearance in scleral lenses with an optical biometer and agreement with subjective evaluation**. Contact Lens and Anterior Eye. 2019 Feb;42(1);28-35.

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6. Macedo-de-Araújo R, van der Worp E, González-Méijome JM. **Success rate over 12 months in a clinical sample of 95 prospective candidates to scleral lens wear**. Submitted to publication,

7. Macedo-de-Araújo R, González-Méijome JM. **Case Report: Improvement of Vision and Ocular Surface Symptoms with Scleral Lenses after Pseudomonas Infection**. Submitted to publication.

8. Macedo-de-Araújo R, van der Worp E, González-Méijome JM. **Clinical findings and ocular symptoms in a clinical sample of scleral lens wearers**. Submitted to publication.

9. Macedo-de-Araújo R, Faria-Ribeiro M, McAllinden C, van der Worp E, González-Méijome JM. **Visual performance over 1-year in a sample of scleral lens wearers**. Submitted to publication

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1. Macedo-de-Araújo R. **Adaptação de Lentes Esclerais: Inquérito Internacional (by invitation)**. 13ª Jornada Cientifico-Técnica de Contactologia (CONTACTUM2019). Braga (Portugal). 5 February 2019.

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3. Macedo-de-Araújo R. **Lentes Esclerais: Resultados Objetivos e Subjetivos de Adaptação de Lentes Esclerais em Córneas Pós-cirurgicas** (by invitation). XII Colóquios UBI. Covilhã (Portugal). October 2018

4. Macedo-de-Araújo R, van der Worp E, Amorim-de-Sousa A, González-Méijome JM. **Previsibilidad de los Parámetros de Altura Sagital de la Topografía Corneal na Adaptación de Lentes de Contacto Esclerales** ,25º Congreso Internacional de Optometría, Contactología y Óptica Oftálmica (OPTOM2018). Madrid (Spain). 13-15 April 2018.

5. Macedo-de-Araújo R, van der Worp E, Amorim-de-Sousa A, González-Méijome JM. **Resultados Objetivos y Subjetivos de Adaptación de Lentes de Contacto Esclerales en Corneas Pos-Quirúrgicas**. 25º Congreso Internacional de Optometría, Contactología y Óptica Oftálmica (OPTOM 2018). Madrid (Spain). 13-15 April 2018

6. Amorim-de-Sousa A, Macedo-de-Araújo R, Queirós, A; Fernandes Paulo, González-Méijome JM. **Evaluación del Vault en la Adaptación de Lentes de Contacto Esclerales con un Biómetro Óptico**. 25º Congreso Internacional de Optometría, Contactología y Óptica Oftálmica (OPTOM2018). Madrid (Spain). 13-15 April 2018.

7. Macedo-de-Araújo R, Amorim-de-Sousa A, van der Worp E, González-Méijome JM. **Six-months Performance of Scleral Contact Lenses: Visual Acuity, Comfort and Handling Perspective.** 15º Congresso Internacional de Optometeria e Ciências da Visão (CIOCV2018). Braga (Portugal). 28-29 April, 2018.

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9. Macedo-de-Araújo R. **Adaptação de Lentes de Contacto Esclerais: Curvas de Aprendizagem do Clínico e do Paciente (by invitation)**. 13ª Jornada Cientifico-Técnica de Contactologia (CONTACTUM2018). Braga (Portugal). 6 February 2018.

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11. Macedo-de-Araújo R, van der Worp E, González-Méijome JM. **Curvas de Aprendizagem na Adaptação de Lentes de Contacto Esclerais: Perspectiva do Clínico e do Paciente**. XIII Conferências Abertas de Optometria (CAOS 2017). Braga (Portugal). 2017

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14. Macedo-de-Araújo R. **Lentes de Contacto Mini-Esclerais** (by invitation). 12ª Jornadas Científico-Técnicas de Contactologia (CONTACTUM'17). Braga (Portugal). 21 February 2017.

15. Macedo-de-Araújo R, González-Méijome JM. **Acuidade Visual e Sintomatologia com Lentes de Contacto de Apoio Escleral em Córneas Irregulares e Altas Ametropias**. 12ª Conferências Abertas de Optometria, (CAO'2016). Covilhã, 12-13 November 2016.

16. González-Méijome JM, Macedo-de-Araújo R. **Adaptação de Lentes de Conacto Especiais - Workshop** (by invitation). Conferências Abertas de Optometria 2016 (CAO'2016). Covilhã (Portugal). 12-13 November 2016

17. Macedo-de-Araújo R, van der Worp E, González-Méijome JM. **Scleral Contact Lenses: Short and Medium Term Changes in Visual Acuity in Pathological and Non-pathological Corneas.** 13º Congresso Internacional de Optometria e Ciências da Visão (CIOCV'16). Braga (Portugal). 23-24 April 2016

18. Macedo-de-Araújo R. **Caso Clínico: Adaptação de Lente Escleral após Infeção Ocular com Cicatriz na Área Pupilar.** Conferências Abertas de Optometria (CAO'2015). 2015

Posters

1. Amorim-de-Sousa, A; Macedo-de-Araújo, R; Amorim, André; Queirós, António; Fernandes, Paulo; JM, González-Méijome. **Influence of scleral contact lens material on the eletrophysiological response of the retina - a pilot study**. 15º Congresso Internacional de Optometria e Ciências da Visão, (CIOCV2018). Braga (Portugal). 28-29 April 2018

2. Macedo-de-Araújo R, van der Worp E, González-Méijome JM. **On-eye breakage by impacting object of mini-scleral contact lens without compromise for the ocular surface.** Global Specialty Lens Symposium (GSLS2018). Las Vegas, Nevada, USA. January 2018

3. Macedo-de-Araújo, R; van der W. E; Amorim-de-Sousa, A; JM, González-Méijome. **Practitioner learning curve in fitting mini-scleral contact lenses in irregular and regular corneas using a fitting trial**. Global Specialty Lens Symposium (GSLS2018). Las Vegas, Nevada, USA. January 2018

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5. Macedo-de-Araújo, R; Amorim-de-Sousa, A; Beerten, R; van der W. E; JM, González-Méijome. **Reduction of night vision disturbances with scleral contact lenses in irregular and normal corneas: subjective and objective analysis**. Barcelona Academy and OPTOM Meeting (EAOO2017) Barcelona (Spain). 12-14 May 2017

6. Macedo-de-Araújo R, van der Worp E, Amorim-de-Sousa A, González-Méijome JM. **Unusual applications of mini-scleral contact lenses: two case reports**. 14º Congresso Internacional de Optometria e Ciências da Visão (CIOCV2017). Braga (Portugal). 2017

Awards

1. Best Poster (1st prize) "**Practitioner learning curve in fitting mini-scleral contact lenses in irregular and regular corneas using a fitting trial**". GSLS2018. Las Vegas, Nevada.

2. Best Oral Comunication (3rd prize): "**Acuidade Visual e Sintomatologia com Lentes de Contacto de Apoio Escleral em Córneas Irregulares e Altas Ametropias**", Conferências Abertas de Optometria (CAO'2016).
3. Best Oral Comunication (2nd prize): "**Adaptação de Lente Escleral após Infeção Ocular com Cicatriz na Área Pupilar**", Conferências Abertas de Optometria (CAO'2015).

Chapter 1

Thesis Overview: Introduction and Rationale

1. Thesis Overview: Introduction and Rationale

1.1 Introduction

Scleral lenses are specialty designed contact lenses that have gained more importance over the last decades. These lenses are made from rigid gas permeable (RGP) materials and vault all the corneal surface, including corneo-scleral limbus. The space between the scleral lens and the corneal surface is filled with liquid – typically preservative-free saline solution – which, together with the RGP material makes them one of the best vision correction options for irregular corneas. After a period in which these lenses were only fitted by a handful of practitioners all around the world, we are facing now an increasing interest in these lenses – which was attributed to improvements in the lens materials and to the implementation of more reproducible computer lathes for lens manufacturing. Even though these lenses were previously fitted - almost exclusively - on irregular-shaped corneas or other ocular surface diseases, the role of scleral lenses has expanded in such a manner that practitioners began to consider to fit these lenses in healthy corneas as well. In fact, this market evolved in such an extraordinary way in recent years that it has been difficult for science to keep pace with this growth. Its consequences? There are few evidence-based clinical practices and long-term prospective studies to prove the visual efficacy and safety for both diseased and healthy eyes. Contrary to other types of contact lenses, the scleral lens fitting process could not be so straightforward. As these lenses do not touch the corneal surface – and because of it are called "scleral lenses" instead of "scleral contact lenses" – the corneal shape assessment will not provide a significant help. Because of that - and before the beginning of this project - scleral lens fittings were considered more "art than science", in which the eye care practitioner needed to use its clinical skills and experience to select the best trial lens for the eye and then the fitting was done by a "trial & error" approach.

The present document integrates a research series nurtured during the last 4 years in the context of the Thesis project entitled: "*Clinical and Biological Interactions During Scleral Lens Wear*". The motivations to conduct the present work arose from the gaps detected during literature review. The lack of long-term prospective clinical reports raised some doubts on the safety of these specialty lenses overtime – in both diseased and healthy corneas. So, the main goal of the present work was to investigate the short, medium and long term interactions of

scleral lenses with the ocular surface and quantify the optical quality enhancement in diseased and non-diseased corneas. Other goals included understand the relationship of scleral lens parameters with corneal and scleral topography and to develop strategies capable of assist the practitioner during the scleral lens fitting process - in order to avoid the use of several trial lenses to achieve the best fit. Also, this work includes an international collaboration in Chapter #13 carried out at Universidad Complutense of Madrid where I had the great opportunity to evaluate the biological interactions of scleral lens on the anterior ocular surface, by means of the goblet cell density assessments in scleral lens wearers with different wearing times.

1.2 Structure of the Thesis Document/ Research Rationale

In order to meet these goals, we designed a prospective dispensing clinical trial. Ninety-five patients (175 eyes) were primarily recruited for scleral lens wear over a 12-month follow-up period. The patients were divided into two groups accordingly to their corneal condition. One group included subjects seeking visual enhancement due to corneal irregularities with different etiologies – primary or secondary ectasias, post-surgical procedures, or trauma. This group included 71 patients (129 eyes). The other group included 24 patients (46 eyes) with healthy eyes – i.e. never underwent an ocular surgery neither had any pathology. This group included patients with high refractive errors that failed any other contact lens wear. All the subjects were evaluated through several appointments – Baseline, Lens Dispensing Visit, and follow-up appointments of 1, 3, 6 and 12 months of lens wear.

Except for Chapter#02 and #03 and some results of Chapter#07 and #09, all the works were developed with measurements performed in the aforementioned 95 patients over their journey of 12 months of scleral lenses wear. In order to make the work easy to follow for the reader, the presentation of this Thesis begins with a brief summary of the rationale of the present organization of chapters. Each one of these chapters configures a research article that has already been published, are submitted awaiting for peer-review or intended to be submitted in the near future. The flow chart in *Figure 1.1* presents the different works that will be presented through this Thesis and is essential for the reader to link the whole work.

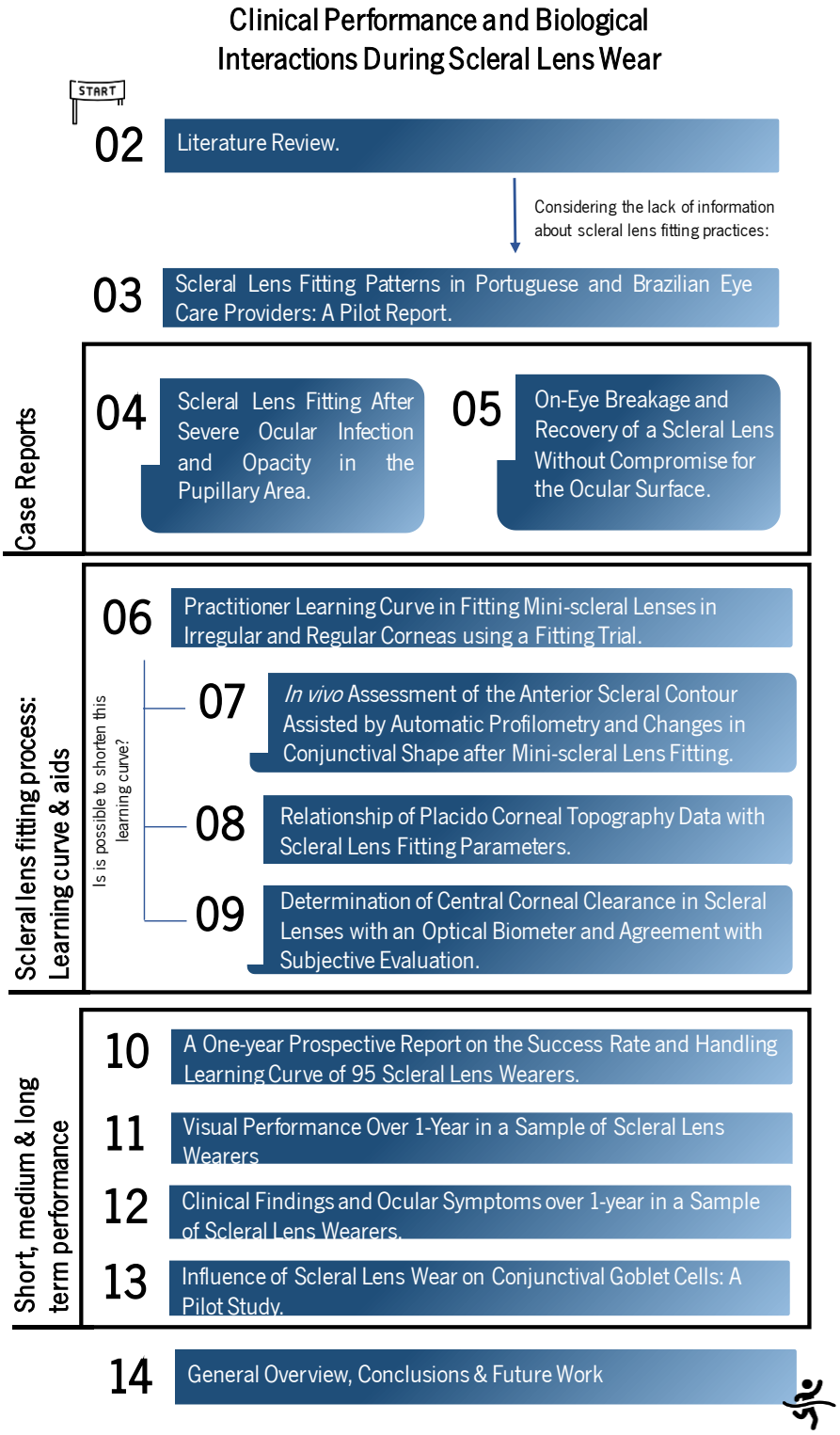

Figure 1.1. Flow chart of the research rationale linking the studies and results chapters included in the thesis document.

Chapter 2
Scleral Lenses: A Review

In this review chapter it is presented a summary of the literature published that served as the basis for the elaboration of this project. This chapter includes a literature review conducted in the beginning of this study on several aspects regarding scleral lenses over the last years. It includes an historical overview of these lenses and how they became the great power in the specialty contact lens industry as they are nowadays. Also the most important aspects regarding indications, fitting process, visual quality, potential complications & contraindications and main fitting issues are revised throughout this chapter. An update on this Review, with more recent peer-reviewed papers and presentations will be overviewed in the "Introduction" section of all the following chapters.

Chapter 3
Scleral Lens Fitting Patterns in Portuguese and Brazilian Eye Care Practitioners: A Pilot Report

This chapter reports the results of an online survey answered by Portuguese and Brazilian eye care providers regarding the scleral lens fitting practice, with respect to scleral lens indications, complications rates, devices used during fitting, care regimens and demographic characteristics of scleral lens fitters and no-fitters. This information allowed to obtain an overview of the role of scleral lenses fitting in Portugal and Brazil, comparing to the known results of other countries and to address the augmented importance of scleral lenses over the last few years in different countries.

Chapter 4
Scleral Lens Fitting After Severe Ocular Infection with Scar and Opacity in the Pupillary Area

This Chapter includes a work that reports the case of one of the first fittings preformed during this Thesis project (patient number 3 of 95). This could be seen as an unusual application of scleral lens fitting. It describes a case in which a low myopic patient, daily disposable contact lens wearer, that had a corneal infection (*Pseudomonas aeruginosa*) 11 months' prior the first

visit with us. Patient and medical efforts saved the eye from being enucleated but an important corneal area became opaque after the infection. Scleral lens fitting has restored the vision for levels that were impossible to achieve with other forms of visual correction, maintaining the corneal integrity and enhancing comfort. The case also comments on the fact that visual acuity by its own could not be a true indication of visual quality enhancement and that the subjective perceptions and other evaluation techniques – such as the evaluation of night vision disturbances – could be important outcomes to take into account.

Chapter 5
On-eye Breakage and Recovery of a Scleral Lens Without Compromise for the Ocular Surface

It describes a case that shows that scleral lenses could have a protective effect to the corneal surface from the direct impact of a high-speed object during a motorbike maintenance. Although the scleral lens suffered an on-eye breakage, the patient didn't suffer any sequel as the pieces of the lens were rapidly removed from the eye. We hypothesized that the lens material, its wide supporting area and the tear film reservoir must have acted as cushioning elements that could both slow down the velocity, absorbing and distributing the kinetic energy of an impacting projectile. Despite the happy conclusions of this case, we did not intent to consider these lenses as protective devices, as they do not replace safety glasses needed during potential risky activities.

Chapter 6
Practitioner Learning Curve in Fitting Mini-scleral Lenses in Irregular and Regular Corneas Using a Fitting Trial

The scleral lens fitting process can be difficult and time-consuming particularly for a non-experienced eye care practitioner. The work versed in this chapter was conducted in order to evaluate my learning curve on scleral lens fitting using a fitting & trials method. With this approach we aimed to characterize the learning curve of a new scleral lens fitter without previous clinical experience in fitting scleral lenses. The number of trial lenses and re-orders that were necessary over the first 156 consecutive fittings performed were counted in a chronological

order. The results of this work led to several other investigations versed in the next 3 chapters – where the main objectives were to investigate new approaches to evaluate the scleral lens fitting (to reduce the number of lens re-orders) and to choose the best trial lens from an objective measure (to reduce the number of trial lenses).

Chapter 7
In vivo Assessment of the Anterior Scleral Contour Assisted by Automatic Profilometry and Changes in Conjunctival Shape After Mini-scleral Lens Fitting

In this chapter, the corneo-scleral topography of candidates to scleral lens wear where measured. Such analysis allowed us to compare the anterior eye surface topography of eyes with irregular and regular corneal surfaces, which could have an important clinical relevance during scleral lens fitting. In the second part of this study, some subjects were selected to wear scleral lenses and the same measurements were performed in order to assess if scleral lens landing zones have some mechanical impact on scleral anatomy. Results from this study allowed to conclude that patients must stop scleral lens wearing if a new lens fit is needed, since sclero-conjunctiva seems to be affected by scleral lens wear.

Chapter 8
Relationship of Placido Corneal Topography Data with Scleral Lens Fitting Parameters

Following the main problem versed on Chapter #6, this work was conducted to find which parameters derived from corneal topography could be eligible to predict the best trial scleral lens for each eye. This was a retrospective study that correlated the scleral lens parameters that patients were wearing and the baseline corneal topographies. Although scleral lenses have unique fitting characteristics, namely the absence of contact with the corneal surface, we found some interesting results that correlate some corneal topographic outcomes with the lenses parameters that patients were wearing. We believe and hypothesized that these kind of metrics will aid the scleral lens fitter in choosing the best trial lens for each eye – however, a prospective investigation is needed to prove that.

Chapter 9

Determination of Central Corneal Clearance in Scleral Lenses with an Optical Biometer and Agreement with Subjective Evaluation

The work presented in this Chapter follows the line of the previous one: find better and more objective ways to aid the eye care practitioner in scleral lens fitting. The central corneal clearance or CCC is almost always measured subjectively with slit lamp (as seen on Chapter #3 results). To have a more objective and quantitative measure of CCC more sophisticated equipments may be needed. The present work aimed to investigate if other clinically available instruments and techniques could be used to have an objective measure of CCC. Three techniques were compared – the subjective technique (slit lamp), image processing technique (ImageJ) and an indirect measure with an optic biometer (IOLMaster).

Chapter 10

A One-year Prospective Report on the Success Rate and Handling Learning Curve of 95 Scleral Lens Wearers

This chapter includes the first work of this document reporting long-term (12 months) scleral lens wear outcomes. Despite the growing body of literature on the indications and possible contraindications of scleral lens wear, there is lack of prospective peer-reviewed works that study the scleral lens fitting process over a long period of time. In this specific work, I overviewed the total 95 patients that were recruited to this project and studied the fitting success of scleral lens wear, by analyzing and comparing those patients that concluded the 12-month follow-up period with those that discontinued scleral lens wear. Scleral lens handling is an important issue that can led to several dropouts, so it was addressed at the second part of the study - here, the mean time to correctly apply the lens for the first time as well as the long term changes in handling routines (number of days per week and hours per day of lens wear, etc) were recorded.

Chapter 11
Visual Performance Over 1-Year in a Sample of Scleral Lens Wearers

This chapter includes the second long-term work. Although the visual acuity enhancement with scleral lenses was previously mentioned in the literature – namely for irregular cornea patients -, this is the first prospective work reporting the visual acuity and other vision quality metrics over the 12-month follow-up in both diseased and healthy corneas. Measurements of high and low contrast visual acuity, aberrometry, night vision disturbances and subjective perceptions of the wearer were assessed at baseline and with scleral lenses at all appointments. Although visual acuity assessment is always used in scleral lens fittings assessment, aberrometry and night vision disturbances are not so common and this work shows that these outcomes add valuable information about the visual quality promoted by these lenses.

Chapter 12
Clinical Findings and Ocular Symptoms Over 1-year in a Sample of Scleral Lens Wearers

This chapter included the third and last long-term report on scleral lens wear. This chapter shows the results over the 12-month follow-up regarding scleral lens fitting, ocular health and symptomatology recorded with different questionnaires. Regarding ocular health, the slit lamp findings of bulbar redness and staining and corneal edema were recorded, as well as the adverse events that occurred over the 12 months. The scleral lens fitting – central corneal clearance and landing zone periphery alignment – were recorded at all follow-up appointments. All these measures allowed to evaluate several research questions that arose from previous peer-reviewed works – Are scleral lenses safe for diseased and heathy corneas? Does the short-term corneal edema induced by scleral lenses and the decrease of central corneal clearance continues over the long-term? In summary, this was the first long-term prospective investigation in a controlled sample that allowed to address several aspects regarding the safety, comfort and fitting characteristics of scleral lens wear over 12-months.

Chapter 13
Influence of Scleral Lens Wear on Conjunctival Goblet Cells: A Pilot Study

Scleral lenses do not interact directly with the corneal surface. However, these lenses rest on the sclero-conjunctiva region, resulting in a mechanical impact in the bulbar conjunctiva which can somewhat modify some conjunctival properties – which, from their part, may have some influence in tear film composition and symptomatology of the patient. The main goals of this work were to use a combined technique (impression cytology and laser confocal microscopy analysis) to evaluate the differences in goblet cell density and mucin cloud amplitude between superior and inferior bulbar conjunctiva and to evaluate the effect of scleral lens wear in both variables. Although this work does not report a longitudinal follow-up, it compared the goblet cells density and mucin cloud amplitude in two groups of subjects wearing scleral lenses: one group included subjects wearing the lenses for less than 4 months (1 to 4 months) and the other group included subjects wearing the lenses for more than 6 months (6 to 18 months).

Chapter 14
Conclusions and Future Work

This last Chapter highlights the main results and their potential implications in the scleral lens area. The last part comments on the future lines of work that can be developed on the basis of this work.

Chapter 2

Scleral Lenses: A Review

2. Scleral Lenses: A Review

2.1 Brief History of Scleral Lenses

Scleral lenses are large diameter contact lenses that have their resting point beyond the corneal borders without any mechanical interaction with the corneal surface. The scleral lenses as they are known nowadays passed through an evolutionary process with several "ups and downs" since their first conceptualization.

The invention of contact lenses is every now and then attributed to Leonardo Da Vinci. Actually, what Da Vinci described was the first concept of neutralizing the corneal power by pushing the head in a bowl of water. [1] Although this was not the invention of the contact lenses, it certainly contributed to the understanding of corneal neutralization that years later was used to inspire the development of the first contact lens. Many theoretical concepts on the corneal neutralization using devices with fluid against the eye emerge in the next years. [2,3]

As a matter of fact, names such as Frederich Müller, Albert Müller, Ernest Abbe, Eugene Kalt, Adolf Fick and August Albert Müller are unknown for the great majority of eye care practitioners. These names are linked to the development and application of the first contact lenses of history. We were in the late 1880's when Müller brothers made the first contact lens. This was actually a scleral lens in its concept – as the lenses had their resting points on the sclera. Müller were artificial eye makers that idealized this "scleral shell" with a protective intent for a patient with palpebral injuries. The lens – made from glass – was similar to an artificial eye, except the corneal area was clear, allowing the patient to see. [4] At about the same time, Ernest Abbe made some glass scleral lenses and shared them with Fick, a German ophthalmologist that was studying the corneal shape in keratoconus – he fitted lenses in six patients, and in one of them (with keratoconus) the vision improved considerably. [3] At the same time, Kalt also investigated these lenses as "orthopedic appliances" for the treatment of keratoconus. [3] In 1889, August Müller described in his dissertation entitled "Spectacle Lenses and Corneal Lenses" the correction of his 14-diopters of myopia, stating that *"... we can give an abnormal eye a new cornea, such that this new refracting surface will produce images in the correct position*".

[5] These early scleral lenses (or scleral shells) were about 20mm in diameter and were made of glass. However, these lenses didn't have the widespread acceptance that one could think. In fact, they were difficult to manufacture and had a potential risk for the corneal integrity, as they were impermeable to oxygen, leading to severe problems of corneal hypoxia. Fortunately, the introduction of molding techniques and the introduction of moldable acrylic plastics (polymethyl methacrylate - PMMA) for contact lenses in the 1930s and 1940s were important breakthroughs in the contact lens field. [6–9] Despite that, their usefulness was compromised by the early findings of corneal epithelial edema and neovascularization in the long term – which were somewhat minimized with corneal lenses, with a much lower diameter. These hypoxic problems led to the emergence and success of new lens materials and designs – first, the hydrogel material in the early 70's and 7 years later the introduction of rigid gas permeable materials (RGP). All of these were good news for the overall contact lenses practice, but made scleral lenses nearly obsolete for several years.

2.2 Modern Scleral Lenses

In the context of modern scleral lenses, other names appear – Donald Ezekiel, Perry Rosenthal, Rients Visser, Ken Pullum, among others. The first successfully use of a scleral lens with RGP material was described in 1983 by Donald Ezekiel. [10] Rients Visser became enthusiastic with this creation. Previously to this invention, Visser was fitting PMMA corneal lenses and hydrogel contact lenses but still prescribed PMMA scleral lenses in certain corneal conditions – however, with reduced wearing times because of the unacceptable level of corneal hypoxia produced by these lenses. With this first description of RGP scleral lenses, Visser and other minority of specialized contact lenses fitters began to prescribe RGP scleral lenses all around the world. Other innovations were made in the following years – in the late 80s, Perry Rosenthal came up with the first non-fenestrated RGP scleral lens; during 90s, front toric lens designs to improve vision [11] and the back-surface toric scleral lenses (by Visser's team and contact lens company Procornea) for better lens alignment with the ocular surface were introduced. [12,13] These breakthroughs, allied to improvements in the ability to evaluate all the corneal surface contour, development of better computer-driven lathes for more reproducible lens manufacture, and development of diagnostic lens sets led to an exponential renewed interest in

scleral lenses. All these "ups and downs" in the history of scleral lenses are depicted in the graphic of *Figure 2.1.*, that shows the rate of publications since 1946. After a period in which some publications were made (60s and 70s) – probably related to the emergence of PMMA lenses - it is seen a period with few publications on the field of scleral contact lenses (until 2000s) – related to the appearance of other materials and designs. After that, an exponential number of publications began to appear, undoubtedly related to the aforementioned reasons – better biocompatibility of RGP materials, more reproducible manufacture and more sophisticated anterior eye surface imaging techniques. In fact, this was a huge increment, but one must take into account that the great majority of the scleral lens literature rely on case reports, retrospective studies describing the use of specific lens designs in individual practices or reviews of ocular conditions for which scleral lenses were prescribed, and prospective or retrospective observational studies. [14]

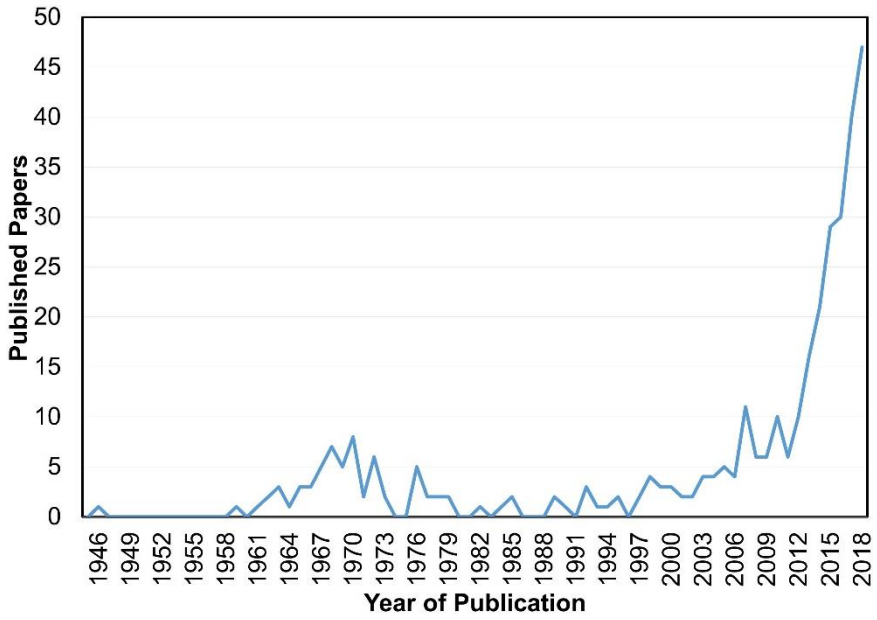

Figure 2.1 Publication rate (yearly) in the field of scleral contact lenses as retrieved from the National Library of Medicine search engine (www.pubmed.com) by December 3rd, 2018, using the same combination of keywords previously described [15] and after excluding the non-related cases (n=340). This graphic was published recently in the Editorial of Scleral Lens special edition (Contact Lens and Anterior Eye). [16]

Scleral lenses have conquered the specialty lens market and are undoubtedly the sum of all the evolutions completed in different areas since the late 1880s. Scleral lenses – in its

modern design – can be described as large diameter, non-fenestrated, RGP lenses that are supported entirely by the sclera. They have unique fitting characteristics that makes them an excellent platform to compensate visual deteriorations due to different etiologies, relief of ocular-surface symptoms and correct high ametropies (see section 2.5.). In fact, the only point of contact of these lenses with the ocular surface is in the scleral underlying the conjunctiva. Theoretically, scleral lenses should be named "conjunctival lenses". However, the conjunctiva is a soft and non-structured tissue – as it only follows the shape of the sclera - and because of that the lenses were named "scleral". In addition, scleral lenses vault the entire corneal surface and limbus – avoiding any mechanical interactions with these structures - promoting a thick liquid reservoir between the back surface of the lens and the corneal epithelium (*Figure 2.2.*) – so these lenses need to be inserted with liquid. These clearance, along with the lens materials, allows to fully correct the irregularities that can be present in the corneal surface, promoting an excellent visual correction. The fact that there is no point of contact with the corneal surface, makes these lenses extremely comfortable when compared to corneal RGPs. All these unique characteristics made scleral lenses one of the best vision correction options available nowadays.

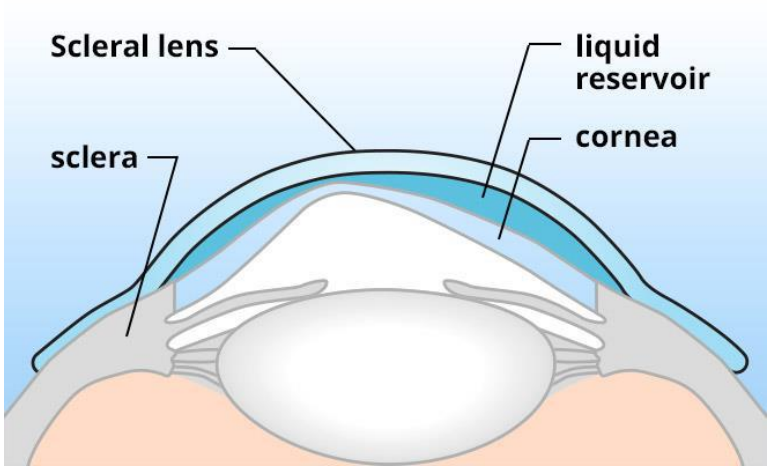

Figure 2.2 Scleral lens – a liquid tear film reservoir is seen underneath the lens. In: http://www.allaboutvision.com/contacts/scleral-lenses.htm

2.3 "Anatomy" of a Scleral Lens

Until recently, these lenses were subdivided in categories accordingly to their diameter – corneoscleral, mini-scleral and full-scleral. However, these definitions were not linked to the

corneal diameter. For example, a 14.5mm was considered a semi-scleral lens, but if the patient had a corneal diameter smaller than the average, the lens could not have any mechanical interaction with the corneal surface and act as a scleral lens. This encouraged the Scleral Lens Education Society (SLS) to introduce, in 2013, a revised terminology based on where the lens distributes its weight rather than the lens diameter (*Table 2.1.*). [3]

Table 2.1. Scleral Lens Education Society (SLS) recommended terminology for modern scleral lenses.

Lens Type	Description	Definition of Bearing Area
Corneal		Lens rests entirely on the cornea
Corneo-scleral		Lens rests partly on the cornea and partly on the sclera
Scleral	Mini-scleral *Lens is up to 6mm larger than HVID** Large Scleral *Lens is more than 6mm larger than HVID*	Lens rests entirely on the sclera

*HVID – Horizontal Visible Iris Diameter

The selection of scleral lens diameter (mini-scleral and large scleral) will be related to the indication for lens fitting. The main difference between mini and large scleral lenses, apart from the diameter, is the amount of clearance that they can create underneath the lens. So, more compromised corneas, with higher irregularities, may benefit from large tear film reservoirs and - every now and then – it only can be achieved with a large scleral, depending on the patient's ocular sagittal height. [17] But is not only for highly compromised corneas that large-scleral lenses can promote benefits. Section 2.5 will revise the main indications for scleral lens fitting.

Scleral lenses could be divided into four main zones – Optic zone, intermediate zone (that can be further divided into mid-peripheral and intermediate zone) and landing zone. More zones could be added and can be labeled many ways by each manufacturer (*Figure 2.3.*). The first zone – optic zone – is the central portion of the lens and will create the dioptric power. It can be labelled in dioptric power, radii of curvature or sagittal height. The definitions of all of these, namely the sagittal height, will vary significantly with the manufacturer. Unique optical properties, such as sphere, cylinder, asphericity and high order aberrations corrections can be added to this zone to enhance visual quality. This zone needs to vault all the corneal surface, avoiding touching

it. The intermediate zone is also very important in scleral lens fitting. These lenses need to vault the entire limbus too, and it could be challenging. The limbus-lens clearance should be lower in order to not compromise the oxygen delivery to the limbal stem cells. Sometimes, due to the infero-temporal deccentrations of the lenses and anatomical features, the limbus clearance on the supero-temporal region is reduced. Last, is the landing zone, considered one of the most important zones as is the zone that contacts with the ocular surface. The shape of the landing zone should be aligned with the overall scleral shape. To perform that correctly, these zone can be spherical, toric, quadrant specific or notched.

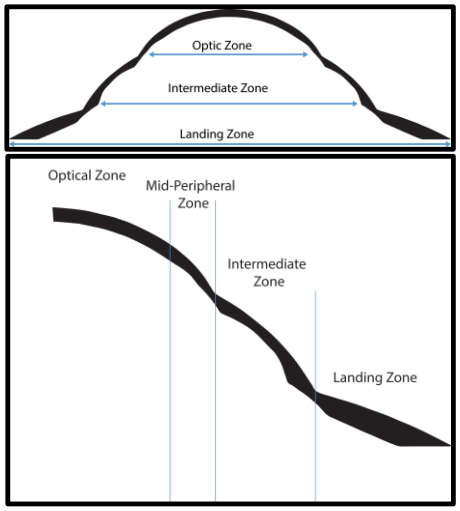

Figure 2.3 The basic four zones of a scleral lens.

2.4 Anatomical Considerations for Scleral Lens Fitting: The Scleral Shape

As scleral lenses land exclusively on the sclera, it is important to know the anatomy of this structure. The truth is that little importance was given to anterior eye's shape, except for corneal shape, but the recent resurgence of scleral lenses led to renewed interest on corneo-scleral junction and scleral shape.

The corneo-scleral junction (limbal area) was thought to be concave but it has been found that it had a tangential shape instead. Considerations on scleral shape, and its asymmetry are very important to consider the geometry of the lens to be fitted – small or large diameter,

toric or quadrant-specific landing zone, notched, etc. Limbal shape is seen as an important parameter when fitting scleral lenses. In 1992, Meier [18], with slit lamp examinations, has defined five types of transition profiles from cornea to sclera (*Figure 2.4*.) that are decreasing in sagittal height (number 1: highest sagittal height; to number 5: lower sagittal height):

1. Gradual transition with the scleral portion being Convex;
2. Gradual transition with the scleral portion being Tangential;
3. Marked transition with the scleral portion being Convex;
4. Marked transition with the scleral portion being Tangential;
5. Convex corneal shape with a concave corneal shape.

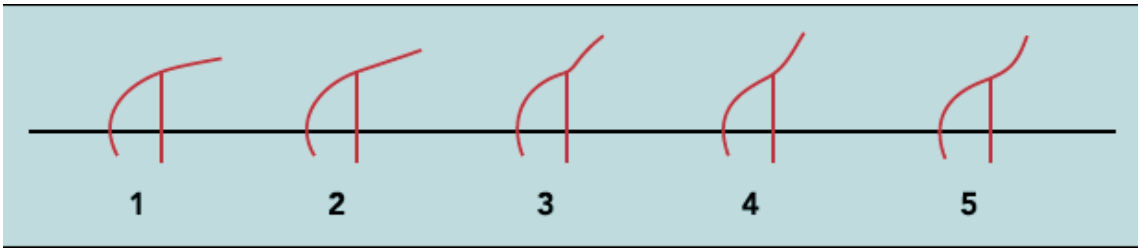

Figure 2.4 The different limbal transitions. Image from: A guide to scleral lens fitting V2.0, by Eef van der Worp. [17]

Theoretically, the scleral shape was assumed to be concave in shape, but measurements with anterior segment optical coherence tomography (AS-OCT) conducted at Pacific University led to conclude that most of corneo-scleral junctions were tangential. [19,20] It was therefore suggested to use tangent angles rather than curvature to describe corneo-scleral and scleral shapes. [21] From the same studies at Pacific University, it was concluded that the nasal part was flatter than the other quadrants of the eye (*Figure 2.5*).

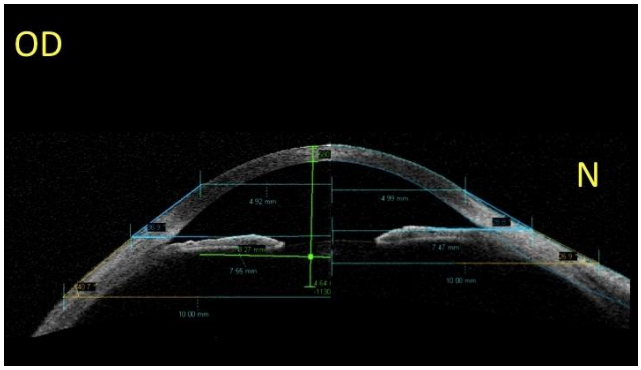

Figure 2.5 OCT image of anterior ocular surface. Here the flatter nasal scleral shape is evident. Image from: http://contactlensupdate.com/2012/09/12/beyond-the-corneal-borders-an-update-on-scleral-lens-fitting/

Further studies with OCT led to conclude that between 10.0mm and 15.0mm chord the angles are very similar through the 8 principal meridians of the eye, but the farther they go (15.0mm to 20.0mm) the greater the asymmetry between the measures of the meridians. As mentioned and seen on *Figure 2.6.*, the sclera has a non-spherical nature, with the nasal side being flatter than temporal (lower tangential angles). This suggests that if we fit a scleral lens with bearing points up to 15.0mm, a non-toric lens may have a good performance; but if we fit a scleral lens with bearing points closer to 20.0, a toric or quandrant specific lens may be needed. These non-rotationally symmetric lenses can minimize conjunctival blanching by reducing localized bearing areas. In fact, this asymmetry will result in a different weight bearing of a spherical scleral lens on the globe which will induce compression of the conjunctival vessels – also known as *conjunctival blanching*. This will have an effect on comfort and wearing time. [13,19] Because of the aforementioned asymmetries, ccleral lenses lenses tend to decenter temporally [22] and also inferiorly due to gravity action. [22]

Other techniques to measure scleral topography have emerged recently. The eye surface profiler (ESP) [23] and sMap3D [24] - based on profilometry – are recent devices that promise to be good allies with scleral lens practitioners, in order to help to understand scleral anatomy and aid the scleral lens fitting process.

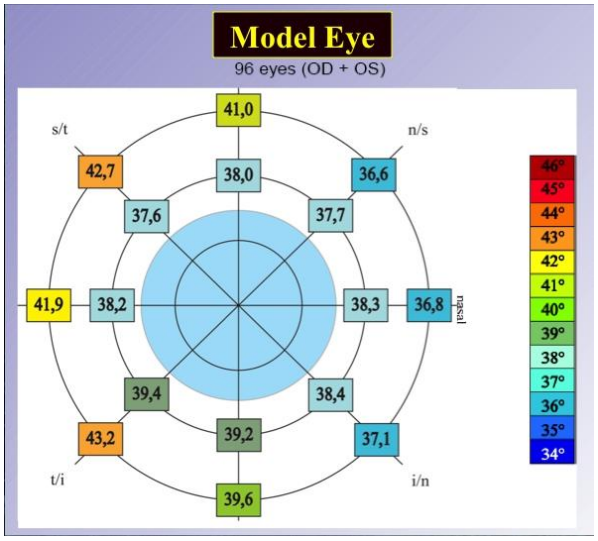

Figure 2.6 Ocular surface shape beyond the cornea: study at the Pacific University College of Optometry (Oregon, USA). Image from: A Guide to Scleral Lens Fitting [17]

2.5 Current Indications for Scleral Lens Wear

Scleral lenses provide unique therapeutic and vision rehabilitative properties for ocular surface diseased and irregularities. Indications for scleral lens fit have been evolving over the years. In the early days, these lenses were fitted exclusively in severely compromised corneas but now some defend that these special lenses can also be fitted to less compromised corneas. In fact, some look after that non-diseased eyes can take advantage of comfort, corneal vaulting and centration promoted by these lenses. [25] Indications for scleral lens wear are now well established and divided into vision improvement, ocular surface protection and support and for sport and cosmetics. [14,25] PMMA hand-painted lenses have been used for several years for cosmetic purposes. Others can also beneficiate from these lenses in cases of ptosis (for example) as large diameter scleral lenses promote a clearance that can increase the aperture size and then diminish ptosis. For sports, these lenses can have benefits in water sports and those activities that involve exposure to dusty environments.

However, the primary clinical indication of scleral lenses is for vision enhancement. Scleral lenses proved to be effective in improve the vision quality in several stages of corneal diseases. [26,27] Since 1984 that studies show that the main focus of these lenses are primary corneal ectasias (PCE) (see *Figure 2.6.)* but also secondary ectasias (normally related to

unsuccessful refractive surgery), with both including large amounts of high order aberrations which leads to a reduced optical quality. [25,28]

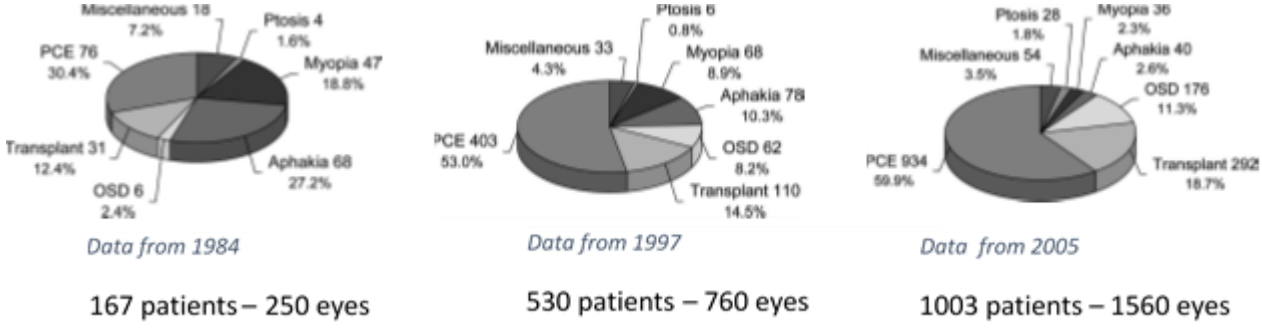

Figure 2.7 Data collected and reproduced from studies from Pullum et al:
1984: The modern concept of scleral lens practice
1997: A study of 530 patients referred for rigid gas permeable scleral contact lens assessment
2005: Scleral contact lenses: the expanding role

The secondary ectasias can be due to unsuccessful post-refractive surgery (LASIK, LASEK, PRK and RK). Some studies evaluated the vision benefit of eyes with irregular corneas and concluded that these patients can have a significant improvement: Romero-Jiménez *et al* found a statistically significant improvement in visual acuity (VA) with the best corrected visual acuity with scleral lenses (0.09) compared to the without correction situation (0.82). [26] Others found an improvement of approximately 2 lines with scleral lenses when compared to best corrected visual acuity and approximately 5 lines when compared to uncorrected visual acuity. [27] Also, other indications for vision improvement is after other kind of surgery in patients with corneal primary ectasias, like intraestromal ring implants and corneal crosslinking. A study [29] concluded that scleral lenses are well-accepted in these cases, with excellent indication to restore vision. Other indication is after corneal transplants (namely penetrating keratoplasty) as they often require a contact lens to restore vision and a scleral lens can be indicated in these cases, as it can help to preserve fragile corneas and prevent mechanical stress on the cornea. [30,31]

Other indication is for ocular surface protection. Patients with dry-eye related diseases (Dry eye, Sjogren's syndrome, Steven-Johnson syndrome, graft-versus-host disease, exposure keratopathy, and others) can benefit from scleral lens wear because of the retention of a fluid reservoir that maintains the bulbar surface moistened. Also, scleral lens can protect the eye in cases of incomplete lid clousure (eyelid coloboma, exophtalmus, or ectoprion). [25]

2.6 Complications and Fitting Challenges Associated with Scleral Lens Wear

The balance between risk and benefit is more evident at this point in diseased eyes than in non-diseased eyes. Although the short-term complications of scleral lens wear on diseased eyes have been thoroughly studied with relatively few reports regarding the unique aspects of their fittings and potential complications, the consequences of long-term scleral lens wear are unknown for the diseased and non-diseased eye, despite the proven benefits in visual quality and comfort. [15] The following sub-sections will have a critical review of scientific peer-review literature regarding several types of complications that could occur during scleral lens wear. *Figure 2.8* compiles some of the adverse events and fitting challenges that can occur during scleral lens fitting process, based on the review of Walker *et al*. [22]

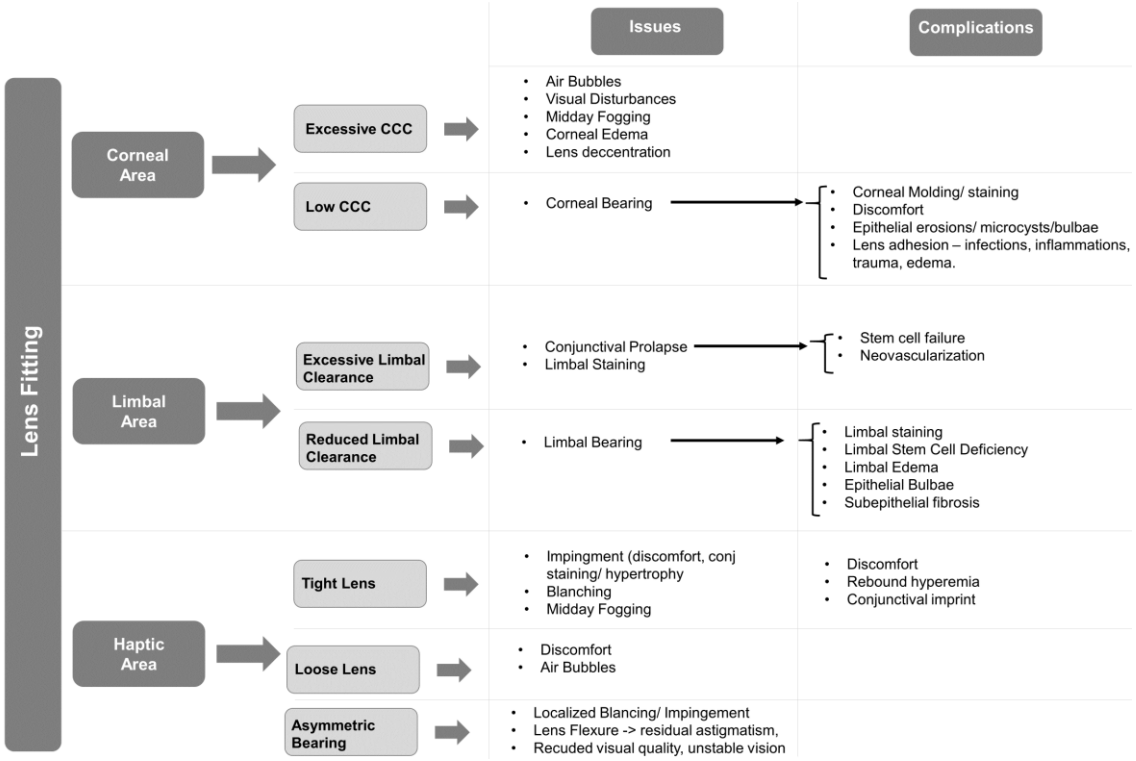

Figure 2.8 Summary of fitting challenges and consequent complications that can occur during the scleral lens fitting process. Contents based on Maria Walker *et al* Review paper. [22]

Infection-related and inflammation-related events

Isolate case reports and congress presentations confirm the occurrence of corneal infections and inflammations during scleral lens wear, which had increased in the last few years, due to the resurgence of scleral lens into the marker. [22] The tear stagnation observed underneath a scleral lens might be related with the incidence of these kind of problems, namely on previously compromised corneas. [15,32]

Relatively to infection-related problems, in a retrospective review with a total of 875 eyes, there was a report of 4 cases of microbial keratitis in patients wearing scleral lenses in an extended basis due to persistent epithelial defects. [32] Other publications referred the same event caused by *pseudomonas* in 2 patients, [33] and other referred a polymicrobial keratitis. [34] The inflammation-related events due to scleral lens wear are even less related on the literature. In a review, Walker *et al* [22] commented that there are inflammation problems during scleral lens wear that are underreported in the peer-review literature but are confirmed by clinical experience. Although inflammation-related events can be attenuated by changing lens parameters, some patients report experiences of discomfort and/or redness. There is a report of an acute red eye related to scleral lens wear in a 44-years old female with keratoconus. Despite the efforts for augment the vault separation, there was a recurrence after few months that was linked to deficient contact lens maintenance. Eye care solutions were changed and no other problems were felt after, so the authors conclude that lens hygiene may be particularly important to avoid these kind of problems during mini-scleral lenses wear. [35] There are two other works referring cases of acute red eye, [36,37] and another related a conjunctival hyperemia after lens removal which was considered to have an inflammatory etiology (*rebound hyperemia*). [35,38] Despite the absence of systematic reports of these kind of problems, they exist. It is confirmed by the numbers of scleral lens discontinuation due to discomfort (about 10% according to 2 different studies). [39,40]

Although there are few publications in the peer-review literature, it is a topic that deserve attention in order to be avoided. In fact, there is an increasing risk of bacterial keratitis infection during extended wear of scleral lenses and attention to hygiene and lens care is needed to prevent these cases. [17,35] Also, all the literature cited is related to previously affected/

diseased eyes and there are no reports in peer-review literature of adverse reaction in uncompromised/ healthy eyes.

Hypoxia-related events

As mentioned in the previous section of this review, hypoxia was the primary reported cause of complications because of the materials used (glass and PMMA). [22] Recent reviews [15,22] refer the same paper in their "complications and fitting challenges" section: the article is from 1995 (retrospective, analyzed 517 eyes), and reported the hypoxia-related incidence of edema (7.4%), corneal vascularization (13.3%), and also abrasion (3.1%), and papillary conjunctivitis (1.7%). [5] The great majority of the eyes were wearing PMMA scleral lenses which is impermeable to oxygen, so it was expected a great incidence of adverse hypoxia-related events with these lenses than with RGP lenses. The fact is that there are no systematically reported adverse hypoxia-related events with RGP that prove or disprove the occurrence of corneal swelling [41] and so we continue to be based on the same scientific evidence from 20 years ago. Some recent works tried to estimate the best combination of lens thickness, lens permeability and postlens tear film thickness that could promote the best oxygen supply to the cornea and avoid hypoxia-related problems. [42–45] Despite the utility, these studies are theoretical and could not be reproduced in clinical practice. One of the studies [42] included also a clinical trial with 8 healthy eyes wearing lenses and concluded that corneal thickness increased significantly after 3h of scleral lens wear with two lenses providing different postlens tear film thicknesses: the shallower (150 μm) caused an increase of 1.59% and the deeper (350μm) caused an increase of 3.86% in corneal thickness. These values are within the expected values of physiological edema that occurs during sleeping (about 4%). This was the only clinical trial that aimed to calculate the amount of edema caused by scleral lens wear; however, the patients only wore the lenses for 3h, which is a relatively short time to assess the real effect of hypoxia during all-day of wear. Also, it is important to know which are the long term effects for the eye that is exposed to some kind of hypoxia, and if the amount of hypoxia is the same for the diseased and non-diseased eyes. Once again, this physiological edema could have no important influence in diseased eyes, since sometimes scleral lenses are the only option to achieve a good visual acuity, but the possible consequences in non-diseased eyes deserve more attention.

Midday Fogging

Clinicians have been reporting a problem called *midday fogging (Figure 2.9.)*. This condition is characterized by the accumulation of particles in the tear film beneath the contact lens, creating a blur image similar to fog sensation in some patients after few hours of wear. It is estimated to occur in approximately 20% to 30% of ScCL wearers, [46] even when it appears to be a "good fit". Although this phenomenon is very discussed among clinicians and at conferences, it is little referred on peer-review literature. Because of it, the mechanisms that led to the formation of these particles or either what these particles really are, are still unknown.

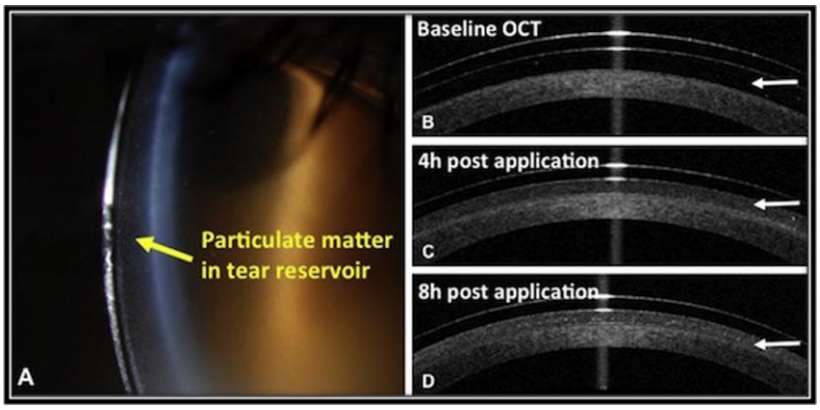

Figure 2.9 A shows an optic section with slit lamp. Images **B, C** and **D** shows images with OCT: a progressive opacification of the tear film reservoir is seen. Images extracted from Walker *et al.* [22]

Some believe that this is related to the absence or lack of tear turn over and others relate this accumulation to fluid forces associated with scleral lens system and pressure at peri-limbal conjunctiva. In this last case, some re-fitted "*foggers*" with new lens design that plugs up the peripheral cornea and the fogging was eliminated. [47] Because we don't know yet the real nature of these particles and why they only appear in some patients, the only way to manage it is by removing the lens, rinsing and refiling them with fresh unpreserved saline solution and reinsert them. With this technique, the patients are able to wear the lenses for a few more hours with reasonable good optical quality. [22] This decrease in optical quality was already referred in the peer-review literature but without the name "midday fogging". Rosenthal *et al* [32] referred that some patients needed to remove the lens periodically due to accumulation of tear debris, but without referring the number of cases/ prevalence.

Lens seal-off

A condition called *lens seal-off* - which is referred as a strong suction of the lens to the eye – is commonly reported. [22] Patients with compromised ocular surfaces suffering from diseases like keratoconus or pos-surgical procedures like LASIK or keratoplasty that suffer *lens seal off* have a higher risk of trauma or rupture of the globe during lens removal. In addition, the stagnation of tear film underneath the lens increases the susceptibility to infections and inflammations. [39] Clinicians are aware of this problem and recommend the midday removal of the lens to avoid this kind of problems.

Conjunctival prolapse

Other fitting challenge rarely mentioned in the literature is the *conjunctival prolapse*. It occurs when the conjunctival tissue migrates and adheres to the peripheral cornea. [22] Only one study reported the occurrence of 1 case, among the 33 patients fitted with scleral lenses. [39] Because of it, the consequences of this conjunctival prolapse are unknown, but, in a clinical perspective, Walker *et al* [22] recommend to fit the lens with less clearance, especially on the limbal zone.

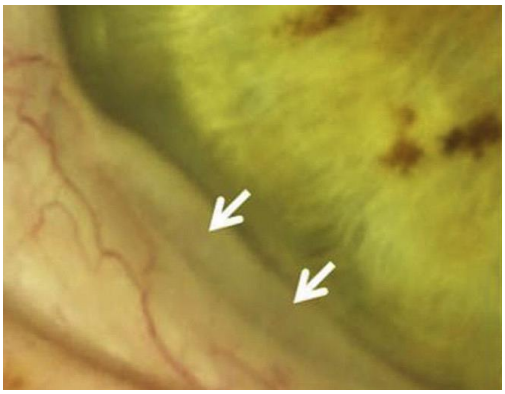

Figure 2.10 Conjunctival prolapse in the inferior-temporal zone (Image adapted from Walker *et al* [22])

The re-birth of scleral lenses in the last few years makes it urgent to complete new investigations in order to support all of these unsolved problems related to scleral lens wear and evaluate the balance between risk and benefit in non-diseased eyes. Also, the fitting patterns over all countries need to be evaluated in order to establish good practice behaviors for scleral lens fitters worldwide.

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Chapter 3

Scleral Lens Fitting Patterns in Portuguese and Brazilian Eye Care Practitioners: A Pilot Report

3. Scleral Lens Fitting Patterns in Portuguese and Brazilian Eye Care Practitioners: A Pilot Report

3.1 Abstract

Purpose: To report the scleral lens fitting practice, with respect to scleral lens indications, complications rates, devices used during fitting, care regimens and demographic characteristics of scleral lens fitters. A secondary goal was to identify the main reasons why some practitioners do not fit scleral lenses.

Methods: An online survey was designed to assess the current fitting patterns and demographic characteristics of the fitters. The results of the present work are based on the answers of the Portuguese version. The survey was anonymous and was disseminated through online platforms in Portugal (PT) and Brazil (BR). A total of 75 responses were retrieved and analyzed – 48 from PT and 27 from BR. Data was analyzed by country.

Results: The mean age of the respondents was 31±8 and 45±7 years for PT and BR, respectively.

33% of PT respondents and 89% of BR respondents reported to have completed at least one fitting of a lens with a diameter larger than the cornea (>13mm). The great majority of PT respondents had an Optometry-related graduation or master (63% and 29%) and worked majorly at Optical Stores (n=34) and the great majority of BR respondents had an Ophthalmology degree (81%) and worked majorly at Private Hospitals and/or Ophthalmology Clinics (n=12 and 22, respectively). All respondents completed their first scleral lens fitting after 2010. The main indication for scleral lens wear reported by scleral lens fitters was keratoconus (100% PT and BR). Scleral lenses were considered as the first option to fit an irregular cornea in 38% of PT and 21% of BR and none of the respondents considered scleral lens as the last option. More than 95% of respondents from both countries use slit lamp and fluorescein during the fitting process, and only one PT practitioner mentioned to use a scleral topographer. The most prevalent scleral lens-related adverse events were acute red eye (PT 25%, BR 58%), handling-related problems (PT 25%, BR 42%), corneal neovascularization (PT 19%, BR 25%) and corneal edema (PT 19%, BR 13%). None of the respondents reported to have any corneal ulcer event. Thirty-eight percent (38%) from PT and 17% from BR respondents reported never had a patient that discontinued scleral lens wear. The more prevalent causes for scleral lens dropout were handling problems (PT 44%, BR 46%) and patient financial aspects (PT 19%, BR 63%). BR respondents also stated that some patients (29%) discontinued scleral lens wear because of some adverse event/ complication.

Conclusion: This pilot report on current scleral lens practice in Portuguese and Brazilian eye care practitioners shows that scleral lens fitting is quite new among PT and BR populations (since 2010) and provide valuable information on scleral lens fitting patterns of both countries. More countries need to be added to this survey in order to have a general overview of the scleral lens practices all around the world and help to identify risky behaviors and to create universal good practices for all practitioners.

3.2 Introduction

Considering their unique characteristics, the scleral lens fitting process could be challenging, especially for a beginner practitioner (Macedo-de-Araújo, Learning Curve, BioMed Int – accepted). Modern scleral lenses are made from rigid gas permeable materials (RGP), like corneal RGPs or hybrid lenses (with a central RGP material and soft skirt in the landing zone). However, and contrary to the other contact lens modalities, scleral lenses do not have any mechanical interactions with the cornea and corneo-scleral limbus. Instead, they vault all this area and only contact with the anterior eye surface on conjunctival area. Considering the mucous and non-structured nature of the conjunctiva (as it only follows the scleral contour), these lenses are called "Scleral Lenses" instead of "Conjuntival Lenses" as it is the sclera that actually supports them. These lenses need to be inserted with liquid, creating a tear fluid reservoir between the posterior part of the lens and the anterior corneal surface, which - together with the lack of interactions with the corneal surface - makes them a comfortable option for the patient. [1–5] Despite the comfort enhancement, the corneal clearance and the lens's material, make scleral lenses one of the best vision correction options for the irregular cornea – as the irregularities are masked by both corneal clearance and the RGP material. [3,5–8]

The resurgence of scleral lenses over the last decade led to a growth in the interest on the field. However, scleral lenses are considered to be in its "infancy" [9], with the body of peer-reviewed literature available nowadays consists majorly of case reports, retrospective reviews or short-term outcomes. [6,10] In this regard, surveys are always an interesting option to have an overview of what is happening all around the world – who is fitting scleral lenses, practice patterns, good or bad practice behaviors, among other important information. The Scleral Lenses in Current Ophthalmic Practice: An Evaluation (SCOPE) was the pioneer group designing an online survey regarding the fitting patterns [11] and demographic characteristics [12] of scleral lens fitters around the world. However, the great majority of the respondents were based on the United States of America (71%). Although more 40 countries were identified, they were not mentioned [12], so one does not know if there were any Portuguese or Brazilian respondents identified. The present work aims to report current scleral lens practices in Portugal and Brazil.

3.3 Methods

A survey was developed by investigators from the Clinical and Experimental Optometry Research Lab (CEROLab – University of Minho, Portugal) and from OCUPHARM (University Complutense of Madrid – Madrid, Spain) The survey consisted on different paths regarding the response to the first question, that aimed to know if the practitioner has already fitted any contact lens larger than the corneal surface (>13 mm). If the respondent answered "no", the survey was designed to show only questions related to the "reasons why". On the other hand, if the respondent answered affirmatively to the first question, he/she was directed to more 17 questions related to the fitting patterns and habits. The last section, related to demographic characteristics of the respondents was showed to both fitters and no-fitters practitioners and included age, gender, country of practice, academic training and year of conclusion, and place of work/practice. All questions had an obligatory answer in order to complete the survey. The scleral lens fitting-related questions included questions regarding the year of first scleral lens fit, indications, devices used to aid fittings, care regimen (disinfecting, storage and fill the lens), adverse events (if any), drop-out reasons (if any), water usage on scleral lenses, recommended hours of lens wear, and handling and satisfaction questions. The Portuguese version of the survey was launched using Google Forms survey tool.

Data were reported by mean ± standard deviation (for age), percentages (%) for categorical variables with only 1 response available, and number of respondents (n) for categorical variables with more than one response accepted.

3.4 Results

3.4.1. Demographic Characteristics

A total of 75 responses were collected – 48 from Portugal (PT) and 27 from Brazil (BR). Each question had an obligatory nature in order to complete all the survey, so the number of responses for each question is the same for both countries. *Table 3.1*. shows the demographic characteristics of the respondents from each country. The mean age of the Portuguese (PT) respondents was inferior than Brazilian (BR) respondents (31.19±8.13 and 44.78±8.56, respectively), and were majorly female (67%) although the BR were majorly male (67%). The great

majority of PT respondents had an optometry-related degree (92%) and none reported to be an ophthalmologist or had a PhD degree completed and worked majorly on Optic Shops (71%) and Optometric clinics (10%). On the other hand, BR respondents were majorly ophthalmologists (81%) or reported to have a PhD degree (15%) and worked on Private Hospitals (44%) or Ophthalmology Clinics (82%).

Table 3.1. Demographic and academic characteristics of the respondents.

		TOTAL SAMPLE		No Fitters		Fitters	
		Portugal (n=48)	Brazil (n=27)	PT (n=32)	BR (n=3)	PT (n=16)	BR (n=24)
Age, years (mean±SD)		31.19±8.13 (22 to 55)	44.78±8.56 (33 to 64)	30.10±7.33 (22 to 45)	49.00±14.11 (36 to 64)	33.44±9.37 (22 to 55)	44.25±7.94 (33 to 59)
Gender (%)	Female	67%	33%	78%	33%	44%	33%
	Male	33%	67%	22%	67%	56%	67%
Degree Completed (%)	Optometry-related Grad.	63%	0%	63%	0%	63%	0%
	Optometry-related Master	29%	4%	34%	0%	19%	4%
	PhD Degree	0%	15%	0%	0%	0%	17%
	Ophthalmology-related	0%	81%	0%	100%	0%	79%
	Orthoptist	4%	0%	0%	0%	13%	0%
	Student	4%	0%	3%	0%	6%	0%
Year of training completion (%)	Before 2005	15%	44%	16%	67%	13%	42%
	2005 – 2010	13%	33%	16%	33%	6%	33%
	2011 – 2015	38%	15%	34%	0%	44%	17%
	2015 - 2019	31%	7%	31%	0%	31%	8%
	Still Studying	4%	0%	3%	0%	6%	0%
Place of work, n (%) *	Public Hospital	1 (2%)	5 (19%)	0 (0%)	0 (0%)	1 (6%)	5 (21%)
	Private Hospital	3 (6%)	12 (44%)	3 (9%)	2 (67%)	0 (0%)	8 (33%)
	Ophthalmology Clinic	2 (4%)	22 (82%)	0 (0%)	3 (100%)	2 (13%)	19 (79%)
	Optometric Clinic	5 (10%)	1 (4%)	5 (16%)	0 (0%)	0 (0%)	1 (4%)
	University	3 (6%)	2 (7%)	1 (3%)	0 (0%)	2 (13%)	2 (8%)
	Optical Store	34 (71%)	0 (0%)	23 (72%)	0 (0%)	10 (63%)	0 (0%)
	Other +	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (6%)	0 (0%)

*respondents were allowed to choose more than one option; +contact lens industry

Figure 3.1. shows the percentage of respondents from each country that answered "Yes" or "No" to the first question of the survey, regarding the fitting of a scleral lens bigger than the cornea (>13 mm). The great majority of PT respondents answered "No" (67%) but the great majority of the BR respondents answered "Yes" (89%).

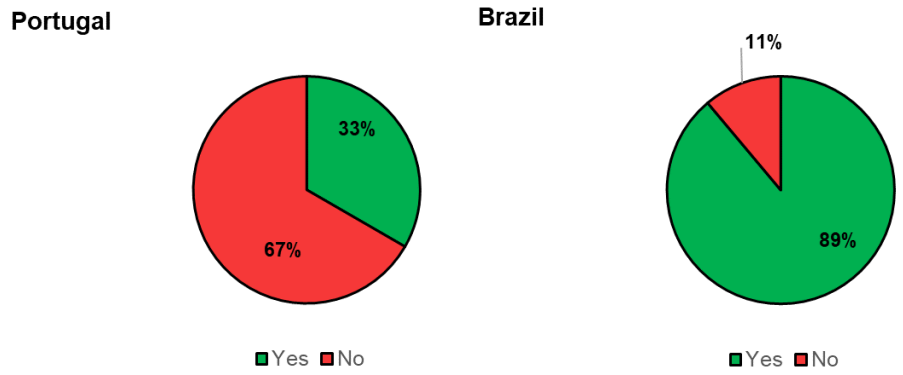

Figure 3.1 Percentage of respondents that answered "Yes" or "No" to the question: *"Have you ever fitted a rigid gas permeable lens with a diameter larger than the cornea (>13mm)?"*

3.4.2. Non-scleral Lens Fitters: Reasons Why

Subjects that reported to never have fitted a scleral or corneo-scleral lens during their practice, where asked about the motifs (*Table 3.2.*). The vast majority of PT respondents considered lack of training (50%) and lack of advanced equipment (75%) as the major motifs to never have fitted a scleral or corneo-scleral lens. Also, 59% reported to never had a case in which was necessary to fit a scleral lens. According to BR respondents, the main motifs were lack of training and advanced equipment, the costs for the patients and the requirement of longer appointments. Six (6%, n=2) from PT respondents and 67% (n=2) from BR respondents reported to not know scleral lenses.

Table 3.2. Motifs to never have fitted a scleral or corneo-scleral lens. Respondents were allowed to choose more than one option.

	PT (n=32)	BR (n=3)
I cannot get significant visual benefits with these lenses	0 (0%)	0 (0%)
I consider these lenses more prone to complications	1 (3%)	0 (0%)
I find these lenses difficult to fit	6 (19%)	0 (0%)
I do not think I have enough training to fit them	16 (50%)	1 (33%)
I think patients have difficulty in adapting to these lenses	3 (9%)	0 (0%)
I do not know these lenses	2 (6%)	2 (67%)
I have never had any case which scleral lens fitting was necessary	19 (59%)	0 (0%)
Requires longer appointments	0 (0%)	3 (100%)
I do not have advanced equipment to perform scleral lens fittings	24 (75%)	2 (67%)
The costs to the patient are high	6 (19%)	2 (67%)

3.4.3. Indications for Scleral Lens Fitting

The no-fitters were also asked about the clinical cases that they considered to be relevant for scleral lens fitting. Accordingly, scleral lens fitters were asked about the conditions in which they already fitted a scleral lens. Both results are shown on *Table 3.3*. Although without any scleral lens fitted yet, 29 out of 32 (91%) and 2 out of 3 (67%) respondents from PT and BR, respectively, considered keratoconus as an indication for scleral lens wear. Other indications majorly selected were pellucid marginal corneal degeneration (PMD - PT 41%; BR 67%), secondary ectasia (PT 31%; BR 100%), and penetrating keratoplasty (PT 53%, BR 33%). PT respondents considered that regular astigmatism (38%), hyperopia (2%) and myopia (9%) could be an indication for scleral lens fitting, although BR respondents didn't consider those cases. None of the respondents considered presbyopia as an indication for scleral lens fitting.

The main indication for scleral lens wear reported by scleral lens fitters was keratoconus (100% PT and BR). BR respondents also had high rates of fittings in PMD (79%) and penetrating keratoplasty (83%). Although most BR no-fitters didn't consider regular cornea conditions as

indications for scleral lens fitting, fitters reported high rates of fitting, especially for regular astigmatism (PT 25%, BR 42%). Although in a minor rate, there were reports of some fittings in presbyopic patients (PT 6%, BR 13%).

Table 3.3. Indications for scleral lens fitting – answered by no-fitters; and conditions in which have fitted a scleral lens – answered by scleral lens fitters. Respondents were allowed to choose more than one option.

	No - Fitters *		Fitters *	
	PT (n=32)	BR (n=3)	PT (n=16)	BR (n=24)
Keratoconus	29 (91%)	2 (67%)	16 (100%)	24 (100%)
Pellucid marginal corneal degeneration (PMD)	13 (41%)	2 (67%)	4 (25%)	19 (79%)
Secondary ectasia	10 (31%)	3 (100%)	7 (44%)	14 (58%)
Penetrating keratoplasty	17 (53%)	1 (33%)	3 (19%)	20 (83%)
Ocular trauma	7 (22%)	1 (33%)	5 (31%)	15 (63%)
Dry eye	10 (31%)	1 (33%)	2 (13%)	13 (54%)
Regular astigmatism	9 (28%)	0 (0%)	4 (25%)	10 (42%)
Hyperopia	2 (6%)	0 (0%)	1 (6%)	5 (21%)
Presbyopia	0 (0%)	0 (0%)	1 (6%)	3 (13%)
Myopia	3 (9%)	0 (0%)	2 (13%)	7 (29%)

*Non-fitters were asked about the possible conditions that they considered to be an indication for scleral lens fitting; Fitters were asked about the conditions in which they already fitted a scleral lens.

3.4.4. Scleral Lens as the First Option?

In a normal scenario, PT and BR scleral lens fitters reported that choose scleral lenses as the first lens modality option to be fitted in a case of corneal irregularity in 38% and 21%, respectively (*Figure 3.2.*). Although the great majority of BR respondents agreed that corneal RGP lenses are the first option to consider to fit in irregular cornea patients (63%), PT answers are very partitioned between scleral lenses (38%) and corneal RGP lenses (31%). Piggyback and

standard soft CL were considered the last option by 50% of PT respondents, and hybrid, piggyback and standard soft lenses by BR respondents (38%, 25% and 25%, respectively). None of the respondents considered scleral lenses as the last option to fit an irregular cornea patient.

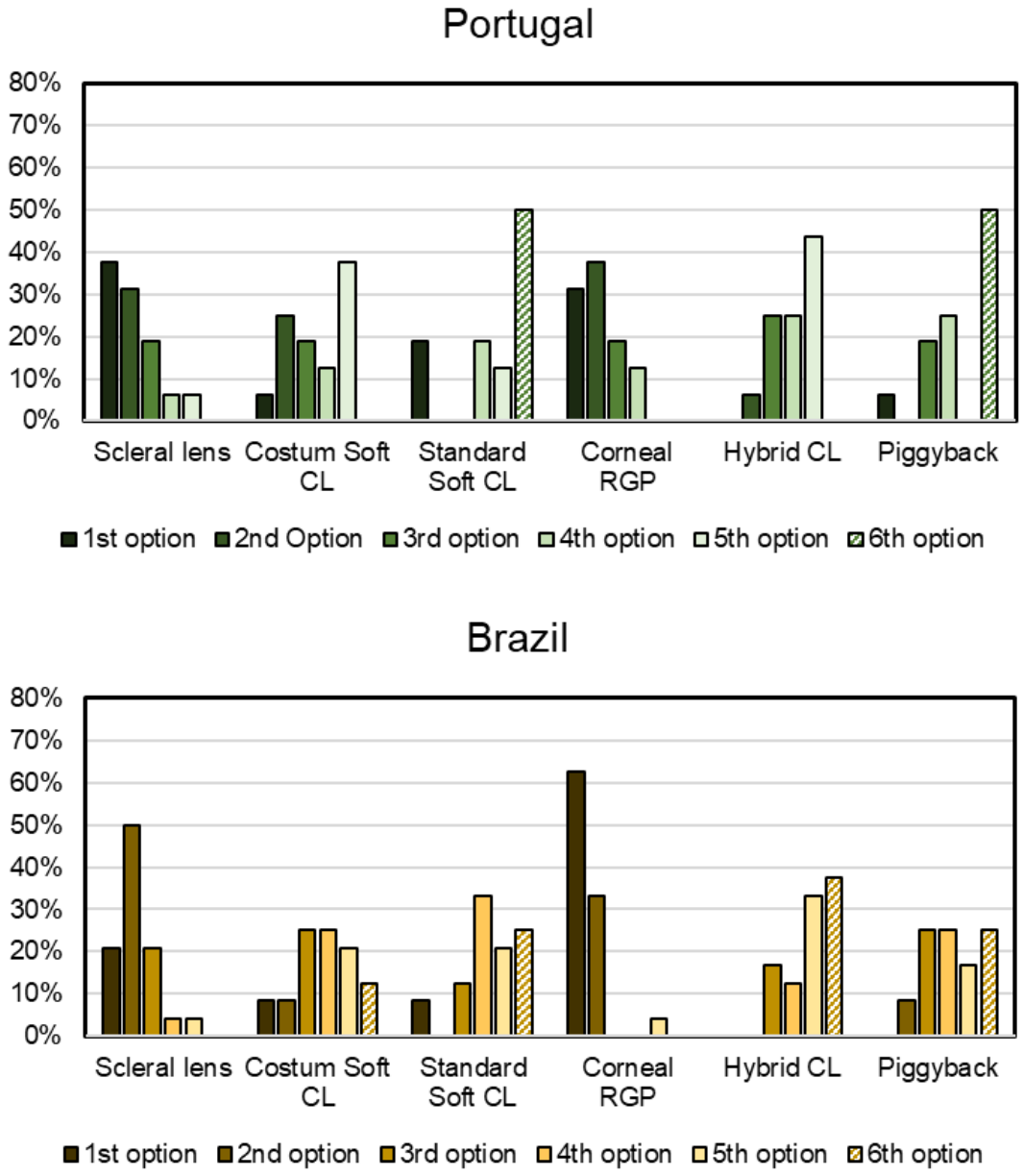

Figure 3.2 Contact Lens (CL) options to consider for an irregular cornea patient. Respondents were asked to order each one of the CL options accordingly to their first consideration for a patient with corneal irregularity (keratoconus, for example).

3.4.5. Number of Scleral Lens Fittings

Sixteen (16) PT respondents and 24 BR respondents (*Table 3.1.*) reported to fit at least one scleral or corneo-scleral lens during their practice. *Figure 3.3.* represents the number of fittings of different lens diameters (13 to 15.5mm, 15.6 to 17mm and/or >17mm) that each respondent reported to have fitted. The great majority of PT respondents (75%) never fitted a scleral lens >17mm, against only 25% of BR respondents.

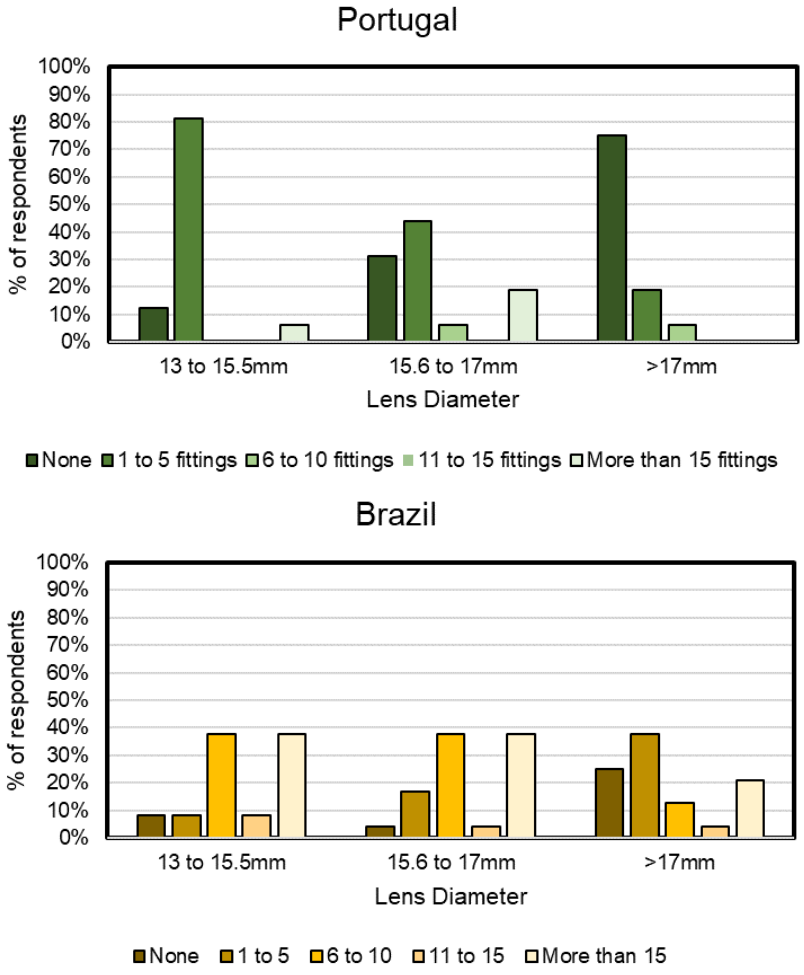

Figure 3.3 Percent (%) of fittings of each lens diameter (13 to 15.5mm; 15.6 to 17mm; >17mm) for the Portuguese (up, n=16) and Brazilian (down, n=24) respondents.

3.4.6. Devices Used During Scleral Lens Fittings

Almost all the PT and BR respondents reported to use slit lamp (PT 100%, BR 96%) and fluorescein (PT 94%, BR 96%) during scleral lens fittings. Nearly half of the respondents reported to use corneal topographers. OCT was used by 38% of BR respondents but only 6% of PT respondents. None of the BR respondents and only 1 PT respondent stated to use a scleral topographer to aid the scleral lens fitting process.

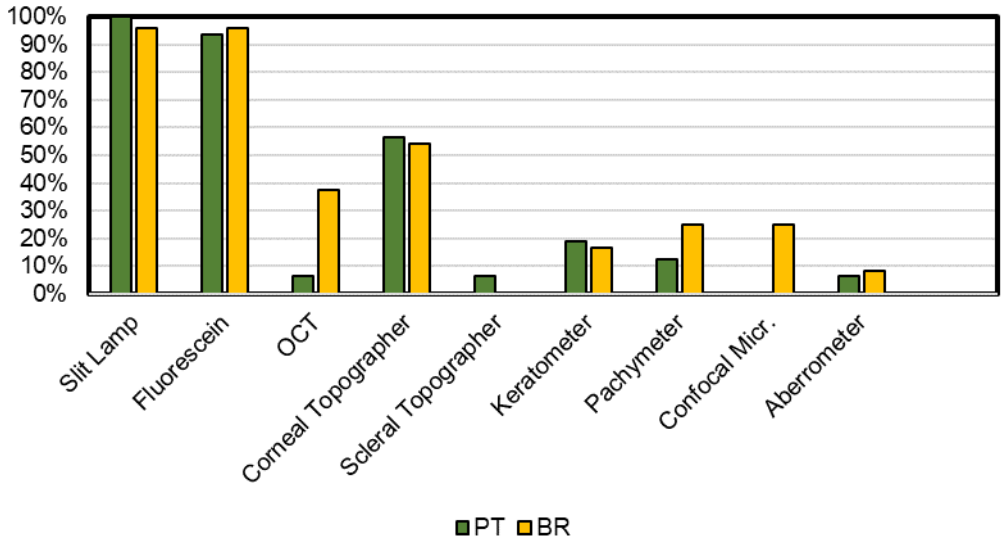

Figure 3.4 Devices that fitters reported to use during scleral lens fittings.

3.4.7. Disinfecting, Storage and Fill-in Solutions

The great majority of practitioners recommend to patients the use of multipurpose solution (MPS) for RGP CL to disinfect scleral lenses (PT 75%, BR 83%) (*Figure 3.6.).* PT respondents recommend more frequently the use of H_2O_2 than BR (50% vs 17%). Some practitioners recommend the use of multipurpose soft CL solutions (PT 13%, BR 25%). Regarding the liquid recommended to fill the scleral lens before insertion, 75% of PT and 83% of BR respondents recommend preservative-free saline solutions. 31% of PT respondents recommend a combination of artificial tears and preservative free saline solution. Some BR respondents recommend MPS (both for soft or RGP lenses) to fill the lenses (13% and 17%, respectively).

Sixty-nine percent (69%) of PT respondents and 63% of BR respondents reported to always inform their patients that water usage on scleral lenses is forbidden. A residual percentage answered that usually do not mention anything about water use (PT 6%, BR 17%), some mention that water can be used on exceptional situations (PT 13%, BR 17%) and others mentioned to recommend patients to rinse their lenses with water only before putting them on lens case (PT 13%, BR 4%). None of the respondents affirm to recommend patients to fill the lens with water.

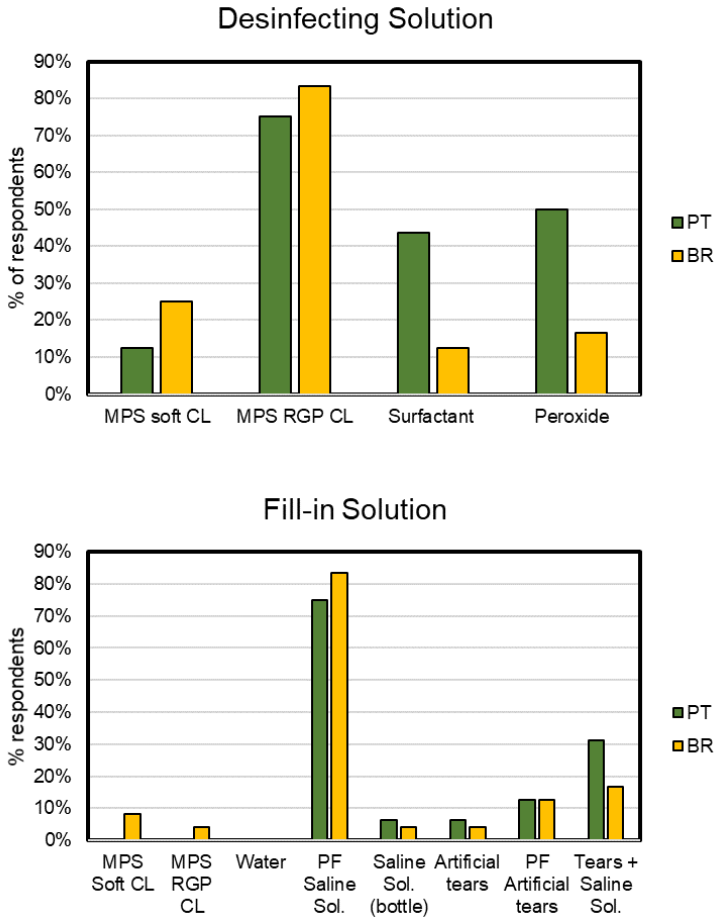

Figure 3.5 Disinfecting (up) and Fill-in (down) solutions that practitioners recommend to patients. More than one answer per respondent was accepted. MPS – multipurpose solution; CL – contact lens; PF – preservative-free; Sol. – solution.

3.4.8. Scleral Lens-Related Complications/ Adverse Events and Drop-Outs

Thirty-eight percent (38%) from PT and 17% from BR respondents reported to never had a patient that discontinued scleral lens wear. The more prevalent causes for scleral lens dropout were handling problems (PT 44%, BR 46%) and patient financial aspects (PT 19%, BR 63%). Regarding visual quality, 6% of PT and 21% of BR didn't continue scleral lens wear because of unsatisfactory visual outcomes. BR respondents also stated that some patients (29%) discontinued scleral lens wear because of some adverse event/ complication. *Table 3.4* shows the percentage of each adverse event seen by scleral lens fitters. 63% and 21% of PT and BR respondents reported that their patients never had an adverse event related to scleral lens wear. The most prevalent adverse events were acute red eye (PT 25%, BR 58%), handling-related problems (PT 25%, BR 42%), corneal neovascularization (PT 19%, BR 25%) and corneal edema (PT 19%, BR 13%). None of the respondents reported to have any corneal ulcer event.

Table 3.4. Percentage of adverse events/ complications reported by scleral lens fitters. More than one response was allowed.

	PT (n=16)	BR (n=24)
No adverse events reported	63%	21%
Corneal Neovascularization	19%	25%
Corneal Edema	19%	13%
Acute Red Eye	25%	58%
Corneal Ulcer	0%	0%
Toxic Keratopathy	0%	8%
Microbial keratitis	0%	4%
Giant Papillary Conjunctivitis	6%	8%
Handling-related problems*	25%	42%
Intolerance	0%	4%

*red eye, conjunctival staining.

3.4.9. Further Considerations About Scleral Lens Fitting Characteristics

Figure 3.6. shows the year of the first fitting of the respondents. Nobody reported to have fitted a scleral lens prior to 2000's and the great majority fitted a scleral lens for the first time in the last 10 years (PT 94%, BR 75%). *Figure 3.7.* illustrates the recommended number of hours of daily wear, showing that the great majority of respondents tend to recommend between 8 to 12h of lens wear or until the patient feels comfortable. The mean number of hours of daily wear recommended by PT respondents was 9.10±1.62 PT and 10.20±2.97 by BR.

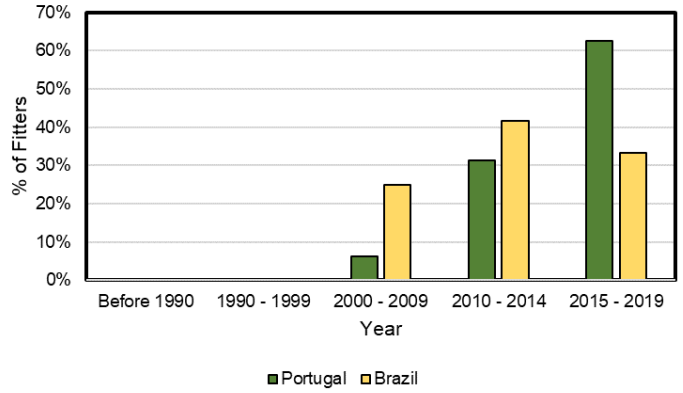

Figure 3.6 Year of the first scleral lens fitting for PT (green, n=16) and BR (yellow, n=24) respondents.

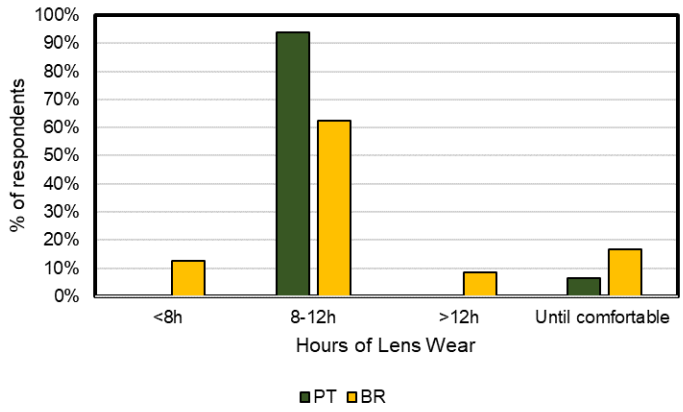

Figure 3.7 Hours of lens wear recommended by the respondents.

Regarding *Midday Fogging* complaints (*Figure 3.8.*), 44% of PT practitioners reported to not know what *midday fogging* was, against only 9% of BR ones. 12% and 8% from PT and BR respondents reported to never had this problem. None of the respondents reported to have this phenomenon in all patients, but 8% of BR practitioners reported to have this problem frequently on their patients. When asked for midday lens removal recommendations (to fill the lens with new solution), 19% of PT and 17% of BR answered that never recommend that to patients, although 19% of PT and 38% of BR recommended the midday lens removal to their patients frequently or always.

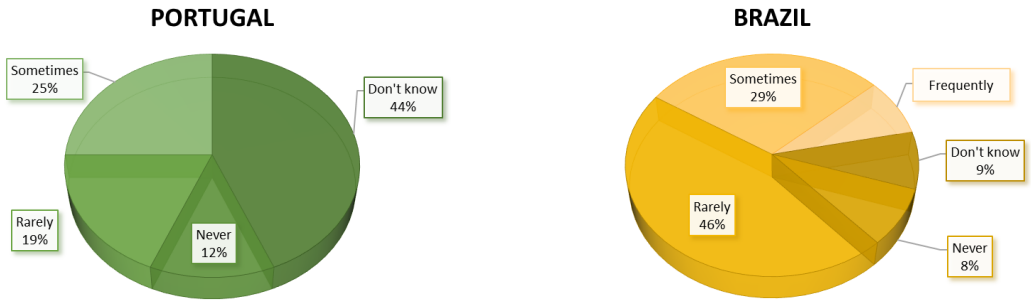

Figure 3.8 Frequency of *Midday Fogging* reported by the practitioners.

Respondents were asked to grade their proactivity (from 0 to 10), handling difficulties and their overall satisfaction (from 1 to 10) regarding scleral lens fitting (*Figure 3.9.).* On average both PT and BR respondents considered lens handling to be easier for the patient than for them (Practitioners, *Figure 3.10. A and B*). On average, BR fitters considered themselves more proactive in the scleral lens fitting area than PT ones (*Figure 3.9. C*) and had a slightly higher satisfaction regarding scleral lens fittings outcomes (*Figure 3.9. D*).

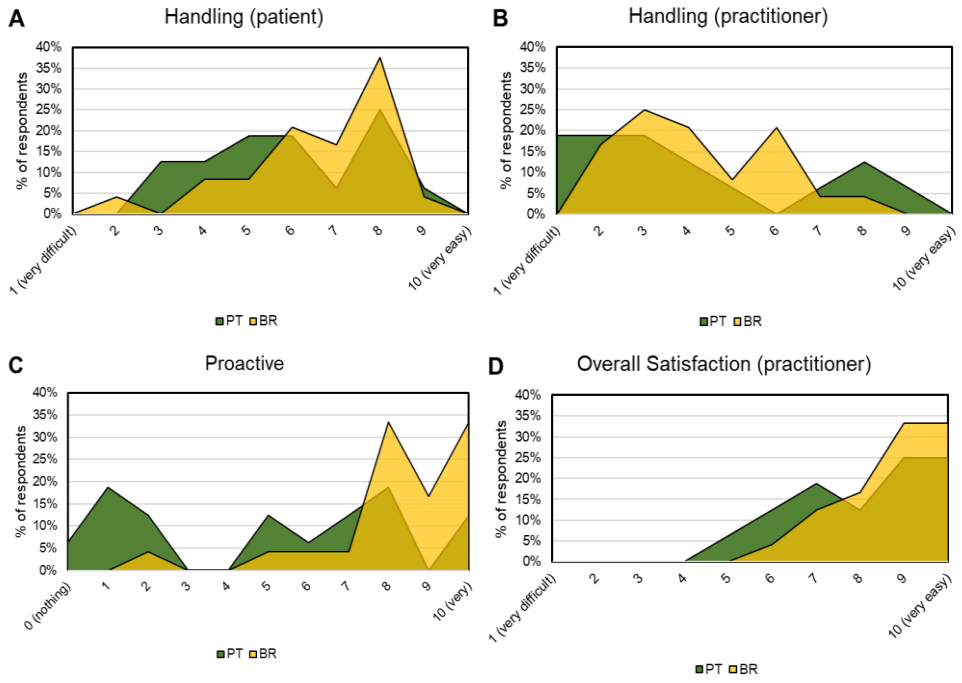

Figure 3.9 Self-reported easiness/difficulty on scleral lens handling (A), perception of handling difficulties of the patients (B), self-reported proactivity on scleral lens field (C) and the overall satisfaction (D).

3.5 Discussion

This is a pilot report on scleral lens fitting perspectives of Portuguese and Brazilian eye care providers. Seventy-five (75) respondents retrieve their answers – 48 from Portugal and 27 from Brazil. Again, one must be aware that this is a pilot report and a small number of eye care providers retrieved their answers, so no solid conclusions can be withdrawal from these results with only 75 respondents. The survey will be online through the next months in order to recruit a larger sample in both countries.

Recently, a survey conducted by SCOPE study group identified 989 eye care providers with some level of interest or proficiency in scleral lens fitting that have fitted 84,375 patients. [12] Although the results are from a worldwide population, 71% of the respondents were based on the United States. Considering the different academic training and practice behaviors among countries, it becomes necessary to assess the profile of scleral lens fitters and fitting

characteristics and practices, in order to identify risky behaviors and develop generalized clinical practices. In the present work, 33% of PT and 89% of BR respondents had fit at least one scleral lens during their clinical practice. PT practitioners seem to have a tendency to fit lenses with smaller diameters – 80% reported to have fitted 1 to 5 lenses with 13 to 15.5mm and 41% reported to have fitted 1 to 5 lenses with 15.6 to 17mm but only 19% reported the same for >17mm lenses. Few PT eye care providers reported to have fitted more than 15 lenses. Contrary, we found a higher percentage of experienced BR fitters: 39% reported to have fitted more than 15 lenses with a small diameter, 39% with medium diameter and 21% with large diameter (>17mm). Similarly to Harthan *et al* [11] findings, there was a higher rate of fittings of lenses with 15 to 17mm diameter, but those working as ophthalmologist in hospital-based practices (BR respondents) commonly prescribe lenses with a higher diameter (>17mm). In fact, there was a big discrepancy between PT and BR respondents with respect to academic background and place of work – the great majority of PT respondents were based on optic shops and had an optometric-related degree, although BR respondents were majorly based on private ophthalmic practices and had ophthalmic-related degrees. Interestingly, only 4% of BR practitioners reported to have an optometry-related degree (Master), and none of PT respondents reported to be an ophthalmologist. Also, BR respondents self-reported to be more proactive in the scleral lens fitting area (*Figure 3.9 C*) than PT respondents. However, a larger sample is needed to develop solid conclusions about the academic background of scleral lens fitters of both countries.

More than 80% of respondents reported to fit their first scleral lens after 2010, similarly to other study where more than half of the respondents began fitting scleral lenses in 2010. [12] Accordingly, nearly 70% of PT and 22% of BR respondents completed their academic degree after 2010, which could be related to an increment/ implementation of more didactic and clinical disciplines related to scleral lens fitting in graduation classes in the last few years, namely in Portugal. Other explanation, along with the previous one, could be the increase in peer-review literature related to scleral lens, which "awaked" the interest of practitioners in this field. [9]

We identified 32 PT and 3 BR eye care providers than never fitted a scleral lens. Comparing those to the scleral lens fitters (*Table 3.1.*), the great majority of PT no-fitters were female (78%) although the PT fitters were majorly male (56%). Controversially, there were more respondents with an optometric-related Master degree in the no-fitters group (34% vs 19%) and the percentage of graduated optometrists was the same (63%) – theoretically, a Master degree in

the PT population ads more training on the specialty contact lens area (including scleral lenses), but it seems to not encourage Masters to venture in the scleral lens field. In addition, 69% of PT no-fitters concluded their last academic degree after 2010, in contrast to the 79% in the fitters group – so, similarly to other results [12], scleral lens modality seems to be embraced more actively by eye care providers that completed their graduation recently. There were no significant differences regarding the place of work of PT fitters and no-fitters – the great majority work in optic shops (63% and 72%, respectively), but controversially there are more no-fitters working in more specialized environments, like private hospitals (9% vs 0% of fitters) and optometric clinics (16% vs 0% of fitters). Regarding BR respondents there were no differences regarding gender of both groups. All the no-fitters were ophthalmologists and in the fitters group there were also a high percentage of ophthalmologists (79%) but also 4% with an optometry-related master degree and 17% with a PhD. All BR no-fitters concluded their graduation prior 2010, but in the BR fitters group there were 25% that completed their training after 2010. Altogether, seem to corroborate the early thought that more specialized practitioners that have concluded their training more recently are more enthusiastic about scleral lenses [11,12], contrary to PT respondents. Still in relation to no-fitters, the reasons given to never have fitted a scleral lens were the lack of advanced training to fit them (50% PT, 33% BR), lack of advanced equipment to perform the fittings (59% PT, 67% BR), and the cost for the patient (19% PT, 67% BR). Interestingly, PT no-fitters are those that have more academic training and work in places where is more regular to find advanced equipment (private hospitals and clinics). Also, 2 PT and BR respondents said that they did not know these lenses, and 59% of PT (and none of BR) reported to never had a case in which scleral lens fitting was necessary – which could be in accordance to the place of work, as PT respondents worked majorly on optic shops and cases of advanced corneal irregularities are often seen by medic-related places.

In agreement to previous literature [12–14], respondents majorly fitted scleral lenses in irregular cornea patients - keratotonus patients (100% of cases), PMD (PT 25%, BR 58%), and penetrating keratoplasty (PT 19%, BR 83%) – but there was also a higher rate of fittings in dry eyes, especially in BR respondents (PT 13%, BR 54%). Although non-scleral lens fitters didn't consider healthy eyes as candidates for scleral lens wear, PT and BR fitters reported to fit at least one scleral lens in cases of regular astigmatism (PT 25%, BR 42%), myopia (PT 13%, BR 29%), hyperopia (PT 6%, BR 13%) and presbyopia (PT 6%, BR 21%).

Although scleral topographers are emerging [15–17], only 1 PT practitioner that works in an optic shop reported to use one during scleral lens fittings. Slit lamp and fluorescein were reported to be used by more than 95% of the respondents. Corneal topographers were reported to be used by more than 50% of respondents. OCT were more reported to be used in BR (38%) by the ones that work in private facilities (hospitals and clinics) and only 1 PT practitioner working in optic shop reported to use one.

Regarding care regimen products, both PT and BR respondents demonstrated some consensus on the disinfecting solution (RGP MPS – more than 70%) and the fill-in solution (preservative-free unidose saline solutions – more than 70%). Although no respondents reported to recommend the use of water to fill the lens, some said that never mention anything about water usage (PT 6% and BR 17%) to their patients. Fortunately, more than 60% of respondents reported to always inform the patient that water usage on scleral lenses is forbidden. Although tap water can eventually be used to rinse the lens before underwent a complete disinfection, it is important to clearly state that to patients and remind them every appointment. However, it is already known that patients do not fully understand or forget initial instructions, reducing compliance. [18] Considering that tap water was previously related to serious ocular infections [19] and that scleral lenses are fitted majorly in diseased eyes (which could be more prone to ocular complications), tap water rinse can be a risky recommendation. In fact, in a previous report, authors became surprised by the number of respondents who reported to recommend (even rarely) tap water to rinse scleral lenses (about 40%) – about 10% of respondents recommended the use of tap water all of the time. [11] They also concluded that past graduates (before 2009) recommended significantly more tap water rinse than recent graduates. In the present study, 4 out 5 BR respondents that recommended tap water rinse in some occasions completed their graduation until 2010, but all PT respondents completed their training after 2011. Along with the thoughts of mentioned authors [11], we also recommend to completely avoid tap water in the lens care regimen until peer-reviewed works conclude otherwise.

Midday fogging is a condition characterized by a progressive clouding of the scleral lens fluid reservoir that worsen vision. [20] That was reported to occur in 22-45% of scleral lens wearers. [20–22] In the present study, midday fogging was reported to occur, even rarely, by 44% of PT and 83% of BR respondents. We didn't found any correlation between the solution recommended to fill the lens and the severity of symptoms of midday fogging ("sometimes" or

"frequently"). Among BR respondents, although 1 reported to recommend MPS for soft lenses and other MPS for RGP to fill the lens, the others recommended preservative-free unidose saline solutions. Among PT respondents, all recommended unidose saline solutions or artificial tears.

Accordingly, the midday lens removal was recommended by 81% of PT and 83% of BR respondents. Harthan *et al* [11] also found that 73% of respondents recommend midday removal at least some of days. Most of the respondents recommended a daily scleral lens wear of 8 to 12 hours. Harthan *et al* [11] also reported a mean recommendable wearing time of 11.8±3 hours. However, considering that most patients seek for the visual enhancement promoted by scleral lenses during all awakening hours, the wearing times recommended by practitioners should not reflect what patients really do. Some patients report to wear their lenses for 16 hours or more (Macedo-de-Araújo, Fitting Success, submitted to publication).

Respondents were also asked to grade the difficulty to handle a scleral lens (from 1 to 10, being 1 very difficult and 10 very easy). More than 70% of respondents self-reported that handling a scleral lens is difficult (grade < 5), but controversially only 44% of PT and 21% of BR respondents attributed the same grade when considering the difficulty to handle a scleral lens by the patient. The overall satisfaction about scleral lens fittings was quite high in both countries (*Figure 3.9 D*), being slightly high among BR respondents. No one reported to not be satisfied with the outcomes of scleral lens fittings.

In conclusion, this pilot survey provides data about eye care providers that are fitting scleral lenses, regarding their fitting practices and indications for lens wear. No-fitters were also identified and asked about the motifs to not fit scleral lens. The results showed that scleral lens fitting is quite new among PT and BR populations (since 2010) and that the great majority of fittings are performed in keratoconus patients. Despite that, respondents also reported to fit some cases of healthy corneas (namely with regular astigmatism). More respondents and countries need to be added to this survey in order to have a general overview of the scleral lens practices all around the world and help to identify risky behaviors and to create universal good practices for all practitioners.

Aknowledgments

We thank all the eye care practitioners who kindly completed the questionnaire.

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Chapter 4

Case Report: Improvement of Vision and Ocular Surface Symptoms with Scleral Lens after *Pseudomonas* Infection

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Submitted to publication: Macedo-de-Araújo RJ, González-Méijome JM. Case Report: Improvement of Vision and Ocular Surface Symptoms with Scleral Lens after *Pseudomonas* Infection

4. Case Report: Improvement of Vision and Ocular Surface Symptoms with Scleral Lens after *Pseudomonas* Infection

4.1 Abstract

Significance: Beyond the common applications of scleral lenses, these devices can also have important roles to rehabilitate other corneal conditions such as corneal scarring as a result of trauma or ocular infections.
Purpose: To report a case successfully rehabilitation with a scleral lens for visual correction of an eye with a scar from a *Pseudomonas aeruginosa* infection. Visual outcomes and subjective and objective measures of ocular surface discomfort and night vision disturbances associated to the condition will be provided.
Case Report: A 38-year-old woman that was a previous compliant daily disposable soft contact lens (CL) wearer with myopia (-1.75D) reported an episode of acute ocular infection during daily disposable CL wear 11-months prior contacting the investigators. The ocular infection was positive for *Pseudomonas aeruginosa*. Infection got under control but remained with sequels: corneal irregularities, infiltrates and opacity. The best spectacle-corrected visual acuity was +0.44 logMAR that recovered to +0.06 with the trial scleral lens with over refraction. The patient was fitted with a 16.4mm scleral lens and was scheduled for several appointments over a 12-month follow-up period. Both high and low contrast visual acuities remained stable over the follow-up. The comfort was assessed with ocular surface disease index (OSDI) questionnaire, which depicted a comfort enhancement from 75.0 to 47.9 over the short-term. Quality of vision (QoV) questionnaire was also administrated and showed an improvement on frequency, severity and bothersome of the vision-related symptoms overtime.
Conclusions: Despite the transparency loss over part of the pupil area, scleral lens had an important role in restoring the visual quality of this patient. The lens has promoted a better comfort and a significant reduction on the night vision disturbances

4.2 Introduction

Scleral lenses are known to have excellent visual quality and comfort enhancement capabilities. Medical indications of gas-permeable scleral lens are majorly divided into visual improvement in cases of severe corneal irregularities, ocular surface protection and refractive error correction. [1,2] Beyond the common applications of scleral lenses, these devices can also have important roles to rehabilitate other corneal conditions such as corneal scarring as a result of trauma or ocular infections. Bacterial, fungal or viral keratoconjuntivitis can cause aftereffects

that can compromise visual function (corneal irregularity, opacities). [3] As scleral lenses will promote a smoother anterior ocular surface upon insertion, visual quality can be also enhanced in those cases, as long as the corneal opacity is not on the visual axis. Notwithstanding, off-axis opacities will also compromise visual function though in a minor extent. Along with the visual enhancement, scleral lens may also have therapeutic benefits in specific cases. Cressey *et al* [4] reported a case of scleral lens fitting in a 58-year woman with extensive vascularized limbal keratitis - the scleral lens helped restore corneal health by means of a decrease in the corneal neovascularization and opacity. In a different approach, scleral lens materials may also help to protect the anterior ocular surface from environmental factors, such as dust [2] or even from corneal injuries that could be promoted by mechanical traumas (impact of high-speed objects/ particles). [5–8]

The present case report illustrates the condition of an eye with a significant opacification and scarring of the cornea covering part of the pupil area after an ocular infection. Despite the clinical presence, the scleral lens device was able to rehabilitate vision to near normal values through the regularization of the irregular but clear corneal area and was also able to promote a significant comfort enhancement. The 12-month follow-up results regarding visual acuity and comfort are presented.

4.3 Case Report

A 38-year-old Caucasian woman referred by the ophthalmologist for potential visual rehabilitation with contact lenses attended to the Clinical and Experimental Optometry Research Lab (CEORLab) at the Center of Physics (University of Minho). The clinical timeline is shown on *Figure 4.1*. The motivations were the possibility to enhance the poor visual acuity on the left eye, caused by a severe ocular infection 11 months prior this visit. Before the onset of the ocular infection, the patient was a daily disposable silicone hydrogel contact lens wearer for three years with -1.75 D in both eyes. The patient reported to wear the lenses for about 8 to 12 hours per day, 5 days per week, and denied overnight contact lens wear. She reported to have no history of other adverse events related to contact lens wear or others and never used topical medications. She had no systemic medical problems and took no medications.

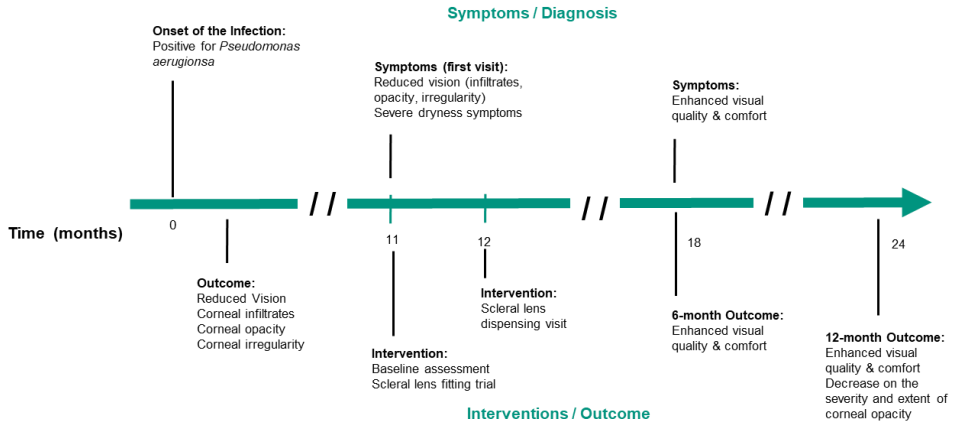

Figure 4.1 Clinical Timeline: 48-year-old Caucasian woman who suffered a *Pseudomonas aeruginosa* ocular infection. The poor visual outcomes were successfully managed with a scleral lens.

The patient described the history of the onset of the infection. She reported that one day she started to feel a burning sensation and pain and attended to an ophthalmologist later on that day, where non-specific medications were applied and the eye was patched. The next morning, the eye pain and secretions were so strong that she immediately went to the hospital and was straightaway hospitalized. The ocular infection - that was positive for *Pseudomonas aeruginosa* – evolved to an endophtalmitis. The prognosis was very poor and enucleation was considered. But because of medical efforts and patient's dedication, the infection got under control and the eye was saved from enucleation. However, the visual acuity on that eye was very poor and the patient also reported severe dry eye symptoms and was dependent on lubricant eye drops every 30 to 60 minutes to maintain minimal comfort. Eleven (11) months after this episode, the patient was examined in our facilities and the best spectacle correction was 0.48 logMAR. The corrected visual acuity of the right eye was within normal values (-0.1 logMAR). It was impossible to better correct the left eye's vision with spectacles because it has part of the corneal surface with an opacity covering a significant pupillary area (*Figure 4.2 A*). A corneal topography (Medmont E300, Victoria, Australia) was performed (*Figure 4.2 B*). Despite the limitations of Placido reflection-based corneal topographies in analyzing no-transparent corneal surfaces, a wide area of irregularity (corresponding to the "clear" pupillary area) was observed.

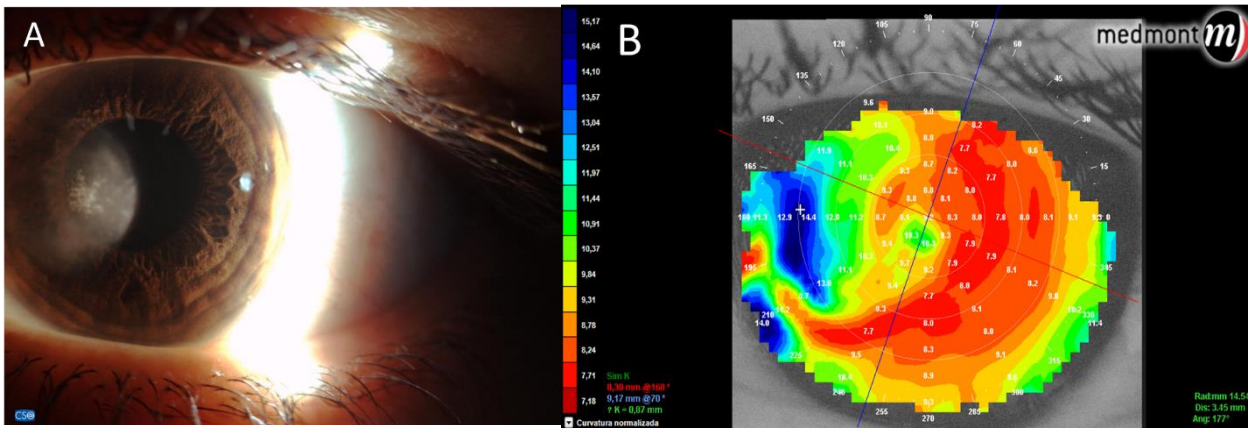

Figure 4.2 (A) Left eye 11 months after the onset of the infection. An opacity over a significant part of the pupil area is seen, as well as corneal infiltrates. **(B)** Corneal topography of the same eye. Large amounts of irregularities are seen. It is important to know that corneal topographers based on the projection principle of Placido rings have limitations to analyze very irregular corneas namely those with transparency loss, so this data needs to be analyzed carefully, since it can be influenced by the corneal health of the patient.

Taking into account the poor visual acuity achieved and the corneal irregularities, a scleral lens was fitted. Corneal rigid permeable contact lenses (RGP) were not considered in order to avoid contact with the affected corneal area. A trial scleral lens from Procornea (Senso Mini-sclera, Procornea, Eerbeek, the Netherlands) was chosen following fabricant recommendations. With the trial scleral lens, the visual acuity improved to 0.2 logMAR. Patient was instructed to stay with the trial scleral lens for more 90 minutes and then the over refraction was performed. With an over-refraction of -0.75 -0.25 x 80 the vision increased to 0.08 logMAR. Following the trial lens assessment, a scleral lens was ordered: diameter of 16.40 mm, BCR 8.20 mm, and sagittal height 3.25 (corresponding to approximately 4573µm) and over-refraction -0.75D. No adjustments were needed on the landing zone of the lens.

Figure 4.3 shows the scleral lens fit over the different quadrants at lens dispensing visit. The scleral lens evenly land on the conjunctival surface, not depicting any conjunctival blanching nor other problems on the landing zone of the lens. Five minutes after lens insertion the central corneal clearance (CCC) was reported to be 250µm that decreased to 150µm after 2h30 of lens wear. The patient reported that the comfort was excellent and rated subjectively the vision as "fantastic". To follow the case over the long-term, some measurements were performed. High and low visual acuity (HCVA and LCVA, respectively) were measured with EDTRS in logMAR

scale. The quality of vision questionnaire (QoV) [9] was applied at Baseline and at all follow-up appointments. This questionnaire has questions regarding night vision disturbances (NVD) such as haloes, glare and starburst and other vision-related complaints. The prevalence, severity and bothersome of each one of the visual symptoms are scored from 0 to 100 and the higher the score, the higher the impairment. Symptomatology was also assessed with the Ocular Surface Disease Index (OSDI) [10,11] – a 12-item questionnaire scaled from 0 to 100, with the highest score representing greater disability/ more symptoms. All these assessments were performed on the Baseline (with the patient habitual correction) and at the scheduled follow-up appoints of 1, 3, 6 and 12 months. For a more comprehensive visual quality assessment, measurements of NVD were taken with the Light Distortion Analyzer (LDA) with previously described methodology. [12–14] This measure allows to quantify the size (LDI, %) and shape (BFCIrreg & BFCIrregSD) of the light distortion induced by a glare source.

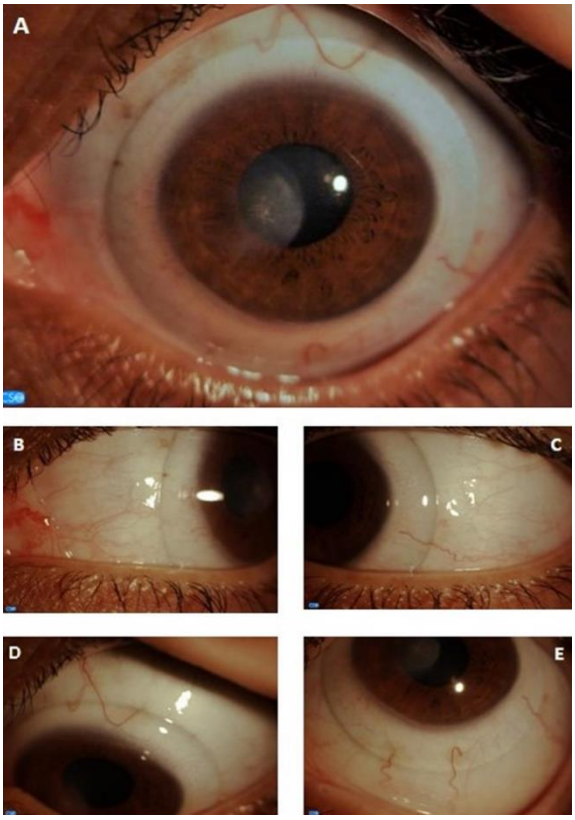

Figure 4.3 Scleral lens fitting in all quadrants. A – overall fitting; B – Nasal; C – Temporal; D – Superior; E – Inferior. Is worth nothing that no conjunctival blanching is seen at none of the ocular quadrants.

Table 4.1 shows the results of HCVA and LCVA and symptomatology over the follow-up period. An improvement of almost 4 lines in HCVA and LCVA was observed with scleral lenses when compared to the habitual correction of the patient. Both HCVA and LCVA were stable over the 12-month follow-up period. Regarding the symptomatology, a decrease on OSDI scores was observed with scleral lenses when compared to Baseline (symptoms felt with habitual correction). Despite the slight augment in the subjective perception of the symptoms overtime, they didn't reach Baseline values. Regarding the questions of QoV questionnaire, there was a decrease in the frequency, severity and bothersome of vision-related symptoms with scleral lenses when compared to Baseline, namely on V6m and V12m.

Table 4.1. High and Low contrast visual acuity (HCVA and LCVA) and subjective perceptions (OSDI and QoV) of the patient. HCVA and LCVA were measured with habitual correction (HC) best spectacle correction (BSC) and with scleral lens at lens dispensing visit (LDV) and over the follow-up period in logMAR scale. Both questionnaires (OSDI and QoV) were administrated at Baseline (symptoms felt with HC) and over the entire follow-up period.

		Baseline		Follow-up (Scleral lens)				
		HC	BSC	LDV	V1m	V3m	V6m	V12m
Visual Acuity	HCVA	0.48	0.44	0.06	0.10	0.10	0.06	0.10
	LCVA	0.72	0.70	0.36	0.36	0.38	0.36	0.38
OSDI	OSDI Score	75.00	-	-	47.92	56.25	64.58	60.42
QoV Score	Frequency	82	-	-	77	77	72	61
	Severity	78	-	-	72	63	63	57
	Bothersome	90	-	-	83	83	71	63

Despite the great augment in both HCVA and LCVA, the subjective perception of the patient about her quality of vision did not suffered a significant change on the short-term. Notwithstanding, both size and shape of light distortion measured with LDA were significantly reduced with the scleral lens, however both measures (without and with scleral lens) were only performed at V12m, so the possible overtime changes in the light distortion analysis were not recorded (*Figure 4.4*). Because the patient had a normal eye with normal vision prior the onset of the infection, it is understandable that the patient did not rate subjectively her vision as normal even with a great reduction seen on the size and shape of the light distortion with scleral lens. However, it is seen a decrease in the visual symptoms (QoV), at V6m and at V12m – this could

indicate that the patient suffered a neuro-adaptation or simply got used to the night vision disturbances.

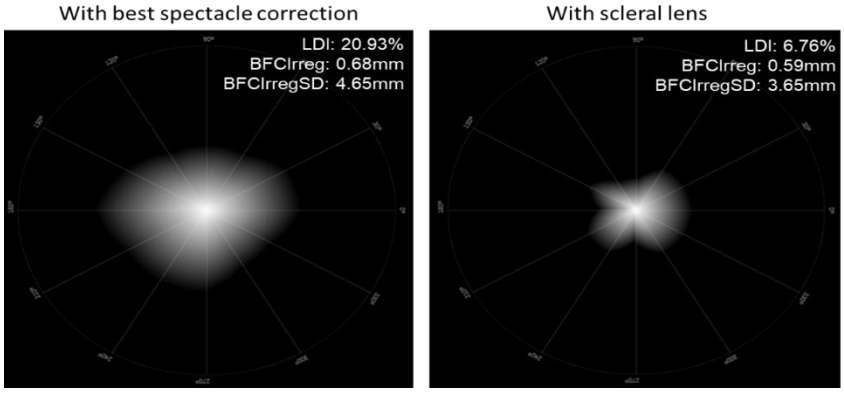

Figure 4.4 Light distortion of the left eye of the patient measured with Light Distortion Analyzer (LDA). Left – measurement performed with best spectacle correction at V12m; Right – measured performed with the scleral lens at V12m. A decrease of 14% in the size of the light distortion was observed.

4.4 Discussion

Eye infections due to *Pseudomonas aeruginosa* have serious prognosis and could have devastating effects. The most common form of infection is a corneal ulcer that can rapidly evolve to panophtalmitis and can cause blindness or led to enucleation in severe cases. The main risk factors for developing *Pseudomonas* keratitis are ocular surface disease, ocular trauma or surgery, but also CL wear. [15,16] Before the widespread of CL wear, ulcerative keratitis was very rare in normal eyes. [17] In a recent review, Subedi *et al* [15] concluded that the prevalence of the bacteria was much higher in contact lens-related microbial keratitis than on other eye infections. However, the mechanisms by which lens wear are a predisposition to the infection are still unknown. [18] The present work reports a case of a complaint daily-disposable CL wearer that developed a severe ocular infection that was successfully managed. Other authors have reported similar cases in women between 34 and 38 years old, all of them compliant daily disposable CL wearers. [19–21] The visual outcomes after treatment of the aforementioned cases included reduced vision, but none of the authors discuss on the possible options to restore vision. In the present case report, and as the visual outcome was poor due to ocular sequels

(corneal irregularities, infiltrates and opacity), the patient was fitted with a scleral lens. The lens was able to restore vision nearly to normal values, providing an improvement of nearly 4 lines of visual acuity when compared to the vision that the patient had with her HC (from 0.44 to 0.06 logMAR). The lens had also improved the comfort, with a mean decrease in the OSDI score of 27.1 (from 75.0 to 47.9). It was also reflected in a less dependency on artificial tear drops that the patient constantly used prior scleral lens fitting. Despite the significant improvement on visual acuity, the subjective perceptions captured with the Quality of Vision (QoV) questionnaire didn't show a significant decrease in the short term, but an improvement was observed after 6 months. QoV questionnaire evaluates the frequency, severity and bothersome of several vision-related symptoms with a great focus on night vision disturbances – such as glare, haloes and starburst. In fact, the 4 lines of visual acuity improvement doesn't account for potential sources of glare and other night vision disturbances under night vision, such as the headlights of the cars. The opacity that remained after the infection can have a potential effect on light scattering, leading to visual disturbances under dim light conditions. A limitation to assess the potential improvement overtime in night visual disturbances was that the measurements with LDA were only performed with BSC at V12m and with the scleral lens at V12m. Despite that, frequency, severity and bothersome of the vision-related symptoms underwent a decrease at V6m and also at V12m. This could be attributed to several reasons. The first one is the subjective perception of the patient of night vision disturbances – the incapacity could be the same as V1m, however the perception of the patient can change during time, maybe due to some neuro-adaptation to these kind of dysphotopsias. Other reason could be the fact that the opacity and corneal infiltrates seem to have reverted over the 12-month follow-up (*Figure 4.5*). Despite this improvement in the perception of the patient, the visual acuity during the follow-up didn't have significant changes, with mean fluctuations of 2 letters between appointments. This points to the need to investigate other outcomes beyond the typical recording of the visual acuity and the medium and long-term reduction in night vision disturbances might be relevant for some patients, even if their visual acuity remains stable.

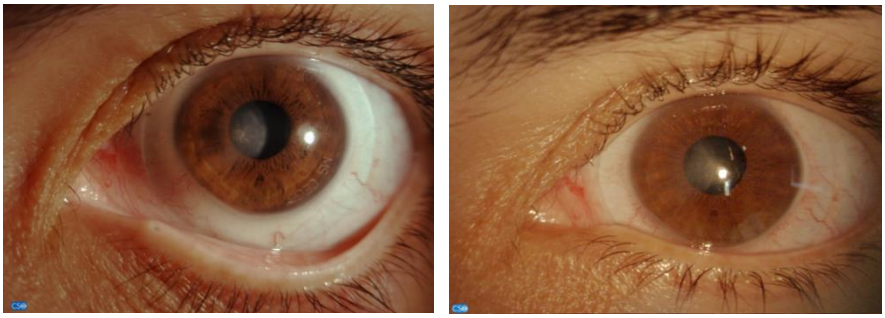

Figure 4.5 Left eye of the patient with the scleral lens in situ at Baseline (left) and at V12m (right). Focus on the decrease in the severity of the opacity and infiltrates.

4.5 Conclusion

Eye care practitioners should be aware that *Pseudomonal* infectious events may occur even in compliant daily disposable contact lens wearers. If the visual outcome of the event is poor, a scleral lens may be a good option to restore vision nearly normal values if the corneal opacity leaves the pupil partially free.

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Chapter 5

On-eye breakage and recovery of mini-scleral lens without compromise for the ocular surface

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Macedo-de-Araújo RJ, van der Worp E, González-Méijome JM. On-eye breakage and recovery of mini-scleral contact lens without compromise for the ocular surface. *Cont Lens Anterior Eye.* 2018 Jun;41(3):311-314.

5. On-eye breakage and recovery of mini-scleral lens without compromise for the ocular surface

5.1 Abstract

Purpose: To report the on-eye breakage of a mini-scleral lens in a healthy cornea after being hit by a speeding object, without causing any severe corneal damage.

Case Report: A 24-year-old Caucasian male involved in a clinical study reported the *in situ* breakage of a mini-scleral lens during motorbike maintenance. The patient reported eye redness and irritation that significantly decreased after all the pieces of the lens were recovered from the eye. Ocular examinations within 48 hours showed absence of corneal damage other than superficial punctate keratitis inferiorly and no fragments of the lens were found in the conjunctival sac. The patient was wearing a 15.2mm mini-scleral lens in a high Dk material. The evolution of rigid materials towards higher Dk values has resulted in a decreased hardness and modulus values, so these materials are more elastic when subjected to mechanical stress, which could be a beneficial aspect in absorbing the energy of an impact before breaking in pieces.

Conclusion: This case report shows that scleral lenses could have a protective effect to the corneal surface from the direct impact of a high-speed object. Mechanical material properties, wide supporting area and post-lens tear volume acted as protective factors helping to absorb and distribute the kinetic energy of the impacting object.

5.2 Introduction

The role of mini-scleral and scleral lenses for correction of irregular corneas with a wide range of etiologies and for ocular protection in cases of ocular surface diseases has been widely reported in the literature. [1–4] The excellent comfort, vision quality, centration and on-eye stability promoted by scleral lens fittings comprise a series of advantages over other kind of contact lenses (CL). [5,6] These are the main reasons why practitioners are now prescribing scleral lenses beyond irregular corneas, namely to correct moderate to high refractive errors in normal corneas, accounting over 10% of the total scleral lens fits. [7]

Some concerns about the long term effects of scleral lens wear have been raised, and the risk/benefit ratio of fitting scleral lenses in normal corneas is not well established. [8] To minimize the potential risks, like hypoxic stress of the cornea [8], scleral lenses are made of high oxygen permeability polymers which promote a better oxygen availability minimizing the corneal hypoxia. [9] However, these materials with higher Dk have a decreased hardness which is potentially related with the higher content of permeable monomers in the bulk of the material. As consequence, modern scleral lenses could hypothetically break more easily compared to PMMA thicker designs. When on-eye, scleral lenses are entirely supported by the conjunctiva and sclera outside the corneal and limbal area. [5] Compared to other kind of contact lenses (CL), a relatively thick liquid reservoir is trapped between the lens and the cornea, acting as protecting environment to avoid direct contact with the scleral lenses.

The following case report shows a 15.2 mm mini-scleral lens potentially acting as a protective shield to the cornea against the impact of a high-speed object and the safety procedures followed to ensure the recovery of the lens fragments, ocular health assessment and hypothesizing on the mechanical behavior of the scleral lens during the impact.

5.3 Case Report

A 24-year-old Caucasian male with a refraction of S +3.75 =C -3.75 x 10° right eye (RE) and S +3.75 =C -3.75 x 160° left eye (LE), participating in a mini-scleral lens clinical study reported the breakage of his right scleral lens on eye during motorbike maintenance. The patient was bilaterally wearing scleral lenses manufactured from Procornea (Eerbeek, Netherlands): the lenses were dispensed the day before the incident, so the subject was wearing the lenses just for one day. The technical details of the scleral lens are presented in *Table 5.1.*

Table 5.1. Characteristics of the scleral lens fitted.

Parameter	Value
Material	Boston XO (hexafocon A)
Dk	100 barrer
Central Thickness	400 µm
Diameter	15.2 mm
Back Optic Radius	8.20 mm
Power	+1.00D (sphere)
Sagittal Depth	2.25
Refractive Index	1.425
Hardness	81/112 (Shore/Rockwell)
Density	1.27
Contact Angle	49

The fitting on the dispensing visit is graphically presented in *Figure 5.1*. depicting a central vault of approximately 370 µm after 30 minutes of lens wear (B). When first contacted the clinical investigator (R.A) he reported that 3 hours before the lens broke after the impact of an object on his RE. The incident happened 6 hours after scleral lens application. He reported eye redness and irritation after the accident and confirmed to have recovered all pieces of the contact lens. He also reported a transient loss of vision after the impact what he attributed to the pieces of the lens floating on the eye. He further confirmed that vision was restored to normal levels and that discomfort was relieved after removal of all lens fragments.

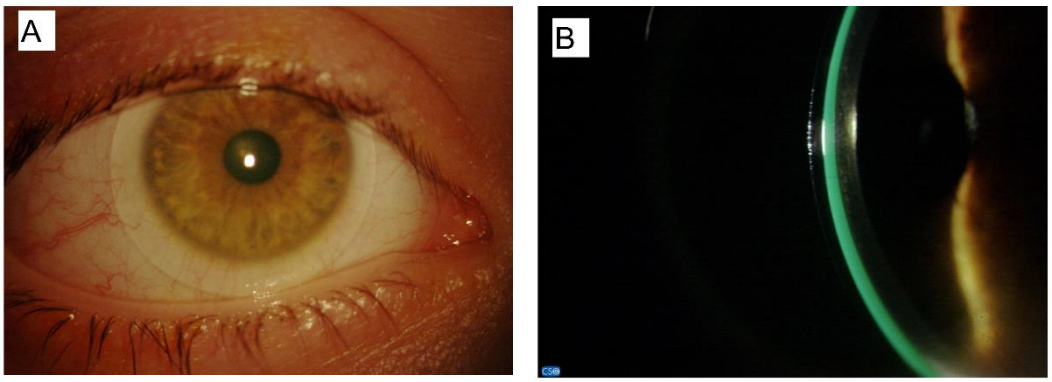

Figure 5.1 Scleral lens fitting at dispensing visit after 1 hour of lens wear; (A) frontal view with absence of conjunctival blanching, (B) optical section with the slit lamp at central area at 16x magnification.

Since the patient only contacted the clinical investigator on Friday night, 3 hours after the incident and considering the relief of symptoms, normal visual perception, and patient's availability to attend the clinic, he was scheduled for a visit on Monday morning. The patient was also advised to report immediately in the event of vision worsening, signs or symptoms and to go to a hospital emergency if necessary. Two days after the accident he showed no irritation or pain, while minor redness was persisting. Ocular examination showed absence of corneal damage other than superficial punctate keratitis in the inferior area (*Figure 5.2*). It should be expected to see some conjunctival staining in the lens bearing points if the evaluation was done after the accident. However, since the patient was not wearing the lenses since the injury, the clinical investigator did not find any clinical differences in conjunctival health according to previous examinations. The scleral lens was reconstructed from the pieces brought by the patient and apparently no fragments were observed (*Figure 5.3a*), nor found in the conjunctival sacs.

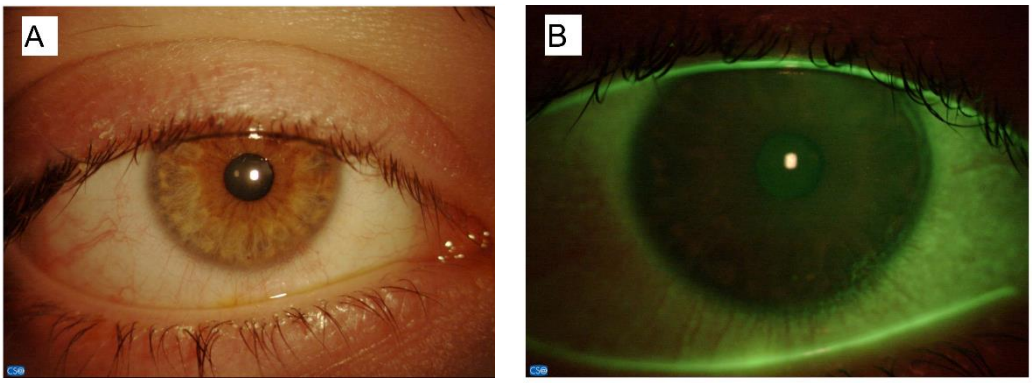

Figure 5.2 Right eye of the subject 2 days after the accident; (A) increased redness in the inferior limbus, (B) positive fluorescein staining in the inferior area of the cornea.

By further investigating the accident, the object was determined to be a black rubber band with two metal square pieces attached to each end (*Figure 5.3b*). The authors presume that one of the metal rings impacted the eye and lens when trying to pull the rubber band to fix a part of the motorbike he was repairing. The scleral supporting area of the lens was estimated using Image J 1.51 (National Institutes of Health, Bethesda, Maryland, USA) image processing software. Considering that the cornea has 11.9 mm diameter (measured with IOL Master, Meditec, Jena, Germany) and the lens 15.2 mm and a band of 0.5 mm in width between the supporting area and the limbus, there is a 1.15 mm width supporting band representing a 50.75 mm^2 area. The same software was used to estimate the lens-cornea separation resulting in 370

microns separation, being quite uniform with a mild asymmetry between the thinner superior and thicker inferior quadrants. This could be attributed to inferior lens deccentration commonly seen in scleral lens fittings due to gravity action and scleral anatomy in the different quadrants of the landing zone.

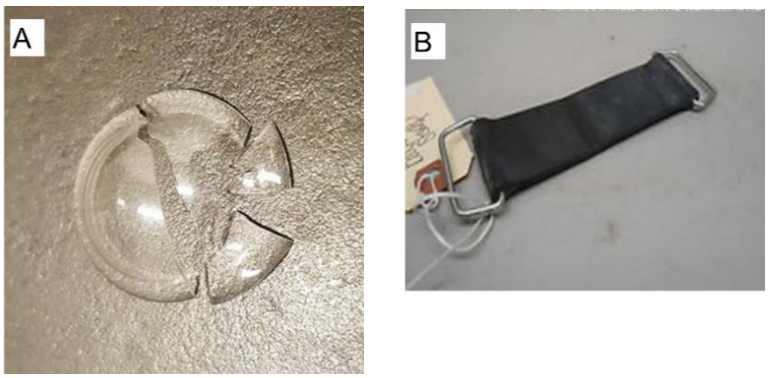

Figure 5.3 (A) Scleral lens fragments recovered by the patient; (B) Object that impacted the eye, consisting of a black rubber with two metal square rings.

Currently, the patient is wearing 15.2mm scleral lenses in both eyes on a regular basis (5 times per week, between 8 and 12 hours per day), reporting excellent comfort and vision (0.00logMar). No other adverse events were reported since the described accident.

5.4 Discussion

Scleral lenses are beginning to enter mainstream contact lens practices, and gradually more specialists are prescribing them as treatment option for irregular corneas and for dry eye related cases. Recently, these lenses are also increasingly being prescribed for normal corneas as alternative to spectacles or other types of CL in cases of high refractive errors. [7] In this case report the authors hypothesized that the absence of clinically relevant damage to the ocular surface was due at least in part to the presence and protective nature of the scleral lens. No impact signs were observed in the eyelids what suggests that the impacting object reached directly the ocular surface. The delay of 2 days in the schedule of an appointment was related with patient's availability and absence of complaints, as he didn't report vision loss, or persistent

redness once the lens pieces were removed. However, the authors want to reinforce the advice that these cases should be observed as soon as possible after the injury. In this case, penetrating injury was not considered possible giving the absence of severe symptoms, but such possibility cannot be ruled out in other similar events.

This is the first case in the peer reviewed literature reporting the potentially protective effect of a gas permeable scleral lens in the event of impacting objects on the lens' surface. Although in this specific case the accident did not cause any severe corneal injury, it is important to know that scleral lenses can have a full breakage on eye which can potentially lead to corneal injuries in specific cases. The repercussions of these kind of accidents could be worse in more fragile corneas like post-surgical cases. However, the hypothetic protective advantage of scleral lens has already been reported recently by Maria Walker *et al* [10] in a case where a projectile hit the lens *in situ* without corneal damage but a hole in the lens. Reports of *in situ* breakage with different kinds of CL are rare but were previously mentioned in the literature before the appearance of rigid gas permeable (RGP) materials, and almost none of the published cases in humans reported significant injuries to corneal surface.

A study done with pig's eyes [11] encountered fewer and less severe corneal injuries from high-velocity projectiles in CL-wearing eyes than in controls and that those eyes wearing soft CL had more corneal damage than those wearing rigid lenses. The results of another early study with rabbits [12] wearing soft (HEMA) and rigid CL (PMMA) showed that when in an environment with hot grid particles the CL (namely PMMA) will act as a protection shield. However, when they were exposed to mechanical damage caused by large solid particles, the energy required for the projectiles to splinter the PMMA lenses was significantly lower than that required to perforate the cornea, so the authors believed that the corneal damage could be higher with these lenses than without them.

However, there are some other reports that contradict those arguments. In 1964, Brown [13] reported traumatic fractures of plastic CL resulting from fist injuries: one patient developed a corneal abrasion with remaining parts of the lens on eye and another patient had a minimal corneal abrasion 24h after the injury. More recently, Caroline *et al* [14] reported another case in which a 35-year-old female has been afflicted by a 3mm piece of a large metal staple that broke her left corneal RGP lens in four pieces. In similarity to this case, the subject needed to remove the pieces immediately. By the time of examination, the subject still had two small epithelial defects and diffuse edema. The authors also hypothesized that the RGP lens had an

important protective role to the corneal integrity (from a severe penetrating injury). They also hypothesized that "*The presence of a RGP lens can both slow down the velocity of an airborne projectile, and distribute the projectile's force over a significantly larger area before the contact lens breaks into multiple pieces.*"

In 1981, Nilsson *et al* [12] concluded that the rigidity of the material is a key factor, as low water content soft CL required a higher energy of the particle for the perforation of the lens than high water content CL, and that PMMA CLs broke at the same energy than that required for perforation of the cornea. Nowadays, patients frequently refer to mechanically break their RGPs during cleaning. Similarly, and considering the lower rigidity of modern RGP materials, it is expected that hard particles require low momentum to break the lenses: however, the remaining pieces of RGP lenses could be a risk for corneal injuries.

The XO material is currently used to manufacture scleral lenses as this material combines a high oxygen permeability required to minimize hypoxic effects. [9] As seen in *Figure 5.4* the evolution of Boston materials towards higher Dk values has resulted in lower hardness and modulus values. Therefore, the authors speculate that XO material is less brittle than older materials (like PMMA) and will present a more elastic behavior when subjected to mechanical stress and this might be a beneficial aspect to resist breakage during handling. In the present case, this might have also been beneficial in absorbing the energy of the impact before breaking in pieces. The authors further hypothesize that the thick (over 300 microns in this case) post-lens tear film also acted as a cushioning factor spreading the incoming pressure over a larger surface and minimizing the risks for the ocular surface.

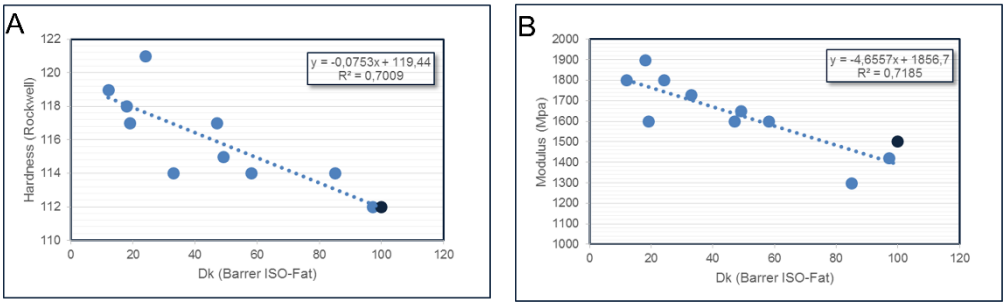

Figure 5.4 Changes in hardness (A) and modulus (B) of RGP Boston materials as Dk values increased. The XO material is highlighted in a darker color. Values extracted from Boston Product Guide.

5.5 Conclusion

In conclusion, this case report describes the potential protective action of a scleral lens device. Although the literature showed other cases where scleral lenses seemed to help protecting the eyes from potentially harmful projectiles, it is not the authors' intention to encourage the use of scleral lenses for eye protection as they do not replace safety glasses during potentially risky activities. However, this case report shows that the scleral lens worn most probably had a protective effect to the corneal surface from the direct impact of a high-speed object. The main hypothesis is that the mechanical properties of the lens material, the wide lens-conjunctiva supporting area and the volume of tear reservoir acted as protective factors helping to absorb and distribute the kinetic energy of the impacting object.

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Chapter 6

Practitioner Learning Curve in Fitting Scleral Lenses in Irregular and Regular Corneas using a Fitting Trial

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Work winner of Best Poster (1st prize) "Practitioner learning curve in fitting mini-scleral contact lenses in irregular and regular corneas using a fitting trial". Global Specialty Contact Lens Symposium, 2018. Las Vegas, Nevada.

6. Practitioner Learning Curve in Fitting Scleral Lenses in Irregular and Regular Corneas using a Fitting Trial

6.1 Abstract

Purpose: To assess the learning curve of a novel practitioner with minor previous experience with scleral lenses (SL) fitting in the initial 156 consecutive fittings in irregular and regular corneas using a fitting trial.
Methods: Prospective dispensing case series involving a total of 85 subjects (156 eyes), 122 eyes with irregular corneas (IC Group) and 34 eyes with regular corneas (RC Group). All lenses were fitted by the same practitioner with minimal previous knowledge and practice on SL fitting. The first 156 consecutive fittings were studied to estimate the number of trial lenses required to achieve the optimal fitting and the number of re-orders required. The results were divided in 8 chronological groups of 20 fittings (eyes) each.
Results: There was a decrease in the number of trial lenses required to achieve the optimal fit from 2.35±0.18 lenses in the first 20 fittings to 1.56±0.13 in the last fittings ($p<0.05$, Wilcoxon). There were no statistically significant differences between IC and RC groups. Regarding the number of re-orders, there was also a decrease from 0.95±0.17 in the first fittings to 0.25±0.11 in the last fittings ($p<0.05$, Wilcoxon). Thought not statistically significant, there was an increase in the use of toric designs with increasing experience.
Conclusions: Practitioner fitting experience reduced both number of trial lenses required to achieve the best fit and the number of re-orders with time. After the first 60 cases, there was a significant reduction in the trial lenses and re-orders necessary.

6.2 Introduction

There is increasing evidence that scleral support rigid gas permeable contact lenses are suitable to compensate a wide range of corneal conditions derived from primary corneal disease, post-surgical complications and even in normal corneas. [1–3] Scleral lenses (SL) have been a matter of research reports in several peer-review journals with an exponential increase in the number of publications over the last years. [4] Although several publications report on long-term outcomes, most recent publications focus on short-term studies with the purpose to evaluate specific features of lens fitting, regarding settling time, [5–8] post-lens tear film characteristics [9–11], or the ocular surface response. [11–13]

The recent rebirth of scleral lens (SL) fitting has been accompanied by a more predictable fitting process, but there is still a significant degree of uncertainty due to the few options of devices to objectively measure anatomical features of the ocular surface beyond the corneal area. Optical coherence tomography (OCT) and scleral topographers are some options that could have an important role during the fitting process, however they are still not widely used in clinical practice all over the world. [4] Fitting recommendations given by several manufacturers use to consider only the clinical features and the degree of severity of the corneal condition to decide the starting point for fitting. Few studies however mention the success rate of the fitting process expressed as the number of lenses needed to accomplish a satisfactory fitting. [14] Understanding this learning curve is relevant for manufacturers and clinicians as this will directly impact the number of lenses required to accomplish a successful fitting. The starting hypothesis for this work is that the number of lenses required to obtain an optimal fit reduces significantly after the initial fitting procedures.

The primary goal of the present study was to analyze the number of trial lenses and re-orders required to obtain a satisfactory fitting and to evaluate the learning process from the clinician perspective by evaluating the changes in fitting over the time of enrollment. A secondary goal was to evaluate the differences in the fitting complexity between irregular and normal corneas.

6.3 Methods

6.3.1 Study Design and Subjects

This was a prospective dispensing, case series involving patients with primary corneal ectasia, penetrating keratoplasty, post-surgical ectasia and regular corneas with high refractive errors between December 2015 and March 2017. The study was conducted at the Clinical and Experimental Optometry Research Lab (CEORLab), at University of Minho (Braga, Portugal). A total of 95 subjects were primarily recruited to participate in a study involving scleral supported contact lens fitting. Lenses were manufactured by Procornea (Eerbeek, Netherlands). Other relevant technical details of the contact lenses are presented in *Table 6.1*. Two trial sets were available, one with 16.4 mm (10 trial lenses) and other with 20.0 mm (9 trial lenses) diameter

each with different parameters. All the subjects included were new SL wearers or previous SL wearers that were switched to a different lens design.

Table 6.1. Characteristics of the mini and full scleral lenses trial sets used in the present study.

Parameter	Mini-scleral lens	Full-scleral lens
Material	Boston XO (hexafocon A)	Boston Equalens II (oprifocon A)
Dk (ISO/Fatt)	100	85
Central Thickness (-3.00 D)	0.25 mm	0.45 mm
Diameter	From 15.20 to 18.00 mm in 0.40 mm steps	From 18.00 to 24.50 mm in 0.50 mm steps
Back Optic Radius	8.20 mm (from 7.00 to 9.40 mm in 0.20 steps)	From 7.20 mm to 9.80 mm in 0.10 mm steps
Power	Sphere +20.00 D to -25.00 D in steps of 0.25 D; Front cyl -0.50D to -3.00D in steps of 0.25D; Axis 0 to 180 degrees in steps of 1 degree	Sphere +30.00 D to -30.00 D in steps of 0.25 D; Front cyl -0.50D to -3.00D in steps of 0.25D; Axis 0 to 180 degrees in steps of 1 degree
Refractive Index	1.415	1.423
Hardness	81/112 (Shore/ Rockwell)	114 (Rockwell R)
Density	1.27	1.24
Contact Angle (deg)	49	30
Sagittal height	From 0.25 to 6.75 in 0.25 steps	From 2.47 to 5.07 in 0.10 steps
Peri Factor / Sclera Opening	From -8 to +8 in steps of 1	From 11.50 to 17.25 in 0.25 steps
Toricity (difference in peri factor)	From 1 to 6 in steps of 1	From 1 to 4 in steps of 1

The subjects were divided into two major groups. One group (IC Group) comprising corneas with primary or secondary ectasias, post-penetrating keratoplasty and other corneal irregularities due to refractive surgery or others. The second group was comprised by subjects with regular and healthy corneas (RC Group) that have failed or rejected other forms of vision correction with contact lenses, whether because of comfort or lens stabilization on-eye (vision). Only subjects with moderate-to-high refractive errors (myopia > 6.00 D, astigmatism > 2.00 D, and/or hyperopia > 4.00 D) that failed other forms of vision correction were included in RC Group. Subjects with previous ocular surgery were excluded. Subjects of each group were further divided into subgroups for some analysis: Prim.IC included subjects from IC Group with primary ectasia or other conditions not induced by corneal surgeries and Sec.IC included those subjects from IC Group with secondary irregularities due to previous surgeries (corneal irregularities due to

refractive surgery, penetrating keratoplasty, intracorneal ring segments implantation, and corneal cross-linking). Subjects from RC Group were separated according to their astigmatism into LA.RC (low astigmatism <2.00 D) and HA.RC (high astigmatism >2.00 D). To be included in the present study patients must have been dispensed with SL and have at least 1 follow-up visit completed (85 subjects).

6.3.2 Measurements

Three repeated measures of corneal topography were done with Medmont E300 (Precision, Vancouver) in each eye in order to assess the severity of each case. Data from simulated keratometry (SimK), that measures the paracentral zone (usually 3mm) of the anterior surface of the cornea, and corneal asphericity (Q) of the the flat and steep corneal meridians were analyzed for each group. High and Low contrast visual acuities (HCVA and LCVA, respectively) with EDTRS LogMAR scale charts were measured with Habitual Correction (HC) and Best Spectacle Correction (BSC). Later, both HCVA and LCVA were also evaluated with SL.

6.3.3 Fitting Procedure Evaluation (Trials and Re-orders)

All lenses were fitted by the same practitioner (R.M-A) who was a licensed optometrist with a Master Degree in advanced optometry but without previous clinical experience of scleral lens fitting. Prior to fitting the lenses, she received a training on the fitting procedure. Following the recommendations of the declaration of Helsinki, all subjects received information from the study before they accept to participate and signed a consent form. The protocol of the study has been reviewed and approved by the Ethics Subcommittee for Life and Health Sciences of University of Minho.

All the subjects enrolled in this study had to attend several appointments during the follow-up: Baseline, lens dispense visit and follow-up visits: 1, 3, 6 and 12-month visits. In this report, only subjects that were dispensed and have at least one follow-up visit were included. At the first appointment (Baseline) SL fitting was done. Fittings were performed using diagnostic fitting sets from Procornea. Subjects that were CL wearers previous to the trial visit were advised to not wear their habitual lenses 3 days before the Baseline appointment. The initial trial lens was

determined following manufacturers' guidelines, considering clinical features and the degree of severity of the corneal condition. Practitioner did not use any objective measurement that could aid in the selection of the first trial lens. All lenses were fitted empirically, based on trial and error process, with diagnostic lens sets. The best trial lens should align evenly on the scleral and vault the entire corneal surface and limbus, with a cornea-lens separation of about 300 μm after insertion. Both scleral alignment and cornea-lens separation were subjectively evaluated with slit lamp. If the on-eye fitting of the first trial lens was not satisfactory (i.e. inadequate alignment on the sclera or inadequate cornea-lens separation), a second trial lens was inserted. The process was repeated in both eyes until the practitioner found the best trial lens for each eye. After this, the final fitting assessment was done after a settling time of at least 90 minutes of lens wear. [7,15,16] Central and peripheral (limbal) clearance and scleral alignment of trial SL and sphero-cylinder over-refraction were assessed to order the final lens. The optimal final SL should align evenly on sclera and vault the entire corneal and limbal area with an ideal cornea-lens separation of 100 to 200 μm after settling. The number of trial lenses needed to obtain a satisfactory SL fitting was recorded for each eye.

When the ordered SLs arrived, subjects went to the lens dispensing visit (LDV), where the on-eye fittings were evaluated after lens insertion and after at least 90 minutes of lens wear. If the fitting was not satisfactory, another lens with different parameters was ordered (and was considered a re-order). The number of re-orders at LDV (when needed) were recorded for each eye. Then, subjects were also evaluated at several follow-up appointments at 1, 3 and 6 months of lens wear (after LDV) – re-orders were also recorded at these visits. It was considered a "re-order" whenever it was necessary to order a new lens with different parameters for the same eye. Erroneous shipments and other factors not directly linked to practitioner fitting process were excluded from this analysis. The number of trial lenses required to prescribe and order the lenses as well as the number of lenses re-ordered to the manufacturer at LDV and through the follow-up period were counted and grouped in 8 chronological groups in 20 fittings (eyes), without accounting for the group of the subject (IC or RC Group). Analysis involving the division into the different groups and subgroups was performed without chronological sequence.

6.3.4 Statistical Analysis

Statistical analysis was conducted using SPSS v.24.0 (IBM Co, IL) to compare the number of trial lenses and re-orders required between groups and subgroups. Normality of data distribution was analyzed with Shapiro Wilk test in different groups and subgroups. Pairwise comparison between groups or subgroups was done using an independent sample T-Test for normally distributed data and Wilcoxon signed ranks test for non-normally distributed data. Multiple comparisons to evaluate the effect of time on number of trials and reorders or subject handling and wearing experience was evaluated with ANOVA test for or normally distributed data and Kruskal-Wallis test for non-normally distributed data. The level of statistical significance was set at $p<0.05$.

6.4 Results

A total of 85 subjects (43 females, 42 males) with a mean age of 34.51±10.41 years were included in this report. Of them, 14 wore lenses in one eye and 71 wore lenses in both eyes representing a total of 156 eyes dispensed with SLs. Since not all fittings were bilateral, there were 5 cases in which both eyes of the same subject fell in different groups – which contributed to increase the chance of final homogenization between all groups. The fittings were divided into 8 groups of 20 fittings, in the chronological order of each fitting, in order to analyze the learning process. The sample was also analyzed separately according to the ocular condition that required the SL fitting in IC Group (irregular corneas, n=122 eyes) and RC Group (high refractive error, n=34 eyes).

Table 6.2 shows the demographic data of the subjects enrolled in the present report including keratometric data, spherical equivalent refraction and best corrected visual acuity with habitual correction (HC), best spectacle correction (BSC) and with SL. Results are presented separately for irregular (IC Group) and regular corneas (RC Group).

Table 6.2. Demographic data of the patients analyzed in each clinical subgroup included in the present report.

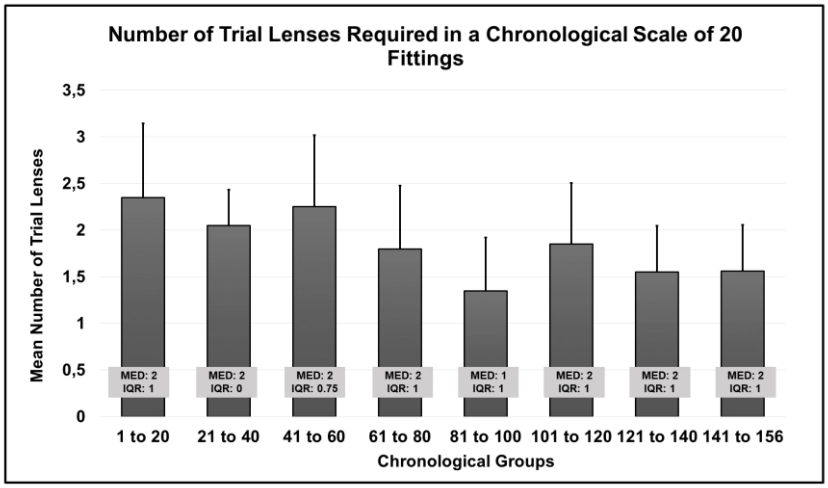
		Total	IC Group	RC Group	p
No. Subjects		85	67 (79%)	18 (21%)	-
No. Eyes Fitted		156	122 (78%)	34 (22%)	-
Gender		43 female (51%) 42 male (49%)	31 female (46%) 36 male (54%)	12 female (67%) 6 male (33%)	-
SubGroup (No. Fittings)			Prim.IC: 80 (66%) Sec.IC: 42 (34%)	LA.RC: 8 (24%) HA.RC: 26 (76%)	-
Age (years)		34.51±10.41 (range: 16 to 65)	35.54± 10.45 (range: 16 to 65)	30.67±9.91 (range: 18 to 35)	0.080+
SimK Flat (D)		43.93±5.51	44.20±6.19 [range: 17.03 to 62.92]	42.99±1.62 [range: 39.45 to 46.01]	**<0.001***
SimK Steep (D)		47.29±6.04	47.78±6.74 [range: 18.83 to 65.38]	45.58±1.71 [range: 43.20 to 45.58]	**<0.001***
Q Flat		-0.65±0.53	-0.71±0.58 [range: -2.89 to +0.84]	-0.43±0.19 [range: -0.86 to -0.11]	**<0.05**+
Q Steep		-0.17±0.69	-0.26±0.71 [range: -1.59 to +2.24]	0.14±0.51 [range: -0.32 to 1.64]	**<0.05***
HC (No. Eyes)	Glasses	73	45	28	-
	Soft CL	19	13	6	-
	RGP	20	20	0	-
	Hybrid	13	13	0	-
	SL	11	11	0	-
	N/P	20	20	0	-
HCVA w/ HC		+0.30±0.30	+0.34±0.31 [range: -0.18 to +1.40]	+0.16±0.21 [range: -0.10 to +0.60]	**<0.001***
LCVA w/ HC		+0.54±0.32	+0.62±0.33 [range:+ 0.10 to +1.80]	+0.31±0.18 [range: +0.08 to +0.9]	**<0.001***
BSC	M (D)	-3.64±3.63	-3.24±3.23 [range: -15.00 to +3.00]	-4.94±4.57 [range: -13.13 to +1.88]	0.078*
	J0 (D)	0.23±1.02	-0.04±0.92 [range: -1.38 to +3.29]	1.09±0.89 [range: -0.44 to +3.20]	**<0.001***
	J45 (D)	0.20±1.13	0.23±1.26 [range: -3.20 to +3.50]	0.12±0.61 [range: -1.10 to 2.09]	0.820*
HCVA w/ BSC (LogMAR scale)		+0.26±0.27	+0.31±0.28 [range: -0.10 to +1.00]	+0.11±0.17 [range: -0.10 to +0.60]	**<0.001***
LCVA w/ BSC (LogMAR scale)		+0.51±0.30	+0.58±0.29 [range: +0.10 to +1.80]	+0.29±0.18 [range: +0.08 to +0.90]	**<0.001***
HCVA w/ SL (LogMAR scale)		+0.07±0.15	+0.08±0.15 [range: -0.18 to +0.62]	+0.06±0.15 [range: -0.20 to +0.48]	0.650+
LCVA w/ SL (LogMAR scale)		+0.32±0.18	+0.34±0.18 [range: +0.02 to +0.94]	+0.24±0.15 [range: +0.04 to +0.60]	**<0.05***

IC – Irregular Cornea; RC – Regular Cornea; ♀ female; ♂ male; PrimIC – primary ectasia; SecIC – secondary ectasia; LA.RC – Low Astigmatism; HA.RC – High Astigmatism; ; HC – Habitual Correction, BSC – Best Spectacle Correction, HCVA – High Contrast Visual Acuity, LCVA – Low Contrast Visual Acuity, SL – Scleral Lenses, N/P – No prescription, Q – corneal asphericity, (+) Independent T-test, (*) Mann-Whitney U independent samples

Regarding the results of VA, in IC Group there were statistical significant differences between both HCVA and LCVA with SL when compared to HC (improvement of more than 2 lines, $p<0.001$). In RC Group those differences were also statistically significant, although clinically insignificant (differences of 2.5 letters, $p<0.05$). Although HCVA with HC was significantly different between groups, there were no differences between them in HCVA measured with SL, meaning that we can achieve an identical HCVA in healthy and irregular corneas with these kind of devices. However, there was a statistically significant difference of 1 line of letters in LCVA with SL between the same groups, which reflects that the optical quality in low contrast is significantly worse in subjects with irregular corneas.

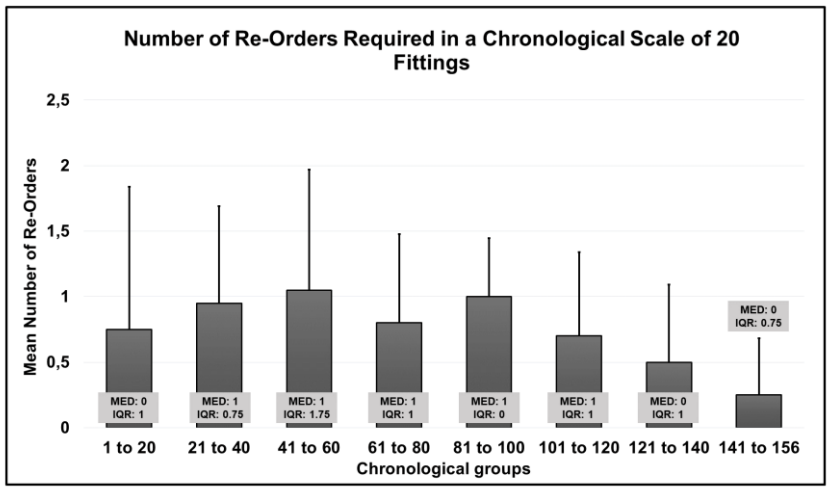
6.4.1 Fitting Trials and Re-orders

Figure 6.1 presents the number of lenses required during the fitting trial in a chronological scale of 20 fittings. According to the chronological order of the fittings we observed a tendency to decrease the number of lenses required to achieve the optimal fitting to be dispensed - a decrease from a mean of 2.35±0.79 in the first 20 chronological fittings to a mean of 1.56±0.50 in the last 16 fittings ($p<0.05$, Wilcoxon). The number of trial lenses required began to be statistically significant lower than the first 20 fittings after fittings 61 to 80 ($p<0.05$, Wilcoxon). The mean number of lenses trialed to arrive to the final dispensing SL in the trial visit was 1.85±0.71 lenses, being 1.84±0.69 for IC Group (range between 1 and 4 trial lenses) and 1.88±0.77 for RC Group (range between 1 and 4 trial lenses). When both groups were compared, there were no statistical significant differences between them regarding the number of trial lenses needed to achieve the best fit ($p=0.970$, Mann–Whitney U test). By further diving the sample into subgroups, it was required, on average, more lenses in Sec.IC (irregular corneas submitted to surgeries, 1.98±0.72 lenses) than on Prim.IC (1.78±0.67 lenses), but without statistical significant differences between them ($p=0.149$, Mann–Whitney U test) and more trial lenses for HA.RC (with astigmatism >2.00 D, 1.96±0.82 lenses) than for LA.RC (1.63±0.52 lenses), also without statistical significant differences ($p=0.413$, Mann–Whitney U test).



Statistical significant diferences between (Wilcoxon):
1 to 20 with 61 to 80; 81 to 100; 121 to 140; 141 to 156 & 21 to 40 with 81 to 100; 121 to 140; 141 to 156 & 41 to 60 with 61 to 80; 81 to 100; 101 to 120; 121 to 140; 141 to 156 & 61 to 80 with 81 to 100 & 81 to 100 with 101 to 120

Figure 6.1 Number of trial lenses required to achieve the best fit. Data is presented in a chronological scale of 20 fittings. Bars represent the Mean number of trial lenses and respective Standard Deviation. Boxes show the Median (MED) and Interquartile Range (IQR) for each chronological group.



Statistical significant diferences between (Wilcoxon):
21 to 40 with 141 to 156 & 41 to 60 with 141 to 156 & 61 to 80 with 141 to 156 & 81 to 100 with 121 to 140; 141 to 156

Figure 6.2 Number of re-orders required after the first lens dispensed. Data is presented in a chronological scale of 20 fittings. Bars represent the Mean number of trial lenses and respective Standard Deviation. Boxes show the Median (MED) and Interquartile Range (IQR) for each chronological group.

Figure 6.2 presents the number of re-orders required in a chronological scale of 20 fittings. According to the chronological order of the fittings there was a decrease on the re-orders required (a reduction of an average of 0.95±0.74 at fittings 21 to 40 to 0.25±0.43 in fittings 141 to 156 ($p<0.05$, Wilcoxon), meaning a reduction of an average of almost 1 re-order per subject to 1 re-order per 4 subjects on the last fittings. The number of lens re-orders began to decrease after fitting number 60 ($p<0.05$, Wilcoxon).

The average number of re-orders needed was 0.76±0.77 lenses, being 0.73±0.76 for the IC Group (range between 0 and 4 trial lenses) and 0.88±0.81 for the RC Group (range between 0 and 3 trial lenses), without statistical significant differences between them ($p=0.303$, Mann–Whitney U test). By further dividing the sample into subgroups, the Sec.IC required statistically more re-orders to achieve the best fit (0.98±0.92) when compared to Prim.IC (0.60±0.63) ($p<0.05$, Mann–Whitney U test). But when comparing the mean number of re-orders between LA.RC and HA.RC (1.00±0.76 and 0.85±0.83, respectively), there were no statistically significant differences ($p=0.537$, Mann–Whitney U test). However, 73.3% of the re-orders performed on RC Group were done on HA.RC subgroup, which also as higher a number of fittings (*Table 6.3*). *Table 6.3* shows the number of lenses ordered to the manufacturer to accomplish a satisfactory fitting. Results are presented separately for each Group and each subgroup according the nature of the irregular astigmatism (primary ectasia or surgically induced in IC Group) and regular astigmatism (low or moderate-to-high astigmatism (≥ 2.00 DC) in RC Group). The visit when the re-orders were needed are also shown.

Most of the re-orders performed were due to inadequate sagittal height (more than 30% in both groups), poor vision (23.6%, IC Group) and a combination between poor vision and inadequate fit (33.3%, RC Group). An important issue is that about 10% of the subjects of each group required a re-order because of lens discomfort, although the fitting seemed satisfactory. Most of the changes were done in the landing zone of the lens, namely refitted with toric designs, which resulted in improved comfort. Another important factor is the number of lenses that broke (5 in IC Group and 1 in RC Group) – 4 of them broke during mechanical handling disinfection (rubbing the lenses), 1 lens felt on the floor during application and 1 lens suffered an in situ breakage after being hit by a high speed projectile, but without compromise to the corneal surface. [17] More than 70% of the re-orders needed in both groups were made in the lens dispense visit, however there were also 3 subjects that required a re-order after 3 months of lens wear – 2 because of lenses that broke and 1 because of continuous discomfort.

Table 6.3. Number of lenses reordered in each group (irregular and regular cornea) and subgroup (surgical/non-surgical and low and high astigmatism).

		TOTAL fittings (n=156)	IC Group			RC Group		
			TOTAL (n=122)	Prim.IC (n=80)	Sec.IC (n=42)	TOTAL (n=34)	LA.RC ≤ 2.00 D (n=8)	HÁ.RC ≥ 2.00 D (n=26)
Cause of re-order	Inadequate Saggital Height*	36 (30.3%)	27 (30.3%)	12 (13.5%)	15 (16.9%)	9 (30.0%)	3 (10.0%)	6 (20.0%)
	Inadequate Landing Zone	7 (5.9%)	5 (5.6%)	2 (2.2%)	3 (3.4%)	2 (6.7%)	0 (0%)	2 (6.7%)
	Poor Vision	23 (19.3%)	21 (23.6%)	16 (18.0%)	5 (5.6%)	2 (6.7%)	0 (0%)	2 (6.7%)
	Discomfort	12 (10.1%)	9 (10.1%)	5 (5.6%)	4 (4.5%)	3 (10.0%)	3 (10.0%)	0 (0%)
	Poor Vision + Fit$^{\Delta}$	21 (17.6%)	11 (12.4%)	6 (6.7%)	5 (5.6%)	10 (33.3%)	2 (6.7%)	8 (26.7%)
	Fit$^{\Delta}$	14 (11.8%)	11 (12.4%)	4 (4.5%)	7 (7.9%)	3 (10.0%)	0 (0%)	3 (10.0%)
	Lens Broke	6 (5.0%)	5 (5.6%)	3 (3.4%)	2 (2.2%)	1 (3.3%)	0 (0%)	1 (3.3%)
Visit of re-order	Lens Dispense Visit (V0)	85 (71.4%)	64 (71.9%)	34 (38.2%)	30 (33.7%)	21 (70%)	5 (16.7%)	16 (53.3%)
	1 week visit	8 (6.7%)	6 (6.7%)	3 (3.4%)	3 (3.4%)	2 (6.7%)	0 (0%)	2 (6.7%)
	1 month visit (V1)	19 (16.0%)	12 (13.5%)	6 (6.7%)	6 (6.7%)	7 (23.3%)	3 (10.0%)	4 (13.3%)
	3 month visit (V2)	4 (3.4%)	4 (4.5%)	3 (3.4%)	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)
	>3 month visit	3 (2.5%)	3 (3.4%)	2 (2.2%)	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)
	Total number of re-orders	119 (100%)	89 (100%)	48 (53.9%)	41 (46.1%)	30 (100%)	8 (26.7%)	22 (73.3%)

n is the number of fittings; *both increased and decreased sagittal height; ΔPoor Fit = both sagittal height and landing zone parameters inadequate.

6.4.1 Fitting Trials and Re-orders

Figure 6.3 A shows the percentage of SL with landing zone toric designs required in a chronological scale of 20 fittings. According to the chronological order of fittings, there was observed an increase on the number of landing zone toric lens designs required. The number of landing zone toric designs duplicated between the first 20 fittings (35%) and fittings no 41 to 60 (97%). In IC Group, 85% of the total lenses fitted were toric and 74% of RC Group were toric.

Figure 6.3 B shows the percentage of SL with front-toric designs required in a chronological scale of 20 fittings. From the 156 total number of fittings, 53% required front-toric lens designs. The value of astigmatism that was required ranged from -0.50 D to -2.00 D (mean of -0.90±0.28 D).

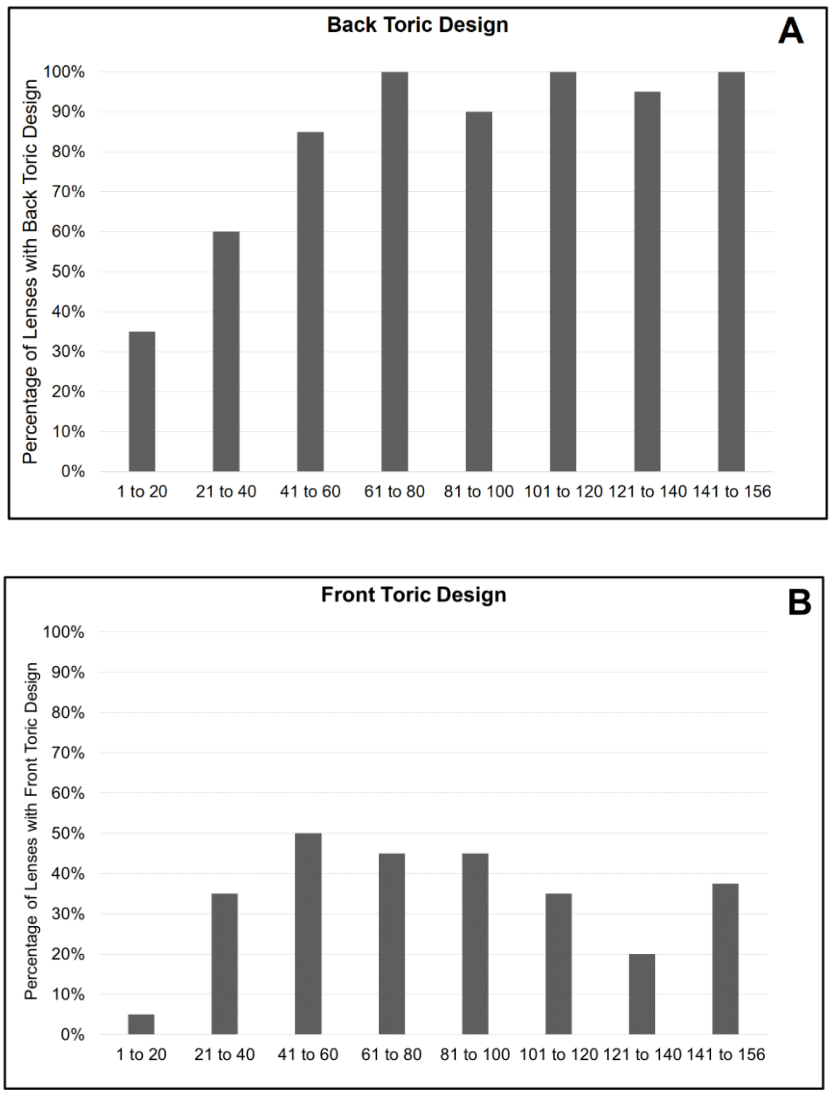


Figure 6.3 Percentage of back-toric lens design (A) and front toric lens design (B) required. Data is presented in a chronological scale of 20 fittings

6.5 Results

Several studies have already proven the visual efficacy of SL for different eye conditions, from normal/regular shaped corneas to the more challenging corneal irregularities. [1,3,4,18] Although many experts state that there is a steep learning curve in fitting these devices, there are no publications regarding the complexity and the learning curve in fitting SL for a beginner practitioner. This is the first study that confirms that SLs can be successfully fitted by practitioners with minor previous training using fitting trials method. However, there is a training period after which there is a reduction in both trial lenses needed and re-orders performed to achieve the best SL that subjects can comfortably wear successfully.

The recently published results of SCOPE online survey on demographic and prescribing patterns of SL fitters [19] revealed that the number of practitioners fitting SL has increased during the past decade. From the total 989 respondents, 19% reported to had fit at least 5 patients with SL. From the practitioners that completed the entire survey (n=678), 65% reported that have fitted 50 or fewer patients during their career and 21% reported that they had fitted only 10 or fewer patients. A limited number of experienced fitters was identified (13%) who reported to have fitted more than 200 patients. Despite the valuable information drawn by this study about how many SL fitters and their demographics and academic background and how many patients are actually wearing SL, there are no results of how many lenses have those two distinct groups of practitioners were required to achieve the best fit for each patient.

In the present study, we identified how many trial lenses were required to achieve the optimal lens to be dispensed and how many re-orders were required after the first dispensed lenses, and how this learning curve evolves overtime in a novel practitioner without previous experience on SL fitting. *Figure 6.1* shows a decrease in the number of trial lenses required to achieve the optimal fit to be dispensed. An average of 2.35±0.79 lenses per eye were necessary in the first fittings, which reduced to 1.50 trial lenses or less after the first 61 to 80 fittings (eyes) were accomplished. Although the time spent in each trial visit was not recorded in this study, this reduction of 1 trial lens per eye could have a significant positive effect in the chair time required. In this study, the practitioner and the devices used in each trial visit were the same, so this improvement of 1 lens per eye reveals an improvement in practitioner's clinical judgment with time. The findings shown in this study might be affected by asymmetry of more challenging or easier to fit cases that might appear at any time during the chronological course of this study.

However, the relatively large sample recruited and the uniformity in inclusion and exclusion criteria should minimize this factor and contribute to a uniform distribution of cases with different degrees of difficulty in reaching the final fitting. A preliminary analysis comparing refractive, topographical and quality of vision parameters between the 8 chronological groups was conducted. Despite statistical significant differences between the 8 groups in some topographical and quality of vision parameters, there was not a pattern that suggests a chronological change in easiness or difficulty between groups. In fact, these parameters are not necessary related to the difficulty of fitting. Regarding proportion of patients without or with previous surgery or different grades of ectasia severity or no ectasia, they were evenly distributed between the 8 chronological groups.

Although there are no studies in peer review literature reporting the potential improvement of practitioner skills over time in fitting SL (learning curve), there are few studies reporting the mean number of trial lenses or lenses ordered per eye to achieve the best fit during the fitting process. Schornack *et al* [20] found an average of 1.5 of lenses ordered per eye and an average of 2.8 visits to complete the fitting process in a sample of 19 patients with keratoconus (30 eyes), and Gemules [21] reported an average of 1.7 attempts per patient for the 9 patients enrolled in the study. Studies with corneal rigid gas permeable contact lenses (RGP) reported the need of a range from 1 to 5 trial lenses per eye to achieve the best fit, with a mean number of trial lenses of 2.3 [22] and 1.73 [23]. According to our results, a mild-experienced SL fitter would need an average of 1.50 trial lenses per eye, which is less than the values provided by those studies for RGP corneal lenses.

The differences between IC and RC groups on the mean number of trial lenses required to achieve the best fit (1.84±0.69 and 1.88±0.77, respectively) were not statistically significant. By further dividing our results in subgroups, post-surgical corneas (Sec.IC) required more trial lenses than those with primary ectasia. Corneas with high astigmatism (HA.RC) also required more trial lenses to achieve the best fit. Although there were no statistical significant differences between them, this means that irregular corneas submitted to surgeries or corneas with high astigmatism could be more challenging to fit in some cases. By personal experience of the practitioner, those corneas that underwent specific surgeries (like penetrating keratoplasty and intracorneal ring implantation) or those with high astigmatic corneas (namely with limbus-to-limbus high toricity) are often more challenging to fit. Possible explanations to this include the more asymmetric corneal surface in the post-surgical corneas and the more asymmetric scleral

shape associated to the highly toric corneas (in the RC Group). Although there is lack of consensus in this regard, some clinical observations revealed that when the corneal astigmatism is higher and congenital in nature, the sclera could also have the same magnitude and orientation of toricity. [24,25] Also, Marcus Ritzmann *et al* [26] did not found a strong association between the orientation and magnitude of corneal astigmatism and scleral toricity in normal corneas, except for some eyes. The authors also concluded that higher corneal astigmatism (>2.00D) could be associated to scleral toricity. Other studies found that the scleral topography of irregular and regular shaped corneas have differences, which could have a direct impact in SL fitting – namely when choosing the best landing zone geometry for the different eyes. [27–29]

Regarding the re-orders needed during the fitting process, we found a 40% optimal fit rate with the first lens ordered. To our knowledge, this have never been established for SL in the peer-reviewed literature. A work presented at GSLS 2018, which analyzed the first 150 fits in a normal clinical practice, reported that 27.9% of the subjects completed the fit with no changes to the initial lens order. [14] In corneal RGPs there are also significantly different reported rates: Romero-Jimenez *et al* reported an optimal fit rate of 77% [22] and Betts *et al* [30] of 33% using the same lenses – discrepancies between studies were justified by differences in the methodology. In our sample, 48% of the total sample required 1 lens exchange, 9% required 2 lenses exchanges and 4% required 3 or 4 lens re-orders. On average, the mean number of lens ordered per eye was 1.76±0.77, which is similar to the reported values of a recent work by Adeline Bauer (1.70 lenses per eye). [14]

Although it seemed to have an increase in the number of re-orders in the first fittings, we rapidly see a tendency of decrease (*Figure 6.2*). That early increase in the number of re-orders was attributed to the augmented complexity of the cases after fitting number 20. After these initial 20 fittings, the experience of the practitioner shows a higher rate of back surface toricity prescription, which could require some additional re-orders in the beginning as the practitioner gets familiar with the clinical impact of different changes in fitting parameters.

The differences between both groups on the mean number or re-orders (0.73±0. 76 and 0.88±0.81, respectively) were small and with no statistical significant difference. When further dividing into subgroups and similarly to what we concluded about trial lenses, Sec.IC subgroup needed more re-orders than Prim.IC ($p<0.05$), which corroborates our thoughts about the complexity of fitting those corneas that underwent some surgeries. Controversially to the findings on the mean number of trial lenses required in each subgroups of RC Group, no

statistical significant differences were found (mean of 1.00±0.76 on LA.RC and 0.85±0.83 in HA.RC). In fact, there is a large difference in the number subjects of each subgroup (8 in LA.RC and 26 in HA.RC), but we can also see that 73.4% of the total number of re-order were from the subgroup of corneas with high astigmatism. As said before, the clinical feeling of the practitioner was that high astigmatic corneas were more complex to fit. In 3 fittings of HA.RC Group it was required to order a different trial lens because none of the lenses from the trial set fitted correctly the scleral shape (landing zone) because of high scleral toricity.

Regarding the prescribing pattern of more specific designs, 83% of the total fits have toric landing zone designs (85% in IC Group and 74% in RC Group). This is in accordance to Gregory DeNayer *et al* [31] findings, that 94.3% of the 140 eyes analyzed with a scleral topographer showed non-spherical like scleral shapes – meaning that the vast majority of the eyes analyzed could benefit from non-spherical landing zone geometries to perfectly align with the scleral shape. There was also an increase in using central and landing zone toric lens designs with increasing experience: 35% of the first 20 fittings had landing zone toric design, that increased to 97% in the last fittings. Once again, the authors recognize that these results should be analyzed with caution. Indeed, eyes requiring SL with toric landing zones or with internal astigmatism requiring central toricity could present at any time during the clinical trials, so it is difficult to address that this could be only related to a change in the practitioner skills.

There are some factors that could be seen as limitations of the study. First, only 1 practitioner/ fitter was evaluated to assess the learning curve: other practitioners could learn faster or slower and this will have a direct impact on the study findings. Second, the results of this study are limited to the fitting of SLs using trial sets with the same characteristics of the ones used in this study. Current fitting approaches by most practitioners use a similar procedure what allows to apply current results to most fitting protocols. However, other designs and manufacturers might not replicate exactly the present results and they need to be independently assessed. Also, technologies such as OCT and scleral topographers are increasingly being used during SL fittings, which could aid during the fitting process and consequently decrease the number of trial lens and re-orders. Also, techniques derived from corneal topography - like the ones described in another study by the same authors [25] - might also aid during the fitting process, but it needs to be prospectively assessed. In addition, other approaches could be used to assess the cornea-lens separation (central corneal clearance – CCC) – such as the use of optic biometers or using an image processing software (like ImageJ) to measure CCC more

objectively than with slit lamp alone. [32] Altogether could have a direct impact in the number of trial lenses and re-orders to the manufacturer.

The authors' decision of using both eyes of each subject (when applicable) was because 78% of the total sample were irregular corneas and is well established that the majority of these conditions are asymmetric in nature. These asymmetries will influence the lens fitting, namely the lens sagittal height for each eye. In addition, SL land on conjunctiva, so the anatomy of the eye beyond the corneal borders has an important role in the fitting process. Despite some degree of correlation in refractive error or corneal power between both eyes (which are not necessary related to the difficulty of SL fitting process), there were poor correlations considering the geometry of the lens landing zone in the two groups ($r=0.364$ IC Group and $r=0.333$ RC Group, Spearman). Considering the clinical experience of the authors that despite similarities that might be present between both eyes of the same subject, the level of complexity of the fitting process is not so straightforward – it is often required specific adjustments. Further limitations include the asymmetric number of patients/eyes in the different subgroups. However, altogether, the present study presents one of the largest case series recently published.

In summary we have observed that contemporary scleral supported rigid gas permeable lenses can be fitted in most cases of moderate-to-severe ocular corneal defects and regular shaped corneas by practitioners with minimal previous training. After the first fittings, a novel practitioner fitting SLs would be able to significantly reduce the number of trial lenses and re-orders to the manufacturer.

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Part of the present results have been presented in a short communication to the Global Specialty Lens Symposium - GSLS2018,Nevada, USA, 2018
Written consent has been obtained from the patients to publish the information reported in this paper. Datasets are available upon request to the corresponding author.

6.6 Results

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Chapter 7

In Vivo Assessment of the Anterior Scleral Contour Assisted by Automatic Profilometry and Changes in Conjunctival Shape after Scleral Lens Wear

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Macedo-de-Araújo RJ, van der Worp E, González-Méijome JM. In vivo assessment of the anterior scleral contour assisted by automatic profilometry and changes in conjunctival shape after miniscleral contact lens fitting. J Optom. 2018 Nov 1.

7. *In Vivo* Assessment of the Anterior Scleral Contour Assisted by Automatic Profilometry and Changes in Conjunctival Shape after Scleral Lens Wear

7.1 Abstract

Purpose: To compare the shape of the anterior sclera of candidates to scleral lens fitting with regular and irregular corneas and analyze the changes induced in the shape of the sclero-conjunctiva after scleral lens wear.
Methods: Thirty-five eyes of 18 subjects (19 eyes with irregular corneas and 16 with regular corneas) were consecutively recruited. Three measures of sclero-conjunctival shape were taken with Eye Surface Profiler (ESP). Tangent angles and ocular sagittal heights (OC-SAG) were analyzed at different chords from 13 to 17mm in the nasal, temporal, superior and inferior regions. The 19 eyes with irregular cornea were selected to wear scleral lenses and the changes in their sclero-conjuntiva surface parameters were compared before and after 3h of lens wear.
Results: Irregular corneas showed higher OC-SAG values than regular corneas in all the chords analyzed, with statistical significant differences in the temporal region. Regarding tangent angles, regular corneas showed lower values (flatter surface), with statistical significant differences at 8 and 8.50mm on the nasal and 8.50mm on the temporal region. Some changes were seen in sclero-conjuctival shape after short-term scleral lens wear. There was an augment in OC-SAG after 3h of scleral lens wear and a reduction on tangent angles, namely on the nasal region at 7.5mm and 8.00mm chord lengths, which is coincidental with the landing zone of the scleral lens.
Conclusions: ESP shows mild differences in scleral shape between eyes with regular and irregular corneas. ESP might be valuable in quantifying the mechanical impact of the scleral lens on the anterior eye surface.

7.2 Introduction

Contact lenses are still the preferred solution for visual correction of the irregular cornea. However, corneal rigid gas permeable, hybrid contact lenses or special soft contact lenses are frequently not suitable for highly distorted corneas. In that cases, the contact lens needs to vault the entire cornea and limbus and rest entirely in the scleral area beyond the limbus. Scleral lenses are useful for visual rehabilitation of highly irregular corneas, and for the relief or severe dry eye symptoms in different ocular surface diseases. [1,2]

Scleral lens fitting is challenged by three main factors. First, scleral lenses are intended to align with the bulbar conjunctival tissue over the anterior sclera. This tissue is a thin layer of columnar epithelial cells supported by connective tissue and deep dense collagen – due to these histological characteristics, conjunctival tissue does not provide a stable support for Scleral lens. Instead, these lenses compress this soft tissue (*Figure 7.1*), decreasing the vault and tightening the lens against the ocular surface over time. [3,4] Second, the tightening effect seals the posterior lens tear reservoir limiting the exchange of the tear film and promoting the formation of tear debris and limiting the oxygen transport to the cornea. [5] This might induce some degree of corneal edema, even though it is, on average, within the physiological limits (edema that occurs during sleep without contact lens). [6] Third, there was a poor understanding of the true scleral shape and until recently it was not possible to assess this relevant parameter in the clinical setting.

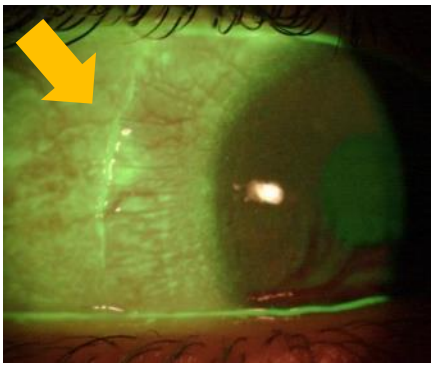

Figure 7.1 Conjunctival staining after scleral lens wear, indicating the landing zone area of the lens. This picture was obtained in one of the patients of the study during the initial fitting trials.

In order to minimize the first two effects, modern scleral lenses have been designed to provide a wider area of support in order to avoid localized impingement and/ or compression of the sclero-conjunctiva tissue. This has been possible by the qualitative and quantitative evaluation of the scleral topography using image processing from anterior segment optical coherence tomography. [1,7–9] However, the inter-individual differences in shape and symmetry of the sclera limits the predictability of the fitting and the need to trial several lenses is frequent, increasing the chair time. Thus, a device that would be able to measure the scleral topography in the clinical setting, could potentially increase the predictability of scleral lens fitting. Eye Surface Profiler (ESP) is a new device that uses optical profilometry to obtain a three dimensional reconstruction of the anterior ocular segment up to approximately 20 mm. This technology allows

to measure the peri-limbal scleral topography in an automated manner [10,11] and could be useful in the evaluation of the areas under pressure and/or more decentered and assist in the decision to adjust Scleral lens parameters to seek a better distribution of the lens support over larger and wider areas using spherical or toric lens haptics designs. [12]

The main goals of the study were to compare scleral shape of eyes with regular and irregular corneas and to measure the changes in the topography of the sclero-conjunctiva where the miniscleral lens align with the ocular surface in order to understand the main areas of compression of the lens.

7.3 Materials and Methods

7.3.1 Study Design and Subjects

This was a prospective study enrolling candidates to scleral lens fitting. The subjects were previously recruited to participate in a prospective clinical trial evolving scleral lens fitting and have undergone the trial lens fitting process and were waiting for the final lens to be dispensed. The contact lens wearers were asked to discontinue the use of their habitual contact lenses prior to the evaluations. This study was divided into two parts. The first part of the study (Part I) aimed to compare the sclero-conjuntival shape between eyes with irregular corneal surfaces and eyes with regular corneal surfaces. Thirty-five eyes of 18 subjects (12 women) with mean age of 35±11 years were analyzed. Subjects were divided into two groups according to their corneal condition. Group I comprised 19 eyes with irregular corneal surfaces due to primary and secondary ectasia (2 eyes with post-LASIK ectasia, 2 eyes with keratoplasty and 15 eyes with keratoconus). The severity of keratoconus (KC) was classified with the Keratoconus Severity Score (KSS). Three eyes were classified as having grade 1, 2 eyes with grade 2, 8 eyes with grade 3 and 2 eyes with grade 5. The Group II comprised 16 regular corneas with high refractive errors (myopia ≥ 6.00 D and/or astigmatism ≥ 2.00 D). The second part of the present study (Part II) aimed to quantify the changes in sclero-conjunctival tissue after 3 hours of scleral lens wear. The measurements were performed only in the 19 eyes from Group I (irregular cornea group) during the scleral lens dispense visit. After Baseline (Part I) measures, these patients wore their brand new scleral lens for approximately 3 hours. Measurements were also performed

after 3 hours of scleral lens wear (5 minutes after scleral lens removal). Patients were informed about the purpose and nature of the evaluations and signed an informed consent form. The protocol of the study was reviewed and approved by the Ethics Committee of the School of Health Sciences of the University of Minho (Braga, Portugal) and followed the 1964 Helsinki declaration and its later amendments.

7.3.2 Scleral Lens Used and Fitting Protocol

The scleral lenses used on the Part II of the present study were from Procornea Nederland B.V. (Eerbeek, The Netherlands). All the lenses had 16.4mm diameter and were fitted according to manufacturers' recommendations. All subjects have already undergone a trial lens visit were the best scleral lens for each eye was selected with a trial-and-error method (Macedo-de-Araújo *et al*, Learning Curve, accepted Int Biomed Research). An ideal fit was achieved if there was no touch over the entire cornea and limbus, with a center corneal clearance between 100 and 200 μm after settling and no conjunctival impingement or compression/ blanching of the conjunctival vessels. *Figure 7.2* shows the appearance of the fitting of a scleral lens on eye. Lens fit was assessed with slit lamp examination and instillation of fluorescein (Fluo Strips, Contacare, India) directly on the lens, prior to its insertion. The measurements of Part II were done at the lens dispense visit, before that the subjects have only attended for a fitting visit more than 1 month ago.

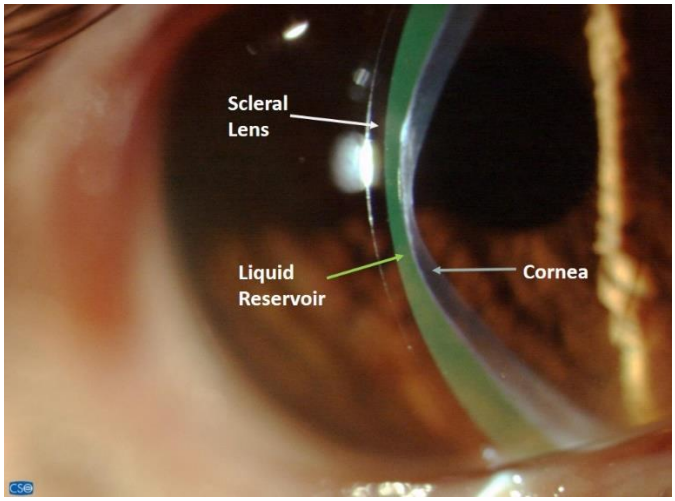

Figure 7.2 Relationship of a scleral lens with the ocular surface.

7.3.3 Measurements

The Eye Surface Profiler (ESP) from Eaglet Eye (Houten, The Netherlands) is a new device to obtain the elevation of the anterior ocular segment using Fourier transform profilometry technique. The ESP has previously been validated. [10,13] It projects two grids over the anterior corneal surface stained with sodium fluorescein and creates a three dimensional reconstruction of the anterior corneo-scleral topography up to 20 mm chord. In our protocol, we stained the surface with a fixed amount of fluorescein diluted in non-preserved saline. Three repeated evaluations were performed 10 seconds after instillation. To compensate the time lapse for processing data, a new drop of sodium fluorescein was applied after the first measurement to ensure consistent measurements. In order to achieve a greater field for analysis, the examiner held both eyelids against the orbital area without pressing the globe. Data was collected from each individual map (3 captures before and 3 captures after lens wear) and the average values at each visit were used for subsequent analysis. Different parameters were collected and analyzed:

- Sagittal height of the anterior ocular surface (OC-SAG) was recorded at 14, 15 and 16 mm in the horizontal meridian (180°). This measures gives the TSag (temporal sagittal height) and NSag (nasal sagittal height) and the difference between them that allows to quantify the scleral asymmetry (TSag-NSag). *Figure 7.3* represents a horizontal cross-section of a typical eye surface (image from ESP user's manual): as it is seen, the OC-SAG was calculated for a total chord of 16mm with the exactly half of the total chord length being attributed to NSag and TSag (8mm nasal and 8mm temporal). The respective sagittal heights are determined from the corneal apex outwards.

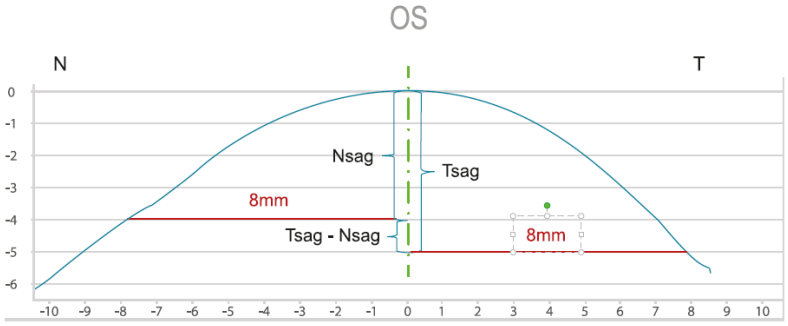

Figure 7.3 Sagittal Height calculation (image from Eye Surface Profiler user's manual). It is observed a flatter nasal (N) side when compared to temporal (T), which leads to a lower sagittal height on this side.

- Tangent Angles at 6.5 mm, 7 mm, 7.5 mm, 8 mm and 8.5 mm in nasal, temporal, superior and inferior quadrants. These attributes will better describe the shape of the sclera rather than radii of curvature, because of its geometric nature. Also, tangent angles could be useful in determining the haptic zone of the lens.

7.3.4 Statistical Analysis

Statistical analysis has been conducted using SPSS v21.0 (IBM Inc. IL). Normality of data distribution was assessed using the Shapiro-Wilk test. Considering the nature of the data distribution, differences between quadrants were assessed using repeated measures ANOVA (normally distributed) or Friedman test (non-normally distributed). The level of statistical significance has been set at $p<0.05$.

7.4 Results

7.4.1 PART I: Differences In Scleral Shape Between Eyes with Regular and Irregular Corneal Surface

Table 7.1 represents the OC-SAG at the different chord diameters analyzed (14mm, 15mm and 16mm) for temporal and nasal quadrants and the difference between them for each meridian separately. As shown, the overall OC-SAG for each semi-meridian is always higher on the temporal region when compared to nasal, for all chord lengths analyzed, with statistical significant differences for all the chord diameters analyzed in both groups ($p<0.005$, paired t-test or Wilcoxon, according to sample distribution). The OC-SAG values are increasing as the analyzed chord length is increasing in both nasal and temporal regions for both groups ($p<0.005$, paired t-test or Wilcoxon, according to sample distribution). This suggests that there is a progressive asymmetry as we move away from limbus. The eyes with irregular corneas (Group I) showed higher values of OC-SAG than those from Group II, in all the chord lengths analyzed and in both nasal and temporal regions. Despite this, statistical significant differences between the two groups were only found on temporal region.

Table 7.1. Differences in OC-SAG (µm) between Regular and Irregular Cornea Eyes at 14mm, 15mm and 16mm in both Temporal and Nasal scleral regions.

OC-SAG (µm)	Regular Cornea (n=19)	Irregular Cornea (n=16)	Difference, µm *(p-value)* [a]
TSag 14mm	3453±134	3628±230	176 (p=0.016) *
NSag 14mm	2909±252	2945±252	36 (p=0.714)
TSag-NSag 14mm	552±295	683±402	131 (p=0.301)
Overall OC-SAG 14mm	3181±128	3287±154	107 (p=0.053)
TSag 15mm	3888±139	4123±237	235 (p=0.003) *
NSag 15mm	3199±281	3312±78	113 (p=0.294)
TSag-NSag 15mm	688±327	810±374	122 (p=0.368)
Overall OC-SAG 15mm	3544±150	3718±171	174 (p=0.008) *
TSag 16mm	4394±179	4599±268	205 (p=0.042) *
NSag 16mm	3524±326	3571±229	48 (p=0.717)
TSag-NSag 16mm	870±356	1077±86	207 (p=0.229)
Overall OC-SAG 16mm	3959±192	4042±127	84 (p=0.253)

[a]Unpaired *t*-test.

Figure 7.4 A represents the Tangent Angles at different chord lengths in nasal and temporal regions. On average, the values at temporal regions are higher than on the nasal region. The values are similar between eyes with regular and irregular corneas, with the first ones showing slightly lower values in nasal, temporal and superior regions, although without statistical significant differences between groups. The only statistical significant differences found between Group I and Group II were seen on the nasal side at 8 mm (31.19±3.86° and 34.96±6.91°, respectively) and 8.50 mm (33.68±5.16° and 38.61±9.50°, respectively) and for 8.50 mm on the temporal region (46.14±2.66° and 51.22±3.41°, respectively). There is a bigger SD in eyes with KC. *Figure 7.4 B* represents the Tangent Angles in superior and inferior regions. Although subjects from Group II showed lower values than irregular cornea eyes (Group I) on the superior zone, there were no statistical significant differences between the two groups for all the points analyzed.

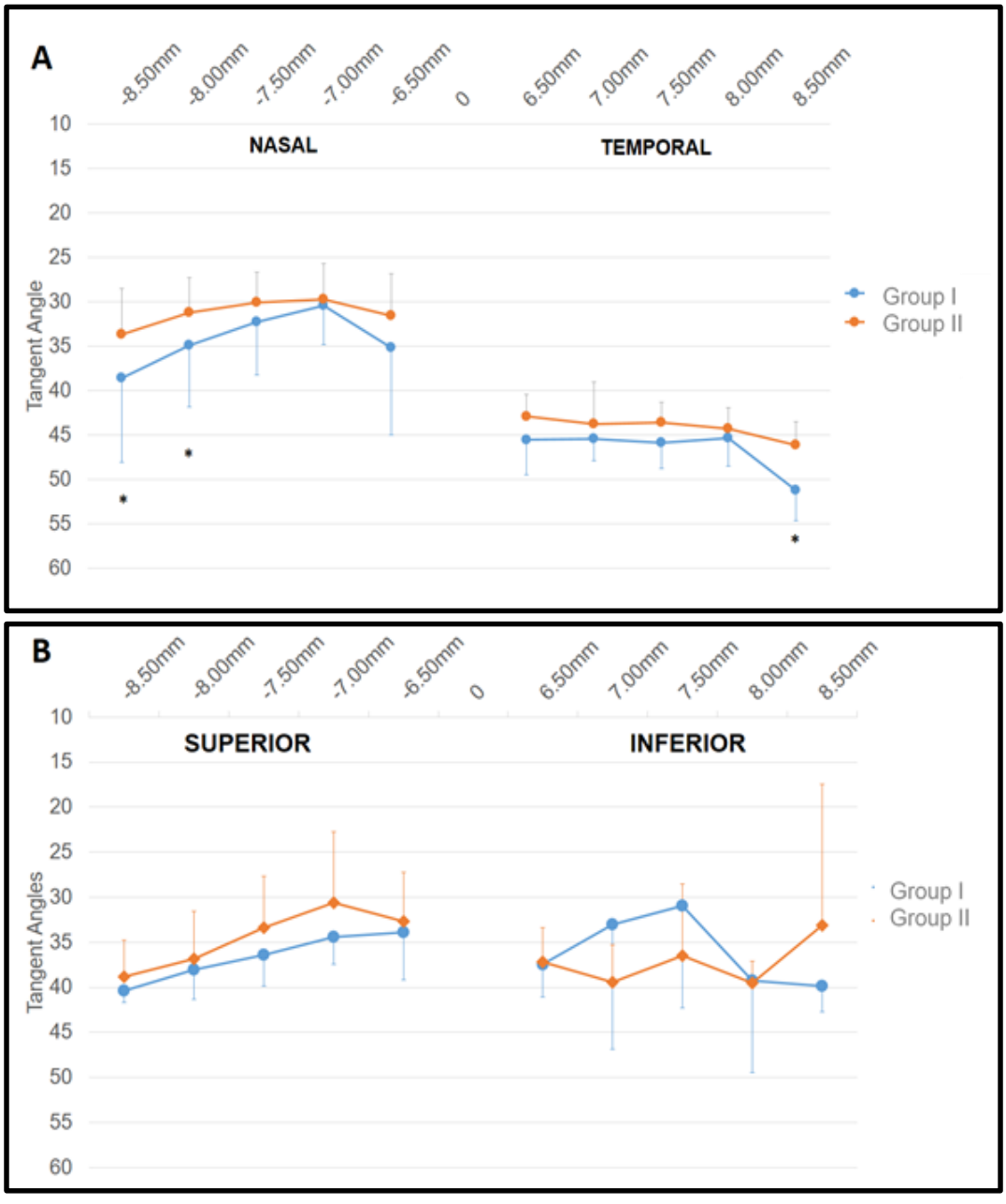

Figure 7.4 Differences in Tangent Angles between Normal Eyes (orange lines) and eyes with Keratoconus (KC – blue lines) on horizontal meridian (A) and Vertical meridian (B). * Unpaired t-test.

7.4.2 PART II: Differences In Sclero-Conjunctival Tissue Before and After 3 Hours of Scleral Lens Wear.

Table 7.2 represents the changes on OC-SAG induced by the landing zone of a scleral lens on eye (baseline and after 3h). Both surfaces become steeper (deeper) after 3 hours of scleral lens wear, namely at 15 and 16mm. There was only a statistical significant difference between measurements at 15mm chord on the temporal region (p=0.049).

Table 7.2. Changes in Sagittal Height from Apex at Temporal and Nasal sides after 3 h of lens wear.

OC-SAG (µm)	Baseline	After 3h of lens wear	Difference (µm) (p-value)*
TSag 14mm	3608±220	3694±192	86 (p=0.066)
NSag 14mm	2911±287	2922±800	11 (p=0.986)
TSag-NSag 14mm	697±401	772±777	75 (p=0.656)
TSag 15mm	4099±228	4185±187	86 (p=0.049)*
NSag 15mm	3256±298	3306±292	50 (p=0.095)
TSag-NSag 15mm	843±385	859±319	16 (p=0.385)
TSag 16mm	4547±245	4599±208	52 (p=0.765)
NSag 16mm	3497±282	3600±340	103 (p=0.143)
TSag-NSag 16mm	1092±400	969±350	123 (p=0.466)

Figure 7.5 shows the differences on Tangent Angles after 3h of scleral lens wear for nasal and temporal regions (*Figure 7.5 A*) and superior and inferior regions (*Figure 7.5 B*). Although there were no statistical significant differences in sclero-conjunctival shape after 3 hours of scleral lens wear, there are some slight alterations namely on the nasal region. As seen, values are slightly higher between 6.50 and 7.50 mm, but after 7.50 mm became lower. On temporal side, the main differences are seen from 7.50 mm, being these values lower (meaning flatter) after 3h of scleral lens wear. In the superior zone there is not a consistent behavior. There are differences among all the chord lengths studied, and a decrease at 8.00 mm is seen, followed by a great augment.

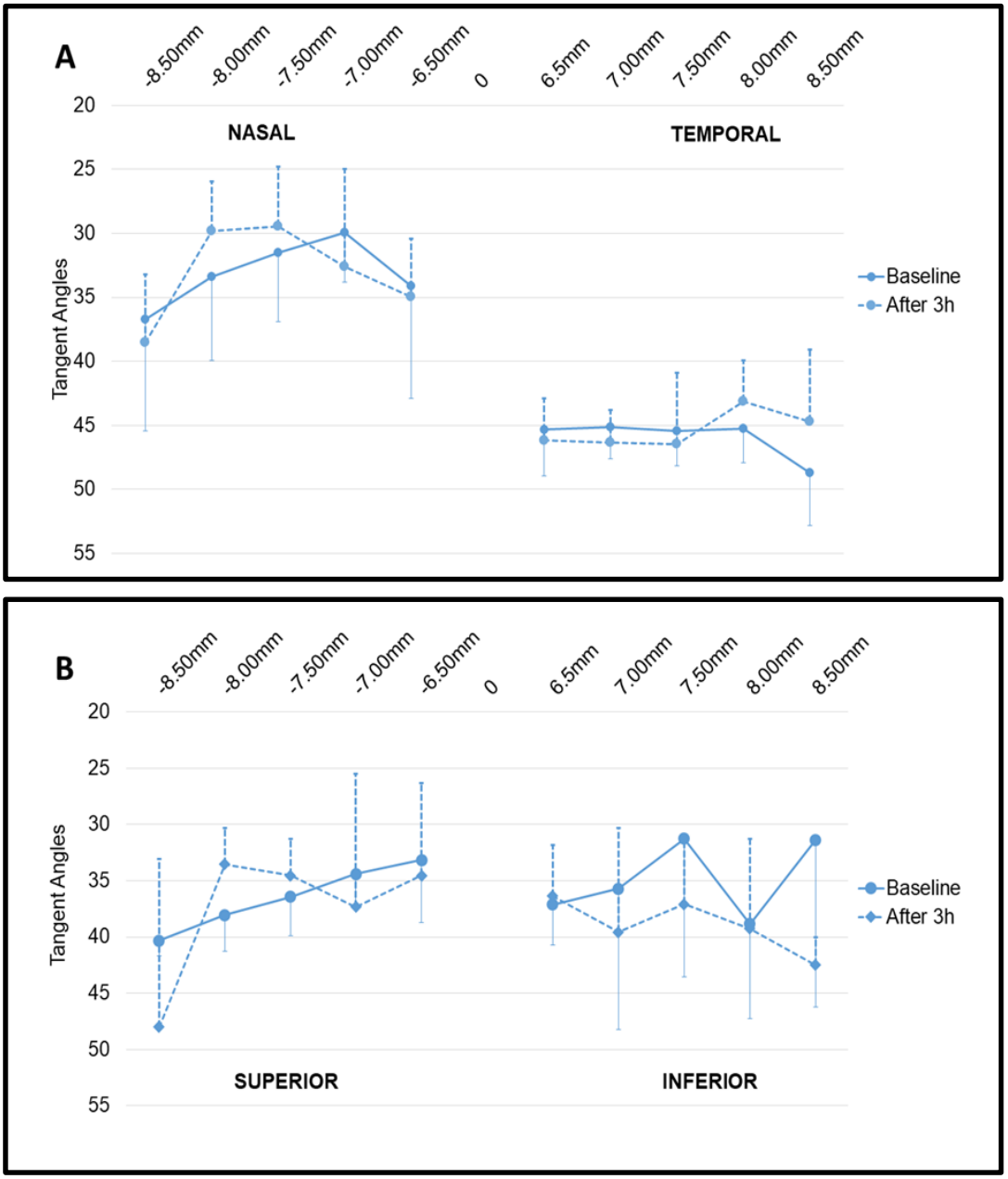

Figure 7.5 Values of Tangent Angles from 6.50 to 8.50mm in Nasal and Temporal regions (Horizontal - A) and Superior and Inferior regions (Vertical - B) at Baseline and after 3h of scleral lens wear.

7.5 Discussion

In the present study a corneo-scleral topographer (ESP) was used to compare the sclero-conjunctiva shape of eyes with regular and irregular corneas and later investigate the influence of short-term scleral lens wear on sclero-conjunctiva. ESP has previously been used to measure scleral radius and limbus shape [14–16], evaluation of scleral changes with accommodation [17] and has also been used to analyze perpendicular meridians to estimate the scleral asymmetry to relate it with scleral lens flexure on-eye [18].

In the first part of the present study we aimed to detect differences in corneo-scleral profile between healthy eyes and eyes with keratoconus. It is important to establish those differences in anterior ocular surface anatomy to aid the scleral lens fitting process. The emergence of recent technologies that allow to evaluate the anterior ocular surface (like scleral topographers and AS-OCT) allowed to characterize the scleral shape for different chords and its asymmetry. [7,9,19,20] Based on several studies with OCT, it is accepted that the OC-SAG of the normal eye is on average about 3750 µm with a range of 1000 µm. [21] Several studies with OCT found values of horizontal OC-SAG at 15mm of 3735±186 µm (Harkness B *et al,* Poster American Academy Optometry 2015), 3740±200 µm [8] and 3740±160 µm [22] for normal eyes, which are higher than those found in the present study for the same chord in eyes with regular cornea (3544±326 µm). Another study with ESP also found an OC-SAG value of 3755±207 µm for 86 normal eyes at 15mm. [23] The sample of the present study has different characteristics, as only eyes with high refractive errors were included and this could influence the mean OC-SAG. The OC-SAG of eyes with ectasias is expected to be higher than in normal eyes. Achong-Coan *et al* found that eyes with keratoconus have an OC-SAG 205 µm higher (on average) than normal eyes. (Achong-Coan *et al*, Poster Global Specialty Lens Symposium 2012). In the present study an average difference of 174 µm was found between Group I and Group II ($p=0.008$) for a 15 mm chord. The mean difference between groups was larger on the temporal region (235 µm, $p=0.03$) than on the nasal region (113 µm, $p>0.05$). Discrepancies between studies could be due to differences in the sample characteristics, as not all the eyes that are included in Group I have keratoconus, and the keratoconic eyes of the different studies might have been evaluated at different stages of severity. Recently, Piñero *et al* [11] used a corneo-scleral topographer to compare the OC-SAG at 11, 12, 13 and 14 mm chord lengths of a large

sample of normal and keratoconic eyes. For normal eyes, they found an OC-SAG of 3130 µm for a 14 mm chord, which was similar to the value encountered in the present study for the same chord length (3181 µm). Similarly to the results of the present study, some differences were also found in OC-SAG between eyes with regular and irregular cornea, but only in moderate and advanced stages of keratoconus, and no statistical significant differences were found between normal eyes and eyes with less severe stages of keratoconus. Although the OC-SAG of regular cornea group at 14 mm was very similar to our study, they found a shallower OC-SAG for KC corneas (3120 µm vs 3287 µm in the present study). These differences could be due to different stages of keratoconus of the population analyzed, that could not be compared as the KC severity was measured with different scales in both studies. In another study from Sorbara *et al* [7], an OCT was used to measure the OC-SAG at HVID and 15 mm chord in normal eyes and eyes with keratoconus in order to compare the differences between them. They analyzed the OC-SAG at steep and flat meridians, contrary to the present study in which the horizontal meridian (nasal and temporal regions) were analyzed. In fact, the great majority of studies conclude that there is no relationship between corneal and scleral toricity (both magnitude and orientation) especially in irregular corneas [19,24,25] (Posters Global Specialty Contact Lens Symposium, Kinoshita et al 2016 and López-Alcón *et al* 2018), however recent studies encountered a relationship between corneal and scleral astigmatism in subjects with healthy corneas and high corneal astigmatism. [24,26] Despite the methodological differences between studies, Sorbara *et al* also found statistically significant differences between normal and KC eyes, and that KC eyes have a higher asymmetry in OC-SAG between steep and flat meridians (at both HVID and 15 mm) than normal eyes, similarly to the present study but in nasal and temporal regions and at 14, 15 and 16 mm chords (*Table 7.1*, Tsag-Nsag). Differences between healthy and irregular eyes were also found in tangent angles, with normal eyes having lower values, in accordance with the results of the present study. Sorbara *et al* [7] also found differences in peripheral tangent angles between the two groups at 15mm but not at HVID. Also, their results confirmed significant asymmetries between different quadrants of the sclera and that these asymmetries increase with the increasing chord diameter analyzed. Also, is confirmed that the nasal quadrant of the sclera is flatter. These asymmetries were already encountered by other studies with OCT and corneo-scleral topographers. [1,7,19,20] In conclusion, the mild differences found between regular and irregular corneas in the Part I of the study were already reported in the literature, but only in samples with normal cornea (typically with low refractive errors) and in keratoconus patients. In

this study, regular cornea with high refractive errors and the irregular cornea group not only comprised with keratoconus (but also post-keratoplasties and post-lasik ectasias) were analyzed, which could justify the differences found between this study and the literature.

The second part of the present study was focused on finding the possible differences in sclero-conjunctival profile after short-term scleral lens wear and if the ESP device was able to detect those differences. Recent studies already showed that, although scleral lens do not mechanically touch the cornea, there is a flattening of the anterior corneal curvature following short term scleral lens wear. [27–29] However, as these lenses land exclusively in the sclero-conjunctival tissue, it is also relevant to assess objectively the mechanical impact of the scleral lens compression on the bulbar conjunctival as a result of lens misalignment or external sources of mechanical compression. [30] Although with no statistical significant differences, this pilot study found that the short-term scleral lens wear (3 hours) caused some changes in sclero-conjunctival tissue. *Table 7.2* shows that after 3 hours of lens wear there is an augment in OC-SAG at all the chords analyzed, meaning that these regions became steeper (deeper), namely at 15 and 16 mm. This steepening could be related to the scleral lens "footprint" on the sclero-conjunctiva due to compression of the tissue. *Figure 7.5* also demonstrates some differences in tangent angles through different chord lengths. The differences in sclero-conjunctiva were more pronounced in the nasal region. This is coincidental with the clinical observations of stronger mechanical pressure of scleral lens in this area (since the nasal region is, on average, flatter than the other meridians).

It is already known (from OCT studies) that there is a tissue thinning/compression over all quadrants after 3 hours of scleral lens wear. [31] A study from Consejo *et al* [32] that aimed to quantify the effect of short-term (5 h) scleral lens wear on sclero-conjunctival topography (with ESP) also concluded that the anterior eye surface was significantly modified by short-term scleral lens wear – an increment in the limbal radius and a flattening in the sclero-conjunctiva was observed. These alterations in the ocular surface were previously found after short-term soft contact lens wear, though of smaller magnitude. [33] They also repeated the measures 3 h after lens removal and concluded that these changes did not recede to baseline values over that period. The tissue thinning found by Alonso-Carneiro *et al* also did not recovered to baseline values 3 hours after lens removal. [31] The time necessary for the sclero-conjunctiva to return to its normal shape is still unknown and should be studied in future studies to better understand the mechanical response of the scleral-conjunctival tissue during scleral lens wear. A major limitation

of previous studies that aimed to quantify the sclero-conjuctival changes after contact lens wear is the limited chord lengths analyzed. The present study ads an important contribution as different chord lengths are analyzed in 0.5 mm steps (*Figure 7.5*). In this way, it is not only possible to conclude that there is an alteration in sclero-conjunctival topography but also perceive which areas have the greatest changes during scleral lens wear. As seen on *Figure 7.5* and *Figure 7.6* regions nearest the limbus become steeper after scleral lens wear and then is seen a flattening in tangent angles (between 7 and 7.5mm nasal and 7.5 and 8mm in temporal). The authors hypothesize that this is related with the landing zone of the lens. Due to anatomical factors, scleral lenses tend to decenter inferiorly and temporally. Because of that, the landing zone of scleral lens will be closer to the limbus on the nasal region than on temporal region – that's why the flattening is seen at different chord lengths in both regions mentioned. The authors acknowledge that, contrary to what occurs when analyzing the results of Part I of the study, the evidence regarding the changes in sclero-conjunctiva after scleral lens wear could not be strong enough to draw clear conclusions, as there were no statistical significant differences between measurements and the standard deviations are quite high.

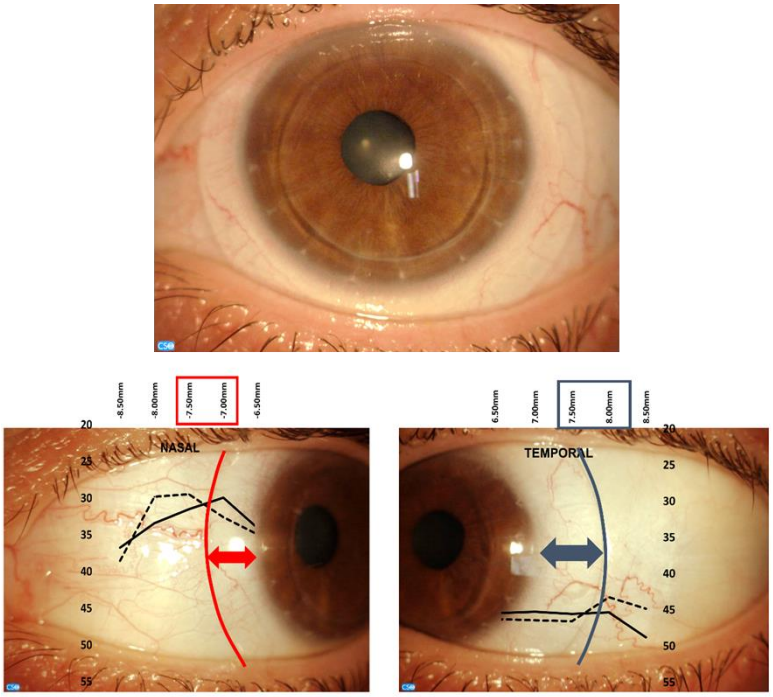

Figure 7.6 (A) Infero-temporal deccentration of a scleral lens. (B) Conjugation of results from Figure 7.5. A with figures from the nasal and temporal portion, demonstrating that the changes found on scleral tangent angles could coincide with the scleral lens haptic zone. Red (nasal) and blue (temporal) lines are overlapped with the landing zone of the lens, that is nearest the limbus on the nasal side than on the temporal side. The inferior-temporal part of the lens is visible in the bottom-right image.

The authors recognize some other limitations in this study. Anatomical structure of the ocular surface and instrument capabilities limits the ability to take measurements at 8 or 8.50 mm in some subjects, particularly in the vertical direction, which leads to the higher values of standard deviations found. The authors ensure that at least 2 complete maps were obtained to process the data.

This is a preliminary study to further investigate the predictability role of scleral shape measurements (both OC-SAG and scleral tangent angles) to allow clinicians in the scleral lenses fitting process, as nowadays the most used method is trial-and-error (diagnostic lens set). When correlated to trial lens information and clinical evaluations, it is expected that the present findings will add valuable evidence to reduce the need to fit several trial lenses to achieve the best fitting, namely on unexperienced/ novel fitters (Macedo-de-Araujo, submitted to publication). Although some authors have already considered this issue, further investigation needs to be done in order to investigate if ESP measurements can anticipate the areas of compression and correlate scleral anatomy parameters with the ideal lens parameters in order to improve the predictability of these increasingly popular fitting strategy. Also, it is important to know if these changes in scleral anatomy after short-term scleral lens wear will maintain at the long term, as well as the time necessary for the sclero-conjunctiva to back to normal values after scleral lens removal.

In conclusion, ESP shows mild differences in scleral shape between eyes with regular and irregular corneas in agreement with previous studies. The preliminary results of this study suggest that the short-term scleral lens wear alters the sclero-conjunctival topography, and that the areas where the changes are more pronounced may be related to the landing zone of the scleral lens. ESP might be valuable in quantifying the mechanical impact of the scleral lens on the perilimbal bulbar conjunctival.

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Chapter 8

Relationship of Placido Corneal Topography Data with Scleral Lens Fitting Parameters

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Macedo-de-Araújo RJ, Amorim-de-Sousa A, Queirós A, van der Worp E, González-Méijome JM. Relationship of placido corneal topography data with scleral lens fitting parameters. Cont Lens Anterior Eye. 2018 Jul 25. pii: S1367-0484(18)30797-5.

8. Relationship of Placido Corneal Topography Data with Scleral Lens Fitting Parameters

8.1 Abstract

Purpose: To analyze the relationship between corneal sagittal height and asymmetry parameters derived from Placido-videokeratoscopy with the parameters of fitted scleral lenses.
Methods: Corneal topographies were measured with MedmontE300 in a total of 126 eyes before initial scleral lens fitting were analyzed. Measurements of sagittal height (OC-SAG) at steep and flat corneal meridians were obtained for 10mm and 12mm chords. Estimated Height (EHChord) parameters were taken for a chord equal to the diameter of the lens that each subject was wearing at different semi-meridians. Corneal asymmetry (difference in OC-SAG between steep and flat corneal meridians) was also assessed. These outcomes were correlated to scleral lenses parameters that subjects were wearing after 1 month (ScCL-SAG, landing zone).
Results: The mean ScCL-SAG was 4696±240μm, and the mean OC-SAG ranged from 1891μm (10mm), 2914μm (12mm), and between 4162μm and 4251μm for EH0-180° and EH30-210°. Higher correlations ($p<0.001$) between OC-SAG and ScCL-SAG were determined for EH0-180° ($r=0.595$) and EH30-210° ($r=0.618$). The mean differences between OC-SAG and ScCL-SAG were between 447±290μm (EH0-180°) and 389±360μm (EH30-210°). There was no relationship between corneal asymmetry and the need to fit a scleral lens with toric haptic design in irregular corneas. Orientation of flat corneal and scleral meridians were similar only in corneas with high astigmatism.
Conclusions: EHChord attributes were the parameters that best correlated with the ScCL-SAG. The corneal asymmetry was shown to be a poor predictor for the need to fit a scleral lens with toricity at landing zone in irregular corneas, but could have some predictive power in healthy corneas.

8.2 Introduction

Scleral-supported lenses rest in the scleral region, vaulting the limbus and cornea. Their use has increased exponentially as several manufacturers have entered the global market providing refined fitting trials and methods as well as reproducible computer lathing techniques in high-oxygen-permeable materials. [1,2] With these fitting approaches, it is now possible to achieve successful fittings with minimal trial lenses and fewer lens exchanges after dispensing (Macedo-de-Araujo *et al,* Chapter 6).

The main challenges when fitting these lenses remain the estimation of the appropriate vault to avoid contact with the cornea while not being so excessive that it could interfere with the corneal physiology [3–5] and choosing the right scleral lens landing zone geometry to match the scleral shape. [6] The shape of the anterior eye, namely the scleral shape, has increasingly been studied over the last few years mainly because of the resurgence of scleral lenses in the global market. Despite great advances in anterior segment (AS) imaging for scleral lens fitting, such as anterior segment optical coherence tomography (AS-OCT) [7–9] and scleral topographers, [10,11] their use to aid scleral lens fitting remains restricted to few clinical practices around the world because of the current costs of this kind of technology. On the other hand, corneal topographers have become increasingly available in contact lens practice and are more accessible to clinicians. Despite their limited coverage of examination (usually up to 7mm to 10mm of chord diameter), they have the potential to provide direct and indirect information that might be relevant for scleral lens fitting. It has been hypothesized that the anterior ocular sagittal height (OC-SAG) provided by corneal topographers could be of predictive value in estimating the sagittal height of the scleral lens. [12,13] When trying to predict scleral lens fitting from ocular surface parameters derived from corneal topography, Schornack *et al* [14] found weak correlations between them.

The present study aims to test this hypothesis using a commercial scleral lens (Senso Mino Sclera, Procornea) and a commercial corneal topographer (Medmont E300, Precision, Vancouver). Another hypothesis is that some of these measures might have predictive value in estimating the need for a toric peripheral geometry as well as the stabilization axis, as it is commonly observed in clinical practice that certain patterns of corneal astigmatism (i.e. limbus-to-limbus astigmatic corneas) seem to be related to the scleral shape. The main purpose was to analyze the relationship between OC-SAG parameters derived from corneal topography at different chord lengths and correlate that with the sagittal height of the scleral lens (ScCL-SAG) that subjects were wearing. A secondary goal was to investigate whether corneal height asymmetry (differences in OC-SAG between flat and steep corneal meridians) and its orientation predicts the need for asymmetric/toric peripheral lens haptic area and corresponding stabilization of the lens.

8.3 Methods

8.3.1 Sample Characteristics

This was a retrospective analysis involving patients with primary corneal ectasia, penetrating keratoplasty, post-surgical ectasia or regular corneas with high refractive errors (myopia ≥6.00D; hyperopia ≥4.00D and/or astigmatism ≥2.00D) fitted between October 2015 and March 2017. Following the recommendations of the Declaration of Helsinki, all subjects received information about the study before they agreed to participate and signed a consent form. The protocol of the study has been reviewed and approved by the Ethics Subcommittee for Life and Health Sciences of the University of Minho. A total of 175 eyes from 95 subjects were primarily recruited to participate in a study involving scleral-supported lens fitting. The initial 40 fittings (22 subjects) were excluded to eliminate the role of practitioner experience on the study outcomes (Macedo-de-Araújo, 2017, submitted for publication). Another 5 subjects (9 fittings) were excluded because of poor quality of the corneal topography acquisition due to highly distorted corneas. A total of 68 subjects (37 females, 31 males) with a mean age of 34±10 years are included in this report. Of them, 10 wore lenses in one eye and 58 wore lenses in both eyes, representing a total of 126 eyes dispensed with scleral lens. The sample was analyzed according to the ocular condition that required the scleral lens fitting: Group I (irregular corneas, n=92 eyes) and Group II (high refractive error with regular corneas, n=34 eyes). For some of the analysis, these groups were further subdivided: subgroup 1 (Subjects with primary ectasias without surgery); subgroup 2 (subjects with irregular corneas due to or with surgery – LASIK, ICRS, crosslinking); subgroup 3 (subjects with healthy corneas with corneal astigmatism <2.00 D); subgroup 4 (subjects with healthy corneas with corneal astigmatism >2.00D).

8.3.2 Scleral Lens Used and Fitting Method

Scleral lenses were manufactured by Procornea (Eerbeek, The Netherlands) using Boston XO material (hexafocon A). All lenses were fitted empirically by the same practitioner. The initial trial lens was determined following manufacturers' guidelines, considering clinical features and the degree of severity of the corneal condition. The optimal scleral lens should align evenly on sclera without conjunctival *blanching* and vault the entire corneal and limbal area with an ideal tear layer thickness of 100 to 200 μm after settling (2 hours). All the lenses fitted had 8.20mm

of radii of curvature. The diameter ranged between 15.2 and 16.4mm. The mean sagittal heights of the final scleral lenses (mean between steep and flat scleral lens sagittal heigh - ScCL_SAG) used by the subjects at 1 month visit ranged from 3948µm to 5428µm (mean 4696±240µm), and the toricity of the landing zones ranged between T0 to T6 (in steps of 1), T0 being a lens with no toric peripheral geometry (same geometry around the entire landing zone) and T6 having the maximum amount of toricity. The exact amount of toricity is not disclosed by the manufacturer. These scleral lenses parameters were compared to the corneal topographer outcomes listed below.

8.3.3 Corneal Topography

8.3.3.1 Sagittal Height Parameters

Three repeated corneal topography measurements were performed with the Medmont E300 (Victoria, Australia) and were analyzed with the Medmont Studio 6.1 in all eyes at the baseline appointment (prior to entering a prospective, dispensing clinical trial). Measurements of corneal sagittal height at two different chord lengths (10mm and 12mm) were analyzed for the flat and steep meridians of each individual eye. The estimated height (EHChord) parameter from the Medmont Studio 6.1 was also analyzed. This attribute provides the sagittal height of the anterior eye surface (OC-SAG) for a chord value set by the user. In this study, a chord equal to the diameter of the lens that the subjects were using was selected for each patient (between 15.2mm and 16.4mm) – i.e., if a subject was wearing a 16.4mm lens, the EHChord attribute was analyzed to a chord value of 16.4mm. Three parameters of estimated height (EH) provided by the topographer used were calculated for the particular chord diameter selected: EH 0-180°, which is the estimated height for the horizontal meridian for that specific chord length selected, EH 150-330°, and EH 30-210°. These data of OC-SAG for different zones and chord lengths were compared with the ScCL-SAG that subjects were wearing at 1 month of lens wear. *Figure 8.1* shows the relationship between OC-SAG (at 10 and 12mm and EH-Chord parameter), ScCL-SAG and cornea-lens separation for different chord lengths.

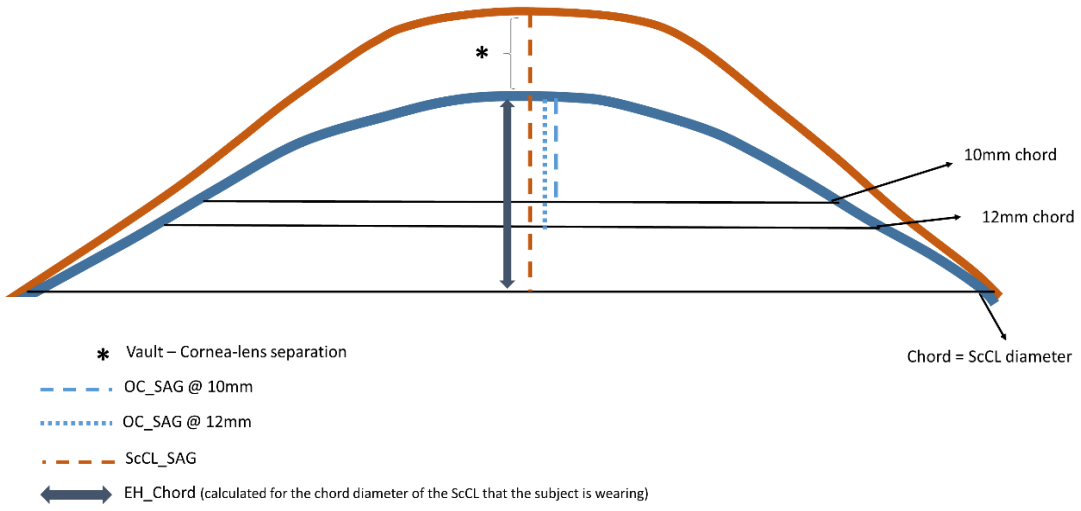

Figure 8.1 Relationship between cornea-lens separation, ScCL-SAG and OC-SAG at 10 and 12mm and EH-Chord parameter.

8.3.3.2 Scleral Lens Stabilization

The scleral lenses used in this study had marks indicating the flattest meridian of the lens in cases in which these lenses had some degree of toricity in the landing zone. The stabilization axis of the lens was measured on-eye during slit lamp examination. Following Visser *et al's* [15] methodology, a narrow slit beam was projected and oriented with the marks present in the lens periphery (indicating the flattest meridian), and the axis was obtained from the protractor incorporated in the slit lamp. The stabilization of the lens through the first day of lens wear was also analyzed for 103 of the 115 lenses that had some degree of toricity; the stabilization of the lenses was recorded 15 minutes after lens application and after more than 90 minutes of lens wear (mean time of wear: 126±74 minutes). This indicated the rotational stability of the lens over time.

8.3.3.3 Corneal and Scleral Asymmetry

The differences in sagittal height between the steep and flat corneal meridians (corneal asymmetry) at 10mm and 12mm was determined to assess the possible relationship between corneal asymmetry and scleral asymmetry (which leads to the need to fit a lens with a toric landing zone geometry). These outcomes were analyzed separately according to the geometry of the lens landing zone that the subjects were wearing; 103 of the 115 lenses that had some degree of toricity in the periphery were analyzed. These lenses had marks in their periphery that indicate the flattest meridian of the lens haptic. This meridian aligned with the flat meridian of the sclera. To further compare corneal and scleral asymmetry, the axis of the flat corneal meridian and the axis of scleral lens stabilization were compared among the different groups and subgroups. These measures were corrected for symmetry before they were analyzed.

8.3.4 Statistical Analysis

Statistical analysis was conducted using SPSS v.24.0 (IBM Co, IL). Normality of data distribution was analyzed with the Shapiro Wilk test in different groups and subgroups. Pairwise comparison between groups or subgroups was done using the Independent sample T-Test for normally distributed data and the Wilcoxon signed ranks test for non-normally distributed data. The level of statistical significance was set at $p<0.05$.

8.4 Results

Table 8.1 shows the demographic data of the subjects enrolled in the present report including keratometric data, spherical equivalent refraction and best-corrected visual acuity with habitual correction (HC), best spectacle correction (BSC) and with scleral lenses and OC-SAG and ScCL-SAG parameters.

Table 8.1. Characteristics of the sample analyzed: results arranged by groups and subgroups.

	Total	Group I (Irregular Cornea)	Group II (Regular Cornea)	p
No. Subjects	68	50 (74%)	18 (26%)	-
No. Eyes Fitted	126	92 (73%)	34 (27%)	-
Gender	37 female (54%) 31 male (46%)	25 female (50%) 25 male (50%)	12 female (67%) 6 male (33%)	-
SG (No. Fittings)		SGI.1: 53 (58%) SGI.2: 39 (42%)	SGII.1: 8 (24%) SGII.2: 26 (76%)	-
Age (years)	34.09±9.94 [range: 18 to 65]	35.74± 10.17 [range: 18 to 65]	29.50±8.17 [range: 18 to 46]	<0.050+
SimK Flat (D)	44.01±4.72 [range: 24.87 to 62.92]	44.42±5.41 [range: 24.87 to 62.92]	42.89±1.62 [range: 39.45 to 46.01]	<0.050*
SimK Steep (D)	47.36±5.06 [range: 29.83 to 65.38]	48.08±5.69 [range: 29.83 to 65.38]	45.40±1.2 [range: 42.87 to 46.01]	<0.001*
Q Flat	-0.67±0.50 [range: -2.89 to +0.43]	-0.75±0.55 [range: -2.89 to +0.43]	-0.44±0.18 [range: -0.86 to -0.11]	<0.050+
Q Steep	-0.20±0.65 [range: -1.56 to 2.24]	-0.30±0.69 [range: -1.56 to +2.24]	0.06±0.43 [range: -0.32 to 1.64]	<0.050*
OC-SAG (µm) – Flat meridian (10mm)	1832 ± 160 [range: 1512 to 2376]	1866 ± 166 [range: 1512 to 2376]	1738 ± 92 [range: 1559 to 1916]	p<0.001 *
OC-SAG (µm) – Steep meridian (10mm)	1950 ± 138 [range: 1686 to 2395]	1965 ± 147 [range: 1686 to 2396]	1908 ± 101 [range: 1779 to 2185]	p<0.05 *
OC-SAG (µm) – Flat meridian (12mm)	2784 ± 279 [range: 2212 to 3552]	2839 ± 293 [range: 2212 to 3552]	2635 ± 165 [range: 2324 to 3015]	p<0.001 *
OC-SAG (µm) – Steep meridian (12mm)	3043 ± 275 [steep: 2546 to 4150]	3064 ± 292 [range: 2546 to 4150]	2986 ± 216 [range: 2604 to 3596]	p=0.139 *
OC-SAG (µm) EHChord 0-180°	4162 ± 373 [range: 3479 to 7103]	4391 ± 539 [range: 3479 to 7103]	4193 ± 324 [range: 3515 to 4918]	p<0.05 *
OC-SAG (µm) EHChord 150-330°	4250 ± 383 [range: 3525 to 6740]	4471 ± 538 [range: 3575 ± 6740]	4307 ± 329 [range: 3525 to 5039]	p=0.127 *
OC-SAG (µm) EHChord 30-210°	4251 ± 339 [range: 3619 to 8223]	4485 ± 610 [range: 3658 to 8223]	4289 ± 316 [range: 3619 to 4908]	p=0.104 *
ScCL-SAG (µm) Flat meridian	4587 ± 254 [range: 3828 to 5307]	4604 ± 261 [range: 3841 to 5307]	4550 ± 233 [range: 3828 to 4883]	p=0.242 *
ScCL-SAG (µm) Steep meridian	4803 ± 248 [range: 4069 to 5548]	4805 ± 244 [range: 4125 to 5548]	4795 ± 263 [range: 4069 to 5293]	p=0.921 *

♀ female; ♂ male; SG – Subgroup; Q – corneal asphericity, OC-SAG – ocular sagittal height; ScCL-SAG – sagittal height of the scleral contact lens used; (+) Independent T-test, (*) Mann-Whitney U independent samples

8.4.1 Relationship between OC-SAG and ScCL-SAG

The mean ScCL-SAG was 4696±240µm (minimum 3949µm, maximum 5428µm). The diameters of the lenses fitted ranged from 15.2mm to 16.4mm; 108 lenses were 16.4mm, 9 lenses were 16mm, 3 lenses were 15.6mm and 6 lenses were 15.2mm. *Table 8.1* also shows the mean OC-SAG values measured at different chord lengths for the 126 eyes analyzed (total and divided by groups). The OC-SAG values from Group I are statistically significantly higher than

in Group II ($p<0.05$, Wilcoxon), except for the sagittal height of the steep meridian at the 12mm and EH Chords at 150-330° and 30-210°. *Figure 8.2* shows the correlations between ScCL-SAG with different parameters derived from the Medmont corneal topographer. Spearman Rho values were <0.500 for the correlations between OC-SAG and ScCL-SAG for 10mm and 12mm, indicating that the correlations for the flat meridian were higher than those for the steep meridian. The correlations were higher for the EHChord results, which represent the estimated height of the anterior ocular surface for a chord equal to the diameter of the lens that each subject was wearing (between 15.2mm and 16.4 mm, depending on the lens that each subject was wearing). The differences between the EHChord at different quadrants and the ScCL-SAG were 447±290µm, 391±260µm and 389±360µm for EH-Chord 0-180°, EH-Chord 150-330° and EH-Chord 30-210°, respectively.

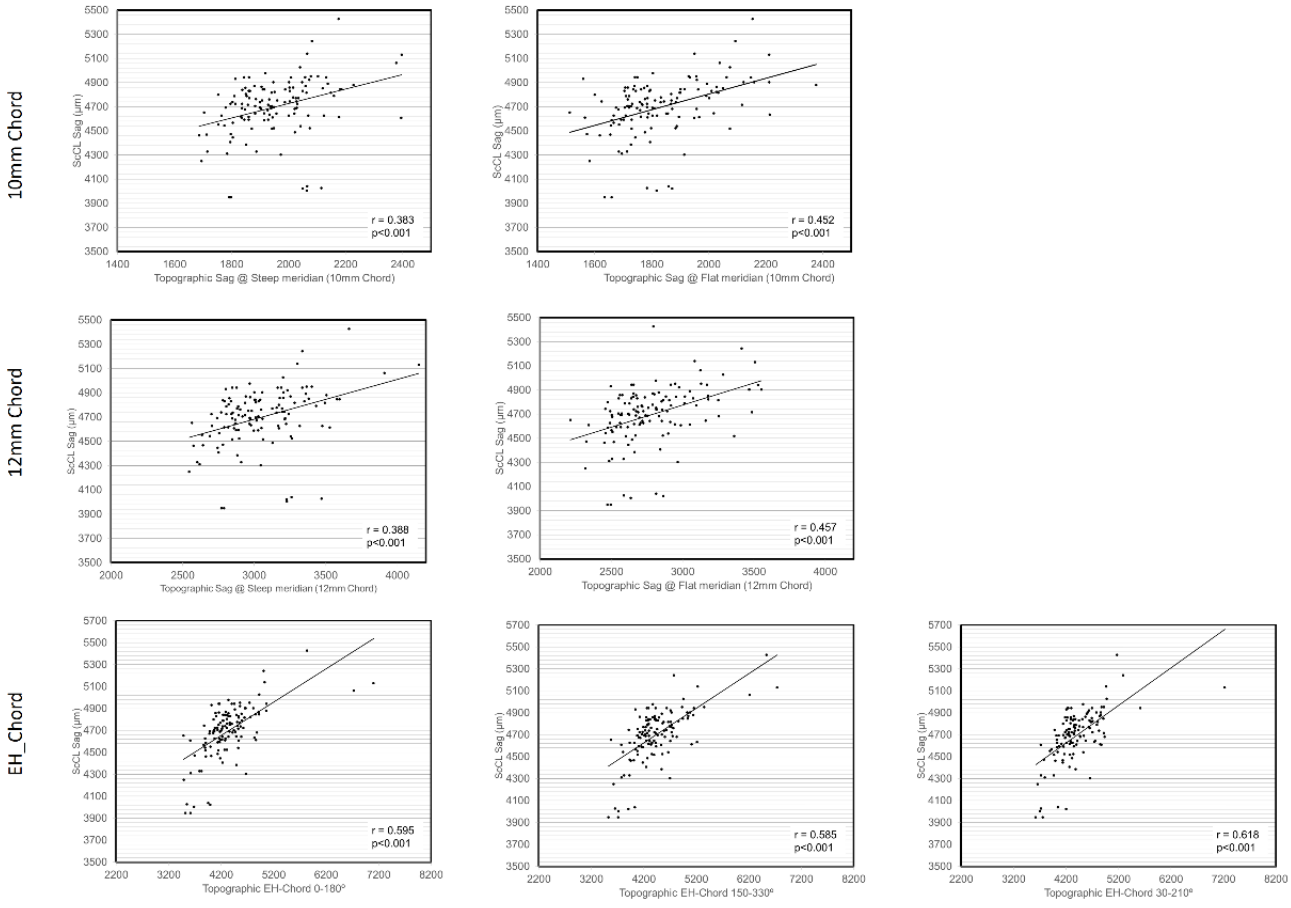

Figure 8.2 Correlations between ScCL-SAG that subjects are wearing with different parameters derived from corneal topography with the Medmont E300. EH-Chord was taken for a chord equal to the diameter of the lenses that subjects were wearing (between 15.2 and 16.4mm).

8.4.2 Relationship between Corneal Asymmetry and Geometry of the Scleral Lens Landing Zone

The vast majority – 115 lenses (91%) - of the 126 lenses fitted had some degree of toricity in the landing zone. Of those, data for 103 lenses were recorded: 44 lenses with toricity of 1 (T1), 49 lenses with T2, 12 lenses with T3, 6 lenses with T4, 3 lenses with T3 and 1 lens with T6. *Table 8.2* shows the differences between the OC-SAG of the steep and flat meridians for the 10mm and 12mm chords, which represents the asymmetry between the principal corneal meridians.

Table 8.2. Corneal asymmetry (differences in OC-SAG between steep and flat meridians) for 10 mm and 12 mm and its relation with toricity of the landing zone.

	Group I Irregular Cornea			Group II Regular Cornea		
T	N	Corneal Asymmetry 10mm (µm)	Corneal Asymmetry 12mm (µm)	N	Corneal Asymmetry 10mm (µm)	Corneal Asymmetry 12mm (µm)
0	5	149 ± 83 [range: 58 to 245]	298 ± 152 [range: 124 to 484]	6	147 ± 52 [range:59 to 213]	313 ± 128 [range: 79 to 460]
1	36	144 ± 91 [range: 4 to 380]	326 ± 210 [range:5 to 786]	8	149 ± 47 [range: 91 to 226]	309 ± 97 [range: 203 to 468]
2	39	136 ± 100 [range: 1 to 446]	318 ± 229 [range:18 to 867]	10	172 ± 67 [range:81 to 284]	372 ± 173 [range:113 to 713]
3	8	169 ± 105 [range: 5 to 332]	305 ± 276 [range:43 to 883]	4	144 ± 78 [range: 88 to 255]	292 ± 163 [range: 175 to 522]
4	4	130 ± 76 [range: 32 to 209]	262 ± 175 [range: 29 to 408]	2	141 ± 117 [range: 59 to 224]	317 ± 198 [range: 177 to 458]
5	0	-	-	3	288 ± 16 [range: 270 to 299]	587 ± 60 [range: 518 to 626]
6	0	-	-	1	254	306
0-1	41	145 ± 89 [range: 4 to 380]	323 ± 203 [range: 5 to 786]	14	148 ± 47 [range: 59 to 226]	311 ± 107 [range: 79 to 468]
2-6	51	141 ± 98 [range: 1 to 446]	311 ± 230 [range: 18 to 311]	20	185 ± 80 [range: 59 to 299]	380 ± 173 [range: 113 to 713]
Diff (µm)		-4	-12		**36**	**69**

T – toricity of the landing zone (0 – no toricity, 6 – maximum toricity); N – number of subjects; Corneal Asymmetry – Difference between the sagittal height of the flat and steep corneal meridians; Difference – difference between the sagittal heights of subjects requiring peripheral spherical lens designs (no toricity) or lower toricity (T 0) and those requiring higher amounts of toricity in the periphery (T between 2 and 6).

There was always a larger difference in the OC-SAG of the flat and steep meridian at 12mm than at 10mm in Group I ($p<0.05$, Wilcoxon) and Group II ($p<0.05$, t test for pairwise samples). There were no statistically significant differences between Groups regarding the differences in both OC-SAGs at 10mm and 12mm ($p>0.05$, t test for independent samples or Mann-Whitney, depending on the distribution). In the Irregular Cornea Group (Group I), there was no relationship between the asymmetry in the OC-SAG at 10mm and 12mm and the toricity required in the landing zone (differences of 4µm and 12µm between the sagittal heights of subjects requiring toricity in the landing zone of 0-1 and 2-6). However, in the Healthy Cornea Group, it was observed that subjects requiring higher landing zone toricity (between T2-T6) also have greater corneal asymmetry (differences in the sagittal height of the principal corneal meridians) than those requiring lower toricity in the landing zone (T0 and T1); this is a difference of 36µm for the 10mm chord and 69µm for the 12mm chord.

To further explore this, the sample was divided into subgroups. *Table 8.3* shows the differences in OC-SAG between the steep and flat meridians at 10mm and 12mm in the different subgroups. There was no relationship between the asymmetry in OC-SAG at 10mm and 12mm and the toricity of the landing zone required in the subgroups of the Irregular Cornea Group. For the subgroups of the Healthy Cornea Group, it was observed that subjects requiring larger amounts of toricity in the lens landing zone (between T2 and T6) had greater corneal asymmetries. The differences in the sagittal height of subjects requiring lower (T0 or T1) or higher (between T2 and T6) landing zone toricity are greater in Subgroup 2 – 36µm at 10mm and 59µm at 12mm - in contrast to Subgroup 1 - 4µm at 10mm and 32µm at 12mm.

Table 8.3. Corneal asymmetry (differences in OC-SAG between steep and flat meridians) for 10 mm and 12 mm and its relation with toricity of the landing zone, analyzed by subgroups.

	Group I Irregular Cornea						Group 2 Regular Cornea					
	SubGroup 1			SubGroup 2			SubGroup 3			SubGroup 4		
Lens Toricity	N	Corneal Asymmetry 10mm	Corneal Asymmetry 12mm	N	Corneal Asymmetry 10mm	Corneal Asymmetry 12mm	N	Corneal Asymmetry 10mm	Corneal Asymmetry 12mm	N	Corneal Asymmetry 10mm	Corneal Asymmetry 12mm
0	2	113 ± 58 [range: 72 to 154]	257 ± 141 [range: 158 to 357]	3	173 ± 101 [range: 58 to 245]	324 ± 284 [range: 124 to 484]	1	59	79	5	165 ± 31 [range: 130 to 213]	360 ± 63 [range: 305 to 460]
1	18	136 ± 80 [range: 4 to 267]	314 ± 203 [range: 5 to 631]	18	152 ± 102 [range: 12 to 380]	339 ± 223 [range: 77 to 786]	3	102 ± 10 [range: 91 to 111]	210 ± 10 [range: 203 to 222]	5	178 ± 33 [range: 141 to 226]	368 ± 68 [range: 285 to 468]
2	25	133 ± 100 [range:18 to 446]	276 ± 207 [range:31 to 752]	14	141 ± 102 [range: 1 to 344]	392 ± 256 [range: 18 to 867]	2	115 ± 48 [range: 81 to 150]	242 ± 182 [range:113 to 370]	8	186 ± 65 [range: 95 to 284]	405 ± 166 [range: 202 to 713]
3	5	201 ± 125 [range: 5 to 332]	359 ± 343 [range: 43 to 883]	3	117 ± 25 [range: 90 to 140]	214 ± 110 [range: 133 to 340]	1	88	175	3	162 ± 84 [range: 89 to 255]	332 ± 174 [range: 180 to 522]
4	3	103 ± 67 [range: 32 to 165]	214 ± 178 [range: 29 to 214]	1	209	408	1	59	177	1	224	457
5	0			0			0			3	288 ± 16 [range: 270 to 299]	587 ± 61 [range: 518 to 626]
6	0			0			0			1	253	306
0;1	20	134 ± 78 [range: 4 to 267]	308 ± 196 [range: 5 to 631]	21	155 ± 100 [range:12 to 380]	337 ± 213 [range:77 to 786]	4	91 ± 23 [range: 59 to 111]	177 ± 66 [range: 79 to 221]	10	171 ± 31 [range: 130 to 226]	364 ± 62 [range: 285 to 468]
2;3;4;5;6	33	141 ± 103 [range:5 to 446]	283 ± 224 [range:29 to 883]	18	141 ± 92 [range: 1 to 344]	363 ± 237 [range:18 to 363]	4	94 ± 39 [range: 59 to 150]	209 ± 112 [range: 113 to 370]	16	207 ± 71 [range: 89 to 299]	423 ± 160 [range: 180 to 713]
Diff (µm)		-7	-26		-14	-27		-4	32		36	59

8.4.3 Scleral Toricity vs Scleral Toricity

8.4.3.1 Corneal and Scleral Asymmetry

The mean stabilization angle of the scleral lenses right after insertion was 112±64° for right eyes and 55±55° for left eyes. After more than 90 minutes of lens wear, the mean lens stabilization angle was 113±65° for right eyes and 54±55° for left eyes. *Figure 8.3* shows the differences in lens stabilization for 103 of the 115 lenses that had some degree of toricity in the landing zone. The vast majority (67%) do not exhibit any rotation, 28.2% exhibited a rotation of 5°, 2.9% a rotation of 10° and 2% exhibited a lens rotation of more than 10° (1 subject with T3 had a lens that rotated 20°, and 1 subject with T2 had a lens that rotated 25°).

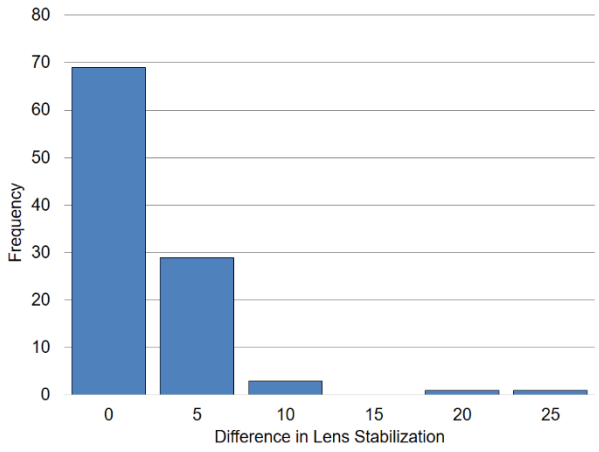

Figure 8.3 Histogram showing the distribution of the differences (lens rotation, in degrees) in scleral lens stabilization between 15 min after lens application and after 126 ± 74 min of lens wear.

8.4.3.2 Corneal and Scleral Asymmetry

Figure 8.4 A shows the distribution of the mean differences between the axis of the flat corneal meridian and the axis of lens stabilization (that will align with the flat scleral meridian) for the total sample. The mean difference was 42±31°, with only 19% having a difference less than 10°. However, when dividing these results by subgroups (*Figure 8.4 B*), it was observed that the vast majority of subjects in Subgroup 4 (yellow bars) have a rotation less than 10°, in contrast with the other subgroups. The mean difference between the flat corneal meridian and

the ScCL stabilization meridian was 51±30° for Subgroup 1, 46±32° for Subgroup 2, 38±18° for Subgroup 3 and 12±14° for Subgroup 4.

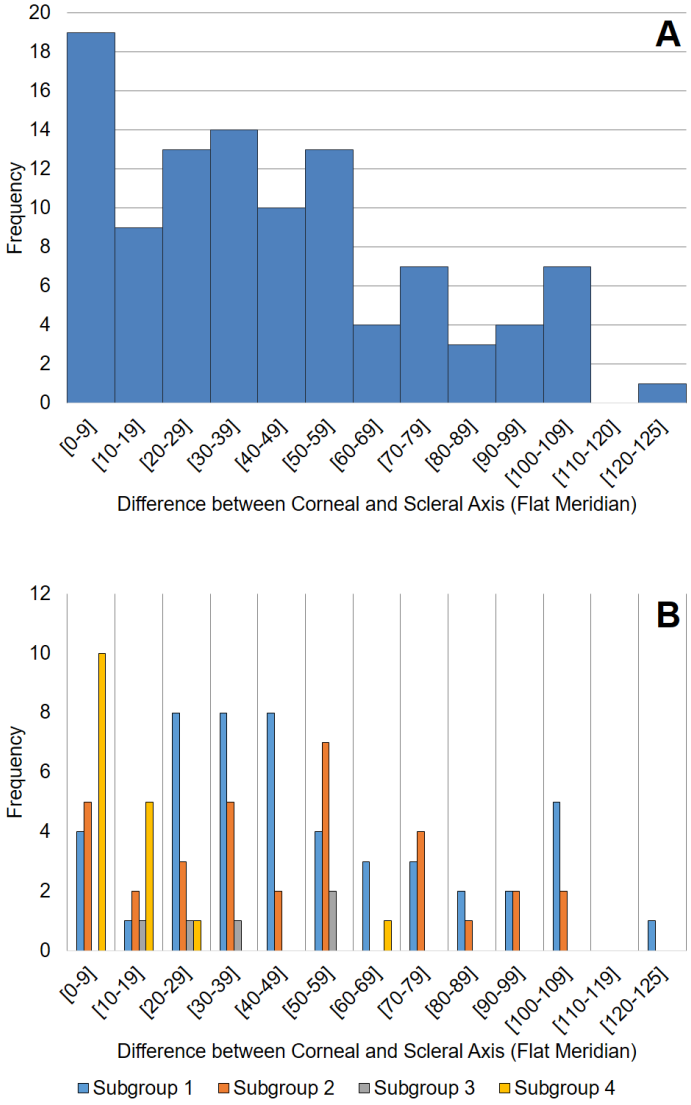

Figure 8.4 Histogram showing the distribution of the differences (in degrees) between flat corneal meridian and stabilization of the lens (that align with the flattest scleral meridian) in the total sample (A) and when dividing by subgroups (B).

The previous results of section 3.2 and the clinical judgment of the practitioner showed that when the corneal astigmatism was higher than 2.00D and had a limbus-to-limbus distribution (Subgroup 4), the sclera also seemed to have a toric shape with the same orientation, requiring back-toric periphery designs for correct alignment. *Figure 8.5* shows 4 cases of limbus-to-limbus corneal toricity with >2.00D of astigmatism for which the axis of

stabilization of the lens (that is on the flattest meridian) is very similar to the axis of the flat corneal meridian.

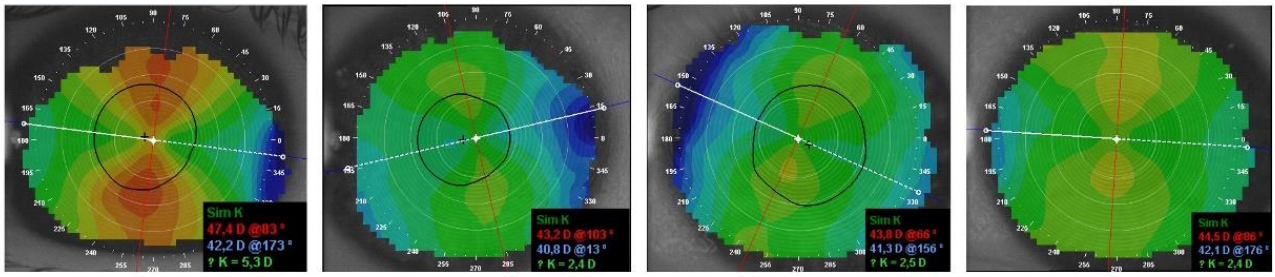

Figure 8.5 Example of corneal topographies (Medmont E300) from the sample of this study (healthy corneas) with limbus-to-limbus astigmatism. Notice that the axis of stabilization of the lens is similar to the axis of the flat corneal meridian.

8.5 Discussion

Currently, the vast majority of scleral lens fittings are based upon observations and estimation as well as the use of diagnostic lens sets (trial and error). One of the main difficulties is the limited information of the anterior ocular surface shape beyond the cornea. Corneal topography has shown to be important in fitting rigid contact lenses that land on the cornea, [16,17] but not for other types of lenses, [18] including scleral lenses. [14] Scleral topographers allow measurement of the amount and direction of scleral toricity and could aid the fitting process, complemented with customized fitting software. [19,20] OC-SAG is a key factor relevant in scleral lens design and fitting and can be measured with different instruments, with minimal differences being found between the Medmont E300 and AS-OCT measurements (3732±159µm and 3728±188µm, respectively). [21]

Corneo-scleral transition is another anatomical factor that plays an important role in defining OC-SAG. [22] However, this cannot be assessed with standard corneal topography devices. When measuring OC-SAG at the 10mm and 12mm chord, it is basically the corneal shape that is being measured. However, scleral lenses land only on the bulbar conjunctiva and underlying Tenon's capsule rather than on the sclera itself. It is a "spongy" surface, so the fitting could be unpredictable because the conjunctiva will be compressed differently under the pressure of the lens from patient to patient. Because of that, weak correlations were expected to

be found regarding scleral lens and corneal parameters. By observing *Figure 8.1*, it is possible to observe weak correlations (r<0.5) between ScCL_SAG and corneal parameters derived from corneal topography (at 10 and 12mm chord analysis). However, moderate correlations were found between EHChord attributes and ScCL-SAG (*Figure 8.2*), that was calculated for the diameter of the lens that subjects were wearing (between 15.2 and 16.4mm). The mean differences between EHChord parameters and ScCL-SAG were 447±290μm, 391±260 μm and 389±360μm for EH-Chord 0-180°, EH-Chord 150-330° and EH-Chord 30-210°, respectively. All of these average values correspond approximately to the cornea-lens separation (vault) that the lenses should have upon application. However, there is a large variability factor that explains why this will not work satisfactorily in every patient These results suggest that when a 16.4mm scleral lens fitting is required, it is possible to predict the best trial lens by measuring EH_Chord for 16.4mm and adding 447μm if EH_Chord0-180° is analyzed or 389 μm if the EH_Chord30-210° is analyzed, for instance. Despite the easiness to use the horizontal direction to perform these measurements due to larger topography coverage, the correlation between ScCL_SAG and EH_Chord30-210° was higher, so the author's recommend to use this value. A potential limitation of the study was the incorporation of different lens diameters into the analysis of EH-Chord outcomes. However, despite absolute values of OC_SAG could not be comparable as they were taken for the chord diameters equal to lens diameter, the differences between ScCL_SAG and OC_SAG are comparable, since they were analyzed for the same chord diameters.

It is known that the sclera is non-rotationally symmetric in nature and becomes more asymmetric with increasing distance from the limbus. [2,9,21,23,24] Because of this, scleral lenses with a diameter larger than 15mm often need to have back-surface toricity to align properly with the conjunctiva to avoid air bubbles and localized conjunctival blanching. [15] According to DeNaeyer *et al*, [6] only 5.7% of scleras have a spherical geometry (defined as less than 300 microns of difference in various meridians). In the present study, all of the ScCLs fitted had diameters larger than 15mm and therefore, perhaps not surprisingly, 91% of the lenses fitted had some degree of toricity in the landing zone. Also, scleral lenses remained rotationally stable during the follow-up exam conducted on the first day of lens wear (difference between 15min and 126min of wear), meaning that the lens did not rotate significantly during these period of lens wear. The vast majority of lenses (67%) did not exhibit any rotation, and 28% rotated up to 5°. These results are similar to those presented by López-Álcon *et al*, [25] who found stability in 87% of cases (with a maximum difference of 5°). In a different approach, Visser *et al* [15] concluded

that scleral lenses rapidly (within 4 to 6 seconds) return to their original positions even when rotated manually. It is important to have a constant stabilization of scleral lenses on-eye, especially in cases in which a front-cylinder or special optical correction is needed.

According to the present study, the corneal asymmetry did not have a predictive power in helping to choose the best landing zone geometry of scleral lens in irregular corneas. However, those from Group II (healthy corneas) wearing lenses with a landing zone toricity larger than or equal to T2 have more than 36μm (at 10 mm) and 69 μm (at 12 mm) of asymmetry compared to those requiring no or low toricity in the landing zone (T0 or T1). For that reason, subjects of Group II were further divided into two subgroups: one subgroup with low corneal astigmatism (subgroup 3) and the other subgroup with high corneal astigmatism (≥2.00D, subgroup 4). Table 3 shows that subjects of subgroup 4 have greater differences between the steep and flat meridians and that the amount of asymmetry is greater in those requiring toricity in the landing zone of ≥T2. In fact, as has been shown in the last section of the results (*Figures 8.4 B and 8.5*), when subjects have high corneal astigmatism, it seems that the sclera has the same geometry; however, it remains relatively unknown whether there is a possible correlation between them. [7] A limitation of the present analysis is the fact that in the surgical group (subgroup 2) the corneal astigmatism is certainly affected by the surgical procedure, and therefore any relationship between corneal and scleral toricity is affected. This might explain why OC-SAG asymmetry derived from topography and lens landing zone toricity in post-surgical corneas are not related in the present sample. Conversely, as expected, in the regular corneas group, larger OC-SAG asymmetry measured with the topographer were associated with higher lens toricity, as seen on the last 3 rows of Table 2.

In this study, it was not possible to objectively measure the scleral shape of the eyes with commercially available devices (such as scleral topographers or anterior segment OCT). However, it was possible to evaluate the axis of stabilization of the lens when a back-toric periphery design was necessary. Although it is well known that the sclera has an asymmetric shape in all quadrants [6], there are some studies concluding that there is no correlation between scleral and corneal shapes in most cases. [26] Nevertheless, some exceptions have already been observed: when the corneal toricity is congenital, it appears that corneal toricity could extend to the sclera. [27] Ritzmann *et al* [9] found that higher corneal astigmatism (>2.00D) appeared to be more associated with scleral toricity compared to eyes with corneal astigmatism between 1.00D and 2.00D; in those eyes, only 27% had the same orientation of

corneal and scleral astigmatism. The present study corroborates these early clinical observations. As *Figures 8.4* and *8.5* show, there is an apparent relationship between the scleral and corneal shapes in subgroup 4, as there are similar orientations on their flat meridians (mean difference of 12±14°). The axis of stabilization of the scleral lens fitted was marked on the flattest meridian and was very similar to the axis of the flat corneal meridian. However, in the present study, this was seen only for the healthy corneas with limbus-to-limbus corneal shapes with high astigmatism – and it did not happen in ectatic or diseased corneas. López-Álcon *et al* [25] didn't find a relationship between corneal and scleral geometries – only in 27% of cases was there a similarity, with a maximum difference of 10° between them. The fact that corneal and scleral flat meridians are not at the same axis in irregular corneas might be related to the fact that the flatter axis determined by the topographer in such corneas must be quite variable and affected by the intrinsic pathological or surgical process.

8.6 Conclusions

In summary, OC-SAG estimated from EHChord attributes (taken for a chord equal to the diameter of the lens that each subject was wearing) were the best of the parameters analyzed for the prediction of ScCL-SAG. The mean difference of approximately 400μm between the OC-SAG and the ScCL-SAG corresponds to the cornea-lens separation that these lenses should have right after lens application. However, there is a large variability factor that explains why this will not work satisfactorily in every patient. Corneal asymmetry (measured by means of the differences in OC-SAG between flat and steep corneal meridians) was shown to be a poor predictor for the need to fit a scleral lens with toric peripheral geometry in irregular corneas. However, in cases of healthy corneas with high corneal astigmatism (≥2.00D), corneal asymmetry could help to predict whether the subject will need a toric landing zone design.

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Chapter 9

Determination of Central Corneal Clearance in Scleral Lenses with an Optical Biometer and Agreement with Subjective Evaluation

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9. Determination of Central Corneal Clearance in Scleral Lenses with an Optical Biometer and Agreement with Subjective Evaluation

9.1 Abstract

Purpose: To compare three methods to measure center corneal clearance (CCC) during scleral lens wear: subjective (slit lamp), image processed (ImageJ) and with an optic biometer. The optic biometer technique was validated in comparison to an OCT in the first part of the study.
Methods: Twenty-two eyes (11 subjects) with healthy corneas were recruited. Three measures of OCT with scleral lens and ten measurements of axial length (AL) with IOLMaster with and without lens were performed. For the second part, 61 eyes (35 subjects) enrolled in a clinical study were selected. Measurements of CCC were done with IOLMaster, SlitLamp and ImageJ.
Results: The measurements of CCC indirectly obtained with IOLMaster had a strong correlation with AS-OCT measurements (r=0.981), showing a mean difference of 122.18±46.05μm (higher with IOLMaster). Regarding the second part, measurements of CCC were 238.66±95.94μm, 250.16±124.31μm and 263.15±90.60μm, for the IOLMaster, SlitLamp and ImageJ, respectively. The correlations were higher for ImageJ vs Subjective measure (r=0.891) than for IOL vs Subjective (r = 0.748) and IOL vs ImageJ (r=0.745). Analysis of differences and correlations between SlitLamp and ImageJ through time showed a mean difference of -32.28±89.95μm (r=0.683) at V1month, 12.53±59.46μm (r=0.850) at V6months and 11.57±32.95μm (r=0.940) at V12months.
Conclusions: It is possible to measure CCC with IOLMaster, considering AL measured with and without lens and lens thickness. The three methods tested have good correspondence, showing that IOLMaster and ImageJ could be objective techniques to measure CCC. Also, it is possible to improve the agreement of subjective measures when compared to objective measures trough time.

9.2 Introduction

Modern scleral lenses are large diameter lenses that have their resting point beyond the corneal borders. They have recently gained more interest among practitioners around the world and are one of the first and best visual correction options for eyes that are unsuccessful with conventional contact lens modalities. Evolutions in lens materials, production techniques and improved knowledge on anterior ocular surface anatomy, boosted the indications of scleral lens fitting, varying from severely irregular corneas to normal/ healthy corneas. [1–3]

Fitting scleral lenses can be a challenge, especially for a practitioner with limited knowledge and practice on scleral lenses (Macedo-de-Araújo R, Poster presented at GSLS 2018, Las Vegas). Knowledge on the several aspects regarding all the anterior ocular surface anatomy characteristics (both corneal, corneo-scleral and scleral geometries), different scleral lens designs and fitting characteristics are topics that must be mastered by practitioners. Regarding the fitting characteristics, one must be aware of several aspects. First, as these lenses land exclusively on the conjunctiva tissue underlying the sclera, practitioners need to fully understand its complex anatomy and geometry [4–6]. This will aid to find the lens landing zone that will be close to the overall scleral shape of the eye being fitted in order to prevent some common scleral lens problem, which can be a challenge for a novel practitioner [7]. Second, as the first aim of these lenses is to bridge the entire cornea and limbus avoiding touching these structures, the scleral lens sagittal height is another important feature. Scleral lenses need to be inserted with liquid - preferably unpreserved saline solutions - that will fill the space between the front corneal surface and the back surface of the lens – the central corneal clearance (CCC). Finding or achieve this best postlens tear fluid thickness or clearance is one of the most difficult challenges during scleral lens fitting process [8,9]. In one hand, scleral lenses should not touch any part of the corneal or limbal area [10]. In the other hand, this CCC should not be very high because of the hypoxia effects [9,11–15]. In addition, it is known that the postlens tear fluid thickness decreases through time, phenomena called settling, making the measurement of this an important issue [16–19]. Objective and subjective methods are available to measure this cornea-lens separation. Subjective methods are dependent on practitioner experience and skills and comprise direct evaluations with slit lamp. If the postlens fluid is dyed before insertion, practitioners can observe the overall fitting and check for areas of corneal or limbal touch. To observe and estimate the thickness of CCC with biomicroscopy, an optic section can be used and compared to central contact lens thickness or central corneal thickness, if known [16,20]. Anterior segment optical coherence tomography (AS-OCT) is an objective method that has been widely used in different studies to measure clearance [16,17,21,22] and corneal swelling. [21,23] However, despite their accuracy and precision, this kind of instruments have a considerable cost and not all practitioners can have easily access to them [24], so it is important to find the accuracy of others methodologies to assess CCC. One must take into account that to have a more precise measurement of CCC, more sophisticated equipment may be needed – like OCT, built-in camera in the slit lamp or other equipment.

The present study has been designed to investigate if other clinically available instruments and techniques could be used to have an objective measure of the *on-eye* cornea-lens separation. Three techniques were compared – a subjective technique (with slit lamp), image processing technique with Image J, and an indirect measure with an optic biometer. The Part I of the present study was conducted in order to validate an optic biometer to measure CCC in the sample of the present study.

9.3 Methods

9.3.1 Part I: Validation of Two Methods for CCC Measurement

9.3.1.1 The use of an Optic Biometer for CCC Measurement

The aim of the first part of the study was to validate an optical biometer to measure cornea-lens separation. This allowed the authors to use this device in the second part of the study. Measurements were performed in 22 healthy eyes of 11 subjects (10 women) with a mean age of 25.51±4.70 years and spherical equivalent of -0.02±1.00 D. Subjects used two different plano scleral lenses from the same manufacturer (Procornea, Eerbeek, the Netherlands), one different in each eye. Both diameter and parameters regarding the landing zone of the lens were the same for the two ScCL selected (16.4 mm) and same radii of curvature (8.20 mm). The sagittal height of the two lenses differed in 100µm: one lens (ScCL1) with 4673 µm and the other with (ScCL2) 4773 µm (values provided by the manufacturer). They were applied randomly in left or right eye in the same subject. The cornea-lens separation (clearance) was measured indirectly with the axial length of the naked eye (AL) and eye with ScCL (Length - LScCL) measurement with the optical biometer IOLMaster (Zeiss, Germany) and directly with AS-OCT RS-3000 (NIDEK, USA). The AL was recorded 10 times before scleral lens insertion. The remain measurements were performed up to 20 minutes after lens insertion to avoid any edema response or warpage. The LScCL was also recorded with IOLMaster 10 times for each eye and the average was calculated. AS-OCT measurements were recorded 3 times for each eye, and the CCC measurements were performed with the same methodology described in previous works – the image was magnified using the software of the instrument and the measurements were

obtained along the central location [25–27]. CCC was measured by the same operator from the anterior corneal surface to the posterior curve of the scleral lens. Later, the values of the two instruments were compared. A simple calculation was made to obtain the value of CCC with IOL: CCC = LScCL – (AL + Lens Thickness) (*Figure 9.1*), being 402µm the central lens thickness. The results showed that both measurements were strongly correlated (r=0.981, p<0.001) with a mean difference of 122.18±46.05µm (higher with IOLMaster). The results of this validation will be used on section 2.2.

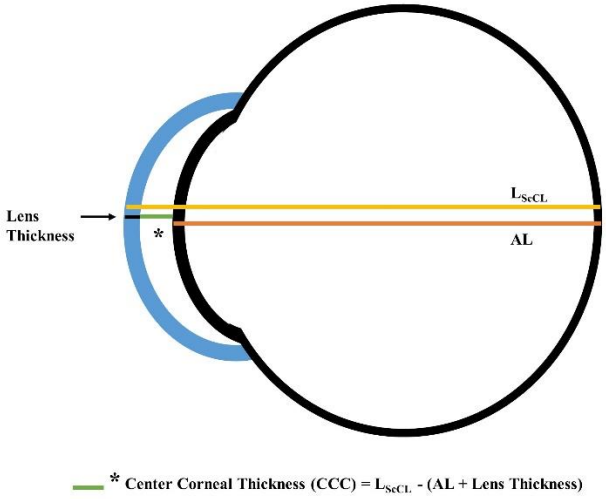

Figure 9.1 Schematic image showing the relationship between the measurements taken with IOLMaster. L_{ScCL} is the distance between pigmented epithelium of the retina and the anterior surface of the scleral lens. AL is the distance between the retinal pigmented epithelium and the anterior surface of the cornea (measurement taken after removing the lens). As the value of clearance is normally the distance between the front corneal surface and the back surface of the scleral lens, the lens thickness must be subtracted.

9.3.1.1 The use of ImageJ for CCC Measurement

To validate the technique to measure CCC with an image processing software, 13 pictures of scleral lenses on-eye were randomly selected. All these pictures (that were randomly selected from the database) were taken with the build-in camera on the slit lamp (CSL990 Elite 5x Digital Video, CSO, Italy) during scleral lens evaluations at different appointments during a clinical trial at Clinical & Experimental Optometry Research Laboratory (CEORLab, University of Minho, Portugal). Posteriorly, these pictures were evaluated with Image J 1.52a software

(National Institutes of Health, Bethesda, Maryland, USA) in order to validate this technique to measure CCC. Images were analyzed in a random order. Measurements of cornea-lens separation and lens thickness were repeated 3 times (not consecutively) for each image (intra-session). All these measurements were randomly repeated 2 more times in 2 different days (inter-session) by the same observer and applying the same criteria.

9.3.2 Part II: Comparison of Three Methods to Measure CCC

The aim of this second study was to compare three methods for CCC measurement: an optic biometer (IOLMaster), a subjective measure (Slit-Lamp) and using an image processing program (Digital Image). Sixty-one eyes of 35 subjects (20 female) enrolled in the clinical trial at CEORLab were randomly selected and voluntarily participated in this study. The ages of the participants ranged between 16 and 60 years with an average age of 35±8 years. As the sample participating in the clinical trial was divided into two groups according to corneal condition, the subjects recruited to this study were from the two groups: 52 eyes of 30 patients with irregular corneas due to different etiologies (Group I) and 9 eyes of 5 patients with normal corneas (Group II) whose motivation and inclusion criteria to enroll the study was having moderate-to-high refractive errors (myopia ≥6.00D, astigmatism ≥4.00D and/or hyperopia ≥4.00D).

The lenses fitted were manufactured by Procornea (Eerbeek, The Netherlands) using Boston XO material (hexafocon A). The overall diameter of the lenses used by the subjects of the present study was 16.4mm. All lenses were fitted by the same practitioner/ examiner following the manufacturer's instructions. Subjects of the present study were already enrolled in a clinical study and fitted with scleral lenses and had several evaluations through the follow-up period (lens dispense visit, and appointments of 1, 3, 6 and 12 months). The measurements of the present study were performed at 6 months visit (6 months after lens dispense visit). The subjects came to the visit with their scleral lenses on-eye for more than 90 minutes of lens wear (mean wearing time: 208±147 min). The fitting of the lenses – and respectively the CCC - was evaluated with slit lamp (CSL990 Elite 5x Digital Video, CSO, Italy). CCC value was obtained by comparing the thickness of cornea-lens separation to the known value of lens thickness (provided by the manufacturer for all the lenses). The same routine was used in all appointments to subjectively

measure CCC – an optic section showing the total lens thickness, post lens tear film reservoir thickness and cornea with 16x magnification and the slit lamp and biomicroscope set at 60 degrees from each other. Pictures of each fitting were taken over a period of about 1-year with the video imaging system build-in the slit lamp with the same technique described above. The Digital Image analysis was performed more than 4 months after the acquisition of the pictures at 6-month appointment with ImageJ with the previously validated methodology (section 2.1.2). All the images were coded and no information of the patient was present at the time of examination, in order to mask the observer. Six repeated measures of lens thickness and six repeated measurements of cornea-lens separation (CCC) were performed by tracing a line between the front and back surface of the lens and the back surface of the lens and the anterior surface of the cornea, respectively. This way, the program can determine the number of pixels within both areas measured. As the observer knew the lens thickness (in microns) provided by the manufacture for each one of the lenses analyzed, a simple conversion of the CCC from pixel to micrometers was done. Previous studies already used this software to measure clearance [20] and turbidity of post-lens tear film [21].

Similarly to the protocol followed in the Part I of the present study, measurements of CCC were also been indirectly obtained with IOLMaster. Again, measurements were performed with the lens on-eye (LScCL) and later after lens removal (AL) (*Figure 9.1*). Taking into account the results of Part I, the CCC value was calculated by:

$$CCC = LScCL - (AL + \text{Lens thickness}) - 122\ \mu m$$

9.3.3 Learning Process of Subjective CCC Measurement vs ImageJ

The aim of this last part of the study was to evaluate the learning process or improvement in the skills of the practitioner to measure CCC subjectively with slit lamp (comparing with ImageJ measurements). Sample was the same from section 2.2. Data from visits of 1 month (V1m), 6 months (V6m) and 12 months (V12m) were analyzed. Slit lamp examination was also performed and pictures from each visit were analyzed with ImageJ. CCC was recorded with the same techniques described on section 2.1.2 and 2.2.

9.3.4 Statistical Analysis

Statistical analysis was conducted using SPSS v.25.0 (SPSS, Inc, Chicago, Illinois, USA). Normality of data distribution was assessed with the Shapiro-Wilk test in different groups of subjects analyzed. The values presented are the mean and standard deviations (mean±SD). Differences between the different techniques and between the same technique within subjects through time (dependent samples) were estimated with Friedman test or ANOVA for repeated measurements, depending on the sample distribution. For pairwise comparisons between techniques and within the same subjects through time, the differences were estimated with Wilcoxon signed-rank test if the sample was no-normally distributed or with paired sample T-test if it was normally distributed. Correlations between instruments were assessed with Spearman's rho. The level of statistical significance was set at $p<0.05$.

9.4 Results

9.4.1 Part I: Validation of Two Methods for CCC Measurement

9.4.1.1 The use of an Optic Biometer for CCC Measurement

The mean CCC values measured were 441.18±197.54µm and 319.00±168.72 µm, for IOLMaster and AS-OCT, respectively. This result shows that measurements performed with IOLMaster are, on average, 122.18±46.05µm higher than measurements performed with AS-OCT (*Figure 9.2A*). Despite these differences, the measurements of CCC indirectly obtained with the optic biometer had a positive and strong correlation with the measurements done with AS-OCT (*Figure 9.2B*: $r=0.981$, $p<0.001$). In addition, the differences between the measurements of the two devices were very similar in the two scleral lenses used: in the ScCL1 the mean difference between instruments was 120.52±52.20µm and in ScCL2 the mean difference between instruments was 123.85±41.49µm.

9.4.1.2 The use of ImageJ for CCC Measurement

Figure 9.3 A and B represents the differences intra- and inter-session in the measurement of lens thickness (LT) (A) and CCC (B) with ImageJ. There were no statistical significant differences between the three measurements of LT and CCC performed at each day except for the measurements of lens thickness at first day ($p<0.05$, Friedman test), between measurement 1 and measurement 3 ($p=0.01$, Wilcoxon). The maximum standard deviation between 3 consecutive measures in the same picture was 4.36, meaning that 95% of the measurements performed had less than 8µm of variability. There were no statistical significant differences between inter-session measurements ($p>0,05$).

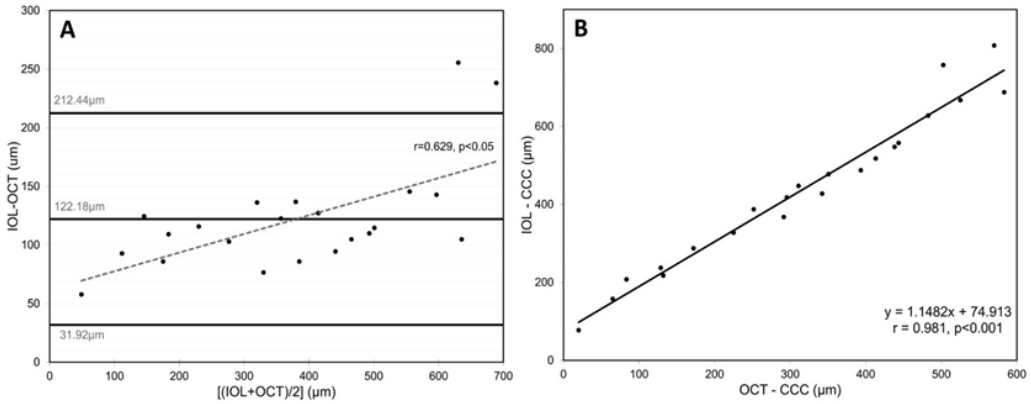

Figure 9.2 (A) Bland-Altman plot of CCC measurements obtained from IOLMaster and AS-OCT. 95 per cent limits of agreement are shown as two darker horizontal lines above and below the mean difference value (mean difference ± 1.96SD). **(B)** Correlation of clearance measurements obtain with OCT and IOLMaster

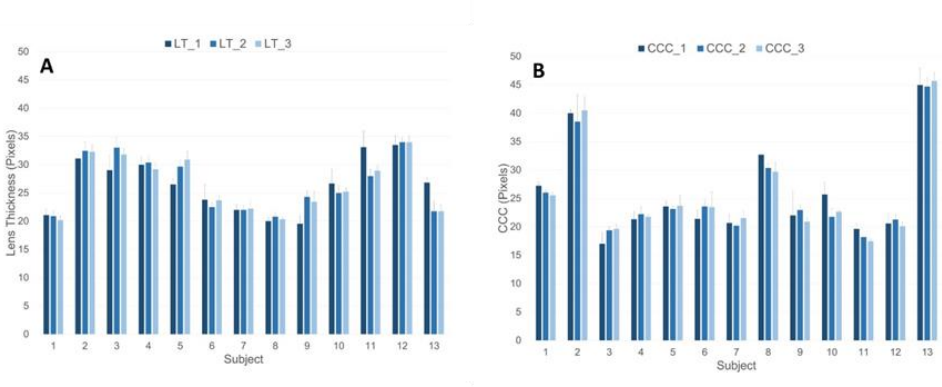

Figure 9.3 (Differences intra- and inter-session in the measurement of lens thickness (LT – **A**) and clearance (CCC - **B**). Each bar represents the Mean±SD of the three repeated measures in the same session (intra-session). LT_1, LT_2, LT_3, CCC_1, CCC_2, CCC_3 represent the measurements performed at each different day at day 1, day 2 and day 3, respectively (inter-session).

9.4.2 Part II: Comparison of Three Methods to Measure CCC

Measurements of CCC at 6 months visit were 238.66±95.94µm, 250.16±124.31µm and 263.15±90.60µm, for the IOLMaster, Subjective measure (Slit Lamp) and Image J processed, respectively. *Figure 9.4* shows the boxplots for the three methods. Comparisons between the three techniques did not demonstrated significant variations between the measurements obtained ($p>0.05$, Friedman test). However, pairwise comparisons showed a statistical significant difference between the measurements performed with IOLMaster and Image J ($p=0.010$, Wilcoxon).

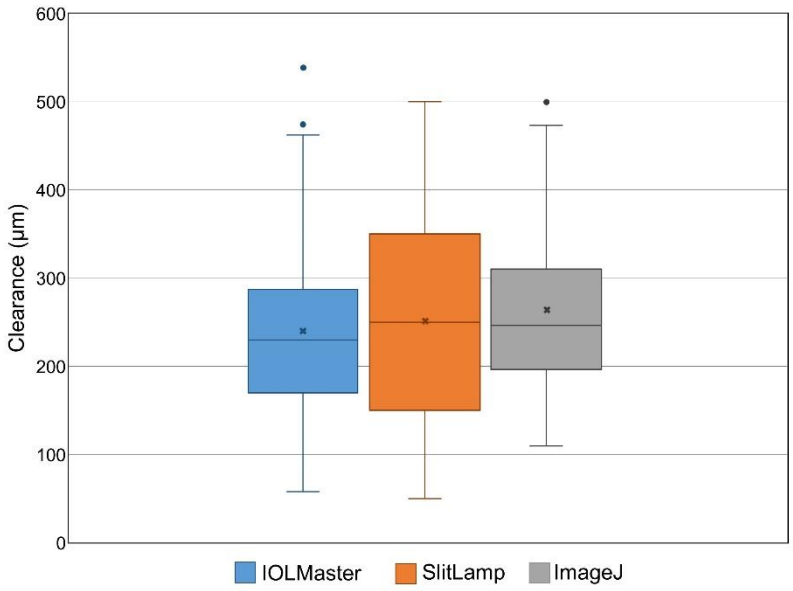

Figure 9.4 Box and whiskers plot comparing the CCC measurements with IOLMaster, subjective method (slit lamp) and Image J processed. It is represented the median value and the 95% confidence interval, as well as the maximum and minimum values.

Figure 9.5 represents the Bland-Altman analysis between IOL, Slit Lamp and ImageJ. The average difference between IOLMaster and Slit Lamp was -12±83µm ($p>0.05$, range: -242min to 158max µm) meaning that Slit Lamp recordings are slightly higher than IOLMaster on average (*Figure 9.5A*). For lower CCC values, measurements with Slit Lamp are underestimated when compared to IOL, but this trend is reversed as higher CCC are assessed. The average difference between IOLMaster and ImageJ was -25±62µm (range: -188 to 90 µm, $p=0.01$), with

the ImageJ measurements being higher on average (*Figure 9.5B*). Lastly, the mean difference between ImageJ and Slit Lamp measurements was 13±59µm (range: -149 to 138 µm, p>0.05), with the Slit Lamp giving lower values on average (*Figure 9.5C*). Measurements with Slit Lamp underestimate the CCC values when the cornea-lens separation is lower, but tends to overestimate this value with increasing cornea-lens separation.

The correlations were higher for Image J vs Subjective measure (r=0.891, p<0.001) than for IOL vs Subjective (r = 0.748, p<0.001) and IOL vs ImageJ (r=0.745, p<0.001).

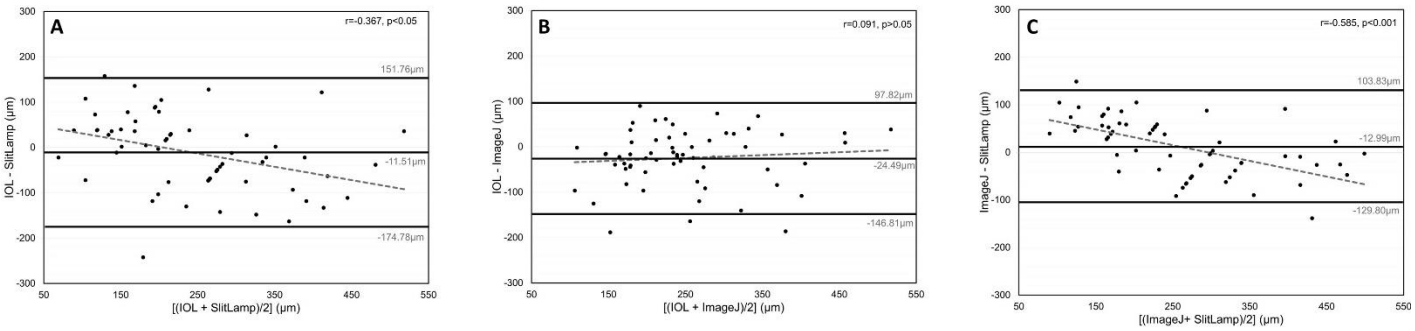

Figure 9.5 Bland-Altman plot of CCC measurements obtained from IOLMaster and SlitLamp (**A**), IOLMaster and ImageJ (**B**) and SlitLamp and ImageJ (**C**). 95 per cent limits of agreement are shown as two darker horizontal lines above and below the mean difference value (mean difference ± 1.96SD).

9.4.3 Learning Process of Subjective CCC Measurement vs ImageJ

Table 9.1 shows the mean difference in clearance measurements performed with two techniques (slit lamp and Image J) through time – V1m, V6m and V12m. A greater difference between both measurements is observed at V1m, being the subjective measures (slit lamp) overestimated (more positive) than the Image J processed images. However, in the remain visits, measurements performed with ImageJ were higher (mean difference of -32.28±89.95µm at V1m, 12.53±59.46µm at V6m and 11.57±33.23µm at V12m). The correlations between both measurements were statistical significant (p<0.001) in all the visits, with increasing correlations through time (r=0.683, r=0.850 and r=0.940, respectively).

Table 9.1. Differences in CCC between subjective measure (with slit lamp) and image processed measure (with ImageJ) at 1, 6 and 12 months visit.

	V1m	V6m	V12m
Image J	290±94.50	257.14±80.07	240.05±87.75
Slit Lamp	322.71±123.44	242.71±105.48	228.47±96.95
Difference	**-32.28±89.95** **(p=0.009)***	**12.53±59.46** **(p=0.089)***	**11.57±33.23** **(p=0.012)***

*Wilcoxon

Figure 9.6 shows the Bland-Altmann analysis between ImageJ and Slit Lamp for the different visits (V1m, V6m and V12m). Notice that the average difference between both measurements tends to decrease with the increasing experience of the practitioner, as well as the 95% limits of agreement.

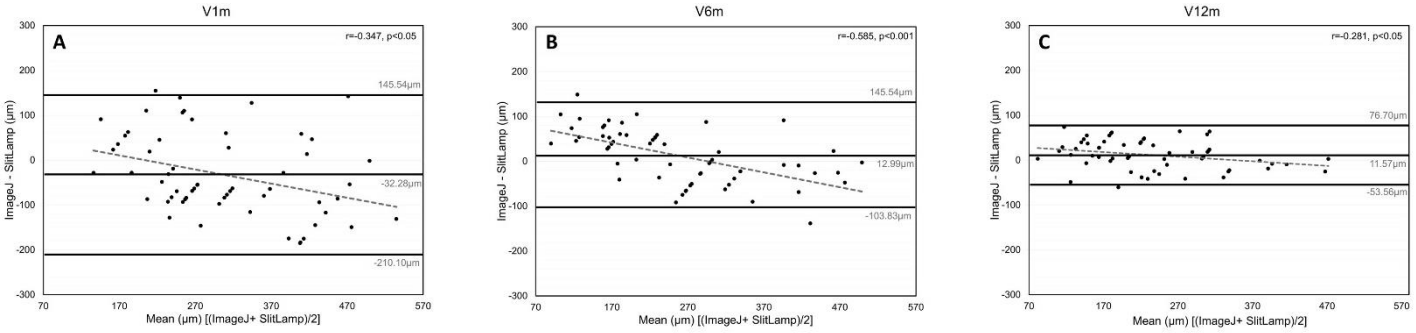

Figure 9.6 Bland-Altman plot of clearance measurements obtained from ImageJ and SlitLamp at the different follow-up visits: 1 month visit (V1m – **A**), 6 months visit (V6m – **B**) and 12 months visit (V12m - **C**). 95 per cent limits of agreement are shown as two darker horizontal lines above and below the mean difference value (mean difference ± 1.96SD).

9.5 Discussion

Over the last few years many advances have been made on scleral lens field. However, specific limitations continue in the fitting process, namely when practitioners do not have advanced instrumentation like AS-OCT available. Although there is lack of consensus on the amount of desired corneal clearance of an ideal fit [28], it is accepted that these lenses shouldn't touch the corneal surface neither have a great cornea-lens separation because of the potentially induced hypoxic stress into the corneal tissue. Moreover, practitioners need to account on lens

settling at the initial fit, as these lenses land on the bulbar conjunctiva that is a soft and compressible tissue that will cause the lens to sink, decreasing CCC overtime. [29] All these details make extremely important to accurately estimate the CCC. The present study intended to compare three different approaches to measure CCC in situ, including the clinical subjective evaluation. In the first part of the study, a method to measure central corneal clearance (CCC) using an optic biometer (IOLMaster) was suggested.

At the first part of the study, measurements of CCC with IOLMaster and AS-OCT in 22 healthy eyes were compared. To measure axial length (AL), IOLMaster takes the measurements from the anterior tear layer above corneal epithelium and the retinal pigmented epithelium. With a scleral lens on-eye, the authors hypothesize that the measurement is performed from the anterior surface of the lens and the retinal pigmented epithelium. Because of that, having the LScCL and subtracting the AL and lens thickness (402µm in the present study) to it, the authors believe that the final result is the CCC. In fact, the CCC measured with IOLMaster was positively and strongly correlated with the measurements made with AS-OCT (*Figure 9.2B*: r=0.981, p<0.001). However, the mean difference in the measurements with these two devices was of 122.18±46.05µm (higher with IOLMaster). The mean differences between devices with the two lenses analyzed were very similar (121µm for ScCL1 and 124µm for ScCL2). The authors hypothesize that this difference could be related to small deviations to the center with the two instruments (differences in measurement position) and differences between acquisitions systems of both instruments. To the author's knowledge, this was the first study that evaluated the viability of an optic biometer to measure CCC, and further studies may be needed to clarify the systematic differences in the measurements performed with these two devices and/or build new devices based on optic biometry technique to measure CCC. The authors consider that this methodology should be reproduced in a larger sample and with different and masked observers (in order to introduce the inter-observer analysis), in order to validate this methodology to use it in the clinical practice. With the results of this first part the authors conclude that the CCC value measured with IOLMaster can be obtained by:

$$CCC = LScCL - (AL + \text{Lens thickness}) - 122\ \mu m$$

and this was the calculation used at IOLMaster measurements in the second part of the study.

In the second part of the study, three techniques for CCC measurement were evaluated: an optic biometer (IOLMaster), a subjective measure (Slit-Lamp) and using an image processing program (Digital Image - where photos recorded during slit lamp evaluation of scleral

lens fitting were posteriorly analyzed with ImageJ software). To guarantee that the digital image technique was reliable to use in the present analysis, 13 photos of scleral lens fitting were randomly selected and measured in the same session and repeated in three different days. In order to use it in a clinical setting, it is mandatory to reproduce it in a larger sample and design the study to add the inter-observer reliability. For the purpose of the present study, the authors conclude that there were no statistical significant differences between the measurements made in the same session (intra-session) neither at the different days (inter-session) (*Figure 9.3 A* and *B*).

The slit lamp is the most used tool to measure CCC - regarding SCOPE study results, Jennifer Harthan *et al* [30] found that the great majority of the 989 practitioners that answered the survey rely on slit lamp (97.3%) and topography (88.7%), but only 47.5% rely on AS-OCT in the scleral lens fitting process. It is important to emphasize that the great majority of the respondents are based in the United States (72%), so future studies are needed to target more practitioners who are fitting scleral lenses outside the United States. [31] So, slit lamp seems to be the most used device to assess scleral lens fitting, and consequently the CCC. However, this is a subjective technique that is somewhat dependent on practitioner experience and skills. In fact, there is no gold-standard method for CCC measurement, and no limits of agreement are established as clinically acceptable between measurements to consider methods interchangeable when comparing different techniques. The 95% limits of agreement in the present study were between -175 and 151 (IOLMaster vs SlitLamp), -147 to 98 (IOLMaster vs ImageJ) and -130 to 103 (SlitLamp vs ImageJ). The average CCC measured with the three techniques were very similar between them: IOLMaster measurements were on average 12±83 and 25±62 μm lower than the measurements with slit lamp and Image J, respectively, and Image J measurements were 13±59 μm higher than those performed with slit lamp. The only statistically significant difference was found between IOLMaster and ImageJ (p=0.01, Wilcoxon), however the authors assume that this has no clinical relevance (25μm).

There are few studies comparing subjective measures using central lens thickness as biometric ruler and AS-OCT. Fuller *et al* [24] concluded that neophyte clinicians tend to overestimate the central clearance when compared to AS-OCT measures, with differences between both measurements of 115 μm (right eye) and 49 μm (left eye). In the present study it was found that measurements performed with slit lamp are overestimated (on average) when compared to objective techniques, like IOLMaster or ImageJ (*Figures 9.5 A* and *B*). However, it was possible to further conclude that for small CCC values, the measurements performed with

Slit Lamp are lower than those recorded with IOLMaster or ImageJ, and that this tendency is reversed as the CCC values became higher. This has an important clinical consequence – if a subject has been fitted in a scleral lens with a lower CCC, the practitioner tends to underestimate the value and will take an action to augment the sagittal height of the lens for preventing the lens from touching the cornea. On the other hand, if the subject was fitted with a higher CCC value, the practitioner tends to overestimate the value and will decrease the lens sagittal height to avoid hypoxia problems. One should think that this bias can be decreased as the fitter gains more experience, however there is some controversy about this. Yeung and Sorbara [20] concluded that, independently of the experience of the observers, there was an overestimation of clearance by an average of 103µm when compared to AS-OCT measurement, with high correlations ($r>0.79$). In the same study, when comparing the estimated clearance with the digital clearance (measured with an image processing software), an average overestimation of 27 µm was encountered, again, with high correlations between both measurements. Along with this, they also concluded that the increasing experience with ScCL fitting did not improve the correlation between measurements (subjective and AS-OCT), but the advanced fitters had significantly less inter-observer variability compared with the neophyte group (less SD). However, they were independent samples and were grouped according to the number of scleral lens fittings done in the past. In the present study, the conclusions drawn from *Figure 9.6* and *Table 9.1* are for the same practitioner – is the learning curve of the practitioner over the follow-up visits. The practitioner began to fit scleral lens without previous experience, but followed 95 consecutive subjects during a follow-up of 12 months – the authors consider that at the end of 3 months following such a large sample, the practitioner was considered experienced. As the clinician gained more experience, it was possible to reduce the average difference between the subjective measures of CCC made with Slit Lamp and the objective measures recorded with ImageJ as well as to narrow the intervals of agreement. In addition, and according to Yeung and Sorbara [20], the overall standard deviation also decreased between V1m and V12m, meaning that there was also a reduction in the variability of the differences. It is also observed on *Figures 9.6 A, B* and *C*, where a reduction in the 95% confidence intervals is observed. Also, the correlations between both measurements were higher at V12m than V6m and V1m ($r=0.94$, $r=0.85$ and $r=0.683$, respectively), meaning that there was an improvement in agreement between techniques with the increasing expertise of the fitter.

Measuring CCC with IOLMaster and with image processing software (like the one used in the present study) could be time-consuming and difficult to implement in the clinical practice. For the first one, it is necessary to take measurements with the lens on eye and later after removing the lens and perform a calculation to have the CCC value. For the second technique, it is required to have a photography acquisition system, preferably incorporated into the slit lamp, and then export the image and perform the measurements (both lens thickness and CCC) with the image processing software. As measurements with ImageJ are given in pixels it is necessary to convert it to microns, which is a simple calculation if the observer knows the central contact lens thickness or other neighbor feature in the image as a "ground-truth". However, both techniques can have significant importance in the investigation fields, where objective measures are preferred to subjective ones to avoid inter-subject variability.

Nowadays, there is no "true" objective measure of CCC. In three of the four methods used in the present study, the observer needs to take an action to have the CCC value: with AS-OCT it is needed to use the calipers within the software, the same way in the ImageJ. The only device that don't need the observer/ practitioner to make an action or manipulate the pictures was the IOLMaster. However, this last technique has some limitations, as both measurements with and without lenses are needed, followed by a calculation. Also, the authors assume that this device was not developed with the purpose of CCC measurement and has an important difference (122μm) when compared with AS-OCT, although with very strong correlation between the measurements of both devices. The authors agree that the development of an optic biometer technique or a software development to measure CCC will have great value.

In summary, central corneal clearance (CCC) can be measured with IOLMaster. The practitioner needs to account on lens thickness and on the systematic error (122μm) found between IOLMaster and AS-OCT measurements. Also, there was a good correlation between the measurements performed with IOLMaster, ImageJ and with slit lamp, making it possible to measure CCC with these three devices. The present study confirms that it is possible to improve the agreement of subjective measures when compared with objective measures with the increasing experience of the practitioner.

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Chapter 10

A one-year prospective report on the success rate and handling learning curve of 95 scleral lens wearers

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10. A one-year prospective report on the success rate and handling learning curve of 95 scleral lens wearers

10.1 Abstract

Significance: Despite the growing body of literature on the indications for modern scleral lens (SL) wear and potential contraindications to their use, there still is lack of peer-reviewed prospective works that study the SLs fitting process over a long period of time.
Purpose: To report the success rate of scleral lens wear and the handling learning curve from the patient perspective.
Methods: Ninety-five patients were consecutively screened for enrollment in a prospective clinical trial comprising SL fitting. Subjects were divided into two groups: ICGroup (71 patients with irregular cornea) and RCGroup (24 patients with regular cornea). Subjects attended several visits: Baseline, Lens Dispense(LDV), 1-month, 3-month, 6-month and 12-month. The number and causes of SL discontinuations and the time to correctly apply the lens fort the first time were evaluated. During follow-ups, patients answered a questionnaire regarding several SL wear aspects.
Results: Sixty-nine subjects successfully completed the 12-month period. Twenty-six subjects discontinued SL wear, none because of adverse events. The success rate was 77% in ICGroup and 58% in RCGroup. The main reason for SL discontinuation were handling issues (35%) and discomfort (19%). 36.2% of the subjects required <15min to correctly apply the lens at LDV, however 13% required >60min (subjects that wore spectacles, soft lenses or had no prescription at Baseline). The number of hours/day and days/week of lens wear had a statistical significant increase over time (7.7h to 9.7h and 5.2 days to 5.7 days), while the number of attempts to correctly apply and remove the lenses decreased significantly.
Conclusions: The success rate was 73% during this prospective 12-month follow-up study. The main reasons to drop-out were discomfort and handling issues. Subjects who continued SL wear have improved significantly their handling skills, and increased the confidence in scleral lens wear.

10.2 Introduction

There is a growing body of literature on the indications for modern scleral lens wear [1–3] as well as potential contraindications to their use. [3] However, there still is lack of peer-reviewed prospective works that study the SLs fitting process over a long term. Prospective studies over the short-term have investigated lens settling [4–9] and the potential hypoxic stress induced by scleral lenses wear. [10–13] In addition to the limitation of being short-termed, the

great majority of these studies are done on normal cornea, which is not the main indication for scleral lens wear. Other studies reported the success rate or failure of scleral lenses, ranging from 62% to 89%. [14–21] However, all of this reports provide a retrospective analysis and differ on scleral lens indications, sample size, scleral lens design, mean follow-up time and study design.

The handling of these lenses was already pointed as one of the main difficulties that patients may face during the fitting process. [16,18,20,22] As the diameter of the lenses is on average larger than the diameter of other kind of lenses, patients may face additional challenges when trying to insert and/or remove them. [18]

The main purposes of this study were to prospectively report the success rate of scleral lens wear over a 1-year follow-up time and the respective reasons to scleral lens wear failure. In addition, the patient learning curve in handling these devices, as well as the wearing time were analyzed during all the follow-up visits.

10.3 Methods

10.3.1 Study Design and Subjects

This was a prospective dispensing, case series involving patients with primary corneal ectasia, penetrating keratoplasty, post-surgical ectasia and regular corneas with high refractive errors. Ninety-five (95) consecutive patients were recruited between December 2015 and March 2017. The subjects were divided into two groups according to their corneal condition: one group with irregular corneas (IC Group) comprising corneas with irregularities due to different etiologies (134 eyes of 71 subjects) and the second group comprising subjects with regular and healthy corneas (RC Group) with high refractive errors (myopia ≥ 6.00 D; astigmatism ≥ 2.00D, hyperopia ≥ 4.00D) that have failed or rejected other forms of vision correction with contact lenses (46 eyes of 24 subjects).

Following the recommendations of the declaration of Helsinki, all subjects received information from the study before they accept to participate and signed a consent form. The

protocol of the study has been reviewed and approved by the Ethics Subcommittee for Life and Health Sciences of University of Minho.

10.3.2 Scleral Lens Used and Fitting Procedure

All patients recruited underwent a full earlier examination (Baseline), which included visual acuity with habitual correction (HC) and best spectacle correction (BSC), anterior eye biomicroscopy and corneal topographic analysis with Medmont E300. The patients with keratoconus were graded with Amsler-Krumeich classification for keratoconus. Visual acuity (VA) was assessed with EDTRS in LogMAR scale in high and low contrast (HCVA and LCVA, respectively). All patients were fitted with scleral lens from Procornea (Eerbeek, The Netherlands) in Boston XO material. Other technical characteristics of the lenses used are described in previous publications in the context of this study. [23,24]

At Baseline, the trial lenses were fitted according to manufacturer's recommendations. The mean trial lenses per eye needed during trials were previously described (Macedo-de-Araújo, Global Specialty Contact Lens Symposium, 2018 - Poster). The practitioner had 4 trial-lens sets available: 2 of mini-scleral lens and 2 of full-scleral lens. The BOZR was the same for all the lenses used (8.20mm) as recommended by the manufacturer. Trial lenses were inserted with unpreserved-free saline solution and sodium fluorescein (Fluo Strips, Contacare, India). The fitting was evaluated with slit lamp 5 to 10 minutes after lens insertion. If the fit was not satisfactory, another trial lens was inserted. When the best trial lens fitting was achieved, patients were asked to continue with the trial lens for more 90 minutes and then come back for another assessment and to perform over-refraction. After the final assessment, minor adjustments were done and the final lenses were ordered.

10.3.3 Patient Learning Curve (handling and wear experience)

The practitioner learning curve in fitting the scleral lens used in the present study in the same subjects was already assessed (Macedo-de-Araújo, Global Specialty Contact Lens Symposium, 2018 - Poster). In the present study the patient learning curve in handling these devices was assessed. In addition to the clinical examination, the time required to correctly apply the scleral lens for the first time (centered and without any air bubbles) at lens dispense visit (LDV) were allocated in one of the following groups: ≤ 15 minutes, between 15-30 minutes,

between 30 to 60 minutes and > 60 minutes. At follow-up visits, subjects were asked to fill a quick questionnaire regarding the number of days per week and number of hours per day of scleral lens wear, and also the methods used to apply and remove the lenses. The degree of easiness in handling these devices was evaluated based on the reported number of attempts that each subject required to correctly apply and remove the lenses (as reported at each follow-up visit).

10.3.4 Follow-up Assessments

All the subjects enrolled in this study had to attend several appointments during the follow-up. After Baseline assessment, subjects were asked to attend several appointments during the 1 year of follow-up: lens dispense visit (LDV), where measurements were performed 10 minutes after lens insertion (LDV1) and more than 90 minutes of lens wear (LDV2), 1-month visit (V1m), 3 months visit (V3m), 6 months visit (V6m) and 12 months visit (V12m).

10.3.5 Statistical Analysis

Statistical analysis was conducted using SPSS v.25.0 (SPSS, Inc, Chicago, Illinois, USA) to compare the different variables between groups and over-time within the same group. Normality of data distribution was assessed with the Kolmogorov-Smirnoff or Shapiro-Wilk test in different groups of subjects analyzed, accordingly to the sample size of each group. Pairwise comparison between groups (IC Group vs RC Group or drop-outs vs patients who continued scleral lens wear) were done with Independent Sample T-test for normally distributed data and Mann-Whitney for non-normally distributed data. Comparisons over-time within the same group were done with Paired Sample T-test or Wilcoxon signed ranks test, according to the sample distribution. The level of statistical significance was set at $p < 0.05$.

10.4 Results

10.4.1 Survival Curve (dropouts)

Table 10.1 summarizes the number of subjects that were recruited and that discontinued during the follow-up time, as well as the respective reasons to fail scleral lens wear. Ninety-five subjects (175 eyes) were primarily recruited to participate in this prospective dispensing case series. In 15 of them, only one eye was fitted, with the remaining being bilaterally fitted. During the follow-up period, a total of 26 subjects (27.37%) of the total sample dropped-out – 16 subjects (22.54%) from IC Group and 10 subjects (41.67%) from RC Group. The main reasons for drop-out were handling issues (9 subjects) and discomfort (5 subjects). Only two subjects complaint about midday fogging due to poor wettability of the anterior surface of the lens, which led to visual complaints and drop-out before trying to modify the lens care system. None of the other patients point out visual issues as a main reason for dropout and none of them discontinued scleral lens wear due to adverse events. A total of 69 subjects (126 eyes) concluded 1-year follow-up period: 55 subjects (99 eyes) from IC Group and 14 subjects (27 eyes) from RC Group.

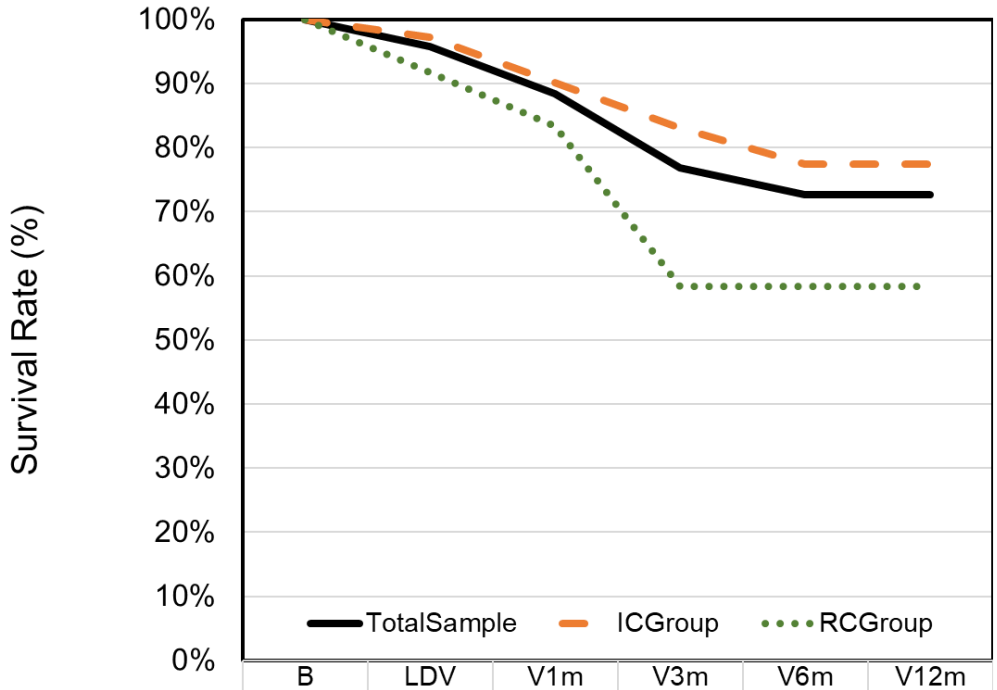
Table 10.1. Number of subjects enrolled in the study and number of subjects that discontinue scleral lens wear.

		Total Sample No. Subjects (No. Eyes)	IC Group No. Subjects (No. Eyes)	RC Group No. Subjects (No. Eyes)
Number of initial subjects		95 patients (175 eyes)	71 patients (129 eyes)	24 patients (46 eyes)
Number of dropouts		26 patients (49 eyes)	16 patients (30 eyes)	10 patients (19 eyes)
Percentage of dropouts		27.37% (28%)	22.54% (23.26%)	41.67% (41.34%)
Reason for drop-out	Never dispensed	4 patients (7 eyes)	2 patients (3 eyes)	2 patients (4 eyes)
	Discomfort	5 patients (10 eyes)	4 patients (8 eyes)	1 patient (2 eyes)
	Handling Issues	9 patients (18 eyes)	5 patients (10 eyes)	4 patients (8 eyes)
	Underwent Surgery	3 patients (6 eyes)	3 patients (5 eyes)	-
	Poor wettability*	2 patients (4 eyes)	2 patients (4 eyes)	-
	Lost to follow-up	3 patients (5 eyes)	-	3 patients (5 eyes)
Number of patients that concluded 1-year follow-up		69 patients (126 eyes)	55 patients (99 eyes)	14 patients (27 eyes)

*vision complaints due to poor wettability of the anterior lens surface.
IC – Irregular cornea; RC – Regular cornea

From the 16 patients from IC Group that discontinued scleral lens wear, 10 wore glasses prior enrolling the study, 2 wore corneal RGP, 1 wore soft lenses and 3 had no prescription. From the 10 patients from RC Group that discontinued, 6 wore glasses and 4 wore soft lenses prior enrolling the study.

Figure 10.1 shows the survival curve. In RC Group, all subjects discontinuing scleral lens wear did it before the 3-month visit. In IC Group, 83% arrived to 3-month visit but then more 6% discontinued – one reported handling as the main issue to this late dropout, another one comfort, another reported visual concerns because of poor wettability of the anterior lens surface, and the last one abandoned the study to underwent cross-linking. In RC group, the great majority of dropouts occurred between V1m and V3m (60%). In IC Group the discontinuation was more gradual.



	B	LDV	V1m	V3m	V6m	V12m
TotalSample	100%	96%	88%	77%	73%	73%
ICGroup	100%	97%	90%	83%	77%	77%
RCGroup	100%	92%	83%	58%	58%	58%

Figure 10.1 Survival curve for the patients wearing scleral lens over a 12-month follow-up period.

Table 10.2 summarizes some of the characteristics of the patients who discontinued scleral lens wear and those who continued (study subjects). There were no differences between the group of subjects that discontinued and the subjects that continued the study for age, gender and baseline symptomatology felt with their habitual correction ($p>0.05$). Regarding baseline symptomatology, in RCGroup the subjects than discontinued scleral lens wear had less symptoms than those who continued (average OSDI Scores: 14.17±11.38 vs 26.96±15.48, respectively) although without statistical significant differences because of the large variability of the data. Differences between subjects that continued and those who discontinued scleral lens wear were found in high contrast visual acuity (HCVA) and low contrast visual acuity (LCVA) with HC in RC Group, with the subjects that discontinued scleral lens wear having better logMAR HCVA (+0.15±0.20 and +0.08±0.14, respectively) and LCVA (+0.31±0.23 and +0.26±0.16, respectively) but without statistical significant differences. There were statistical significant differences between the same groups regarding HCVA and LCVA with scleral lens in RC Group, with the subjects that discontinued scleral lens wear having a better logMAR HCVA (+0.08±0.13 vs -0.02±0.09, P = 0.013, Mann-Whitney) and LCVA (+0.28±0.15 vs +0.17±0.07, P = 0.020, Mann-Whitney). Regarding the time to correctly apply the lens the great majority of subjects from ICGroup that continued the study applied the lens in less than 30min when compared to those who discontinued scleral lens wear (71% vs 53%) and the same in RCGroup (36% vs 50%).

10.4.1 Patient Learning Curve (Handling and Wear Experience)

Table 10.3 shows the ability to correctly apply the lens for the first time at LDV. Regarding the total sample, 36.2% of the subjects required less than 15 minutes to correctly apply the lens for the first time (34.5% in IC Group and 42.9% in RC Group), 33.3% required between 15 and 30 minutes (36.4% in IC Group and 21.4% in RC Group), 17.4% required between 30 to 60 minutes (20.0% in IC Group and 7.1% in RC Group), and 13.0% required more than 60 minutes to correctly apply the lens for the first time at LDV visit (9.1% IC Group and 28.6% RC Group).

Table 10.2. Characteristics of those who continued the study and those who discontinued the study.

	Group	Study Subjects (n=69)	Dropouts (n=26)	*p*
Age	IC	36.65±10.14	35.29±13.98	*0.454* ▪
	RC	30.00±10.04	32.90±8.14	*0.285 †*
		0.019 †	*0.941 †*	-
Gender	IC	26 F / 28 M	8 F / 9 M	-
	RC	10 F / 4 M	8 F / 2 M	-
Condition	IC	KC (77%) PK (11%) SE (8%) Other (4%)	KC (80%) PK (10%) SE (7%) Other (3%)	
	RC	HM (22%) HA (78%)	HM (32%) HA (68%)	
Baseline OSDI Score	IC	46.99±22.52	45.22±21.72	*0.797*▪
	RC	26.96±15.48	14.17±11.38	*0.070 †*
		0.02 †	***0.002 †***	-
HCVA (with HC)	IC	+0.34±0.35	+0.34±0.33	*0.828 †*
	RC	+0.15±0.20	+0.08±0.14	*0.353 †*
		0.008 †	***0.002 †***	-
LCVA (with HC)	IC	+0.59±0.35	+0.53±0.27	*0.509 †*
	RC	+0.31±0.23	+0.26±0.16	*0.633 †*
		<0.001 †	***<0.001 †***	**-**
HCVA (with lens at LDV)*	IC	+0.08±0.14	+0.09±0.17	*0.871 †*
	RC	+0.08±0.13	-0.02±0.09	***0.013*** *†*
		0.825 †	*0.030 †*	-
LCVA (with lens at LDV)*	IC	+0.34±0.17	+0.37±0.19	*0.481* ▪
	RC	+0.28±0.15	+0.17±0.07	***0.020*** *†*
		0.036 †	***<0.001 †***	-
Time to correctly apply the lens at LDV*	IC	<30 min (71%) >30 min (29%)	<30min (53%) >30min (47%)	-
	RC	<30min (64%) >30min (36%)	<30min (50%) >30min (50%)	-

IC – Irregular cornea; RC – Regular cornea; KC – Keratoconus; PK – penetrating keratoplasty; SE – secondary ectasia; other – cases of corneal injuries that led to irregular corneal surfaces, and post-lasik with visual complaints but without ectasia; HM – High Myopia (≥6D); HA – high astigmatism (≥2D); HCVA – High contrast visual acuity; LCVA – Low contrast visual acuity; LDV – lens dispense visit; *data available only for those who were dispensed. (▪) Unpaired Sample T-test; (†) Mann-Whitney

Table 10.3. Time required to correctly apply the scleral lens for the first time at lens dispense visit.

	TOTAL SAMPLE	IC Group	RC Group
< 15 min	25 subjects (36.2%)	19 subjects (34.5%)	6 subjects (42.9%)
15 – 30 min	23 subjects (33.3%)	20 subjects (36.4%)	3 subjects (21.4%)
30 – 60 min	12 subjects (17.4%)	11 subjects (20.0%)	1 subject (7.1%)
> 60 min	9 subjects (13.0%)	5 subjetcs (9.1%)	4 subjects (28.6%)
	69 subjetcs (100.0%)	*55 subjects (100.0%)*	*14 subjects (100.0%)*

IC – Irregular cornea; RC – Regular cornea

Figure 10.2 shows the ability to correctly apply the lens for the first time regarding the habitual correction used prior entering the present study. Eleven (11) subjects had no prescription before enrolling the study, 28 subjects wore glasses, 7 wore soft contact lenses, 10 wore corneal RGP, 6 wore hybrid contact lenses and 7 subjects were already scleral lens wearers prior entering the study. Those subjects who wore glasses, soft contact lenses or with no prescription where those that required more time to correctly apply the lens for the first time at LDV. Subjects already wearing scleral lens prior enrolling the study were the ones that needed less time to correctly apply the lens.

Table 10.4 shows the average number of days per week and hours per day of lens wear and number of attempts to correctly apply and remove the lenses during the first month (reported at V1m), between 1 and 3 months of lens wear (reported at V3m), between 3 and 6 months of lens wear (reported at V6m) and between 6 and 12 months of lens wear (reported at V12m). On average, subjects reported to wear the lenses for 9.9 hours per day during 5.2 days per week at V1m. Both underwent an increase during the follow-up visits, and at V12m the subjects reported to wear the lenses on average 11.4 hours per day during an average of 5.7 days per week. Subjects from IC Group reported to wear the lenses more hours and more days per week at all follow-up visits. Regarding the number of attempts that each subject required to correctly apply the lens for the first time, it also had a decrease from an average of 2.3 attempts at V1m to 1.5 at V3m (mean decrease of 0.6 in IC Group and 1.4 in RC Group). From V3m to

V12m, there was also seen a decrease from 1.5 to 1.1 (mean decrease of 0.4 in IC Group and 0.6 in RC Group). Regarding the number of attempts to correctly remove the lens, there was also a decrease between V1m and V3m (an average of 1.8 at V1m and 1.6 at V3m). It also decreased until V12m (average of 1.1 attempts).

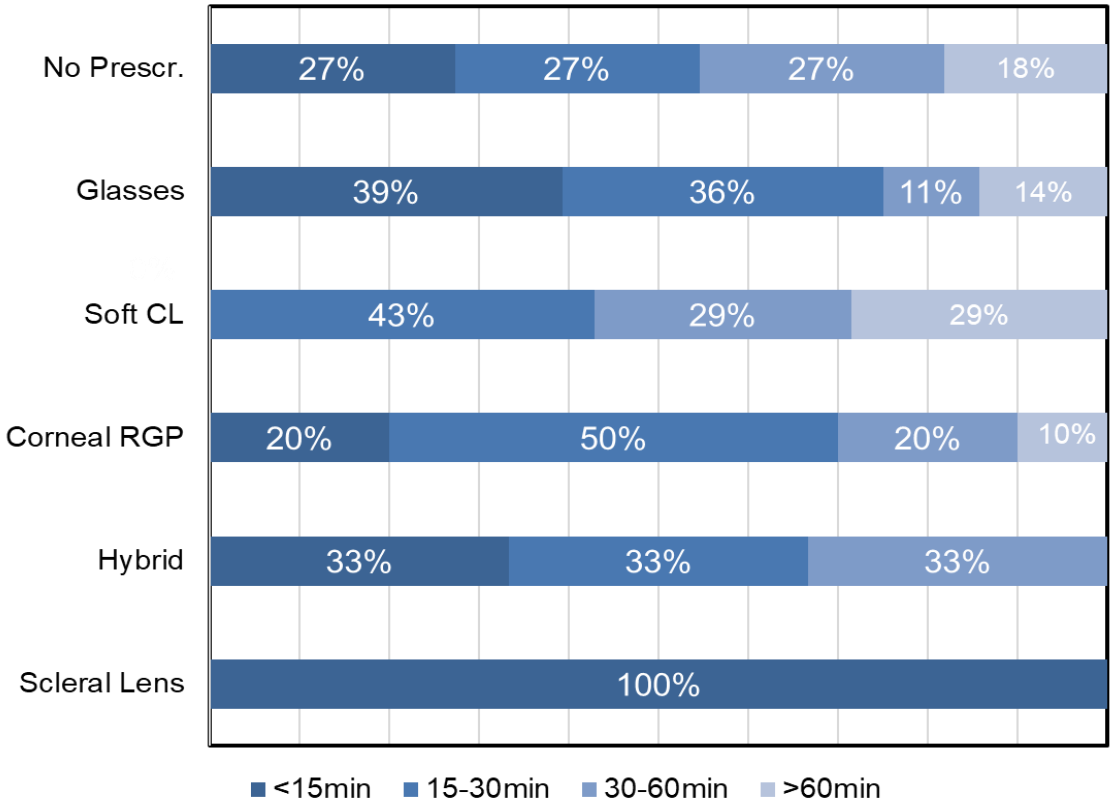


Figure 10.2 Frequency of the responses that each subject gave in each one of the follow-up questionnaires about scleral lens wear and handling, regarding the of number of days per week of lens wear (A), number of hours per day of lens wear (B), number of attempts to correctly apply the lens for the first time (C), number of attempts to correctly remove the lens for the first time (D), method to apply the lens (E) and method to remove the lens (F). Results are divided per group: IC (ICGroup – irregular cornea group) and RC (RCGroup – regular cornea group with high refractive errors).

Table 10.4. Number (mean±SD), median and range regarding the number of days per week and hours per day of lens wear, the number of attempts to correctly apply and remove the lenses and the methods elected for handling these devices.

		V1m	V3m	V6m	V12m
Number of days per week of lens wear	IC Group	Mean: 5.6±1.5 Median: 6.0 [range: 2 to 7]	Mean: 5.6±1.4 Median: 6 [range: 3 to 7]	Mean: 5.8±1.5 Median: 7 [range: 3 to 7]	Mean: 5.9±1.3 Median: 7 [range: 3 to 7]
	RC Group	Mean:3.9±1.3 Median: 3.0 [range: 3 to 7]	Mean: 4.1±1.3 Median: 4 [range: 3 to 7]	Mean: 4.2±1.2 Median: 4 [range: 3 to 7]	Mean: 5.0±1.4 Median: 5 [range: 3 to 7]
	Total Sample	Mean: 5.2±1.6 Median: 5.0 [range: 2 to 7]	Mean: 5.3±1.5 Median: 5 [range: 3 to 7]	Mean: 5.5±1.6 Median: 6 [range: 3 to 7]	Mean: 5.7±1.4 Median: 6 [range: 3 to 7]
Number of hours per day of lens wear	IC Group	Mean: 10.5±3.2 Median: 10 [range: 4 to 16]	Mean: 11.2±3.2 Meadian: 12 [range: 4 to 16]	Mean: 11.6±3.2 Median: 12 [range: 4 to 16]	Mean: 11.8±3.0 Median: 12 [range: 6 to 16]
	RC Group	Mean: 7.7±2.3 Median: 7 [range: 5 to 15]	Mean: 8.3±2.9 Median: 8 [range: 4 to 15]	Mean: 8.9±2.4 Median: 10 [range: 6 to 14]	Mean: 9.6±2.8 Median: 10 [range: 6 to 16]
	Total Sample	Mean: 9.9±3.2 Median: 10 [range: 4 to 16]	Mean: 10.6±3.3 Median: 10 [range: 4 to 16]	Mean: 11.0±3.2 Median: 12 [range: 4 to 14]	Mean: 11.3±3.1 Median: 12 [range: 6 to 16]
Number of attempts to insert the lens	IC Group	Mean: 2.1±1.5 Median: 2 [range: 1 to 10]	Mean: 1.5±1.0 Meadian: 1 [range: 1 to 5]	Mean: 1.2±0.6 Median: 1 [range: 1 to 4]	Mean: 1.1±0.4 Median: 1 [range: 1 to 5]
	RC Group	Mean: 3.1±2.1 Median: 3 [range: 1 to 7]	Mean: 1.7±0.8 Median: 2 [range: 1 to 3]	Mean: 1.1±0.4 Median: 1 [range: 1 to 2]	Mean: 1.1±0.3 Median: 1 [range: 1 to 2]
	Total Sample	Mean: 2.3±1.7 Median: 2 [range: 1 to 10]	Mean: 1.5±1.0 Median: 1 [range: 1 to 5]	Mean: 1.2±0.6 Median: 1 [range: 1 to 4]	Mean: 1.1±0.4 Median: 1 [range: 1 to 5]
Number of attempts to remove the lens	IC Group	Mean: 1.8±1.0 Median: 1 [range: 1 to 4]	Mean: 1.5±0.8 Median: 1 [range: 1 to 4]	Mean: 1.3±0.7 Median: 1 [range: 1 to 4]	Mean: 1.1±0.3 Median: 1 [range: 1 to 2]
	RC Group	Mean: 1.9±1.2 Median: 1 [range: 1 to 4]	Mean: 1.6±0.9 Median: 1 [range: 1 to 4]	Mean: 1.1±0.4 Median: 1 [range: 1 to 2]	Mean: 1.1±0.4 Median: 1 [range: 1 to 3]
	Total Sample	Mean: 1.8±1.1 Median: 1 [range: 1 to 4]	Mean: 1.5±0.8 Median: 1 [range: 1 to 4]	Mean: 1.3±0.6 Median: 1 [range: 1 to 4]	Mean: 1.1±0.3 Median: 1 [range: 1 to 3]

IC – Irregular cornea; RC – Regular córnea

Figure 10.3 reveals the frequency of the responses regarding each one of the questions mentioned above. The percentage of subjects that reported to wear the lenses more than five days per week increased during the follow-up time, as well as the number of subjects that reported to wear the lenses between 9 and 12h and more than 12h per day. Regarding the number of attempts to correctly apply and remove the lenses (*Figure 10.3 C* and *D*), the

frequency of subjects than answered 1 or 2 attempts have increased. Regarding the methods to correctly apply and remove the lenses, the percentage of subjects that reported to apply and remove the lenses with hands augmented through time, namely on ICGroup

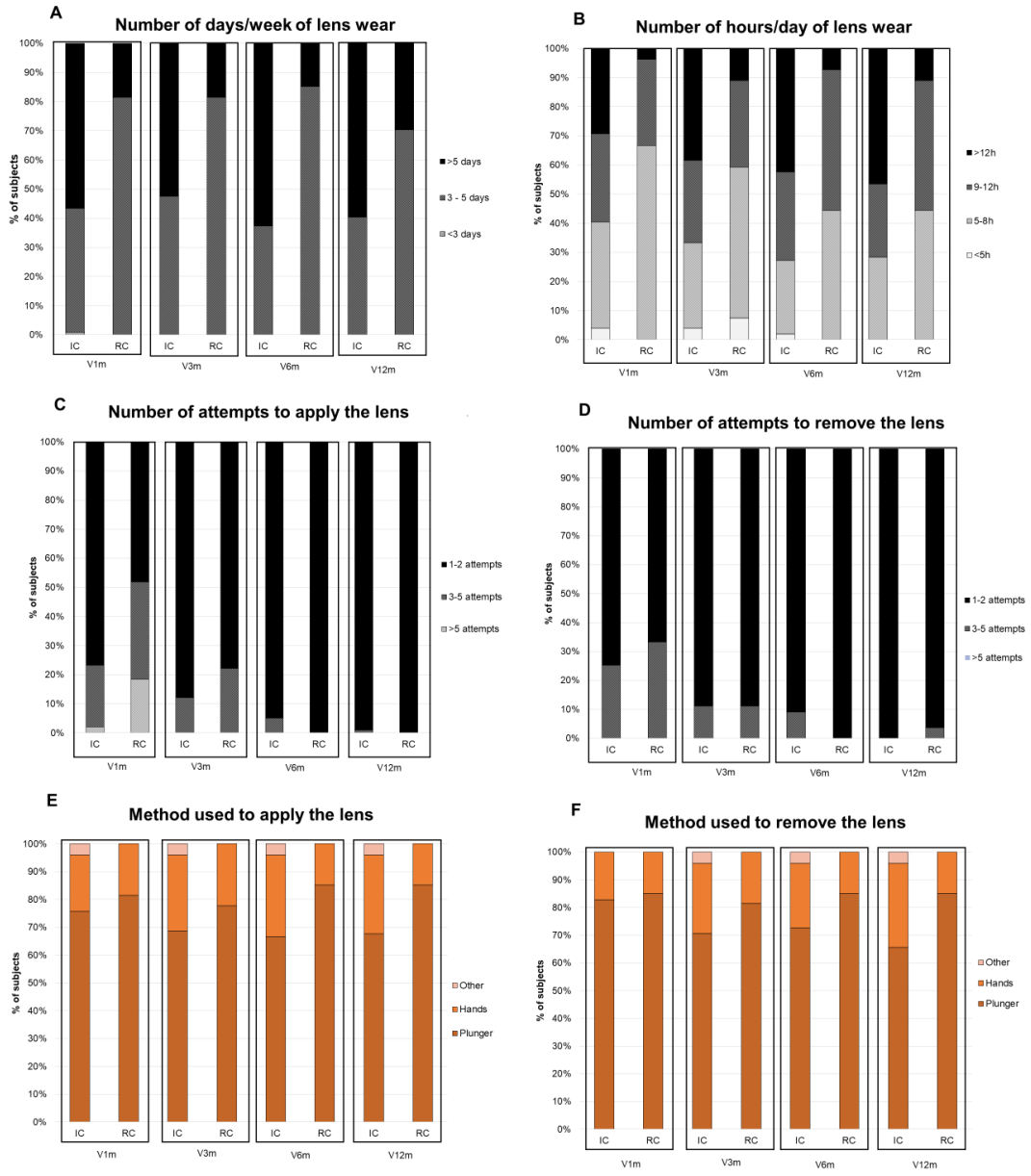


Figure 10.3 Frequency of the responses that each subject gave in each one of the follow- up questionnaires about scleral lens wear and handling, regarding the of number of days per week of lens wear (A), number of hours per day of lens wear (B), number of attempts to correctly apply the lens for the first time (C), number of attempts to correctly remove the lens for the first time (D), method to apply the lens (E) and method to remove the lens (F). Results are divided per group: IC (ICGroup – irregular cornea group) and RC (RCGroup – regular cornea group with high refractive errors)

10.5 Discussion

The success rate of scleral lens wear is an important clinical outcome that has already been reported in the literature. However, the vast majority of the reports are retrospective analysis. In the present study, the average success rate was 72.63%, being this significantly superior in the IC Group (77.46%) than on RC Group (58.33%). The IC Group comprised patients with corneal abnormalities of different etiologies: keratoconus (77% of those who continued and 80% that fail), penetrating keratoplasty (11% of those who continued and 10% that fail), secondary ectasia (8% of those who continued and 7% that fail) or other irregularities (4% of those who continued and 3% that failed). By previous reports, it is known that these lenses are majorly indicated for these kind of cases, being primary ectasia the major indication. [14,16,19,25,26] However, because of their advantages in promoting an improved optical quality, comfort and on-eye stability, scleral lenses started to be also fitted in eyes with normal corneas. In the present study, the main indication for scleral lens wear in healthy corneas was high regular astigmatism (≥2.00D, 78%). However, the success rate of scleral lens fitting in these kind of eyes is significantly lower than for eyes with corneal irregularities. The main reasons for scleral lens discontinuation/ failure were handling issues (35% of the subjects: 31% of IC Group and 40% of RC Group) and discomfort (19% of the subjects: 25% of IC Group and 10% of RC Group). None of the subjects of the IC Group was lost to follow up, but it happened in 15% of the patients from RC Group. None of the patients directly attributed poor VA as the main reason to drop out. However, the HCVA and LCVA with habitual correction (HC) were similar or even better in the dropouts sub-group when compared to those who continue the study ($p<0.05$, *Table 10.2*). The vast majority of patients who discontinued scleral lens wear wore glasses as their HC prior enrolling the study (10 patients from IC Group and 6 patients from RC Group). So, although the vision with scleral lenses was good, the benefit/ convenience ratio was not sufficiently strong to stop wearing glasses and wear scleral lenses as their primary visual correction option – namely because of handling issues and comfort, as mentioned previously. Those patients who had poor VA with their HC may face the same handling challenges/ issues, but the visual benefit that scleral lenses provide might have made them "battle" to correctly apply and remove their lenses. Despite for VA in RC Group, there were no statistical significant differences between the patients that continue wearing scleral lenses and those who stopped wearing them regarding age, gender

distribution, ocular condition, baseline comfort, and handling (*Table 10.2*). Differences between those who continued and those who discontinued were found in HCVA and LCVA with HC, namely on RC Group, suggesting that better VA at baseline in regular cornea patients might imply the patient will be less likely to be motivated to wear the lenses. However, no statistical significant differences were encountered in those parameters. Other authors have not found statistical significant differences between dropouts and scleral lens wearers for topographic data (Sim K and Δ K) and visual acuity [21] neither for mean age, mean scleral lens diameter nor distribution of genders. [20]

Other studies found a success rate similar to the present study. Ortenberg *et al* [15] reported a success rate of 73% in their retrospective analysis of 97 consecutive patients with irregular cornea due to different etiologies in a mean follow-up time of 34.9±18.5 months. The patients who discontinued were grouped into dropouts (17 subjects) because of lack of motivation (n=12), poor visual acuity (n=4), diplopia (n=1), and the remaining (9 subjects) have failed because of ocular complications (intolerance, corneal graft rejection, neovascularization, limbal and bulbar hyperemia and corneal edema). [15] In the present study, a success rate of 77% was found over the 12-month follow up period in a group of patients with similar characteristics (IC Group). It can be further concluded that all of these discontinuations happened before the 6-month appointment and none was due to ocular complications. It is important to notice that in the present study the patients had to attend several periodic appointments which could led to less ocular complications than those reported in retrospective analysis. In addition to Ortenberg *et al* [15] report, other success rates have been described (retrospectively) for shorter follow-up times: success rates of 88% [21] and 77% [20] at 6 and 3 months, respectively. Similarly, in 1997 Pullum and Buckley [16] reported a discontinuation rate of 22%, either due to scleral lens trial failure or stopped scleral lens wear. More recently, other retrospective studies showed similar failure rates: Severinsky *et al* [17] reported a failure rate of 21%, Schornack *et al* [18] reported that 38% of their keratoconus patients choose to not proceed with the fitting process after initial evaluation, and Segal *et al* [19] reported a failure rate of 10.4%. Reasons to fail scleral lens wear were reported to be lack of visual benefit [15,18,20,21], handling [18,19,21], discomfort [20,21], ocular complications (intolerance, graft rejection, neovascularization, corneal epithelial defects, hyperemia and corneal edema) [15,22,27] or abandoned scleral lens wear to underwent surgery (penetrating keratoplasty, cataract surgery). [17,18]

To the authors knowledge, this is the first case series informing on the handling and wearing learning curve from the patient perspective during a 12-month follow-up comprising a relatively large sample and a good retention rate. In the present work (*Table 10.3*) is seen that 36% applied the lens for the first time in less than 15min, but there was a significant proportion (13%: 9% from IC Group and 27% from RC Group) that needed more than 60min to correctly apply the lens for the first time – those patients needed 1 or more training appointments for handling. Regarding the HC prior enrolling the study (*Figure 10.2*), 100% of the patients that already wore scleral lenses have correctly applied the lenses in less than 15 minutes. On the other hand, there are the subjects that wore soft lenses or glasses or had no prescription prior entering the study, where 29%, 14% and 18% of the patients needed more than 60 minutes to correctly apply the lens for the first time, respectively. In those cases, the patients needed one to three more visits for handling instructions. The handling of scleral lens could be an initial obstacle for a great number of patients. In the present study, handling difficulties were pointed as the reason to dropout in 35% of the subjects that discontinued scleral lens wear. Despite the initial difficulty to correctly apply the lens for the first time, patients also need to face a learning process during time to correctly handle these devices. The handling learning curve from the patient perspective and the wearing time are reported on *Table 10.4* and *Figure 10.3*. Regarding the number of attempts to correctly apply and remove the lenses, there was a decrease over the entire follow-up period, reflecting the learning process of the patients. The application of the scleral lens was more problematic than the removal, namely at the first visit (V1m, *Table 10.4*). Despite this, the authors acknowledge that there are some problems related to the lens removal than can occur sporadically, such as extreme suction of the lens to the eye.

Several studies refer to the average wearing time at follow-up appointments as a measure of success but only for a specific time, not over a follow-up period. In early studies, the wearing time was reported in order to compare the success of the fittings between PMMA or glass scleral lenses and rigid gas permeable lenses (RGP scleral lenses). Several studies [14,16,28] reported an increase in wearing time after switching PMMA scleral lenses to RGP materials. Mean scleral lens wearing times were reported to be between 8 and 16 hours [29], 13.7 hours (range: 4 to 18 hours) [22], ≥10h in 59% of the 538 patients, [30] and 16.2h (range 3-18h). [19] In this last one, authors stated that 1 patient experienced difficulty in achieving lens wear beyond 3h, while 83% were able to wear the lenses for 18h. [19] A more recent report (from 2010) [15] defined “success” as the ability to wear the lenses for at least 10h per day,

partial success wearing 8 to 10h, less than 8h was low success, and failure was the complete lens discontinuation. The authors reported a mean wearing time of 10.5 h/day (range: 2 – 18h) and that 65% wore the lenses successfully (≥10h per day). The authors also conclude that the keratoconus patients achieved a higher success (≥10h per day) than PK group (72% vs 50%). [15] In the present study a mean wearing time of 9.9±3.2 hours was documented at V1m, which suffered a constant increase during the follow up appointments, and was 11.3±3.1 hours at V12m (range: 6 to 16). The average wearing time was higher in the IC Group at all the appointments, which reflects the higher necessity for scleral lens wear in those patients. The number of days per week of lens wear was also recorded and an increase from V1m to V12m was also reported (5.2±1.6 days to 5.7±1.4). The range was between 3 to 7 days (*Table 10.3*) - the great majority of subjects from IC Group reported to wear the lenses >5 days per week, however, subjects from RC Group reported to wear the lenses between 3 and 5 days per week in the great majority of the cases (*Figure 10.3 A*). Many studies refer the need to take brief breaks during the day to enhance vision and comfort, [14,15,19,22,25,31] namely because of the tear debris than may be entrapped in the liquid reservoir between the lens and corneal epithelium which can decrease the quality of vision (midday fogging). [31] In the present study, only two patients from IC Group reported to do that frequently (3 to 5 days per week), with others reporting to do that few times (<2 days per week). Contrary to these results, there are other reports considering that 62% of the patients with PMMA lenses needed to take wearing breaks but only 46% of the RGP patients do that. [14,25] Others reported that almost half of the patients need to take breaks (49%). [31] Recently Ortenberg *et al* [15] reported that 71% of the sample reported brief wearing breaks during the day – they were instructed to do that for replenishing the lenses. Although symptoms of midday fogging are usually reported to occur in 20-33% of scleral lens wearers [32–34], this issue was only reported in 2 patients of the 95 that were recruited (2.11%). None of the 69 patients that completed this 1-year follow-up subjectively complaint about decreasing vision during lens wear.

10.6 Conclusions

There was an overall 73% success rate in scleral lens fitting during this prospective 12-month follow-up study. The success rate was 77% in the group of patients with corneal irregularities due to different etiologies but only 58% in the group of patients with healthy cornea but high refractive errors. The main reasons to drop-out were discomfort and handling issues. Those who continued through the 12-month follow-up period have improved significantly their handling skills, and increased the confidence in scleral lens wear (measured by means of number of days per week and hours per day of lens wear).

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Chapter 11

Visual Performance Over 1-Year in a Sample of Scleral Lens Wearers

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11. Visual Performance Over 1-year in a Sample of Scleral Lens Wearers

11.1 Abstract

Purpose: To evaluate the 12-month visual and optical quality outcomes with scleral lenses (SL) in irregular and regular cornea patients.

Methods: Sixty-nine patients completed the 12-months of follow-up. Considering their corneal condition, patients were divided into two groups: one comprising subjects with irregular corneas (99 eyes) and the other one with regular corneas (27 eyes). Visual quality assessments were performed in all patients at Baseline, lens dispensing visit (LDV) and over the follow up visits of 1, 3, 6 and 12months. High and low contrast visual acuities (HCVA and LCVA) in logMAR scale. The size (LDI, %) and shape (BFCIrregSD, mm) of nigh vision disturbances (Light Distortion Analyzer - LDA, CEORLab, Portugal) were measured at Baseline with habitual correction (HC), best spectacle correction (BSC) and with scleral lenses at all appointments. Aberrometry (IRX3, ImaginEyes) was assessed at Baseline (without lens) and at all follow-up visits without and with the scleral lens. Results of low order astigmatism and defocus, as well as high-order comatic aberrations (3rd order), spherical aberration (4th and 6th order), and the root mean square (RMS) up to 8th order of spherical aberration (RMS_SA), comatic aberrations (RMS_COMA), secondary astigmatism (RMS_SecAstig), trefoil (RMS_Trefoil) and high order aberrations (RMS_HOA), were analyzed.

Results: After SL fitting, HCVA improved significantly when compared to HC and BSC in IC group (average improvement of +0.35±0.32 and +0.29±0.26 to +0.08±0.14, $p<0.001$) and RC Group (+0.17±0.23 and +0.12±0.23 to +0.10±0.23, $p<0.05$) without statistically and clinically significant differences up to the 12-months. LCVA presented the same performance. LDI decreased significantly with SL when compared to HC and BSC from 13.85±13.99% and 15.89±13.38% to 5.75±4.51% in ICGroup ($p<0.001$) and 6.16±5.38 and 5.98±5.39 to 3.99±3.05 in RCGroup ($p<0.05$). Irregularity of the light disturbance also decrease significantly, namely on ICGroup (mean decrease of 51% on ICGroup and 21% on RCGroup). Frequency, severity and bothersome of the vision-related symptoms also had a statistically significant decrease with SL ($p<0.05$). Regarding each type of aberrations, there were statistically significant differences between the NE and SL for Defocus, Vertical COMA, SA4th ,VSOTF and for all RMS calculated except for RMS_SA ($p<0.001$) in IC Group and Defocus, VerticalAstig, VerticalCOMA, RMS_trefoil and VSOTF ($p<0.05$).

Conclusions: Scleral lenses promote a better subjective and objective visual quality, namely on patients with irregular cornea. The results of the present work also suggest that high contrast visual acuity assessment alone could not be enough to characterize the visual enhancement promoted by scleral lenses on irregular cornea patients. Additional measurements such as night vision disturbances, aberrometry and subjective visual perception should be considered.

11.2 Introduction

The first goal of a contact lens (CL) is to correct refractive error and enhance visual quality of the retinal image. This is particularly straightforward when correcting low order aberrations (LOAs) such as myopia, regular astigmatism and hyperopia. However, when irregular astigmatism and higher-order aberrations (HOAs) are present – in corneal disorders such as keratoconus, for instance - the wavefront acquires a quite complex shape and disables the visual correction with conventional methods. [1–4] Hopefully, CL with rigid gas permeable (RGP) materials – such as corneal CL, hybrid or scleral lenses - have important roles when other modalities fail. Those materials are able to mask/ neutralize corneal surface irregularities and provide a smoother and regular refractive surface, reducing HOAs. [5–9] This is particularly convenient in patients with keratoconus or other corneal ectatic disorders that degrade the retinal image quality because of the large magnitude of HOAs presented on the corneal surface - typically more 5 to 6 times than a normal eye. [9]

Scleral lenses (SL) are becoming more commonly used for visual correction. [10,11] They are mostly fitted to improve visual quality in cases of irregular astigmatism or for providing a therapeutic environment for managing severe anterior eye diseases. [12,13] These lenses have unique benefits. Along with other CL with RGP materials, the efficacy of these lenses to effectively reduce HOAs has already been proved. [6,14] In addition, the proper alignment of these lenses with the scleral shape will minimize the dynamic movement of the lens [15] – that, in addition to the larger optic zones, make them an important platform to incorporate complex optical designs such as astigmatic correction or wavefront-guided optics to reduce residual HOAs. [9,15] Also, as they do not touch the corneal surface they will promote a better comfort for the patient and mechanical protection. Considering those benefits, scleral lenses are now being increasingly considered for visual correction in healthy eyes. In fact, moderate to severe astigmatic patients tend to prefer corneal RGP lenses to soft lenses with respect to visual tasks. [16] Considering that scleral lenses could potentially promote an increased comfort because of the aforementioned reasons, patients with normal corneal will potentially have more benefits with scleral lenses than with corneal RGPs (both visual and comfort). However, one must consider that the risk/benefit ratio of these lenses in normal corneas seeks to be assessed.

Notwithstanding, and considering the optimal visual acuity results achieved with these lenses [5,6,17–19], patients with corneal irregularities may still have a reduction in their quality of vision/ contrast sensitivity due to residual HOAs. [20,21] Thus, along with standard visual

acuity assessments, objective evaluations of the visual quality (aberrometry and night vision disturbances) will add additional information. Night vision disturbances could be an important limiting factor for patients with corneal irregularities due to ectatic diseases or pots-refractive surgery, compromising daily life activities such as driving. In post-refractive surgery patients, the changes in the corneal shape will induce optical aberrations – such as spherical aberration and coma - that can lead to image degradation, especially under low lighting conditions (larger pupil sizes). [22,23] Similarly, patients with keratoconus – with high amounts of HOAs - will also experience considerable visual degradations under dim light conditions. [24] So, even when the visual acuity is enhanced to nearly normal values, some problems could remain present when under dim light conditions. Along with this, the individual's unique perceptions of their own vision – that account not only on visual factors but also physiological factors – are also important to consider to full understand the visual condition of the patients. [25]

The present work intended to evaluate the long-term optical quality and visual performance over 12 months in two samples of scleral lens wearers, comprising subjects with irregular and regular corneal surfaces.

11.3 Methods

11.3.1 Study Design, Subjects and Scleral Lens used

The present work was a prospective dispensing case series that aimed to report the visual outcomes – fully covering all the above mentioned visual quality metrics – over a 12 months of follow-up in two groups of patients fitted with scleral lenses: one group with irregular corneas and other group with regular/ healthy corneas.

Ninety-five (95) consecutive patients were recruited to participate in this prospective dispensing case series. Twenty-six (26) dropped-out over the follow-up period (Macedo-de-Araújo, Fitting Success, submitted to publication – Chapter 10), so 69 patients completed the 12-month follow-up period. The subjects were divided into two groups according to their corneal condition: one group including patients with irregular corneas (IC Group) involving irregularities due to different etiologies (99 eyes of 55 subjects) and the second group including subjects with regular

and healthy corneas (RC Group) with high refractive errors (myopia ≥ 6.00 D; astigmatism ≥ 2.00D, hyperopia ≥ 4.00D) that have failed or rejected other forms of vision correction with other contact lenses (27 eyes of 14 subjects). Visual acuity and symptoms assessment were performed in all subjects. Due to equipment availability in our facilities, night vision disturbances assessment was only performed in 55 subjects (43 ICGroup and 12 RCGroup) and aberrometry in 46 subjects (34RCGroup 9 RCGroup) – some patients' aberrometries were impossible to capture due to highly distorted corneas.

All patients were fitted with mini-scleral lens from Procornea (Eerbeek, The Netherlands) manufactured in Boston XO material. Other technical characteristics of the lenses used and fitting procedure were already described in previous publications in the context of this study. [26–28] The mean trial lenses per eye and re-orders necessary were also previously described. [28] The power profiles of the scleral lenses used for different power diopters are displayed on *Figure 11.1*, depicting the spherical /non aspheric nature of the profile of the lenses used in the present study.

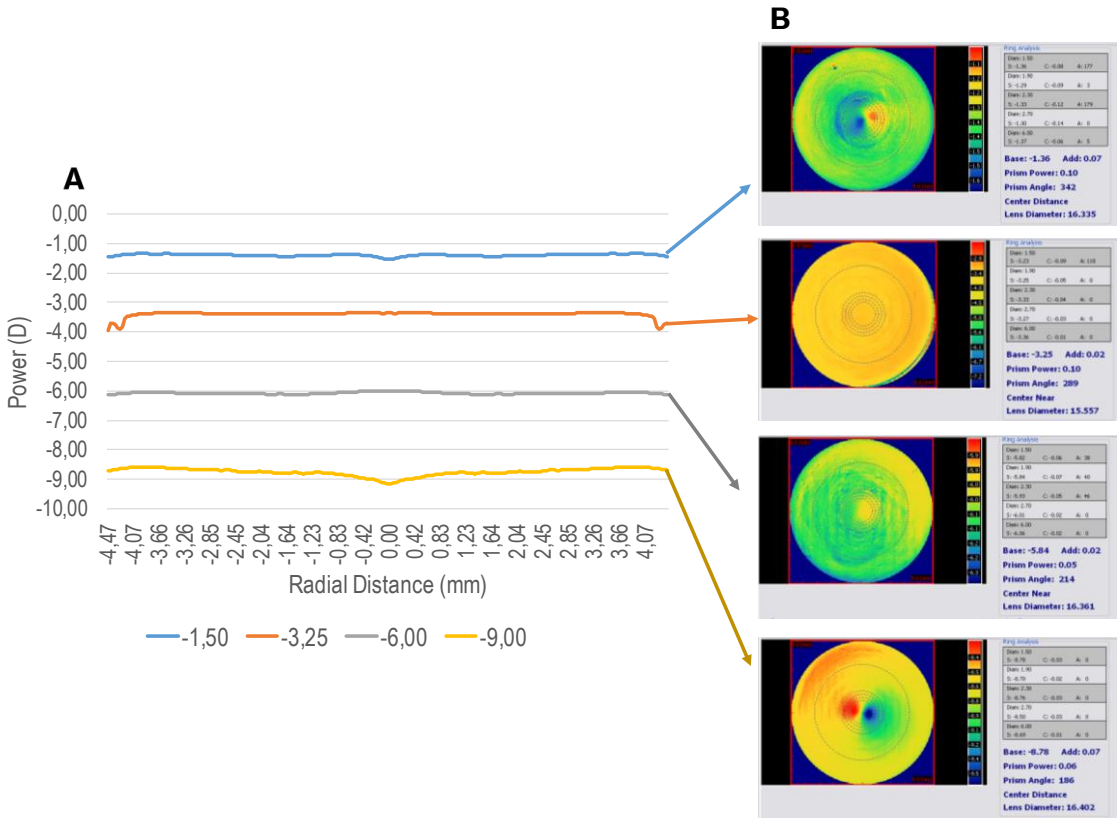

Figure 11.1 (A) Power Profiles of the scleral lenses fitted in the present study for different dioptric powers; (B) Respective Power Maps of the same lenses.

Following the recommendations of the declaration of Helsinki, all subjects received information from the study before they accept to participate and signed a consent form. The protocol of the study has been reviewed and approved by the Ethics Subcommittee for Life and Health Sciences of University of Minho.

11.3.1 Follow-up Assessments

All the subjects enrolled in this study had to attend several appointments during the 1 year of follow-up: Baseline, LDV - where measurements were performed 10 minutes after lens insertion (LDV1) and after more than 90 minutes of lens wear (LDV2) - 1-month visit (V1m), 3 months visit (V3m), 6 months visit (V6m) and 12 months visit (V12m). At all follow-up appointments the patients were asked to attend to the visit after at least 90 minutes of lens wear to allow time for lens settling after evaluation.

11.3.1.1 Objective Visual Quality Assessment

Measurements of light disturbance and ocular aberrometry were performed (n=46) in order to assess the visual quality during the entire follow-up period and baseline. Measurements of light disturbance (n=55) were performed using an experimental device – the Light Disturbance Analyzer (LDA, CEORLab, University of Minho, Portugal). [29–31] This device provides a comprehensive number of metrics that allows to quantify the size and shape of the light disturbance triggered by a central high-intensity light source (LED). Following the methodology of previous works [29,30], the in-out 30° routine exam was selected – a peripheral LED was presented from the center to periphery in a random order over the 12 semimeridians with an angular separation of 30°, surrounding the central LED. Subject was positioned at a distance of 2 meters in a darkened room with one eye occluded (measurements were performed monocularly, in a random order). To perform the measurement, subjects were instructed to always fixate the glare source (high-intensity central LED) and click in the mouse control anytime they saw the peripheral stimulus (smaller LEDs with lower intensity disposed over 12 semimeridians). Three evaluations were performed in each semi-meridian before the instrument calculates the mean

limit of the light disturbance. Parameters of size (light disturbance index – LDI, %) and irregularity (best-fit circle irregularity – BFCIrreg and BFCIrregSD, mm) were evaluated in this study. LDI is the percentage of the total area that is not visible due to light disturbance. BFCIrreg and BFCIrregSD are the sum of the deviations (positive and negative) between the disturbance area and the BFC, and the sum of those differences squared, respectively. [29–31] Measurements were performed at Baseline, with HC and BSC, and at follow-up appointments (V1m to V12m) with scleral lenses in 55 of the 69 patients.

The IRx3 Hartmann-Schack aberrometer (ImaginEyes, France) was used to obtain the total low and high order aberrations (LOAs and HOAs, respectively) up to the eight order, expressed as Zernike polynomials. The results were analyzed for a 5-mm pupil. The root mean square (RMS) up to the 8th order of the total HOAs (RMS_HOA), spherical-like (RMS_SA), coma-like (RMS_COMA), secondary astigmatism (RMS_SecAstig) and trefoil (RMS_Trefoil) were considered. Separated analyzes of low order aberrations (LOAs) – defocus, oblique and horizontal astigmatism –, spherical aberration of 4th (SA_4) and 6th (SA_6) order and vertical and horizontal 3rd order coma-like aberrations were also considered. Several measurements were performed over the follow-up time. At lens dispensing visit (LDV), measurements were performed without lens (Baseline) and right after lens insertion (LDV1), and at each one of the follow-up assessments (V1m to V12m) measurements were performed with and without scleral lenses (with scleral lens – SL and without – No Lens). Due to availability of the devices in our lab, vision quality measurements (LDA and aberrometry) were not performed at all follow-up visits in all patients. Because of that, only subjects that had all the appointments evaluated were considered.

11.3.1.2 Subjective Visual Quality Assessment

Visual quality was also subjectively assessed with the quality of vision (QoV) questionnaire in all patients. [25] This is a 10-item questionnaire, each one with three questions regarding the Frequency, Severity and Bothersome of the visual-related symptom. Questions regarding glare, haloes, starburst, hazy vision, blurred vision, disturbance, double/ multiple images, fluctuations, focusing and depth perception are included. The first 7 questions are accompanied with an image that was developed to aid in understanding the questions and reduce the possibility of inconsistent responses. [25] Similarly to visual acuity assessment, this questionnaire was administrated to all the patients at Baseline (subjects instructed to fill the

questionnaire with the perceptions felt with their HC), and at all follow-up appointments (V1m to V12m - subjects were instructed to fill the questionnaire regarding the perceptions felt when wearing scleral lenses). The questionnaire was already validated with the Rasch-analysis, with the Rasch-scaled scoring being between 0 and 100, with higher scores indicating worse quality of vision. [25,32] The Portuguese version of the QoV questionnaire was administrated in previous studies. [33,34]

11.3.2 Statistical Analysis

Statistical analysis was conducted using SPSS v.25.0 (SPSS, Inc, Chicago, Illinois, USA). Normality of data distribution was assessed with Kolmogorov-Smirnov or Shapiro-Wilk tests according to the number of subjects to be analyzed at each part of the study. Considering the distribution of variables, parametric or non-parametric tests were used. When comparing different follow-up visits within the same group Paired Sample T-test or Wilcoxon test with post hoc corrections were performed. When comparing the two groups, Unpaired T-test or Mann-Whitney test were performed, accordingly to the distribution of the variable in analysis. The descriptive values presented are the mean and standard deviations (mean±SD) for each studied variable at all parts of the study. The level of statistical significance was set at $p<0.05$.

11.4 Results

From the 95 patients primarily recruited, 69 patients completed the 12 months of follow-up: 16 patients from IC Group and 10 patients from RC Group dropped out due to different reasons. (Macedo-de-Araújo RJ, One-year report on success rate, submitted to publication – Chapter 10).

11.4.1 Visual Acuity

Table 11.1 shows the mean ± SD of logMAR HCVA and LCVA with habitual correction (HC), best spectacle correction (BSC) and with scleral lenses at all appointments. The mean ± SD HCVA and LCVA with scleral lenses improved significantly when compared to HC and BSC in

IC Group (p<0.001, Wilcoxon). For the RC Group, there was a statistically significant improvement in HCVA with scleral lenses when compared to HC (p=0.024, Wilcoxon) but not compared to BSC (p=0.294, Wilcoxon) and the difference between HC and BSC had a statistically significant difference (p=0.012, Wilcoxon). Regarding LCVA, there was only a statistical significant difference between BSC and HC (p=0.043, Wilcoxon). Visual acuity improved two logMAR lines or more (≥0.2 logMAR) with respect to BSC in 58% and 66% (HCVA and LCVA, respectively) of eyes in IC Group and 11% and 7% (HCVA and LCVA, respectively) on RC Group.

Although the average HCVA and LCVA show no significant differences over the entire follow-up period, the differences between the maximum and the minimum visual acuity reached over the follow-up visits (LDV to V12m) showed some differences (*Figure 11.2*). A great number of eyes (n=44 and n=51) showed HCVA and LCVA fluctuations of 0.1 to 0.2 logMAR in IC Group. In RC Group the fluctuations were fewer – the great majority (n=16) suffered fluctuations of 0.04 to 0.10. However, one should take into account that these fluctuations do not mean that the vision has worsen – in some cases, it reflects a visual improvement overtime.

Table 11.1. Mean±SD HCVA and LCVA outcomes. IC Group (n=96 eyes), RC Group (n=27 eyes).

		BASELINE		SCLERAL LENS						
		HC	BSC	LDV1	LDV2	1 month	3 months	6 months	12 months	*p (DBV-SL)*
HCVA	IC Group	+0.35 ±0.32	+0.29 ±0.26	+0.08 ±0.14	+0.07 ±0.14	+0.08 ±0.15	+0.08 ±0.14	+0.08 ±0.13	+0.09 ±0.13	*p=0.243 **
	RC Group	+0.17 ±0.23	+0.12 ±0.23	+0.10 ±0.23	+0.09 ±0.23	+0.08 ±0.23	+0.07 ±0.23	+0.07 ±0.23	+0.08 ±0.23	*p=0.396 ** *LDV1 vs 6m †*
P (DBG)		***p=0.006 •***	***p=0.001 •***	*p=0.659 •*	*p=0.571 •*	*p=0.854 •*	*p=0.619 Δ*	*p=0.762 •*	*p=0.441 •*	
LCVA	IC Group	+0.61 ±0.34	+0.58 ±0.27	+0.35 ±0.17	+0.34 ±0.17	+0.35 ±0.19	+0.36 ±0.20	+0.35 ±0.17	+0.37 ±0.17	***p=0.024 **** *LDV1 vs 12m; LDV2 vs 12m; 6m vs 12m†*
	RC Group	+0.34 ±0.23	+0.30 ±0.23	+0.28 ±0.23	+0.28 ±0.23	+0.26 ±0.23	+0.26 ±0.23	+0.26 ±0.23	+0.26 ±0.23	*p=0.477 **
P (DBG)		***p<0.001 •***	***p<0.001 •***	***p=0.001 Δ***	*p=0.054 Δ*	***p=0.028 •***	***p=0.012 Δ***	***p=0.013 Δ***	***p=0.002 •***	

IC Group – Irregular cornea group; RC Group – Regular cornea group; HC – habitual correction; BSC – Best spectacle correction; LDV1 – lens dispensing visit right after lens insertion; LDV2 – lens dispensing visit after more than 90 minutes of lens wear; DBG – differences between groups; DBV-SL – Differences between visits with scleral lenses.*Friedman; †Wilcoxon; ΔUnpaired T-test; • Mann-Whitney

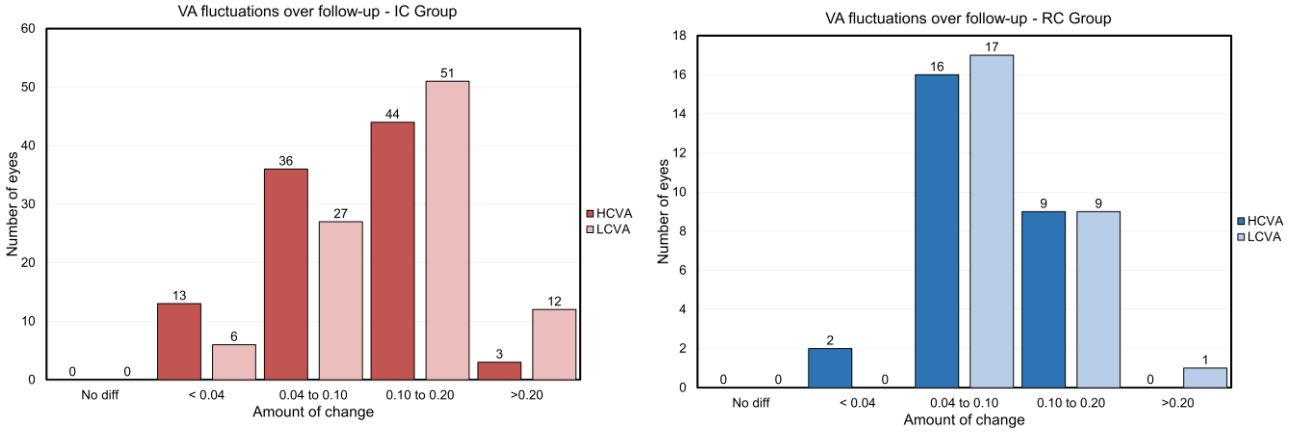

Figure 11.2 Frequency of eyes that underwent specific visual fluctuations over the entire follow-up time with scleral lenses on IC Group (right, n=96 eyes) and RC Group (left, n=27 eyes). The results are the maximum difference between visits (from LDV to V12m) - note that not all HCVA and LCVA fluctuations mean a decrease in the visual acuity overtime – in some cases, the visual acuity improved between visits.

11.4.1 Night Vision Disturbances

Figure 11.3 shows the results of light disturbance analysis measured with HC, BSC and with scleral lens at all the follow up visits. There were statistically significant differences between all visits regarding LDI in both groups ($p<0.001$, Friedman). Pairwise comparisons revealed differences between measurements performed with HC and BSC with all measurements performed with scleral lenses in both groups (from V1m to V12m, $p<0.05$, Wilcoxon). There were also statistically significant differences between LDV1 vs LDV2 and V1m in RC Group ($p<0.05$, Wilcoxon) and between LDV1 vs LDV2, V1m, V3m and V12m in IC Group ($p<0.05$, Wilcoxon). Considering shape parameters (BFCIrreg and BFCIrregSD) there were statistically significant differences between all visits in IC Group ($p<0.001$, Friedman) but not on RC Group. Similar to LDI results, the differences were found between HC and BSC measurements with all scleral lens measurements in IC Group ($p<0.05$, Wilcoxon). In RC Group some pairwise comparisons revealed statistically significant differences in shape parameters, namely between HC and measurements with scleral lenses ($p<0.05$, Wilcoxon).

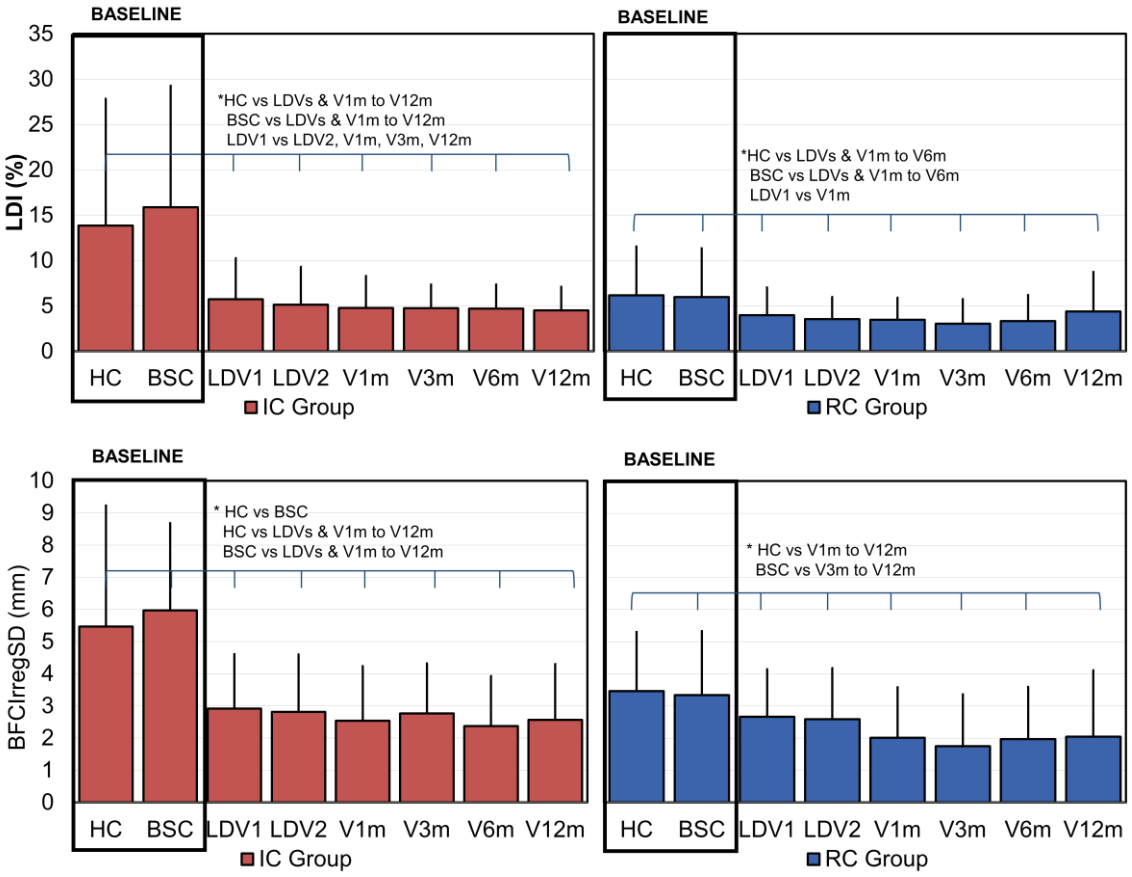

Figure 11.3 Light disturbance index (LDI, top) and irregularity (BFCIrregSD, down) analysis for Baseline measures (with HC and BSC) and over the follow-up appointments with scleral lens. Results for IC Group (right, n=77 eyes) are shown in red and results for RC Group in blue (left, n=23 eyes).

11.4.1 Subjective Visual Quality – Quality of Vision (QoV) questionnaire

Figure 11.4 shows the results of Quality of Vision (QoV) questionnaire. The vision-related symptoms decreased in the follow-up visits (V1m to V12m) when compared to Baseline. There were statistically significant improvements in the Frequency, Severity ($p<0.001$) and Bothersome ($p<0.05$) scores between Baseline visit (with HC) and all the follow-up visits for IC Group. Regarding RC Group, there were only statistically significant differences between Baseline and V1m and V6m for Frequency and Severity ($p<0.05$) but not for Bothersome. No statistically significant differences were observed between follow-up visits (symptoms with scleral lens) showing stability over the follow-up time.

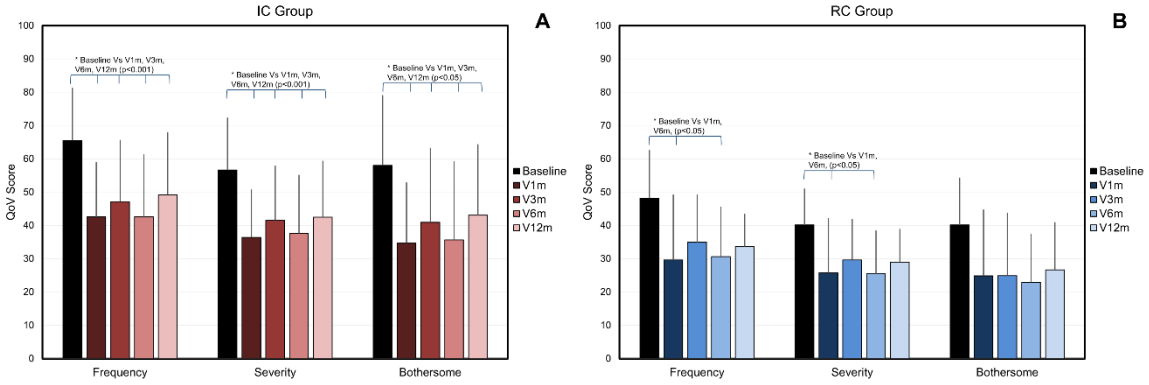

Figure 11.4 Quality of vision (QoV) questionnaire results for IC Group (A) and RC Group (B) for frequency, severity and bothersome scores at Baseline (with HC) and over the follow-up appointments. *ANOVA and paired sample t-test with Post-hoc Bonferroni

11.4.1 Ocular Aberrations with and without Scleral Lenses

Table 11.2 and *table 11.3* show the descriptive statistics of Zernike polynomials aberration coefficients analyzed for IC and RC Groups, respectively. Regarding the comparisons between no-lens and with scleral lens situations, there were statistically significant differences for Defocus, Vertical COMA, SA_4th,VSOTF and for all calculated RMS except for RMS_SA ($p<0.001$) in IC Group and Defocus, VerticalAstig, VerticalCOMA, RMS_trefoil and VSOTF ($p<0.05$). Few statistically differences were found between all visits (no lens situation) and all visits with scleral lenses (p(A)). Regarding both groups, there were statistically significant differences ($p<0.05$, Kruskal-Wallis) between IC and RC Groups for VerticalAstig (NoLens V6m), Defocus (NoLens V6m), VerticalComa (Baseline and LDV), RMS_SA (Baseline and NoLens V12m), RMS_COMA (all visits), RMS_AstigSec (all visits, except NoLens V6m), RMS_Trefoil (Baselline, LDV, V1m, NoLens V3m, SL V6m, NoLens V12m), RMS_HOA (all visits, except NoLens V6m), and VSOT (V1m, V3m, NoLens V6m).

Table 11.2. Descriptive statistics of aberrometry (IC Group). Results are represented by Mean±SD (MIN to MAX).

		BAS./ LDV +	V1M	V3M	V6M	V12M	P (A)
ASITIGOBLIQ	NO SL	-0.32±1.98 (-5.75 to 4.61)	-0.22±1.68 (-4.07 to 4.07)	-0.44±2.18 (-6.04 to 4.44)	-0.45±2.02 (-6.36 to 4.33)	-0.44±1.79 (-5.69 to 2.49)	-
	SL	0.00±0.59 (-2.44 to 1.06)	0.06±0.64 (-2.42 to 2.54)	0.02±0.45 (-0.96 to 1.23)	0.06±0.47 (-0.97 to 1.52)	0.01±0.50 (-2.03 to 1.09)	-
	p (B)	-	-	-	-	-	
DEFOCUS	NO SL	4.35±3.47 (-1.86 to 5.37)	3.98±3.57 (-0.82 to 15.32)	4.69±3.82 (-1.15 to 18.89)	4.52±3.33 (-1.62 to 15.47)	4.59±3.12 (-0.42 to 12.58)	-
	SL	0.35±1.72 (-3.16 to 5.43)	0.55±1.55 (-2.91 to 5.28)	0.42±1.49 (-2.59 to 5.38)	0.55±1.32 (-2.53 to 4.41)	0.51±1.30 (-2.45 to 4.58)	-
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
ASTIGVERT	NO SL	-0.32±1.87 (-4.46 to 5.37)	-0.14±1.54 (-4.75 to 4.90)	-0.40±1.78 (-5.01 to 3.08)	-0.32±1.97 (-5.20 to 5.67)	-0.35±1.84 (-5.22 to 3.64)	-
	SL	-0.01±0.56 (-1.02 to 1.82)	-0.06±0.54 (-1.90 to 1.12)	0.07±0.47 (-0.74 to 0.91)	-0.01±0.49 (-0.84 to 1.28)	0.06±0.68 (-1.01 to 2.97)	-
	p	-	-	-	-	-	
VERTICAL_COMA	NO SL	-1.28±1.14 (-4.12 to 2.01)	-1.16±1.02 (-3.74 to 0.12)	-1.12±1.01 (-4.41 to 0.25)	-1.25±0.92 (-3.57 to 0.60)	-1.17±0.95 (-3.79 to 0.20)	-
	SL	0.50±0.54 (-2.06 to 1.62)	0.48±0.46 (-1.37 to 1.75)	0.53±0.33 (-0.02 to 1.27)	0.51±0.43 (-1.62 to 1.28)	0.50±0.33 (-0.24 to 1.29)	-
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
HORIZONTAL_COMA	NO SL	0.01±0.52 (-1.62 to 2.01)	0.07±0.46 (-1.08 to 1.54)	-0.07±0.48 (-1.44 to 0.72)	0.04±0.51 (-1.32 to 1.59)	0.02±0.55 (-1.38 to 2.75)	-
	SL	-0.02±0.28 (-0.58 to 0.57)	-0.01±0.33 (-0.77 to 0.68)	-0.02±0.36 (-0.81 to 1.10)	0.00±0.33 (-0.84 to 0.83)	-0.02±0.33 (-0.73 to 1.08)	-
	p	-	-	-	-	-	
SA_4TH	NO SL	-0.10±0.38 (-1.57 to 0.22)	-0.08±0.34 (-1.05 to 0.95)	-0.18±0.47 (-1.41 to 0.74)	-0.11±0.39 (-1.77 to 0.64)	-0.15±0.50 (-2.44 to 0.53)	**Baseline vs V12m ; V1m vs V3m**
	SL	0.20±0.19 (-0.23 to 0.70)	0.18±0.21 (-0.33 to 0.71)	0.21±0.20 (-0.47 to 0.69)	0.20±0.17 (-0.12 to 0.59)	0.21±0.19 (-0.20 to 0.78)	-
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
SA_6TH	NO SL	0.00±0.07 (-0.14 to 0.22)	0.01±0.08 (-0.13 to 0.22)	0.03±0.09 (-0.18 to 0.25)	0.01±0.08 (-0.14 to 0.28)	0.01±0.09 (-0.18 to 0.38)	-
	SL	-0.01±0.04 (-0.08 to 0.10)	-0.01±0.05 (-0.15 to 0.11)	-0.01±0.06 (-0.26 to 0.10)	-0.02±0.05 (-0.09 to 0.09)	-0.01±0.05 (-0.18 to 0.12)	**LDV vs V1m & V3m & V6m & V12m; V1m vs V3m**
	p	-	-	**p=0.015**	-	-	
RMS_SA	NO SL	0.29±0.30 (0.01 to 4.14)	0.27±0.23 (0.01 to 1.07)	0.35±0.37 (0.02 to 1.43)	0.26±0.32 (0.01 to 1.79)	0.31±0.43 (0.02 to 2.45)	-
	SL	0.23±0.16 (0.02 to 0.70)	0.23±0.16 (0.05 to 0.71)	0.25±0.15 (0.03 to 0.69)	0.23±0.14 (0.01 to 0.59)	0.24±0.17 (0.02 to 0.78)	-
	p	-	-	-	-	-	
RMS_COMA	NO SL	1.46±1.10 (0.05 to 4.14)	1.29±0.98 (0.08 to 3.78)	1.27±0.97 (0.03 to 4.47)	1.40±0.87 (0.05 to 3.59)	1.31±0.94 (0.04 to 3.82)	**Baseline vs V12m; V3m vs V6m**
	SL	0.67±0.42 (0.03 to 2.16)	0.67±0.36 (0.02 to 1.82)	0.65±0.35 (0.10 to 1.69)	0.67±0.36 (0.08 to 1.69)	0.61±0.35 (0.09 to 1.52)	-
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
RMS_ASTIGSEC	NO SL	0.33±0.24 (0.02 to 2.43)	0.30±0.23 (0.01 to 1.01)	0.31±0.21 (0.03 to 1.01)	0.32±0.25 (0.03 to 1.11)	0.31±0.27 (0.02 to 1.13)	-
	SL	0.13±0.09 (0.02 to 0.38)	0.16±0.10 (0.03 to 0.58)	0.17±0.16 (0.02 to 0.99)	0.15±0.10 (0.02 to 0.45)	0.15±0.12 (0.02 to 0.56)	-
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
RMS_TREFOIL	NO SL	0.62±0.44 (0.06 to 2.43)	0.59±0.49 (0.07 to 2.06)	0.57±0.39 (0.10 to 1.97)	0.60±0.42 (0.05 to 2.38)	0.59±0.41 (0.09 to 2.07)	-
	SL	0.17±0.10 (0.02 to 0.50)	0.18±0.09 (0.03 to 0.46)	0.17±0.11 (0.02 to 0.68)	0.16±0.12 (0.04 to 0.92)	0.17±0.13 (0.02 to 0.94)	**LDV vs V12m; V1m vs V3m**
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
RMS_HOA	NO SL	1.76±1.11 (0.24 to 0.07)	1.59±1.03 (0.15 to 4.05)	1.62±0.95 (0.32 to 4.61)	1.69±0.90 (0.13 to 3.94)	1.63±1.01 (0.19 to 4.09)	**Baseline vs V12m**
	SL	0.78±0.42 (0.13 to 2.28)	0.79±0.36 (0.15 to 1.99)	0.78±0.38 (0.22 to 1.80)	0.79±0.37 (0.15 to 1.97)	0.74±0.37 (0.18 to 1.68)	
	p	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	
VSOTF	NO SL	0.02±0.02 (0.00 to 0.07)	0.02±0.01 (0.00 to 0.05)	0.02±0.02 (0.00 to 0.07)	0.01±0.01 (0.00 to 0.07)	0.02±0.02 (0.00 to 0.10)	**V3m vs V6m**
	SL	0.05±0.05 (0.01 to 0.31)	0.05±0.03 (0.01 to 0.18)	0.04±0.03 (0.00 to 0.17)	0.04±0.03 (0.00 to 0.15)	0.05±0.04 (0.01 to 0.22)	
	P	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	**p<0.001**	

+ Baseline refers to the no-lens measures; LDV refers to the lens dispense visit (measure with lens); p(A) – pairwise differences between all visits (no lens situation) and differences between all visits with scleral lens; p(B) – differences between measurements performed without lens and with the lens for the different follow-up visits.

Table 11.3. Descriptive statistics of aberrometry (RC Group). Results are represented by Mean±SD (MIN to MAX).

		BAS./ LDV +	V1M	V3M	V6M	V12M	P*
ASTIGOBL	NO SL	-0.23±0.99 (-1.92 to 1.78)	-0.10±0.43 (-1.08 to 0.32)	-0.160.67 (-1.51 to 0.72)	-0.08±0.90 (-1.77 to 1.84)	-0.12±1.13 (-1.97 to 1.78)	-
	SL	0.09±0.25 (-0.19 to 0.50)	0.04±0.33 (-0.47 to 0.73)	-0.03±0.34 (-0.53 to 0.62)	0.04±0.29 (-0.41 to 0.75)	0.09±0.29 (-0.31 to 0.68)	-
	p	-	-	-	-	-	
DEFOCUS	NO SL	6.67±5.67 (-4.10 to 14.81)	8.78±4.38 (0.00 to 13.62)	5.61±2.82 (1.91 to 9.90)	5.99±4.72 (-4.24 to 11.52)	5.09±6.16 (-4.47 to 14.72)	-
	SL	0.44±2.05 (-3.01 to 3.45)	0.34±1.65 (-2.48 to 3.38)	-0.46±1.80 (-3.85 to 1.73)	0.53±1.54 (-2.58 to 3.44)	-0.12±2.26 (-3.06 to 4.79)	-
	p	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.05***	
ASTIGVERT	NO SL	-2.24±1.92 (-5.84 to 1.37)	-1.09±1.42 (-3.62 to 1.07)	-1.61±0.62 (-2.62 to -0.88)	-2.08±1.94 (-5.63 to 0.90)	-2.59±2.08 (-6.37 to 0.00)	**Baseline vs V3m**
	SL	0.11±0.66 (-1.33 to 1.18)	0.22±0.43 (-0.48 to 1.34)	0.14±0.39 (-0.48 to 0.65)	0.16±0.44 (-0.60 to 1.31)	0.14±0.51 (-0.69 to 1.42)	**LDV vs V1m**
	p	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.001***	
VERTICAL_COMA	NO SL	0.15±0.26 (-0.32 to 0.47)	0.02±0.26 (-0.47 to 0.23)	0.16±0.28 (-0.25 to 0.68)	0.11±0.32 (-0.29 to 0.81)	0.07±0.36 (-0.48 to 0.62)	-
	SL	0.30±0.32 (-0.11 to 0.85)	0.36±0.30 (-0.18 to 0.82)	0.40±0.26 (0.09 to 0.73)	0.28±0.24 (-0.17 to 0.69)	0.30±0.25 (-0.12 to 0.83)	-
	p	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.05***	
HORIZONTAL_COMA	NO SL	-0.03±0.10 (-0.21 to 0.17)	-0.03±0.10 (-0.19 to 0.10)	0.00±0.08 (-0.10 to 0.15)	-0.05±0.11 (-0.27 to 0.08)	-0.04±0.16 (-0.40 to 0.19)	-
	SL	-0.05±0.24 (-0.36 to 0.45)	0.02±0.28 (-0.39 to 0.53)	-0.05±0.18 (-0.28 to 0.30)	0.00±0.25 (-0.38 to 0.38)	-0.02±0.25 (-0.40 to 0.41)	**LVD vs V1m**
	p	-	-	-	-	-	
SA_4TH	NO SL	0.17±0.30 (-0.17 to 0.89)	0.14±0.18 (-0.03 to 0.43)	0.15±0.16 (-0.03 to 0.39)	0.04±0.17 (-0.21 to 0.36)	0.21±0.36 (-0.25 to 0.86)	**V6m vs Baseline & V3m**
	SL	0.16±0.26 (-0.03 to 0.66)	0.26±0.30 (-0.04 to 0.85)	0.11±0.13 (-0.08 to 0.28)	0.18±0.26 (-0.05 to 0.70)	0.29±0.36 (-0.06 to 1.10)	-
	p	-	-	-	**p<0.05***	-	
SA_6TH	NO SL	-0.01±0.04 (-0.10 to 0.06)	0.02±0.04 (-0.03 to 0.09)	-0.01±0.03 (-0.08 to 0.02)	-0.01±0.05 (-0.12 to 0.09)	0.00±0.05 (-0.08 to 0.10)	**Baseline vs 12m, V3m vs V1m & V6m, V6m vs V12m**
	SL	0.02±0.03 (-0.01 to 0.07)	0.01±0.03 (-0.04 to 0.06)	0.00±0.02 (-0.03 to 0.04)	0.02±0.03 (-0.02 to 0.08)	0.00±0.03 (-0.03 to 0.06)	-
	p	-	-	-	-	-	
RMS_SA	NO SL	0.22±0.26 (0.03 to 0.89)	0.15±0.17 (0.00 to 0.44)	0.16±0.14 (0.03 to 0.40)	0.15±0.10 (0.03 to 0.36)	0.30±0.28 (0.00 to 0.86)	-
	SL	0.18±0.25 (0.00 to 0.66)	0.27±0.29 (0.02 to 0.86)	0.14±0.09 (0.04 to 0.29)	0.19±0.25 (0.02 to 0.71)	0.30±0.35 (0.00 to 1.10)	**V3m vs V12m**
	p	-	-	-	-	-	
RMS_COMA	NO SL	0.29±0.13 (0.08 to 0.51)	0.23±0.14 (0.00 to 0.51)	0.27±0.18 (0.11 to 0.69)	0.28±0.22 (0.09 to 0.87)	0.34±0.20 (0.00 to 0.63)	-
	SL	0.40±0.29 (0.00 to 0.92)	0.50±0.22 (0.17 to 0.83)	0.46±0.24 (0.11 to 0.74)	0.40±0.19 (0.07 to 0.70)	0.41±0.21 (0.00 to 0.84)	-
	p	-	**p<0.05***	-	-	-	
RMS_SEC_ASTIGM	NO SL	0.12±0.09 (0.02 to 0.34)	0.08±0.06 (0.00 to 0.18)	0.07±0.07 (0.02 to 0.23)	0.08±0.06 (0.01 to 0.20)	0.12±0.06 (0.00 to 0.20)	**V6m vs V12m**
	SL	0.06±0.04 (0.00 to 0.14)	0.06±0.03 (0.02 to 0.11)	0.08±0.06 (0.01 to 0.22)	0.05±0.04 (0.02 to 0.14)	0.06±0.03 (0.00 to 0.10)	**V1m vs V6m**
	p	-	-	-	-	**p<0.05***	
RMS_TREFOIL	NO SL	0.25±0.10 (0.04 to 0.42)	0.19±0.15 (0.00 to 0.37)	0.17±0.14 (0.01 to 0.48)	0.21±0.10 (0.06 to 0.42)	0.27±0.14 (0.00 to 0.44)	**V3m vs V6m**
	SL	0.09±0.07 (0.00 to 0.19)	0.09±0.05 (0.02 to 0.18)	0.07±0.05 (0.02 to 0.18)	0.09±0.06 (0.03 to 0.23)	0.11±0.08 (0.00 to 0.24)	-
	p	**p<0.05***	**p<0.05***	-	**p<0.05***	**p<0.05***	
RMS_HOA	NO SL	0.52±0.25 (0.14 to 1.04)	0.38±0.24 (0.00 to 0.76)	0.40±0.26 (0.13 to 0.98)	0.42±0.25 (0.14 to 1.00)	0.59±0.32 (0.00 to 1.12)	-
	SL	0.51±0.30 (0.00 to 0.94)	0.64±0.23 (0.20 to 0.93)	0.51±0.25 (0.14 to 0.78)	0.51±0.21 (0.12 to 0.83)	0.60±0.32 (0.00 to 1.14)	-
	p	-	-	-	**p<0.05***	-	
VSOTF	NO SL	0.00±0.00 (0.00 to 0.02)	0.00±0.00 (0.00 to 0.00)	0.00±0.01 (0.00 to 0.02)	0.00±0.01 (0.00 to 0.01)	0.00±0.00 (0.00 to 0.02)	-
	SL	0.04±0.04 (0.00 to 0.14)	0.05±0.06 (0.01 to 0.24)	0.05±0.06 (0.01 to 0.20)	0.05±0.06 (0.01 to 0.23)	0.03±0.02 (0.00 to 0.06)	**V6m vs V12m**
	p	**p<0.05***	**p<0.05***	**p<0.05***	**p<0.001***	**p<0.05***	

+ Baseline refers to the no-lens measures; LDV refers to the lens dispense visit (measure with lens); p(A) – pairwise differences between all visits (no lens situation) and differences between all visits with scleral lens; p(B) – differences between measurements performed without lens and with the lens for the different follow-up visits.

Figure 11.5 shows the box and whiskers plots for some of the variables studies for both groups – while RC Group presents greater improvements on Defocus with the scleral lenses, the differences in vertical coma, RMS_COMA and RMS_HOA are more pronounced on IC Group.

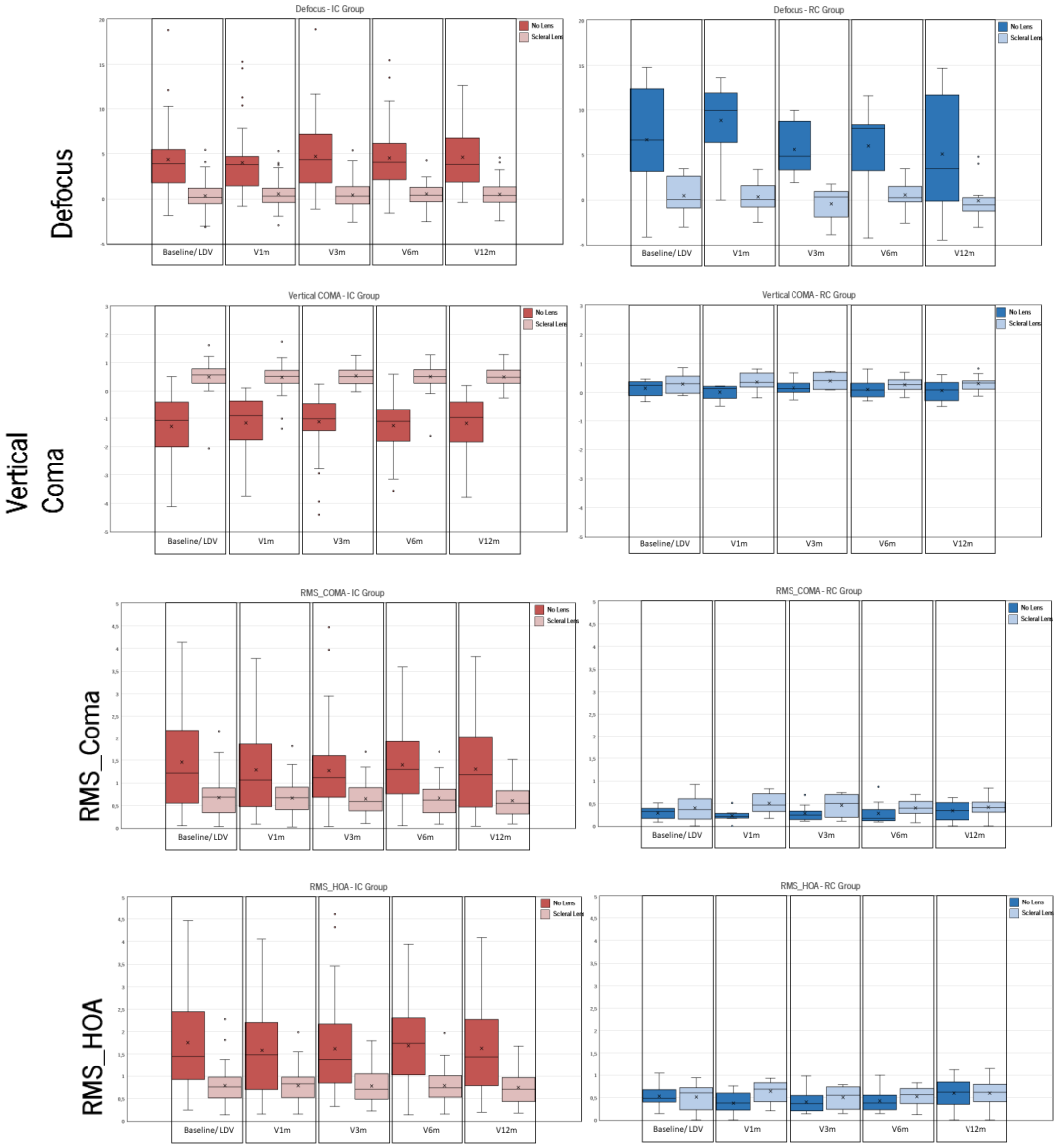

Figure 11.5 Box and whiskers plots comparing different Zernike polynomials with and without a scleral lens on-eye throughout the entire follow-up period. IC Group is presented in the right side (red) and RC Group on left side (Blue). Measurements performed without the lens are presented in a darker color, and measurements performed with scleral lenses are represented in a lighter color.

Table 11.5 shows the correlations between the studied Zernike polynomials and HCVA, LCVA, LDI, BFCIrregSD and QoV outcomes (frequency, severity and bothersome of the symptoms) in IC Group for all the visits. Vertical coma, RMS_HOA, RMS_COMA and RMS_AstigSec were moderately correlated with HCVA and LCVA at almost all visits (r between 0.200 and 0.600, $p<0.05$).

Table 11.4. Correlations (Spearman) between Zernike polynomials and all the variables studies (for IC Group only).

		VSOTF	HCVA	LCVA	LDI	IrregSD	Freq	Sev	Both
AstigObl	Baseline	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	LDV	<0.200	<0.200	<0.200	<0.200	<0.200	-	-	-
	V1m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	V3m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	V6m	<0.300	<0.200	<0.200	<0.200	<0.300	<0.200	<0.200	<0.200
	V12m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
Defocus	Baseline	**-0.739***	**0.502***	**0.470***	**0.427***	**0.299***	<0.200	<0.300	<0.300
	LDV	<0.200	<0.200	<0.200	<0.200	<0.200	-	-	-
	V1m	**-0.318***	<0.200	<0.200	<0.200	<0.200	0.324	0.335	0.345
	V3m	<0.200	<0.200	<0.200	<0.300	<0.200	<0.200	<0.200	<0.200
	V6m	**-0.460***	<0.200	<0.200	<0.200	<0.200	<0.300	**-0.340***	<0.300
	V12m	**-0.420***	<0.200	<0.200	<0.200	**-0.500***	<0.200	<0.200	<0.200
AstigVert	Baseline	<0.200	<0.300	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	LDV	<0.200	<0.300	<0.200	<0.200	<0.200	-	-	-
	V1m	<0.200	<0.200	<0.200	<0.200	<0.300	<0.200	<0.200	<0.200
	V3m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	V6m	<0.200	<0.200	<0.200	<0.200	<0.200	**0.436***	**0.429***	0.309
	V12m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.300	<0.300	<0.300
Vertical_COMA	Baseline	<0.200	<0.300	<0.300	<0.200	<0.200	<0.300	<0.300	<0.300
	LDV	**-0.471***	<0.200	**0.397***	<0.300	**0.538***	-	-	-
	V1m	**-0.471***	**0.343***	**0.458***	<0.200	<0.300	**-0.389***	-0.331	-0,399
	V3m	**-0.725***	**0.387***	**0.464***	**0.356***	**0.408***	-0.362	-0.367	-0.375
	V6m	**-0.556***	**0.395***	**0.422***	<0.200	<0.200	<0.200	<0.200	<0.200
	V12m	**-0.663***	**0.422***	**0.495***	<0.200	<0.200	**-0.448***	**-0.442***	**-0.468***
Horizontal_COMA	Baseline	<0.300	<0.200	<0.200	<0.200	<0.200	<0.300	<0.200	<0.200
	LDV	<0.200	<0.200	<0.200	<0.200	<0.200	-	-	-
	V1m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.300	<0.300	**-0.356***
	V3m	<0.200	<0.200	<0.200	<0.200	<0.200	-0.363	-0.303	**-0.392***
	V6m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.300	<0.300	-0.326
	V12m	<0.200	<0.200	<0.200	<0.200	<0.200	<0.300	<0.300	<0.300
SA_4th	Baseline	<0.300	**-0.284***	<0.300	<0.200	<0.200	<0.300	<0.200	<0.200
	LDV	<0.200	<0.200	<0.200	<0.200	<0.200	-	-	-
	V1m	<0.300	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	V3m	**-0.465***	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	V6m	**-0.361***	**0.306***	<0.300	<0.300	<0.200	<0.200	<0.200	<0.300
	V12m	**-0.537***	<0.200	<0.200	<0.200	**0.539***	<0.300	<0.300	<0.300
SA_6th	Baseline	**-0.280***	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200
	LDV	<0.200	<0.300	<0.300	<0.200	<0.300	-	-	-
	V1m	**0.405***	**-0.299***	**-0.406***	<0.200	<0.300	<0.300	<0.300	<0.300
	V3m	<0.300	**-0.349***	**-0.506***	<0.200	<0.200	<0.200	<0.300	<0.200
	V6m	<0.200	<0.200	<0.300	<0.200	<0.200	<0.200	<0.200	<0.200
	V12m	**0.342***	**-0.298***	**-0.362***	<0.200	<0.200	<0.200	<0.200	<0.200
RMS_SA	Baseline	<0.200	**0.288***	<0.300	<0.300	<0.300	<0.200	<0.200	<0.200
	LDV	<0.300	<0.200	<0.200	<0.200	<0.200	-	-	-
	V1m	**-0.478***	<0.200	<0.300	<0.200	<0.200	<0.200	<0.200	<0.200
	V3m	**-0.620***	<0.300	<0.300	**0.401***	<0.200	<0.200	<0.200	<0.200
	V6m	**-0.434***	**0.324***	**0.275***	<0.300	<0.200	<0.200	<0.200	<0.200
	V12m	**-0.639***	<0.300	**0.261***	<0.300	**0.567***	<0.300	<0.200	<0.300
RMS_COMA	Baseline	<0.300	**0.314***	**0.285***	<0.200	<0.300	<0.200	<0.200	<0.200
	LDV	**-0.664***	**0.322***	**0.582***	0.307	**0.611***	-	-	-
	V1m	**-0.688***	**0.492***	**0.592***	<0.200	<0.300	<0.200	<0.200	<0.200
	V3m	**-0.763***	**0.420***	**0.485***	**0.343***	**0.439***	-0.324	-0.322	-0.354
	V6m	**-0.722***	**0.297***	**0.388***	<0.200	<0.300	<0.200	<0.200	<0.200
	V12m	**-0.700***	**0.467***	**0.536***	<0.300	**0.331***	**-0.462***	**-0.423***	**-0.471***
RMS_AstigSec	Baseline	<0.200	**0.457***	**0.425***	**0.292***	**0.286***	<0.200	<0.300	<0.200
	LDV	**-0.548***	**0.358***	**0.521***	<0.300	**0.357***	-	-	-
	V1m	**-0.654***	**0.489***	**0.401***	<0.300	**0.319***	<0.200	<0.200	<0.200
	V3m	**-0.662***	**0.408***	**0.470***	**0.361***	0.316	<0.200	<0.200	<0.200
	V6m	**-0.655***	**0.309***	**0.412***	<0.300	<0.300	<0.200	<0.200	<0.200
	V12m	**-0.756***	**0.433***	**0.487***	**0.301***	**0.343***	<0.200	<0.200	<0.200
RMS_trefoil	Baseline	<0.200	**0.370***	**0.374***	**0.325***	**0.303***	<0.200	<0.300	<0.200
	LDV	**-0.453***	<0.300	**0.415***	**0.391***	**0.389***	-	-	-
	V1m	**-0.368***	<0.200	<0.200	<0.200	<0.200	<0.200	<0.200	**0.380***
	V3m	**-0.459***	<0.300	<0.300	**0.337***	0.320	<0.200	<0.200	<0.200
	V6m	**-0.546***	<0.200	<0.200	<0.200	<0.300	<0.300	<0.300	<0.300
	V12m	**-0.617***	**0.277***	**0.306***	**0.333***	<0.300	<0.300	<0.300	<0.300
RMS_HOA	Baseline	<0.200	**0.392***	**0.362***	**0.312***	**0.318***	<0.200	<0.200	<0.200
	LDV	**-0.675***	<0.300	**0.535***	0.316	**0.611***	-	-	-
	V1m	**-0.762***	**0.465***	**0.590***	<0.200	<0.300	<0.200	<0.200	<0.300
	V3m	**-0.819***	**0.453***	**0.508***	**0.413***	**0.431***	<0.300	-0.308	-0.305
	V6m	**-0.831***	**0.321***	**0.401***	<0.300	<0.300	<0.200	<0.200	<0.300
	V12m	**-0.839***	**0.496***	**0.565***	**0.305***	**0.382***	**-0.433***	**-0.390***	**-0.449***
VSOTF	Baseline	-	**-0.529***	**-0.492***	**-0.556***	**-0.298***	<0.300	-0.317	-0.319
	LDV	-	<0.200	**-0.331***	<0.200	**-0.539***	-	-	-
	V1m	-	**-0.348***	**-0.517***	<0.200	<0.300	<0.200	<0.200	<0.200
	V3m	-	<0.300	**-0.401***	<0.300	<0.300	<0.300	<0.300	<0.300
	V6m	-	<0.300	**-0.390***	<0.300	-0.328	<0.200	<0.200	<0.200
	V12m	-	**-0.358***	**-0.501***	<0.300	**-0.399***	<0.300	<0.300	<0.300

11.5 Discussion

The correction of corneal irregularities to restore vision is one of the main indications for SL fitting. [35–39] Many authors have reported huge improvements in visual acuity with scleral lenses with respect to best spectacle correction - however, many reports are retrospective analysis or focus on short-term outcomes. The present work reports prospectively the performance in both high and low contrast visual acuity and describes its changes throughout a 12-month follow-up period. Almost 100% of the patients with irregular and regular corneas had their visual acuity improved with scleral lenses with respect to BSC. Those improvements were higher on irregular cornea group (IC Group) with 58% of the eyes fitted achieving 2 or more lines of visual acuity – 16% of them had an improvement of more than 4 lines - 41% an improvement between 0.01 and 0.19 and only 1% had no change. On RC Group, only 12% had an improvement of 2 or more lines, 73% had an improvement between 0.01 and 0.2 and 4% had no visual acuity changes with scleral lenses. Other authors reported these kind of augment in the VA. Montalt *et al* [6] reported an improvement from 0.23±0.30 to 0.00±0.14. Pullum *et al* [36] reported that 70% of their patients achieved a VA ≥ 6/12. Other work [40] examined prospectively the visual acuity in 80 consecutive patients and found a mean improvement on best-corrected VA of -0.39 logMAR (converted from Snellen), being these changes of -0.54 in patients with ectasia and -0.22 in patients with ocular surface disease.

In the present work, the mean HCVA and LCVA remained stable over the follow-up period. However, when analyzing the differences between the maximum and minimum VAs over the follow-up period, some fluctuations were identified. Most patients showed an improvement, what might be due to some degree of neural recovery after restoring good vision after years without correction. [41,42] However, some patients could also experience a decrease in visual acuity that could be related to the intrinsic deterioration of the contact lenses overtime or the progression of the disease (in the case of patients with keratoconus). Taking into account the large sample recruited (especially in IC Group), we assume that an eye care practitioner should expect the VA with scleral lenses to be stable at least over the first 12 months of lens wear (which is the time recommended by manufacturers to change the lens).

An important conclusion to be taken about visual acuity assessment is that the HCVA could not reflect the actual visual performance of the irregular corneal patients. As seen on Table 1, the scleral lenses enhanced the HCVA to similar levels in both groups, however when

analyzing LCVA some differences between both groups arise – and those differences are of almost 1 line of visual acuity.

Apart from visual acuity, the present work adds other important assessments: the night vision disturbances and aberrometry measures. Since SL promote a uniform refracting surface for the irregular cornea patients, a reduction of HOAs should be expected [14] and therefore an improvement in the sensations of night vision disturbances. In fact, the subjective sensation of the patients about those and other vision-related phenomena improved significantly with SL – both frequency, severity and bothersome. However, patients from IC Group remain with higher visual symptoms when compared to RC Group, even after SL fitting.

The mentioned subjective enhancement was accompanied by an improvement in the objective perception of nigh vision disturbances (measured with LDA) – both size (LDI) and irregularity (BFCIrregSD) underwent a decrease with scleral lenses. However, the correlations between those shape factors and subjective perceptions were weak at all visits ($r<0.500$) in IC Group. On RC Group (n=12), some correlations between 0.600 and 0.800 were found between LDI and severity and bothersome at some visits, however those correlations had no statistical significance. The improvements in the size and shape of the light disturbance were larger on IC Group patients – enhancement of 64% and 51% in IC Group and 33% and 21% in RC Group, respectively. However, the values remained higher on IC Group patients when compared to RC Group (similarly to subjective analysis and LCVA results).

Considering aberrometry outcomes – analyzed for a 5-mm pupil size – it is seen that some aberration terms decreased significantly with SL when compared to the No Lens condition. Those improvements were already reported in the literature with corneal RGP lenses [43–45] and specifically scleral lenses. [9,14] Similarly to the findings of the present study, some reported a decrease in Total HOAs with corneal lenses in keratoconic patients but not on normal cornea patients. [46,47] In fact, on Table 4 a non-statically significant worsening in the RMS_HOA is seen in RC Group. The main reductions on ocular aberrations of RC Group were seen in Defocus, Vertical astigmatism (LOAs) and vertical coma, although the main reductions of IC Group were seen on Defocus, Vertical coma, SA_4th and in all RMS analyzed, except RMS_SA. From observation of the graphics from Figure 5, it is also seen that despite the IC Group patients benefited from a higher reduction in the LOAs and HOAs, these did not reach the RC Group values – maybe due to some residual aberrations. Sabesan *et al* [9] demonstrated that the HOAs that remain after a conventional SL fitting could be effectively reduced by 3.1 times with a

customized scleral lens with a wavefront-guided technique, achieving levels of aberrations similar to a normal population. This kind of technology (wavefront customized SL or aspheric surfaces [48]) can be effective in improve visual quality by reducing residual HOAs, however it can have a significant cost and complexity. [9,20] Considering the overtime results, some statistical significant differences were observed between some visits in some outcomes – however it does not indicate a progressive reduction or augment in the amount of aberration, but some fluctuations instead. Those fluctuations could be related with several factors such as the lens wearing time and scleral lens cleanness on the day of the appointment. Montalt *et al* [6] followed a group of 36 patients with keratoconus fitted with corneo-scleral lenses for 1-year. They found a decrease of 55% in total HOAs with scleral lenses and found a statistically significant decrease on spherical aberration (mean reduction from +0.32±0.22 to 0.25±0.36) and other HOAs (reduction from 0.31±0.13 to 0.26±0.09) after 1-year of follow-up. They also concluded that the residual HOAs remained slightly elevated when compared with normal eyes after fitting scleral lenses – the mean total HOAs value was 0.73±0.44 and 0.70±0.39, which are similar to the values reported in the present study (0.78±0.42 μm at LDV and 0.74±0.37 μm at V12m). The results of the present study emphasize the idea that RGP materials can compensate a large amount of corneal HOAs, however residual aberrations – possibly arising from posterior corneal surface or other ocular components – remain uncompensated. [6,20]

Strengths of this study are the study design (a prospective dispensing case series with a total of 12-months of follow up), the large sample recruited, the controlled nature – with scheduled follow-up appointment that were done always at the same time of lens wear for all the patients -, the follow-up time and the measurements performed at each appointment were equal and in the same order for all patients. In accordance to the previous reported studies, the present work adds valuable information on the visual performance over the 12-months of follow-up, comparing different visits performed at the same wearing times for all patients (V1m, V3m, V6m and V12m). Another strength is the inclusion of a group comprising patients with healthy corneas (but high refractive errors) – which could be seen as a control group. In fact, some conclusions of the present work – such as the use of different devices/ measures to assess the visual enhancement in irregular cornea patients – could not be withdrawal with the absence of this control group. A limitation is that some of the results could not be extrapolated to clinical practice – as these patients were carefully followed-up, with programmed visits and had the lenses and disinfecting solutions for free.

11.6 Conclusions

In summary, the scleral lenses fitted in the present study had significantly improved the visual acuity in both groups of patients studied – in the short and long-term -, especially on irregular cornea patients. Those improvements were followed by a significant reduction in ocular aberrations, night vision disturbances perception and subjective perceptions of the patients. The results of the present work also suggest that high contrast visual acuity assessment alone could not be enough to characterize the visual enhancement promoted by scleral lenses on irregular cornea patients. Although the average high contrast visual acuity was practically the same on both group of subjects, other metrics such as low contrast visual acuity, night vision disturbances, aberrometry assessments and subjective perceptions demonstrate that the visual performance of irregular cornea patients fitted with scleral lenses is worse than healthy cornea patients fitted with the same lenses. This opens a window for the development of new designs or for customization of scleral lens fittings in the future. However, the visual improvements promoted by standard scleral lenses – even without being perfect – could be a life-changing event for an important number of irregular cornea patients.

11.7 References

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Chapter 12

Clinical Findings and Ocular Symptoms in a Sample of Scleral Lens Wearers: 1-year Follow-up

12. Clinical Findings and Ocular Symptoms in a Sample of Scleral Lens Wearers: 1-year Follow-up

12.1 Abstract

Purpose: The present work aims to report the fitting aspects and clinical findings in the slit-lamp and symptoms over 12 months of scleral lens (SL) wear.
Methods: Sixty-nine patients with ectasia, surgical procedures and irregular cornea (ICGroup) or high ametropia or high astigmatism but regular corneas (RCGroup) completed the 12-month follow-up period. Patients were evaluated at baseline, lens dispensing visit (LDV), 1-month, 3-month, 6-month and 12-month for assessment of comfort, fitting aspects and slit lamp findings. Comfort was assessed with Ocular Surface Disease Index (OSDI) questionnaire and 8-question Dry Eye Questionnaire (DEQ). Slit lamp evaluations comprised on-eye lens fitting (lens alignment and central corneal clearance – CCC) and anterior ocular surface health (edema, hyperemia, staining, adverse events).
Results: SL wear significantly reduced the symptoms presented at Baseline (OSDI Scores: from 47.0±22.7 to 23.9±14.7 $p<0.001$ in IC Group and 27.0±16.1 to 17.0±13.7 $p=0.029$ in RC Group, $p<0.05$, Wilcoxon). CCC had a significant reduction at LDV (101µm on ICGroup and 113µm in RCGroup, $p<0.05$), and continued overtime until V12m (195µm and 184µm lower compared to Baseline ($p<0.05$, Wilcoxon). Regarding clinical findings, hyperemia and staining were significantly higher with scleral lens when compared at all follow-up appointments when compared to baseline ($p<0.05$). IC group patients showed higher grades of hyperemia and staining. There were no severe adverse events during the entire follow-up period.
Conclusions: Short-term comfort enhancement promoted by SL remained over the entire follow-up. SL wear was related to higher hyperemia and staining grades when compared to no-lens situation. Despite this, SL can be considered a safe modality as there were no severe adverse-events recorded over the 12-month.

12.2 Introduction

The emergence of modern scleral lenses has changed the contact lens practice and management of corneal disorders and other ocular conditions. Their indications and visual benefits are well kwon and have been described in the literature. [1–4] Also, their stability on-eye and comfort opened a window to prescribe them in healthy eyes seeking for visual corrections as well, particularly in cases of high spherical and/or astigmatic refractive errors.[5,6] The widespread fitting of scleral lenses and the lack of long-term prospective studies has raised other concerns over past few years. Theoretically the hypoxic problems would be minimized with the

change from polymethyl methacrylate (PMMA) to rigid-gas permeable (RGP) contact lens. However, hypoxic effects of modern scleral lenses continue to be a concern among practitioners, and despite some important works on the field, [7–12] the long-term consequences of the exposure to a continuous amount of corneal edema during scleral lens wear remains unknown. Peer-reviewed reports regarding other adverse events and its prevalence during scleral lens wear are scare. [11,13,14] Daddi Fadel [14] and Maria Walker *et al* [11] published works that summarize the few literature reports regarding scleral lens complications (non-severe and severe) and fitting challenges. Apart from hypoxic stress that can be amplified by excessive corneal clearance [7,10], many other issues were reported to occur, though in a smaller scale. A lens with low corneal clearance can end in corneal bearing which will most likely promote lens adhesion, micorcysts, staining, among others.[14,15] Other possible issues can arise from inappropriate alignment of the lens with the limbus and conjunctiva: limbal stem cell deficiency[16], conjunctival impingement and blanching[17,18], conjunctival prolapse[11,14,19], lens deccentration[15,18], lens flexure[20], or midday fogging.[21] When these issues are not correctly evaluated and resolved, some complications may also occur. [11] Although the prevalence is still unknown, one must be aware that there are some reports of scleral lens-related infectious and inflammations events[22–25] and that epithelial microcysts, severe corneal edema, neovascularization, chemosis, giant papillary conjunctivitis, among others adverse events could occur.[11,26] All these matters are assessed clinically in the slit lamp and might have implications in the tolerance of the contact lenses by the patient. Therefore, their careful inspection is of paramount relevance considering the current expansion of the role of modern scleral lenses in clinical practice.

To our best knowledge, no previous studies have reported the slit-lamp findings in terms of fitting aspects, ocular surface findings and symptoms in the medium and long term of clinical samples. The present work aims to report the clinical findings and symptoms over a follow-up period of 12 months in a clinical sample of scleral lens wearers.

12.3 Methods

12.3.1 Study Design and Subjects

This was a prospective clinical study involving patients with primary corneal ectasia, penetrating keratoplasty, post-surgical ectasia and regular corneas with high refractive errors, recruited between December 2015 and March 2017. Ninety-five (95) consecutive patients were recruited to participate in this prospective dispensing case series. The subjects were divided into two groups according to their corneal condition: one group including patients with irregular corneas (IC Group) covering corneas with irregularities due to different etiologies (134 eyes of 71 subjects) and the second group including subjects with regular and healthy corneas (RC Group) with high refractive errors (myopia ≥ 6.00 D; astigmatism ≥ 2.00D, hyperopia ≥ 4.00D) that have failed or rejected other forms of vision correction with contact lenses (46 eyes of 24 subjects).

Following the recommendations of the declaration of Helsinki, all subjects received information from the study before they accept to participate and signed a consent form. The protocol of the study has been reviewed and approved by the Ethics Subcommittee for Life and Health Sciences of University of Minho.

12.3.2 Scleral Lens Used and Fitting Procedure

All patients recruited underwent a full examination (Baseline), which included high and low contrast visual acuity (HCVA and LCVA) with habitual correction (HC) and best spectacle correction (BSC) assessed with ETDRS in LogMAR scale, anterior eye biomicroscopy and corneal topographic analysis with Medmont E300. All patients were fitted with mini-scleral lens from Procornea (Eerbeek, The Netherlands) in Boston XO material. Other technical characteristics of the lenses used are described in previous publications in the context of this study. [5,27] At Baseline, the trial lenses were fitted according to manufacturer's recommendations. The mean trial lenses per eye was previously described (*Macedo-de-Araújo, Learning Curve, BioMed*

International, accepted for publication – Chapter #6). The practitioner had 4 trial-lens sets available: 2 of mini-scleral lens and 2 of full-scleral lens. Trial lenses were inserted with unpreserved-free saline solution and sodium fluorescein (Fluo Strips, Contacare, India). The fitting was evaluated with slit lamp 5 to 10 minutes after lens insertion. If the fit was not satisfactory, another trial lens was inserted. When the best trial lens fitting was achieved, patients were asked to continue with the trial lens for more 90 minutes and then come back for another assessment and to perform over-refraction. After the final assessment, minor adjustments were done and the lenses were ordered. At lens dispensing visit (LDV), the lens fit was evaluated and a new lens was re-ordered if any adjustment was required (*Macedo-de-Araújo, Learning Curve, BioMed International, accepted for publication* – Chapter #6).

12.3.3 Follow-up Evaluations

All the subjects enrolled in this study had to attend several appointments during the 1 year of follow-up: Baseline, LDV - where measurements were performed 10 minutes after lens insertion (LDV1) and after more than 90 minutes of lens wear (LDV2) - 1-month visit (V1m), 3 months visit (V3m), 6 months visit (V6m) and 12 months visit (V12m). After LDV, patients were dispensed with care solutions and an information leaflet explaining all the procedures (care regimen and handling issues). Patients were advised to wear the lenses on a daily basis for a maximum recommended time of 12 hours. Lens care consisted of cleaning, wetting and disinfecting with standard RGP lens cleaner (Boston AdvanceTM Cleaner) and multipurpose solution systems (Boston Simplus). Before lens insertions, patients were instructed to rinse the lenses with unpreserved saline solution in 5 ml unidosis (Avizor, saline unidosis) to remove all the preservatives from the disinfecting solution that was on the lens case, and then fill the lenses to the top with the same unpreserved free saline solution. After lens removal, subjects were instructed to rinse the lenses with lens cleaner, then rinse with saline solution to remove the cleaner and put the lens on the case with the multipurpose solution.

At all follow-up appointments the patients were asked to attend to the visit after at least 90 minutes of lens wear to allow time for lens settling after evaluation.

12.3.3.1 Comfort Assessment

The comfort was assessed with two questionnaires: the Ocular Surface Disease Index (OSDI) and the 8-question Dry Eye Questionnaire (DEQ). [28] Both questionnaires were administrated at all the appointments, including Baseline (symptoms felt with HC) and all the follow-up appointments (from V1m to V12m) where subjects reported the symptoms felt with their scleral lenses. The DEQ was selected instead of the Contact Lens DEQ (CLDEQ) [29] because it allows to be administrated at baseline even without previous CL experience and compare the results over the follow-up time.

The OSDI questionnaire [30,31] is a 12-item questionnaire which are divided into three main categories: symptoms, functional limitations and environmental factors. The OSDI Score is scaled from 0 to 100, with the highest score representing greater disability/ more symptoms. The Total OSDI Score was calculated using the following formula: Total OSDI Score = (sum of the scores of all questions x 100)/(total number of questions answered x 4). According to the Total OSDI Score, subjects were allocated into 4 subgroups: Normal, OSDI Score between 0 and 12; Mild, OSDI Score between 13 and 22; Moderate, OSDI Score between 23 and 32; Severe, OSDI Score greater than 33. The OSDI sub-scores were also recorded according to Mathews *et al* [32] methodology: OSDI Symptom-related score (questions 1 to 3 and 10 to 12) comprising symptoms related to irritation or discomfort and environmental-related scores, and OSDI Vision-related score (questions 4 to 9) comprising the effect on visual functioning. Subscale scores ranged from 0 to 50.

The DEQ was designed to assess the prevalence, frequency and diurnal severity of several ocular surface symptoms. The 8-question version was used in this work and contains questions regarding 8 different symptoms including discomfort, dryness, gritty/ scratchy, burning sensation, itching, foreign body sensation, sore/ irritated eyes, and light sensitivity. Following the criteria of Begley and Caffery *et al* [33], subjects were considered symptomatic when answered the questions regarding frequency with “frequently” or “constantly”. Regarding the questions related to the intensity, where subjects were instructed to grade the intensity of each symptom felt in the morning and at the end of the day, it was considered as “intense” if subjects answered “4” or “5”, and any other response was considered non-intense.

12.3.3.2 On-Eye Lens Fitting

Anterior ocular surface health was assessed with slit lamp (CSL990 Elite 5x Digital Video, CSO, Italy) with scleral lens on-eye and after lens removal. With the scleral lens on-eye, the relationship scleral lens – anterior ocular surface was assessed by means of cornea-lens separation evaluation (comparing the known lens central thickness provided by the manufacturer with the post-lens tear layer thickness) – this is a subjective measure of the central corneal clearance (subjective CCC). Pictures of the cornea-lens relationship were also taken with the built-in slit lamp camera to posteriorly analyze it with Image J 1.52a software (National Institutes of Health, Bethesda, Maryland, USA) with a previously validated technique, [34] which allowed to have an objective measure of the central corneal clearance (objective CCC). It was calculated comparing the known central lens thickness with the cornea-lens separation thickness with the calipers of ImageJ software. This technique also allowed to record the corneal thickness over time in order to find some edema response during the entire follow-up (by comparing the baseline measure – without lens – with the measures taken in each follow-up visit after different wearing times).

The relationship of the haptic lens zone with the sclero-conjunctival region was also assessed during slit lamp evaluation with the lens in situ. A scale was used to grade the degree of impingement or edge lift in all quadrants (nasal, temporal, superior and inferior). The edge lift was judged according to the point of blanching (if noticed) – the more internal (closer to the limbus) the larger the edge lift. Also, illuminating tangentially to the edge (from the opposite side) should provide a sensation of "shadow" on the conjunctiva that will reflect the edge lift. Graphical examples are represented in *Figure 12.1*. Each quadrant was graded from +2 to -2, in 0.5 steps, being +2 a lens with extreme edge lift and -2 a lens with a haptic zone too tight (extreme blanching). If it was graded as 0, the lens was perfectly aligned with the sclero-conjunctival surface.

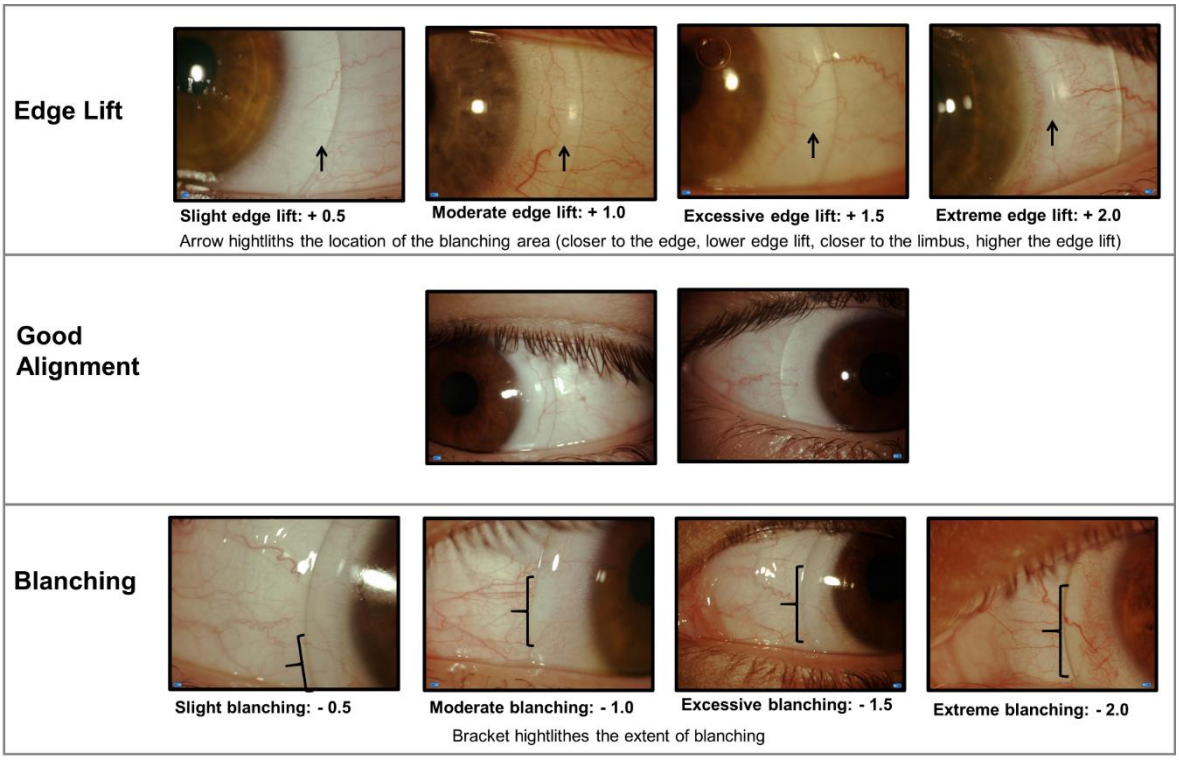

Figure 12.1 Graphical examples of the relationship between scleral lens landing zone and anterior eye surface.

12.3.3.1 Anterior Ocular Surface Health Recording

Bulbar and limbal redness and corneal and conjunctival staining were recorded five to ten minutes after lens removal. This was recorded using the Cornea and Contact Lens Research Unit (CCLRU) Grading Scales (School of Optometry and Vision Sciences – University of South Wales, Australia). This is a photographic scale that comprises four categories that increase in severity of the condition: 0, absent (this is not shown in the CCLRU System); 1, very slight; 2, slight; 3, moderate; 4, severe. All the assessments were conducted by the same experienced examiner (R-MA) and graded in 0.1 steps. The subjects were examined with diffuse white light in the slit-lamp biomicroscope at x10 magnification and in different positions of gaze in order to properly observe and grade the nasal, temporal, superior and inferior quadrants. Both bulbar and limbal hyperemia were also defined as the average of scores of all quadrants.

Corneal staining was assessed 10-20 seconds after sodium fluorescein instillation (Fluo Strips, Contacare, India) using cobalt blue light and yellow filter (written 12) – the cornea was divided into 5 areas (central, nasal, temporal, superior, and inferior) and the staining type, extent and depth of each area was graded:

-Type: (0, no staining; 1, micropunctate; 2, macropunctate; 3, coalescent macropunctate; 4, patch);

-Extent (1, between and 1 – 15% of the surface; 2, between 16 to 30%; 3, between 31 to 45%; 4, >45% of the surface);

-Depth (1, superficial epithelium; 2, deep epithelium, delayed stromal glow; 3, immediate localized stromal glow; 4, immediate diffuse stromal glow).

The scores of the 5 regions for each one of these "categories" were summed to obtain a total corneal staining grading (of type, extent and depth). The results by area where also analyzed to compare with the lens fitting over all quadrants.

12.3.4 Statistical Analysis

Statistical analysis was conducted using SPSS v.25.0 (SPSS, Inc, Chicago, Illinois, USA). Normality of data distribution was assessed with Kolmogorov-Smirnov test. Considering the distribution of variables, parametric or non-parametric tests were used. When comparing different follow-up visits within the same group Paired Sample T-test or Wilcoxon test were performed, according to sample distribution. When comparing the two groups, Unpaired T-test or Mann-Whitnney test were performed, accordingly to the distribution of the variable in analysis. Bonferroni corrections were considered in the analysis that include multiple comparisons. The descriptive values presented are the mean and standard deviations (mean±SD) for each studied variable at all parts of the study. For some results of DEQ, corneal swelling and ocular health recordings, the frequency (%) was analyzed. The level of statistical significance was set at $p<0.05$.

12.4 Results

Visual acuity (LogMAR) with scleral lenses improved significantly when compared to visual acuity with habitual correction: from 0.35±0.33 to 0.08±0.14 in IC group ($p<0.001$, Wilcoxon) and 0.17±0.23 to 0.10±0.23 in RC group ($p<0.05$, Wilcoxon). The average visual acuity at V12m was 0.09±0.13 in IC group and 0.09±0.23 in RC group, reflecting the stability on visual acuity overtime. More detailed results on visual acuity and other visual quality outcomes are presented on Chapter #11.

12.4.1 Comfort: OSDI Scores and DEQ Results

Figure 2A shows the mean OSDI Scores during the entire follow up period for the 2 groups. A statistical significant decrease in the OSDI Scores (meaning less symptoms) is seen when comparing scores recorded at all the follow-up visits in both IC Group ($p<0.001$) and RC Group ($p<0.05$) against baseline. There were no statistical significant differences between the follow-up visits in both groups. Regarding the comparisons between groups, there was a statistical significant differences is OSDI score at Baseline visit ($p=0.033$) and V12m ($p=0.010$), with IC Group showing higher values of symptomatology in all visits. *Figures 2 B* and *C* show the average OSDI sub-scores: symptom-related sub-score (ocular symptoms and environmental triggers) and vision-related sub-score (vision-related functions). In IC Group, statistically significant differences between the Symptom-related sub-scores and the Vision-related sub-scores are show at all follow-up visits but not at Baseline, with Symptom-related issues revealing a higher sub-score. There were statistically significant differences between Baseline and all the follow-up visit regarding the Symptom-related sub-scores ($p<0.001$, paired sample t test) and Vision-related sub-scores ($p<0.001$, Wilcoxon) in IC Group. Regarding Vision-related sub-scores there were also statistical significant differences between V1m and V3m ($p<0.05$, Wilcoxon) and between V1m and V12m ($p<0.05$, Wilcoxon). Regarding RC Group, statistically significant differences between Symptom and Vision-related sub-scores were found at Baseline, V1m, V3m and V6m ($p<0.05$, Wilcoxon). There were statistical significant differences only between Baseline and V3m ($p=0.049$, paired sample t test) and Baseline and V6m ($p<0.05$, paired sample t test) regarding Symptom-related sub-scores and between Baseline and V1m, V3m and V6m ($p<0.05$, Wilcoxon), regarding Vision-related sub-scores.

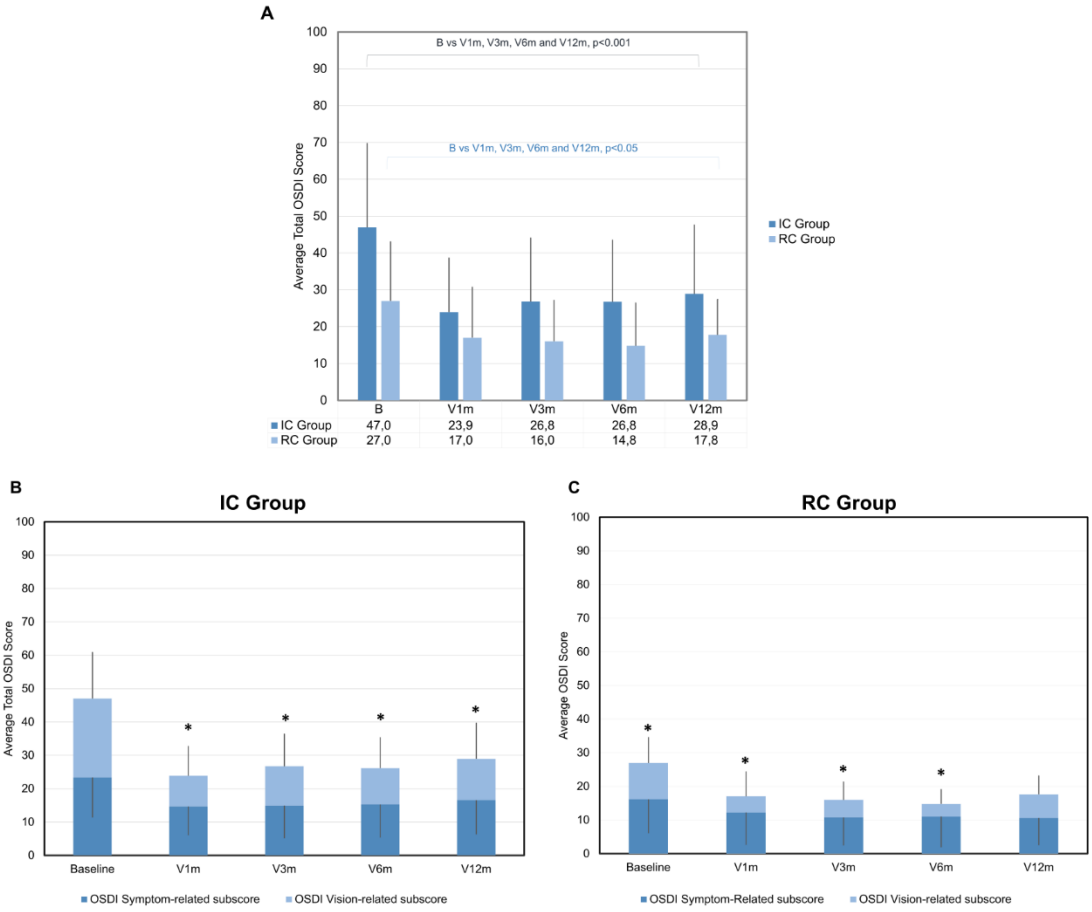

Figure 12.2 (A) Average OSDI Scores for the 68 subjects that completed the 12 months of follow-up; (B) OSDI subscores for IC Group (n=55); (C) OSDI subscores for RC Group (n=14). Statistical significant differences between Symptom-related and Vision-related sub-scores are shown on the images with (*). IC Group - Differences in Symptom-related sub-scores over time: Baseline and V1m, V3m, V6m and V12m ($p<0.001$, paired sample T test) and in Vision-related sub-scores between Baseline and V1m, V3m, V6m, V12m and V3m vs V1m and V1m vs V12m ($p<0.05$, Wilcoxon). RC Group – Differences un Symptom-related sub-scores between Baseline and V3m and V6m ($p<0.05$, paired sample t test) and in Vision-related sub-scores between Baseline and V1m, V3m and V6m ($p<0.05$, Wilcoxon).

Figure 12.3. shows that the great majority (71%) of subjects from IC Group had severe symptoms of dry eye (average OSDI score greater than 33) which decreased to 20% with scleral lens wear (V1m). In RC Group, the proportion of subjects with severe symptoms maintained from Baseline to V1m (21%), but the number of subjects with normal OSDI Scores (average OSDI

Score from 0 to 12) increased from 14% to 50%. The proportion of subjects with severe symptoms.

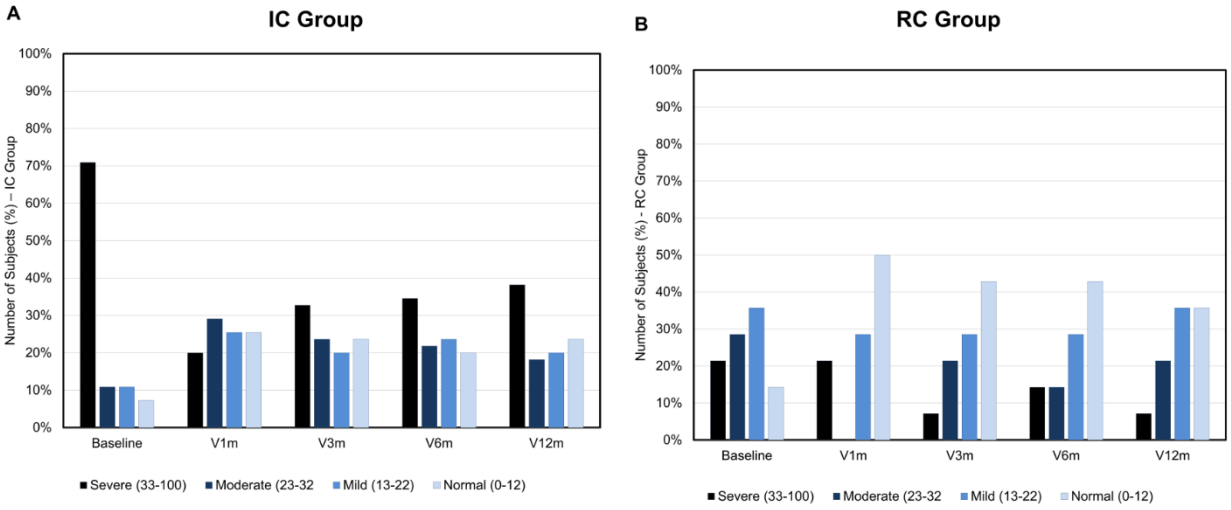

Figure 12.3 Bar chart showing the severity of the symptoms according to the average OSDI Score at the different follow-up appointments in IC Group (A) and RC Group (B). Percentage of subjects shown are proportions within each group (IC Group, n=55; RC Group, n =14).

Table 12.1 shows the percentage of subjects that were considered symptomatic, i.e., that answered "frequently" or "constantly" in the questions regarding the frequency of each symptom in DEQ. Regarding the total sample, all symptoms were more prevalent at Baseline (symptoms felt before enrolling the study, with habitual correction) when compared to V1m (symptoms felt with scleral lenses). Regarding the subjects of IC Group, the most frequent symptoms at Baseline were Discomfort, Dryness and Light sensitivity (prevalence ≥ 70%), which reduced significantly at V1m to a prevalence ≤ 52%. The frequency of all the symptoms decreased with scleral lens wear. Regarding the RC Group, the most prevalent symptoms at Baseline were Discomfort, Burning sensation, Irritated eyes (prevalence ≤ 50%) and Light sensitivity (prevalence of 71%). The great majority of the symptoms underwent a reduction with scleral lens wear, except for Discomfort, Dryness, Sand and Foreign Body sensations. With the exception of Light Sensitivity, all the other symptoms remained equal or worse after 12 months of lens wear, when compared to Baseline values in RC Group.

Table 12.1. Dry Eye Questionnaire (DEQ) outcomes regarding the percent of patients that answered "frequently" or "constantly" in the questions related with the frequency of each symptom. The data are the number of patients reporting each symptom and, in parenthesis, the percentage of patients reporting that symptom to be "frequent" or "constant". Total, n=69; IC Group, n=55; RC Group, n=14.

		BASELINE n (%)	V1m n (%)	V3m n (%)	V6m n (%)	V12m n (%)
Discomfort	Total	55 (80%)	36 (52%)	39 (57%)	37 (54%)	38 (55%)
	IC Group	48 (87%)	28 (51%)	29 (53%)	30 (55%)	31 (56%)
	RC Group	7 (50%)	8 (57%)	10 (71%)	7 (50%)	7 (50%)
Dryness	Total	51 (74%)	28 (41%)	35 (51%)	35 (51%)	39 (57%)
	IC Group	46 (84%)	23 (42%)	28 (51%)	29 (53%)	32 (58%)
	RC Group	3 (36%)	5 (36%)	7 (50%)	6 (43%)	7 (50%)
Gritty/ Scratchy	Total	29 (42%)	12 (17%)	12 (17%)	14 (20%)	14 (20%)
	IC Group	26 (47%)	8 (15%)	9 (16%)	12 (22%)	11 (20%)
	RC Group	3 (21%)	4 (29%)	3 (21%)	2 (14%)	3 (21%)
Burn/ Sting	Total	46 (67%)	25 (36%)	26 (38%)	25 (36%)	30 (43%)
	IC Group	39 (71%)	21 (38%)	19 (35%)	20 (36%)	22 (40%)
	RC Group	7 (50%)	4 (29%)	7 (50%)	5 (36%)	8 (57%)
Itching	Total	44 (64%)	35 (51%)	36 (52%)	29 (42%)	26 (38%)
	IC Group	41 (75%)	34 (62%)	32 (58%)	26 (47%)	23 (42%)
	RC Group	3 (21%)	1 (7%)	4 (29%)	3 (21%)	3 (21%)
Foreign Body	Total	24 (35%)	11 (16%)	17 (25%)	14 (20%)	13 (19%)
	IC Group	23 (42%)	9 (16%)	15 (27%)	12 (22%)	9 (16%)
	RC Group	1 (7%)	2 (14%)	2 (14%)	2 (14%)	4 (29%)
Sore/ Irritated	Total	45 (65%)	31 (45%)	34 (49%)	39 (57%)	41 (59%)
	IC Group	38 (69%)	26 (47%)	27 (49%)	33 (60%)	32 (58%)
	RC Group	7 (50%)	5 (36%)	7 (50%)	6 (43%)	9 (64%)
Light Sensitivity	Total	57 (83%)	33 (48%)	27 (39%)	32 (46%)	34 (49%)
	IC Group	47 (85%)	28 (51%)	23 (42%)	27 (49%)	29 (53%)
	RC Group	10 (71%)	5 (36%)	4 (29%)	5 (36%)	5 (36%)

At Baseline, all the symptoms that were considered intense (answers "4" or "5") where worse at the end of the day (*Figure 12.4*). Almost all the subjects of IC Group who reported to feel Light Sensitivity at Baseline, referred that this was very intense both in the morning and in the afternoon. As seen of *Table 12.1*, the prevalence of subjects that reported to feel light sensitivity (severe) decrease from 85% to 51%, and also the intensity of the condition has decreased.

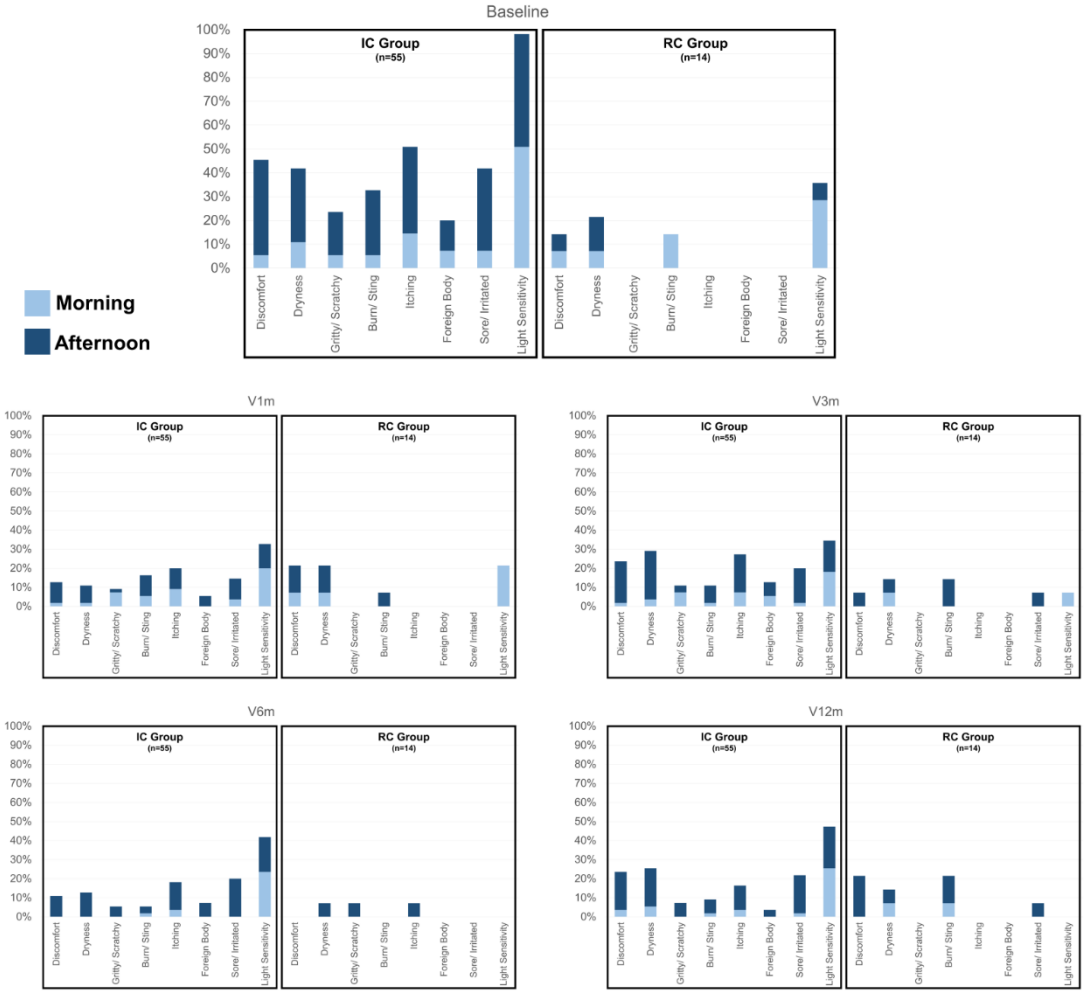

Figure 12.4 Dry Eye Questionnaire (DEQ) regarding the percentage of patients with intense (4 or 5) dry eye symptoms at the beginning of the day (light color) and the end of the day (darker color) for each one of the symptoms at the different follow-up visits. The intensity of the symptoms were recorded in the morning an evening and here are represented the percentage of subjects that answered "4" or "5" regarding intensity (intense and very intense).

12.4.2 On-Eye Lens Fitting

Patients were evaluated with the lens on-eye at each follow-up visit. The haptic zone (*Figure 12.5*), central corneal clearance (CCC – *Figure 12.6*) and corneal thickness changes regarding Baseline (*Figure 12.7*) were recorded through time.

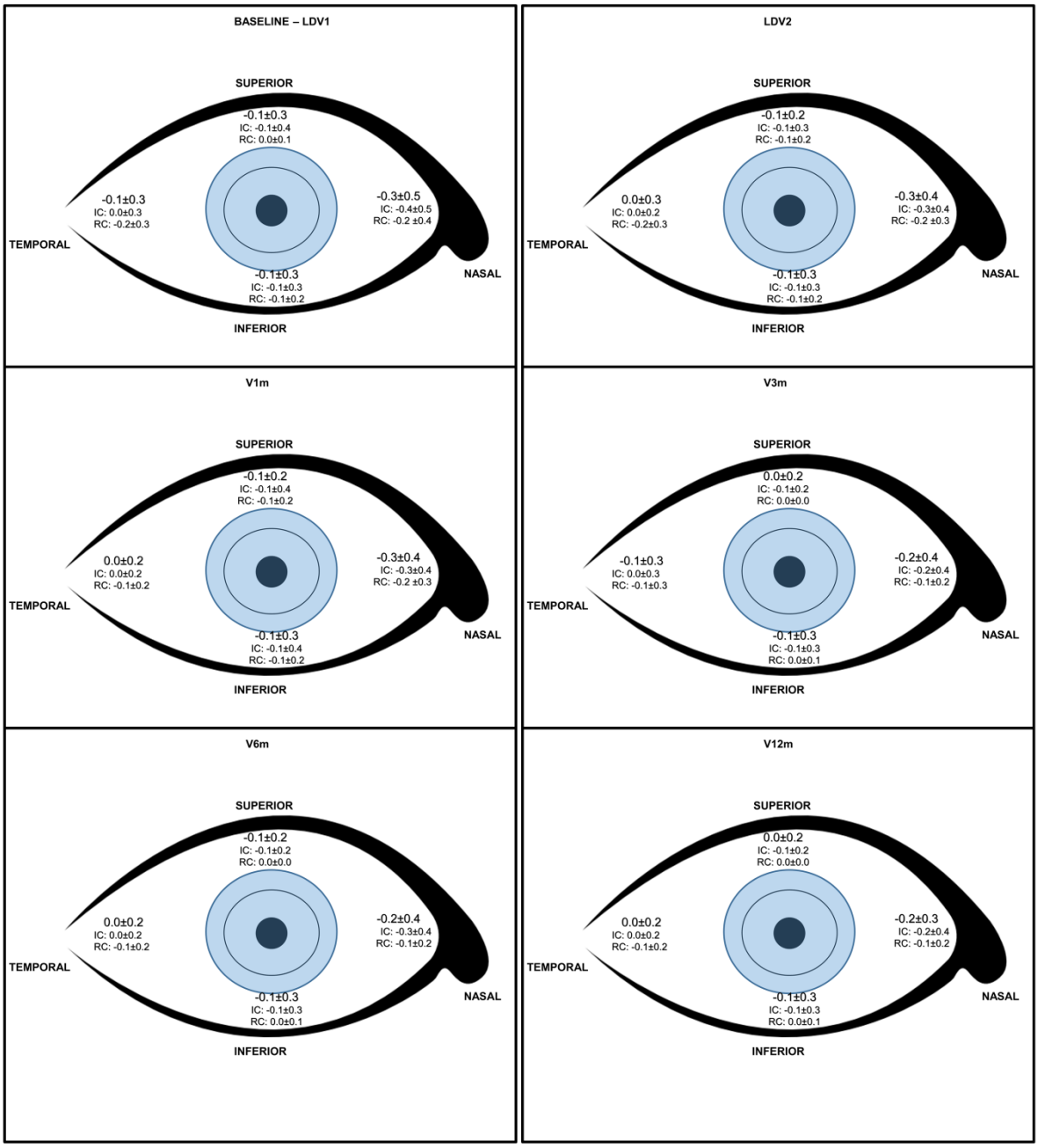

Figure 12.5 Haptic zone alignment during the entire follow-up period, -2 means extreme compression, -1 compression, 0 perfect alignment, +1 edge lift, +2 extreme edge lift. The mean±SD is present for each quadrant (nasal, temporal, superior and inferior) for each one of the follow-up visits.

Haptic zone alignment (*Figure 12.5*) preserved the same characteristics overtime, without statistical significant differences. The average values where slightly negative, indicating the tendency to have a slight conjunctival blanching (*Figure 12.1*), namely on the inferior and nasal areas.

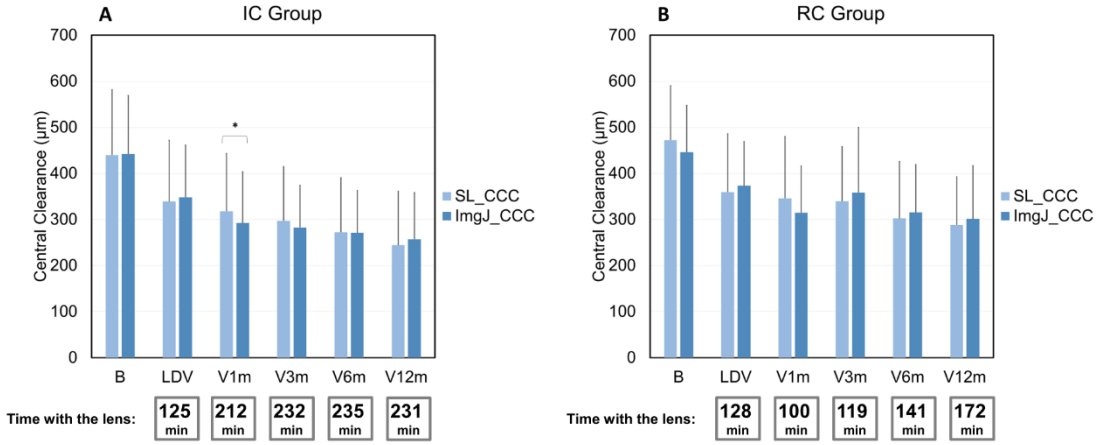

Figure 12.6 Values (in microns) of central corneal clearance (CCC) measured with slit lamp and ImageJ in IC Group (A) and RC Group (B). Underneath each graphic is represented the mean wearing time (in minutes) at each follow-up appointment (time of lens wear at the moment subjects arrived to the appointment). IC Group Subjective measure – Statistical significant differences between all visits in pairwise comparisons ($p<0.001$, Wilcoxon); IC Group ImageJ measure – Statistical significant differences between all visits ($p<0.05$, paired sample T-test) with exception of V3m vs V6m; RC Group Subjective measure – Statistical significant differences between Baseline and all follow up visits ($p<0.05$, Wilcoxon) and between V1m and V6m & V12m ($p<0.05$, Wilcoxon); RC Group ImageJ measures – Baseline and V1m, V6m & V12m ($p<0.001$, Paired Sample T-test) and between LDV2 and V1m, V6m & V12m ($p<0.05$, Paired Sample T-test).

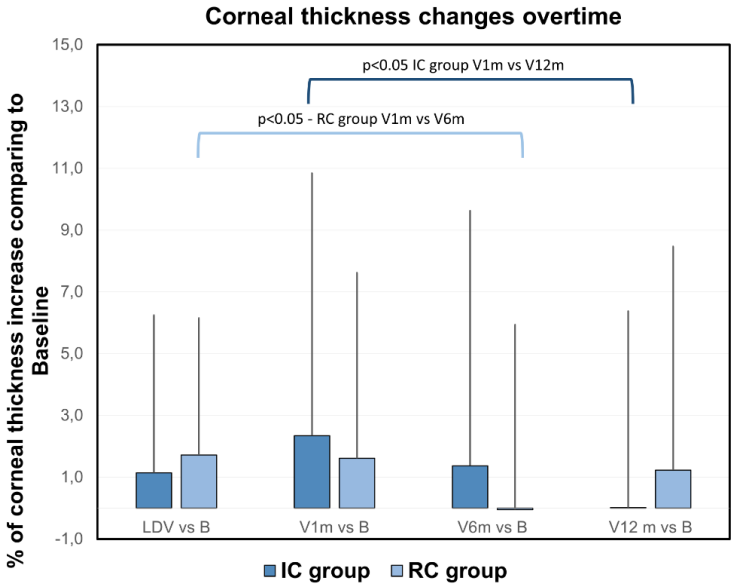

Figure 12.7 Mean percentage (%) of corneal swelling at each follow-up time with respect to Baseline measurements. The mean wearing time (in minutes) of lens wear at each follow-up visit are represented on *Figure 12.6*.

Regarding the central corneal clearance (CCC- *Figure 12.6*), the subjective – CCC (slit lamp) and objective-CCC (ImageJ) were on average very similar, with only one statistical significant difference between them at V1m in IC Group (p=0.018, paired sample t test). Statistically significant differences between Baseline measure (right after lens insertion) and LDV measure (at the same day, after >90 minutes of lens wear) were found in IC Group and RC Group in both subjective and ImageJ measures. Regarding IC group, mean CCC decrease was 101 µm (subjective measure) and 94 µm (ImageJ measure) and was 113 µm (subjective measure) and 73 µm (ImageJ measure) in RC Group. There were also statistically significant differences between follow-up visits, with a tendency for a decrease in CCC overtime in both groups.

Regarding the corneal thickness (*Figure 12.7*), there was an increase in the corneal thickness between the baseline measure and at the end of LDV, with mean short-term corneal swelling of 1.1±5.1% in IC group and 1.7±4.4% in RC group (average wearing times of 125 and 128 minutes, respectively). Corneal thickness increases with respect to baseline measure were continually <3 %. At V12m the mean corneal thickness was the same as Baseline in IC group (mean increase of 0.02±6.37%) and 1.2% higher in RC group.

12.4.3 Anterior Ocular Surface Health Recording

Figure 12.8 represents the mean values of limbal and bulbar redness in the four quadrants analyzed at all the follow-up appointments. Regarding the average values of all the zones analyzed, there are differences between all appointments in limbal and bulbar redness ($p<0.001$, Friedman), corneal staining relating to type, extent and depth ($p<0.001$, Friedman) and conjunctival staining ($p<0.001$, Friedman) – these differences are namely between Baseline and all the follow-up appointments ($p<0.001$, Wilcoxon).

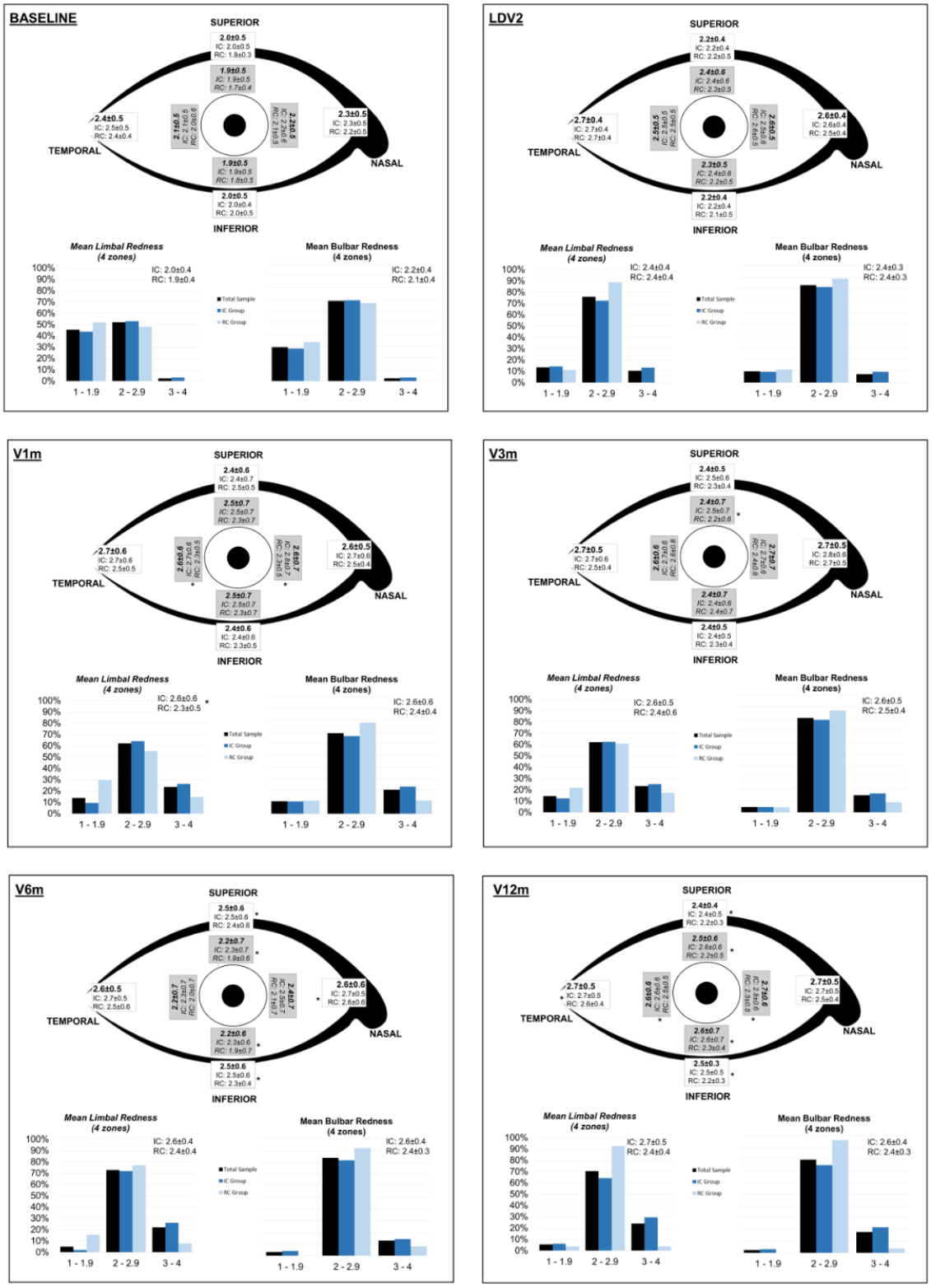

Figure 12.8 Mean values of limbal and bulbar redness in the four quadrants analyzed (images) and frequency of each score in mean for each group (bar charts). Results are the mean of the Total Sample (IC Group and RC Group). Results per appointment: Lens dispensing visit before scleral lens wear (Baseline), Lens Dispensing Visit after lens wear (LDV2), 1-month visit (V1m), 3 months visit (V3m), 6 months visit (V6m) and 12 months visit (V12m). * represents the differences between the two groups.

Figure 12.9. shows the frequency observed of each one of corneal staining grades regarding type (A), depth (B) and extent (C). The frequency of Type 1 (range: 1 to 1.9) and Type 2 (range: 2 to 2.9) corneal staining suffered a slight increase at V1m when compared to Baseline, and remained within the same frequency during the follow-up visits. Regarding Depth (B), an augment was observed in V3m for Type 1, which decreased in the subsequent visits to values similar to V1m. Regarding Extent (C), the frequency of Type 2, 3 and 4 was higher from V1m to V12m when compared to Baseline.

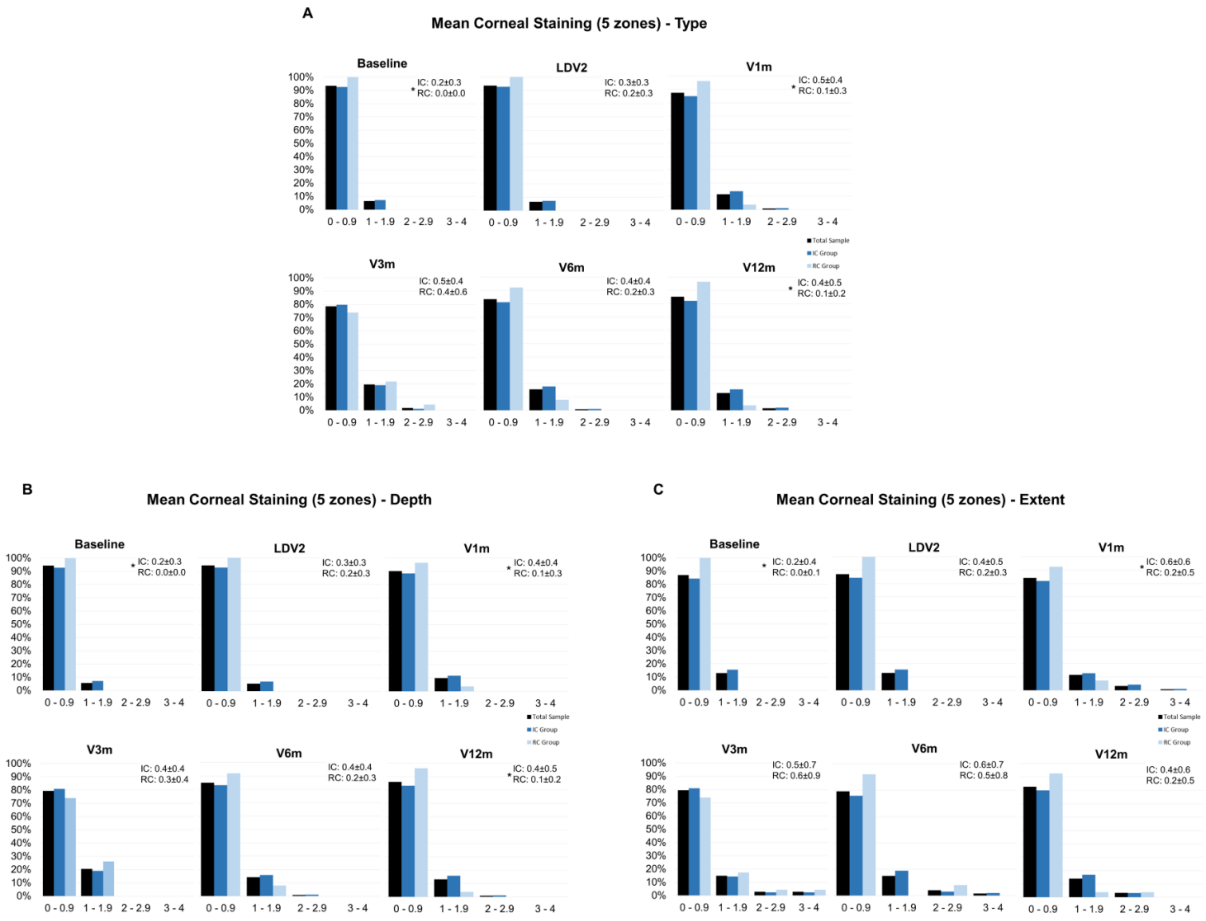

Figure 12.9 Frequency of each one of corneal stainning grades regarding type (A), depth (B) and extent (C). The mean of the 5 corneal zones was considered for this analysis.

Table 12.2 show the mean conjunctival staining recorded over the 12 months of follow-up. Conjunctival staining at different quadrants analyzed was significantly higher during all the follow-up visits comparing to Baseline condition ($p<0.001$, Wilcoxon) and was statistically higher on IC group.

Table 12.2. Conjunctival staining records over the 12 months of follow-up. The mean±SD is represented for each one of the quadrants analyzed (nasal, temporal, superior and inferior).

		Baseline	LDV2	V1m	V3m	V6m	V12m	*p*
Nasal	Total Sample	1.46±0.63	2.31±0.62	2.23±0.69	2.40±0.68	2.45±0.65	2.36±0.71	<0.001 ▵ * Baseline vs LDV2, V1m, V3m; V6m, V12m; V1m vs V12m
	IC Group	1.52±0.66	2.32±0.65	2.32±0.67	2.47±0.66	2.55±0.63	2.41±0.72	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V6m; V1m vs V6m
	RC Group	1.25±0.44	2.27±0.55	1.91±0.65	2.13±0.73	2.08±0.57	2.19±0.67	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V1m
p †		***0.037***	*0.642*	***0.005***	*0.078*	***0.001***	***0.034***	
Temporal	Total Sample	1.39±0.56	2.22±0.65	2.18±0.73	2.25±0.67	2.39±0.68	2.23±0.72	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V6m; V1m vs V6m
	IC Group	1.44±0.60	2.26±0.64	2.32±0.70	2.31±0.65	2.50±0.65	2.31±0.73	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; V6m vs LDV2, V12m
	RC Group	1.20±0.27	2.09±0.69	1.71±0.63	2.02±0.70	1.99±0.64	1.98±0.66	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m;
p †		*0.068*	*0.279*	***<0.001***	*0.173*	***0.001***	***0.027***	
Superior	Total Sample	1.230.45	1.97±0.53	2.13±0.75	2.21±0.68	2.41±0.71	2.25±0.74	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V1m, V3m, V6m, V12m; V6m vs V1m, V3m, V12m
	IC Group	1.28±0.49	2.03±0.52	2.28±0.72	2.30±0.68	2.49±0.72	2.33±0.77	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V1m, V3m, V6m, V12m; V6m vs V1m, V3m, V12m
	RC Group	1.06±0.16	1.77±0.54	1.60±0.58	1.86±0.61	2.13±0.58	1.97±0.60	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; V1m vs V6m, V12m; V3m vs V12m
p †		***0.014***	***0.049***	***<0.001***	***0.011***	***<0.001***	***0.016***	
Inferior	Total Sample	1.27±0.48	1.97±0.60	2.12±0.72	2.19±0.65	2.33±0.68	2.24±0.73	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V3m, V6m, V12m; V6m vs V1m, V3m
	IC Group	1.30±0.51	2.02±0.61	2.26±0.67	2.27±0.62	2.43±0.68	2.32±0.76	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V1m, V3m, V6m, V12m; V3m vs V6m
	RC Group	1.15±0.33	1.80±0.52	1.64±0.69	1.89±0.66	1.95±0.51	1.97±0.56	<0.001 ▵ * Baseline vs LDV2, V1m, V3m; V6m, V12m; V12m vs V1m, V3m
p †		*0.180*	*0.127*	***<0.001***	***0.020***	***0.030***	***0.035***	
Mean (4 zones)	Total Sample	1.34±0.49	2.12±0.49	2.17±0.65	2.26±0.58	2.40±0.59	2.27±0.65	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V6m, V12m; V6m vs V3m, V12m
	IC Group	1.39±0.53	2.16±0.48	2.29±0.61	2.34±0.55	2.49±0.58	2.34±0.66	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; LDV2 vs V1m, V3m, V6m, V12m; V6m vs V1m, V12m
	RC Group	1.16±0.21	1.98±0.49	1.72±0.58	1.98±0.60	2.04±0.46	2.03±0.56	<0.001 ▵ * Baseline vs LDV2, V1m, V3m, V6m, V12m; V1m vs LDV2, V6m, V12m; V3m vs V12m
p †		*0.081*	*0.106*	***<0.001***	***0.033***	***0.034***	***0.016***	

*IC – Irregular Cornea group; RC – Regular Cornea group; †Mann-Whitney test – comparison between IC and RC groups; ▵ Friedman test – comparison between all visits; * Wilcoxon – pairwise comparison between visits*

Table 12.3. Non-severe adverse events reported by the patients and/or observed by the clinician recorded over the 12 months of follow-up. No severe adverse events were observed.

Dia – Lens diameter; LP – lens periphery alignment; CCC – central corneal clearance

Issue	Number of Eyes	Group	Visit	Fitting characteristics at the Visit where the Issue was reported / observed	Description of the event
Conjunctival Prolapse	2	IC	V1m	Dia: 20mm LP: good peripheral alignment CCC: 350 µm RE; 300 µm LE (90 min of lens wear)	Aggravation of conjunctival prolapse (present at Baseline, previous full SL wearer)
	2	RC	V12m	Dia: 16.4mm LP: good peripheral alignment CCC: 200 µm RE; 280 µm LE (330min of lens wear)	Onset of visible inferior conjunctival prolapse observed during slit lamp examination
	1	IC	V12m	Dia: 16.4mm LP: infero-nasal slight blanching (-0.5) CCC: 200 µm LE (360min of lens wear)	
	2	IC	V6m	Dia: 16.4mm LP: good peripheral alignment CCC: ~ 150 µm RE; 180 µm LE (420min of lens wear)	
	2	IC	V6m	Dia: 15.2 mm LP: good peripheral alignment CCC: 100 µm RE & LE (240min of lens wear)	
	2	IC	V6m	Dia: 16.4 mm LP: good peripheral alignment CCC: 180 µm RE; 120 µm LE (360min of lens wear)	
Conjunctival Prolapse TOTAL	6 patients (8.7%) 11 eyes (8.7%)				
Handling-related issues	1	IC	V3m	Dia: 16.4 mm LP: good peripheral alignment CCC: 450 µm RE; 400 µm LE (90min of lens wear)	Corneal Erosion: Reported by the patient at V3m (but happened 1 month). Recovered after temporary discontinuation without further treatment.
	1	IC	V1m	Dia: 16.4 mm LP: good peripheral alignment CCC: 20 µm RE; 300 µm LE (300 min of lens wear)	Difficulties removing the lens. Reported eye redness and discomfort for 2 days that recovered after temporary discontinuation of scleral lens wear without further treatment. No ocular signs neither visual changes at the time of the appointment.
	2	IC	<V3m	Dia: 16.4 mm LP: good peripheral alignment CCC: 350 µm RE; 250 µm LE (150min of lens wear)	Patient called complaining strong difficulties in removing the lenses. Reported eye redness and discomfort in the next day that recovered without further treatment.
	2	IC	< V3m	Dia: 16.4 mm LP: good peripheral alignment CCC: 350 µm RE; 250 µm LE (150min of lens wear)	Extreme lens suction requiring the help of the practitioner to remove both lenses. Reported eye redness and discomfort in the next day that recovered without further treatment.
	1	IC	V6m	Dia: 16.4mm LP: infero-nasal slight blanching (-0.5) CCC: 250 µm LE (120min of lens wear)	Was wearing the lens with a big air bubble for more than 5 hours. Big discomfort and corneal staining.
	1	IC	V12m	Dia: 16.4mm LP: good peripheral alignment CCC: 250 µm LE (120min of lens wear)	Superficial epithelial erosion during lens removal (after wearing the lenses for more than 16 hours), which recovered after 1 weak without wearing the lenses and topical medication.
	2	IC	V6m	Dia: 16.4mm LP: nasal and inferior slight blanching (-0.5) CCC: 250 µm RE; 180 µm LE (120min of lens wear)	Superficial epithelial erosion during lens removal. Patient reported extreme redness, discomfort and photophobia and was 3 weeks without using the lens and with topical medications. No visual reduction.
	2	IC	V12m	Dia: 16.4mm LP: nasal, temporal, inferior and superior slight blanching (-0.5) CCC: 120 µm RE & LE	Subject stated that didn't remove the lenses for more than 1 week. She was doing that, without informing the practitioner, for about 1 month, because she said she felt the eyes "tired" after removing the lenses.
Handling-related Issues (TOTAL)	8 patients (11.6%) 12 eyes (9.5%)				
Other issues	1	IC	V1m	Dia: 15.2 mm LP: good peripheral alignment CCC: 450 µm RE & 380 µm LE (150min of lens wear)	Corneal hypoxic signs potentially related with high CCC. Re-fitted with new scleral lens with lower sagittal height. No further hypoxic signs observed, no visual reduction associated with the event.
	2	IC	V3m	Dia: 15.2 mm LP: good peripheral alignment CCC: 100 µm RE & LE (240min of lens wear)	Limbal staining – the subjects claimed to have used tap water to clean the lens early that morning. Also stated that he knew that was forbidden to use tap water on sclerals.
	2	RC	V3m	Dia: 15.2mm LP: good peripheral alignment CCC: 150 µm RE; 80 µm LE (360min of lens wear)	Corneal staining related to toxicity to the care system/ insufficient lens rinsing before insertion.
	1	RC	1 day*	Dia: 15.2mm LP: good peripheral alignment CCC: 370 µm (30min of lens wear)	On-eye lens breakage without compromise for the ocular surface. (Macedo-de-Araújo *et al*)
Other Issues (TOTAL)	4 patients (5.8%) 6 eyes (4.8%)				

12.4.1 Adverse Events Reported Over the 12-months of Scleral Lens Wear

Table 12.3 summarizes the issues reported over the 12 months of follow-up. Some issues were encountered in 26.1% of the participants of the study: 8.7% had conjunctival prolapse onset/ aggravation during the follow-up, 11.6% had handling-related issues and other non-severe events were reported in more 5.8% of the subjects. Apart from those, 5 subjects broke the lenses (6 lenses) during the follow-up during lens rinsing or because the lens fell into the floor. (*Macedo-de-Araújo R, Learning Curve, BioMed Research – accepted for publication, Chapter #6)* One patient (listed in *Table 12.3*) suffered an on-eye breakage by an impacting speeding object without compromise to the ocular surface. [5]

12.5 Discussion

12.5.1 Comfort

As scleral lenses do not contact with the highly innervated corneal surface, well-fitted scleral lenses are typically comfortable for the wearer since there is lack of lens awareness. Previous works have already confirmed the comfort enhancement promoted by scleral lens wear in different cases. [35] However, comfort is somewhat subjective and it is worth to have an initial comfort score to compare with. Yan *et al* referred that all eyes were comfortable at the beginning of scleral lens wear and that 91% maintained the comfort at 3-month appointment. [36] Lee *et al* [35] administered OSDI questionnaire prior scleral lens fitting and after several months of lens wear by telephone and concluded that the average OSDI score improved significantly (from 58.42±46.22 to 18.99±17.93). In the present study, patients' comfort was assessed by means of two different questionnaires that were administrated at Baseline (symptoms with habitual correction - HC), and later at each one of the follow-up appointments (V1m to V12m). This way, it was possible to have a chronological overview of the symptomatology, and not only at a specific moment in time. Regarding Total OSDI Scores, it is clearly seen on *Figure 12.2* the reduction in the symptomatology with scleral lenses when compared to baseline score, in both group of subjects (from 47.0±22.7 to 23.9±14.7 $p<0.001$ in IC Group and 27.0±16.1 to 17.0±13.7

p=0.029 in RC Group). As there were no statistically significant differences between the follow-up visits, it is possible to confirm that the comfort ratings remained stable after V1m (average OSDI score at V12m: 29.0±18.6 in IC group and 17.6±9.8 in RC group, p>0.05). The number of subjects with Severe OSDI score symptoms (OSDI scores > 33) at V12m was higher on IC group than on RC group (*Figure 12.3*). This could be related to the higher wearing times and number of days of lens wear by the subjects of IC Group. (*Macedo-de-Araújo, Success Rate, submitted to publication – Chapter #10*). As OSDI questionnaire provides questions related to ocular symptoms but also related to visual concerns, it is important to know in which category of symptoms there is a great reduction. Results show that the reduction was majorly observed in the vision-related sub scores, which is in accordance with the visual acuity enhancement promoted by these lenses with respect to HC.

Similar to OSDI score results, DEQ scores showed that the great reduction in symptomatology occurs in IC group patients. In fact, those patients are the ones that are aiming to wear scleral lenses to reduce their visual and symptom complaints. *Figure 12.5* shows the frequency of subjects with "intense" symptoms (answered 4 or 5 in the questionnaire) in the morning and in the afternoon. Light sensitivity was the most frequent symptom felt with high intensity at Baseline by IC Group subjects, which decreased significantly with scleral lens. Light sensitivity might reflect night vision disturbances commonly seen in a higher extent in subjects with high order aberrations (HOAs), such as irregular cornea patients. As scleral lenses partly correct the HOAs of these eyes, it is expected that patients will experience a reduction in light sensitivity along with an improvement in visual acuity. [37] The impact of scleral lenses in night visual disturbances could be the object of more specific studies. To authors' knowledge there are no results on peer-review literature reporting symptomatology records with these questionnaires over a 12-month follow-up period. The results of both questionnaires show a reduction in the symptomatology with scleral lenses over a short-term and that there is a tendency to augment the symptom scores over time, although without statistically significant differences.

12.5.2 On-Eye Lens Fitting

Regarding the lens alignment with the ocular surface, no significant changes were seen over the follow-up period. These were the expected results since the authors did not expected the sclera to change its shape/ anatomy over this follow-up period. There could have been some factors, such as lens flexure or changes in scleral structure or conjunctival inflammation, that could change this lens – scleral relationship. However, these results reveal that the on-eye lens fitting is expected to be stable over time with regard to lens alignment with the sclera and that there is a tendency of the practitioner to fit more tight lenses. However, the average values are <-0.5, meaning that the lens is well aligned or with slight blanching, namely in the nasal and inferior zones, which are coincidental with the zones where the sclera is flatter. [18,38,39]

It is already known that central corneal clearance (CCC) decreases during scleral lens wear, [34,40–44] but such information has not been previously reported over longer periods in clinical samples. In the present study (*Figure 12.6*) a decrease is seen over the short-term (LDV) in both groups. The mean decrease was 101µm after 125±68min of lens wear in IC group and 113µm after 128±57min of lens wear on RC group (measured subjectively with slit lamp). This settling time over approximately 120 minutes of lens wear was higher than those reported in previous studies. Several studies reported different amount of settling with different lens designs after 8 hours (480 minutes) of lens wear. Caroline *et al* [42] found a settling of 96 µm, and Kauffman *et al* [40] found different settlings with different lens designs, which ranged from 88.1 and 133.7 µm. The authors also concluded that settling occurs namely in the first 4 hours of lens wear [40,43,45], but the greater amount of settling is seen within the first 120 minutes of lens wear. Other study concluded that practitioners can evaluate the lens 30 min post insertion and estimate the amount of total settling by doubling the value obtained. [41] However, all studies revealed great inter and intrasubject variability which demonstrates the importance of considering a proper time period to observe scleral lens settling before final prescription. Kauffman *et al* hypothesized in their work that scleral lenses could undergo also a long-term settling, which could occur over months or years of lens wear. [40] In the present study, a statistically significant decrease in CCC over time was also observed in both groups: at V12m, the mean CCC was 195µm and 184µm lower than the values measured at Baseline in IC and RC groups, respectively. As the mean lens wearing times at the time of the appointments were similar between visits of the same group of patients, these statistically significant differences in

CCC overtime could be related to a long-term scleral lens settling. Both techniques used to estimate CCC – the subjective measure with slit lamp and the image processing technique [34] – showed similar values, with only one statistical significant difference between techniques on LDV in RC Group ($p<0.005$). With the same image processing technique and following previously described methodology [34], the corneal thickness was also assessed (*Figure 12.7*). Following the concerns of hypoxic effects during scleral lens wear, previous studies already measured corneal thickness changes over the short term. After 3 hours of lens wear, Vincent *et al* [46] found a 0.85% swelling (5 µm), and after 8 hours of lens wear, Esen *et al* [43] revealed a corneal swelling of 1.3% (between 6.4 and 10.4 µm). Other authors found a central corneal swelling between 2.4-3.5% after 3 hours of daywear and 4.9-17.4% with extended wear of scleral lenses. [47] Similarly, other study concluded that modern scleral lenses evoke less that physiological hypoxic swelling (< 4%), however closed-eye scleral lens wear appeared to be unsafe. [48] As discussed in scleral lens settling, there is also no reports regarding corneal thickness changes over long-term scleral lens wear. It is important to know if the previously reported corneal swelling is present over a long follow-up time and which are the consequences of this continued edema. In the present study, it is observed an augment in corneal thickness at lens dispensing visit - increase of 1.14% (5µm) after 125 minutes of scleral lens wear in IC group and 1.7% (10 µm) after 128 minutes of lens wear in RC Group. These results confirm that there is a corneal swelling followed short term scleral lens wear. The corneal thickness values were also assessed at all appointments, showing that at V1m, the corneal thickness also suffered an augment with respect to Baseline values (corneal swelling of 2.3% in IC group and 1.6% in RC group). Here, the corneal swelling was higher on IC Group, probably because the patients were evaluated after more hours of lens wear – 212min vs 100min. Patients included in IC Group went to all the follow-up appointments with the lens on-eye for more hours than RC Group – in fact, IC Group patients wore the lenses more hours per day (on average – Chapter #10). Also, the great majority of RC Group patients were from Braga, while IC Group patients lived in other cities of Portugal – which meant that more time was needed for displacement to the local of the appointment. Notwithstanding, after V1m, corneal thickness values began to decrease, and at V12m the value was very similar to the value encountered at Baseline in IC group (mean corneal swelling of 2µm) and that was statistically significant lower than the value encountered at V1m ($p=0.045$, Wilcoxon). Regarding RC Group, the corneal thickness values measured with ImageJ maintained below 2% over the 12 months of follow-up.

12.5.3 Anterior Ocular Surface Health Recording

Following lens removal, conjunctival and limbal hyperemia and conjunctival and corneal staining were assessed. Both limbal and conjunctival hyperemia augmented after short-term scleral lens wear (Baseline vs LDV) and also overtime (V1m to V12m) in all the four main quadrants analyzed and in both groups. The hyperemia assessment was performed after lens removal, which could somewhat augment the hyperemia response - rebound hyperemia – which could have an inflammatory etiology. [14,49] Regarding conjunctival staining, it was significantly higher at all appointments when compared to Baseline (*Table 12.2*). IC group showed also higher values than RC groups, with punctual statistically significant differences between them – this could be related to the higher hours per day and days per week of lens wear of IC group when compared to RC Group (*Macedo-de-Araújo et al, submitted to publication*).

Some clinical reports and clinical experience of some scleral lens fitters around the world have enumerated a series of adverse events (non-severe and severe) that could happen during scleral lens wear. [11,14,23] Severinsky *et al* [23] reported several complications related to graft rejection in their clinical sample wearing scleral lens after penetrating keratoplasty and two eyes that had microbial keratitis episode. Other complications were edema and corneal erosions. In contrast, Montalt *et al* [50] reported lack of adverse events including hyperemia, vascularization and corneal damage, however none of them were quantified during the result section of the article. In the present study, no severe adverse events were reported over the 12-month follow-up period. Most of the events were reported by the patients and the practitioner didn't have the opportunity to take an action on them, since the patients only reported the issues when they came to the next appointment and after issue resolution. Despite that, none of the issues encountered during the follow-up visits led to scleral lens discontinuation. Most of them were handing-related issues that led to superficial corneal lesions (11.6%). Other issues were related to the onset or aggravation of conjunctival prolapse (8.7%). This benign complication was already reported in 1 out of 33 eyes (3%). [23] Although conjunctival prolapse was related to high CCC and tight peripheral landing zones, [11] in the present study this issue was also found in properly fitted lenses (good alignment and CCC within the desired values), which indicates that there is a patient-related factor to develop this kind of issues ("rigidity" of conjunctival tissue, ocular surgeries, age...). [11,51,52] None of the patients self-reported discomfort neither esthetical problems related to the conjunctival prolapse incidence. The lack of complicated

adverse events could be related to lens characteristics and proper fitting – use of high oxygen permeable materials, correct alignment with the scleral surface, and CCC within the desired values. Also, the periodic appointments (V1m, V3m, V6m, and V12m) could have been an important factor in preventing some issues, since patients were always reminded of care compliance and handling topics.

12.6 Conclusions

In conclusion, the visual and comfort enhancement promoted by scleral lens wear over the short-term, continued over the 12 months of follow-up. Despite that, scleral lens wear was related to higher hyperemia and staining when compared to no-lens situation (baseline). The known short-term cornea-lens separation decrease was observed, but it seems that these lenses undergo a long-term settling as well. Corneal swelling was continually <3% with respect to Baseline measure in both groups. Scleral lenses were a safe visual correction modality in both groups (irregular and regular corneas), since no severe adverse events were recorded over the 12 months of follow-up. The issues reported were related to handling problems or conjunctival prolapse onset/ aggravation.

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Chapter 13

Influence of Scleral Lens Wear on Conjunctival Goblet Cells: A Pilot Study

This study was conducted at Universidad Complutense de Madrid. I would like to thank to Maria Serramito-Blando and Gonzalo Carracedo for the help during these measurements.

13. Influence of Scleral Lens Wear on Conjunctival Goblet Cells: A Pilot Study

13.1 Abstract

Purpose: To evaluate the differences in goblet cell density (GCD) and mucin cloud amplitude (MCA) between superior and inferior bulbar conjunctiva and to evaluate the effect of scleral lens wearing time (months) in CGD and MCA.
Methods: A total of 26 eyes randomly selected from 26 subjects (11 females) with different grades of keratoconus (KC) enrolling in a prospective clinical series were analyzed. The subjects were divided into two groups, according to the time (in months) of lens wear: Group I included 15 eyes that were wearing scleral lenses for ≤ 4 months (range: 1 to 4 months) and Group II included 11 eyes that were wearing scleral lenses for > 4 months (range: 6 to 18 months). Superior and Inferior conjunctival impression cytology, combined with scanning laser confocal microscopy (LCM) were performed to evaluate GCD and MCA.
Results: There were no differences in symptomatology (OSDI score) between both group of subjects (24.65 vs 22.21, p=0.878 Mann-Whitney). Regarding the differences of GCD and MCA between the samples taken in superior and inferior conjunctiva, there were no statistical significant differences in both groups. Regarding the comparison between groups, the mean GCD was higher on Group 1 than Group 2, but without statistical significant differences. The MCA remained unchanged with respect to scleral lens wearing time.
Conclusions: Scleral lens wear might have some implications on goblet cells density in the superior conjunctiva, but seem to not affect the mucin secretion. The mean GCD and MCA was higher on the superior zone than on the inferior zone for subjects wearing the lenses for less than 4 months. Subjects that were wearing the lenses for more than 6 months showed less GCD on the superior zone, although with no statistical significant differences.

13.2 Introduction

Keratoconus (KC) is a bilateral, progressive and asymmetric ectatic disorder that alters the corneal surface resulting in decreased quality of vision, reduced tear film quality and stability and discomfort. [1,2] The prevalence and incidence of this disease ranges from 0.05 to 2.34% [2–7] and 0.001 to 0.03% [5,8], respectively. More recently, Godefrooij *et al* [9] reported an incidence and prevalence 5-fold to 10-fold higher than previously reported (incidence of 13.3 per 100 000 and prevalence of 265 per 100 000). The discrepancy in the rates reported are attributed to the different definitions and subjective criteria often used to diagnosis, as well as more sophisticated diagnostic devices. The well-known visual impairment produced by KC progression is also accompanied by a decrease in the quality of life. [10,11] Promoting better

visual quality is crucial to augment the quality of life of these patients. Scleral lenses are increasingly being fitted in a great variety of cases and primary corneal ectasias, such as KC, that continue to be the main indication. [12,13] Although the visual efficacy of these lenses is well known in this kind of diseases, it remains unknown if these lenses incite any other changes in the anterior ocular surface.

As scleral lenses do not interact directly with the corneal surface, it should be expected to have no significant alterations on this surface. However, these lenses rest on the sclero-conjunctival region, resulting in a mechanical impact in the bulbar conjunctiva which can somewhat modify some conjunctival properties. Scleral lenses tend to decenter inferior and temporally because of anatomical features and gravity. Because of that, the lens will not land at the exact same distance from the limbus in the 4 main ocular quadrants; i.e. it will land more close to the limbus in the superior zone than on the inferior zone. [14] One could hypothesize that the lens edge compression on the conjunctival surface might change the mucin production and secretion impacting some clinical findings, such as post-lens tear film clouding (midday fogging), in the short-term and impact the density and viability of the goblet cells responsible for such secretion in the long term. Midday fogging is reported to happen in 20-33% of scleral lens fits. [15–17] Walker *et al* [18] found a great concentration of lipids in the postlens tear reservoir of patients with incapacitating midday fogging, but the exact composition of the debris entrapped between cornea and lens has yet to be reported. [19] McKinney *et al* [17] concluded that this phenomenon is more commonly reported by dry eye patients and when a great central corneal clearance combined with edge tightness is seen. In fact, several studies demonstrate that contact lens wear (both soft and corneal) may alter the goblet cell density and function [20–23] and that it is also reduced in dry eye patients. (refs) Conjunctival goblet cells are secretory epithelial cells responsible for the production, package and secretion of the mucinous component of the tear film (MUC5AC). [24] They are critical for maintaining ocular surface integrity. [25] A reduced mucin discharge will trigger some symptoms such as itching, burning and dryness. [26] Conjunctival cytology, which is considered the gold standard measure for dry eye disease diagnosis [27], allows to assess the density of conjunctival goblet cells. Peral and Pintor [25] concluded that some goblet cells are not secreting mucins, so they suggested a new technique that combines impression cytology with laser confocal microscopy (LCM) that can provide more meaningful details about the mucins secreted.

The main purposes of the present study were to use a combined technique (impression cytology and LCM analysis) to compare the goblet cell density (GCD) and mucin cloud amplitude (MCA) in the superior and inferior conjunctival zones and to compare the same outcomes between two groups of subjects: one wearing scleral lenses for ≤4 months and another wearing the lenses for more than 6 months. Secondary goals included correlate those findings with slit lamp evaluations, comfort ratings and on-eye lens fitting.

13.3 Methods

This pilot, experimental study included 26 eyes randomly selected from 26 keratoconus (KC) subjects (11 female) with a mean age of 34.12±8.75 years (range: 20 - 54), all included in a prospective clinical trial related to scleral lens wear. All subjects were wearing the same lens design (Senso Mini Sclera – Procornea, Eerbeek, the Netherlands) and were fitted according to fabricant recommendations. All subjects took part of this study voluntarily and provided informed consent after the nature of the research and risks were explained. The study followed the tenets of the Declaration of Helsinki and the protocol was approved by the Ethics Subcommittee for Life and Health Sciences of the University of Minho.

Subjects were divided into two groups according to the time (in months) of scleral lens wear: Group 1 comprised 15 eyes of 15 patients wearing the lenses for ≤ 4 months (range 1 to 4 months) and Group 2 comprised 11 eyes of 11 subjects wearing the lenses for ≥ 6 months (range 6 to 18 months). These and other demographic characteristics of the sample are shown on *Table 13.1.*

Measurements were performed in a random eye. Subjects were advised to come to the appointment with the lens on eye for more than 90 minutes in order to account on lens settling (Table 1). A regular appointment included in the prospective clinical trial, involving visual quality outcomes, lens fitting, ocular health and symptomatology, was performed and later the lenses were removed. After lens removal, conjunctival cytology was performed with EyePrimTM (OPIA Technologies SAS, Paris, France), equipped with a polyethersulfone (PES) membrane. The measurements were taken approximately 1.5-2.0mm from corneal limbus in the superior and inferior bulbar conjunctiva, using a gentle contact for 2 seconds, following the methodology of

previous works. [28–30] No anesthetic was needed. Right after sample collection, the impression cytology papers were preserved in 96% ethanol. Later, the samples were stained using periodic acid Shiff (PAS) reagent, dehydrated though an ethanol series to xylol, and mounted on coverslips for microscopic observation in Entellan. Samples were analyzed using a laser scanning confocal microscope (LCM) (Zeiss LCM Pascal; Carl Zeiss, Jena, Germany), following a modification to the protocol described by Peral e Pintor. [25] Peral and Pintor used a different paper to conduct the conjunctival cytology, and were able to measure the mucin cloud height (MCH) and cell layer thickness (CLT) independently. The PES membrane used in the present study was way more thin and it was not possible to measure those independently. So, we measure the mucin cloud amplitude (MCA) only. Samples were viewed at magnifications of 20x for Cell density evaluation and 40x for MCA. This LCM is able to scan samples on Z-axiz at 0.01 microns (but we used 0.25 microns).

Table 13.1. Demographic characteristics of the participants in the study.

	Total Sample	Group 1 (n=15)	Group 2 (n=11)
Age (years)	34.12±8.75 (range: 20 to 54)	34.20±9.73 (range: 21 to 54)	34.00±7.67 (range: 20 to 45)
Gender	11 Female 15 Male	7 Female 8 Male	4 Female 7 Male
Eye	13 Right Eyes 13 Left Eyes	9 Right Eyes 6 Left Eyes	4 Right Eyes 7 Left Eyes
Habitual Correction	Nothing: 6 Glasses: 7 Soft CL: 1 Corneal RGP: 4 Hybrid CL: 3 Scleral lens: 4 Piggyback: 1	2 2 1 1 1 3 1	4 5 0 3 2 1 0
KC Grade (KSS)	Grade 1: 0 Grade 2: 10 Grade 3: 11 Grade 4: 5	0 6 5 4	0 4 6 1
Months of lens wear	6.69±5.92 (range: 1 to 18)	2.27±1.16 (range: 1 to 4)	12.64±3.91 (range: 6 to 18)
Mean wearing time at appointment (min)	139.23±53.29 (range: 90 to 270)	125.33±40.15 (range: 90 to 180)	158.18±64.50 (range: 90 to 270)

13.4 Results

All the patients of the study were diagnosed with KC and graded with the KC severity score grading scale [31]: 10 had Grade II, 11 had Grade III and 5 had Grade IV. All the results are shown on *Table 13.2*. The mean OSDI score was 24.65±18.18 on Group 1 and 22.21±10.25, without statistical significant differences between groups. For goblet cell density, there were no statistical significant differences between the groups analyzed, but there is a reduced number in the superior zone in Group 2. Similarly, there were no statistical significant differences between the samples of superior and inferior zones in none of the groups, despite there is a smaller number of goblet cells in the inferior zone for Group 1. Regarding MA, no differences were found between superior and inferior samples neither between groups.

Table 13.2. Comparison of parameters between groups. The results of GCD are the mean±SD of the 5 zones randomly selected and analyzed, MCA are the mean±SD of 15 goblet cells randomly selected from different zones of the sample.

	Total Sample			Group 1 (<4meses)			Group 2 (>6meses)			Diff G1 vs G2
	Superior	Inferior	p-value	Superior	Inferior	p-value	Superior	Inferior	p-value	
OSDI (score)	23.62±15.12 (range: 0 to 63.64)			24.65±18.18 (range: 0 to 63.64)			22.21±10.25 (range: 2.08 to 38.64)			0.878^
GCD (cells/ mm²)	74.70±57.55 (range: 13.81 to 222.93)	55.91±34.80 (range: 14.8 to 141.06)	0.137+	86.34±70.57 (range: 13.81 to 222.93)**	54.04±33.51 (range: 14.80 to 125.27)	0.109+	58.83±28.77 (range: 19.73 to 114.42)	58.29±37.89 (range: 19.73 to 141.06)	0.969*	Sup: 0.878^ Inf: 0.851^
MCA (µm)	21.81±3.30 (range: 16.28 to 31.88)	20.72±2.95 (range: 15.85 to 27.58)	0.201+	22.23±4.01 (range: 16.28 to 31.88)	20.80±3.24 (range: 15.85 to 27.58)	0.300+	21.23±2.02 (range:18.24 to 25.53)	20.62±2.67 (range: 17.03 to 24.88)	0.421*	Sup: 0.357^ Inf: 0.979^

*t test for dependent samples
+Wilcoxon
^U-Mann Whitney
** this includes 3 outliers: 222.93, 193.33, 178.54 (>Mean+2xSD)

Correlation analysis between GCD and MCA in superior and inferior zones whit other clinical parameters related to on-eye scleral lens fitting were performed (CCC and lens periphery alignment with the ocular surface in the four principal meridians – nasal, temporal, superior and inferior). All the correlations were weak and without statistical significance. Also, there were no statistical significant correlations between GCD and MCA in the two zones considered in the present study. The correlations were weak: GCD and MCA in the superior zone (Spearman's rho

0.238, p=0.241) and GCD and MCA in the inferior zone (Spearman's rho 0.136, p=0.516). Weak correlations were also encountered between the same parameters and OSDI Scores. When considering age, there was a statistical significant moderate correlation between age and GCD in the superior zone (r= -0.531, p=0.005). However, the other results between age and GCD and MCA were weak and without statistical significance.

Considering the correlation analysis by groups, only one statistical significant correlation ($p<0.05$) was found between age and GCD in the superior zone (r=-0.735), but not in the inferior zone (r=-0,189, p=0.517) in Group 1. The other correlations were weak ($r<0.406$) and with no statistical significance. Regarding the results for Group 2, one statistical significant correlation was found between age and GCD in the inferior zone (r=0.746, p=0.008) and between inferior GCD and OSDI Score (r= -0.665, p=0.026). Other interesting correlations were found between lens periphery alignment of the inferior zone and GCD in the inferior zone (r= -0.400) and lens periphery alignment in the superior zone and MCA and GCD in the superior zone (r= 0.400), but without statistical significance.

13.5 Discussion

There is some controversy on the influence of contact lens on GCD. Some studies found a decrease in GCD after contact lens (both rigid corneal and soft) fitting [20,22] although others report statistical significant increases or no change during soft lens wear. [21,32,33] One study [20] found a greater reduction in GCD in symptomatic patients (mean reduction of 29%) than on asymptomatic patients (mean reduction of 13%), concluding that GCD is reduced in contact lens wearers and is greater in those patients that developed contact lens-related symptomatology. These incongruences between studies may be attributed to a series of factures related to the impression cytology technique and data analysis: the filter paper used during impression cytology, the inconsistent pressing/ force exerted during cytology, number of images analyzed, criteria for identifying the goblet cells, and conjunctival regions assessed. Some studies perform conjunctival cytology on the superior conjunctiva [25], others temporal conjunctiva [28–30] and others on nasal zone. [20] In the present study, a comparison between the measures done in the superior and inferior conjunctiva was done. There were no statistical significant differences between superior and inferior GCD in Group 2 (58.83 vs 58.29 cells/mm2).

However, it is seen a difference between superior and inferior GCD in Group 1 (86.34 vs 54.04 cells/mm2) but the difference was not statistical significant (p=0.109, Wilcoxon).

To the author's knowledge, this is the first work analyzing goblet cell density and function in KC patients wearing scleral lenses. The GCD is usually estimated by the number of cells per mm2, but there are a wide range of values reported. GCD for the contact lens wearers with healthy eyes was reported to be between 10.5±1.1 cells/mm2 and 152.85±29.0 cells/mm2. [28,34–37] Other studies have found a relationship between changes in GCD and duration of contact lens wear, with a decrease overtime. [35,38] However, other studies found an increase in GCD with contact lens wearing. [21,32] In addition, keratoconus patients typically have lower GCD when compared to healthy subjects. [1,28] The mean GCD of keratoconus patients was reported to be 84.88±32.08 cells/mm2 [28] in a sample of 15 keratoconus patients wearing corneal rigid gas permeable contact lenses for the last 5 years. In the sample of the present study, the mean GCD was 74.70±57.55 and 55.91±34.80 cells/mm2 in the superior and inferior regions, respectively. Though without statistical significant differences, it seems that there is a decrease in the GCD in the superior conjunctival surface with increased wearing time (86.34±70.57 versus 58.83±28.77 cells/mm2). The mean value at Group 1 considers 3 cases that could be considered outliers (Table 2). As this is a comparative study between 2 independent groups and not a follow-up of the same group of subjects, it is difficult to withdraw solid conclusions about this. Some of the subjects of the present study were contact lens wearers prior entering the study. Four (4) were scleral lens wearers before enrolling the study, 1 used piggyback, 3 used hybrid CL and 13 wore spectacles or had no prescription. So, the authors believe that some of the ocular surfaces were somewhat influenced by previous contact lens wear experiences. Future works should focus on changes on goblet cell density and production before and after the short and long term of scleral lens wear, preferably in new contact lens wearers, to confirm if there are any changes in the goblet cell density in the superior zone as suggested by the results of the present study.

Regarding OSDI, there were no differences between Group I and Group II, suggesting that the time of scleral lens wear do not influence the symptoms felt by these patients, which could be related to the unchanged GCD through time as well.

Regarding MCA, there were no statistical significant differences between superior and inferior samples neither between groups (Table 2), suggesting that the mucin secretion through

the tear film is not influence by the wearing time of scleral lenses. Previous studies that analyzed this outcome found a reduced mucin cloud height (MCH) and cell layer thickness (CLT) in keratoconus patients when compared to healthy patients [28], an increase in MCH and CLT after intrastromal corneal rings surgery accompanied by a GCD loss [29], and no differences with orthokeratology lens wear in healthy eyes. [30]

As mentioned in the introduction of the present work, the well-known clinical phenomenon of midday fogging was already related to edge tightness of the lens and the ocular condition of the patient (dry eye). [17] In a prospective clinical dispensing series conducted by Macedo-de-Araújo *et al,* none of the 69 subjects that concluded the 1-year follow-up complained about incapacitating fogging (submitted to publication). The 25 eyes of the present study were randomly recruited from that study. As there were no statistical significant differences in the GCD neither in MCA through time (months of lens wear), one could thing that there could be some relation between the absence of conjunctival cell changes and absence of midday fogging complaints. In our sample we tended to use more lenses with toric haptics [39] (Macedo-de-Araújo *et al*, Poster presented at GSLS 2018) in order to create a uniform landing area, and the lens clearance was intended to be among the recommended values. [40] This also might justify the absence of differences in GCD and MCA between superior and inferior samples. Other studies found a significant percentage of scleral lens wearers complaining about this problem, and this has been justified among other reasons with a hypothetical increase in the mucin secretion trapped underneath the lens, but the precise cause of fogging and the exact content is ultimately unknown. (ref) Our study did not report this and the cytology analysis supports the finding that mucin secretion might not be altered during scleral lens wear with the lens and materials used in this study.

13.6 Conclusion

The mean GCD and MCA was higher on the superior zone than on the inferior zone for the group of subjects that were wearing the lenses for less than 4 months. Subjects that were wearing the lenses for more than 6 months showed less GCD on the superior zone, although with no statistical significant differences. Scleral lens wear might have some implications on goblet cells density in the superior conjunctiva, but seem to not affect the mucin secretion.

13.7 References

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Chapter 14

General Conclusions and Future Work

14. General Conclusions and Future Work

14.1 Conclusions

The work developed over the last 4 years integrates important information for scleral lens fitters - both experienced and beginners – regarding the scleral lens performance over a medium to long-term and potential techniques to be included in clinical routines for scleral lens trial and fitting assessment through time. With this work we have achieved a more exhaustive knowledge on the scleral lens fitting process efficacy and safety. The main conclusions of the present work can be summarized as follow:

- Scleral lenses are already adopted as potential devices for visual correction by a significant number of Portuguese and Brazilian specialty contact lens prescribers;

- Contemporary scleral lenses can be successfully fitted in a wide range of conditions – ranging from severe corneal defects to regular shaped corneas - by practitioners with minimal previous experience in fitting these devices. Practitioner fitting experience will allow to reduce both number of trial lenses and re-orders required to achieve the best fit – especially after the first 60 eyes fitted. The experience of the fitter also allowed to fit more special lens designs such as front and back toric designs;

- Beyond the classic options to assist during the fitting process, the present work addressed new measurements that could aid practitioners in choosing the best lens for each eye and the assessment of scleral lens fittings through time:
    - One of the measurements were provided by a scleral topographer, which proved to be capable of measuring the differences in scleral shape after lens wear and therefore could be used to identify the main areas of impingement of the lens on-eye – and, therefore help practitioners in the evaluations or in choosing the best haptic lens design for each eye;
    - Although scleral lenses do not mechanically interact with the corneal surface, we revealed that some metrics given by a common corneal topographer (such as

EHChord for the diameter equal to the diameter of the lens) could aid the practitioner in choosing the sagittal height of the trial lens to be fitted;

- Some techniques not used for this purpose, such as IOLMaster measurements and the analysis of slit-lamp photography with an image processing software (ImageJ) provide an objective value of the central corneal clearance – which were moderately-to-highly correlated with subjective evaluations with slit lamp. Therefore, those measurements could replace or support the common subjective assessment and assist the scleral lens fitting process and evaluations through time;

- The fitting success rate– i.e. patients that successfully wore scleral lenses through the 12-month follow-up - was 73%. It was higher in irregular corneas (77%) when compared to regular cornea patients (58%). The main reasons for drop-out were discomfort and handling issues. Scleral lens fitters should be aware of these potential difficulties to overcome them and manage the expectations of the patients before lens fitting – considering that normal cornea patients will eventually discontinue scleral lens wear more easily. For those patients that continue scleral lens wear, this work indicated that despite the difficulty on lens handling at the beginning, subjects will improve significantly their handling skills and confidence in scleral lenses with time – more hours per day and days per week of lens wear;

- Scleral lenses provide enhanced subjective and objective visual quality, namely on patients with irregular cornea. We also suggest that high contrast visual acuity assessment alone could not be enough to characterize the visual enhancement promoted by scleral lenses on irregular cornea patients. Additional measurements such as night vision disturbances, aberrometry and subjective visual perception (quality of vision questionnaires) should be considered. However, the visual improvements promoted by standard scleral lenses, like the ones used in the present study – even without being perfect – could be a life-changing event for an important number of irregular cornea patients;

- Although *midday fogging* is oftentimes mentioned in the literature to occur in several scleral lens wearers, this was not subjectively reported by the 69 subjects that completed the 12-month of follow-up;

- Scleral lenses could be considered a safe modality as there were no significate adverse events over the entire follow-up period. Despite this, scleral lenses were related to higher hyperemia and staining grades when compared to no-lens situation;

- Scleral lenses reduced the dry eye-related ocular symptoms in both groups, being those enhancements higher in the irregular cornea group. The short-term comfort enhancement that subjects reported remained stable over the entire follow-up time;

- Scleral lenses undergo a long-term settling on-eye that continues up to 12 months. Although the short-term settling (120 minutes of wear) comprised more than 50% of the total settling, practitioners should be aware that scleral lenses will undergo a 12-month settling. This needs to be considered when evaluating the central corneal clearance of the lens;

- Scleral lenses induce a small degree of corneal swelling within the normal physiologic values, in both regular and irregular corneas. However, this hypoxic effect was continually inferior to 3% with respect to Baseline values in both regular and irregular corneal surfaces up to 12 months of follow-up;

- Scleral lens wear seem to induce significant changes in goblet cells density in the superior conjunctiva, but overall seem not to affect the mucin production.

14.2 Future Work

Several questions arose from the discussion of the contents of the present thesis. Examples of areas with potential interest for the industry and clinicians are the following ones:

- Extend the present study design and assessments to other scleral lens designs and diameters not included in the present work;

- Comparative or cross-sectional study to compare scleral lenses with other specialty contact lens modalities commonly fitted in irregular cornea patients – corneal RGP, hybrid lenses, piggyback – in order to assess the differences in their visual and comfort performances and compare them in terms of safety for the ocular surface;

- Further explore the capabilities of scleral topographers to predict the best lens for each eye – both haptic zone and sagittal height for different scleral lens designs;

- Expand the results of Chapter #3 to more countries in order to have a general overview of the scleral lens practices all around Europe and South-America – this can help to identify risky behaviors and propose good practices for practitioners;

- Although midday fogging was not a main issue on the present work, many practitioners around the world continue to complain about this – a study is needed to be performed in order to assess the etiology of this problem and the reasons why it not happened in the present sample;

- Since scleral lenses are increasingly being fitted in normal cornea patients, many evaluations needed to be performed in order to prevent drop-outs:

    - To evaluate the scleral lens performance under different and controlled environmental conditions;
    - Investigate tear film stability and quality changes with scleral lenses and its relation to comfort;

  - Given the emergence of multifocal scleral lenses, we strongly suggest new studies to evaluate the optical quality promoted by multifocal scleral lenses;

- To investigate the role of retinal electrical activity and visual cortex activity after scleral lens fitting in patients who presented very poor vision before fitting in order to evaluate the eventual adaptation phenomena and potential visual enhancement overtime;

- The study outcomes also opened a window for the development of new designs or for customization of scleral lens fittings in the future;

- Assessment of the changes in the conjunctival goblet cells (both number and production) in a prospective study and with different lens diameters.

"The process of fitting scleral lenses requires more than simply using your hands and your head; you also need to use your heart.

The ability to regain visual acuity often after years of suffering with poor vision, helps get patients back to work and back into society; this is what has driven me for four decades and continues to drive me every day. Helping patients is – of course – at the heart of what we do. But we cannot stop there. Continuing to develop new and improved fitting techniques and teaching colleagues through practical courses and lectures help ensure that scleral lenses and scleral lens practice will continue to improve."

Rients Visser, 2017. In Contemporany Scleral Lenses: Theory and Application; Prologue; p.VII.