SIMULATION METHODS TO EVALUATE AND OPTIMIZE OPTICAL DESIGNS IN ORDER TO IMPROVE THE PRESBYOPIA CORRECTION

TESIS DOCTORAL

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SIMULATION METHODS TO EVALUATE AND OPTIMIZE OPTICAL DESIGNS IN ORDER TO IMPROVE THE PRESBYOPIA CORRECTION

Memoria presentada por

María Caridad Pérez Vives

Para optar al grado de

DOCTOR en OPTOMETRÍA Y CIENCIAS DE LA VISIÓN

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DECLARATION

No portion of the work referred to the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institution of learning.

El Profesor D. Robert Montés Micó, Catedrático de la Universidad de Valencia y la Doctora Dña. Teresa Ferrer Blasco, Profesora Ayudante Doctor de la Universidad de Valencia,

CERTIFICAN que la presente memoria "SIMULATION METHODS TO EVALUATE AND OPTIMIZE OPTICAL DESIGNS IN ORDER TO IMPROVE THE PRESBYOPIA CORRECTION", resume el trabajo de investigación realizado, por Dª Cari Pérez Vives y constituye su Tesis para optar al Grado de Doctor en Optometría y Ciencias de la Visión.

Y para que así conste, y en cumplimiento de la legislación vigente, firma el presente certificado en Valencia, a

de de dos mil catorce.

Fdo: Dr. Robert Montés Micó Fdo: Dra Teresa Ferrer Blasco

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RESUMEN

El envejecimiento tiene dos grandes consecuencias en la visión, la presbicia y las cataratas. La presbicia es el resultado de la declinación natural, relacionada con la edad, de la capacidad para enfocar objetos cercanos. Existe una gran población présbita, en edades comprendidas entre los 45 y 65 años. Las cataratas se producen en personas mayores como resultado natural del proceso del envejecimiento, causando una pérdida de visión debido a la opacificación del cristalino. La cirugía de cataratas es la cirugía más habitual en oftalmología, pero también la intervención quirúrgica, no sólo ocular, más practicada a nivel mundial. Un 30% de la población mayor de 65 años presenta algún tipo de opacidad cristaliniana, siendo en algunos casos necesaria su extracción. Se estima que las cataratas que provocan una pérdida de visión afectan a unos 17 millones de individuos en todo el mundo. Durante los últimos años, el deseo de independizarse de las gafas ha aumentado entre estos pacientes con cataratas y presbicia, debido a múltiples factores, tales como el aumento de las demandas visuales en cerca, la estética o una mayor esperanza de vida, entre otros. Por ello, desde hace varios años, se han llevado a cabo diseños de lentes intraoculares multifocales o acomodativas, cuyo objetivo es reducir la dependencia de gafas tras la cirugía de cataratas o bien como una opción quirúrgica refractiva en aquellos pacientes présbitas.

La presbicia se compensa de manera más común mediante el uso de lentes oftálmicas con adición bifocal o progresiva. Aunque esta opción sufre de inconvenientes ergonómicos y psicológicos, como la distorsión y restricción del campo visual, la inestabilidad binocular, la dificultad para conseguir visión precisa en una variedad de tareas cotidianas, la incompatibilidad con numerosos deportes y los cambios estéticos son a menudo mal aceptados por el usuario. Las lentes de contacto suelen estar mejor adaptadas a los estilos de vida modernos. Dado que normalmente siguen todos los movimientos oculares, no sufren de las desventajas antes mencionadas. Actualmente para la corrección de la presbicia mediante lentes de contacto se emplea la monovisión, donde un ojo es corregido para visión próxima y el otro para visión lejana, y la visión simultánea, donde ambas lentes siguen un diseño multifocal especial con objeto de incrementar la profundidad de foco del ojo. A pesar de los esfuerzos en el desarrollo de lentes de contacto multifocales para présbitas, actualmente en el mercado todavía encuentran una aceptación clínica limitada, siendo su tasa de éxito menor al 10%.

Además de las lentes oftálmicas y las lentes de contacto, existen diferentes soluciones, como la cirugía refractiva corneal o la implantación de una lente intraocular de cámara anterior, también llamadas lentes fáquicas. La opción más común para corregir el error refractivo es mediante cirugía refractiva corneal, aunque actualmente, otras opciones como la implantación de una lente intraocular de cámara anterior se están haciendo más populares, ya que son una buena alternativa para aquellos pacientes que no son buenos candidatos a la cirugía refractiva corneal, debido a altos defectos refractivos o espesores corneales reducidos.

Las ICLs (Implantable Collamer Lens, STAAR surgical, Nidau, Switzerland) son lentes intraoculares de cámara anterior, aprobadas por la FDA *(en inglés, Food and Drugs Administration)* para el tratamiento de la miopía. Se ha demostrado que las ICLs son efectivas para la corrección de la miopía, hipermetropía y astigmatismo. Además, varios estudios científicos han mostrado que este procedimiento quirúrgico es mejor que la cirugía refractiva corneal en aquellas medidas de seguridad, eficacia, predictibilidad y estabilidad, incluso en ojos con baja miopía. Estos resultados se deben, principalmente, a que la ablación requerida durante la cirugía refractiva corneal cambia la forma de la córnea, incrementando las aberraciones de alto orden, especialmente la aberración esférica. Por otro lado, la implantación de una ICL no requiere ablación quirúrgica del tejido corneal, dejando la córnea virgen. Por tanto, este procedimiento quirúrgico induce significativamente menos aberraciones de alto orden que la cirugía refractiva corneal. La implantación de una ICL puede inducir aberraciones de alto orden debido a las propiedades innatas de la propia lente y también debido al tipo de incisión durante el procedimiento quirúrgico.

Uno de los principales inconvenientes de estas lentes es la formación de cataratas tras su implantación, algunos estudios de la FDA mostraron que la incidencia de la formación de una catarata secundaria en pacientes implantados con una ICL fue del 2.1% en el primer año y del 2.7% en el tercer año tras la cirugía. La causa de esta complicación puede ser por el contacto entre la ICL y el cristalino, o bien por una malnutrición localizada debida a la pobre circulación del humor acuoso. Para mejorar la circulación del humor acuso crearon un pequeño agujero en el centro de la ICL, de tal forma que no afectaba la calidad visual de los pacientes y era suficiente para mejorar la circulación del humor acuso de la cámara anterior al cristalino, previniendo así la formación de cataratas secundarias.

El objetivo de este trabajo es caracterizar y evaluar en profundidad estas lentes intraoculares fáquicas, específicamente las ICLs, con el fin de encontrar la solución para que estas lentes corrijan la presbicia. Para llevar a cabo este proyector se utilizó un instrumento llamado NIMO (Lambda X, Belgium), el cual nos permite caracterizar las diferentes lentes mediante la medida de las aberraciones de las mismas; y un simulador visual basado en la óptica adaptativa (crx1, Imagine Eyes, Orsay, France), que nos permite medir, corregir y simular diferentes patrones de aberraciones.

Los sistemas de óptica adaptativa permiten mejorar la calidad de un sistema óptico, limitado por la presencia de aberraciones inducidas por la luz al atravesar un medio no homogéneo, midiéndolas y corrigiéndolas simultáneamente. La óptica adaptativa tiene sus orígenes en la astronomía, la cual se propuso para solucionar el problema de la degradación de las imágenes producida por la atmósfera que se obtenían de las estrellas, introduciendo la idea de la óptica adaptativa como elemento para medir y corregir simultáneamente las aberraciones causadas por una atmósfera turbulenta. Debido a las múltiples aplicaciones de esta técnica, los sistemas de óptica adaptativa tuvieron un gran desarrollo, extendiéndose hasta el campo de la biomedicina, principalmente en el ámbito de la óptica visual. El ojo humano como sistema óptico presenta aberraciones que degradan la imagen que se forma en la retina y, por tanto, la visión, de modo que una de las principales aplicaciones de la óptica adaptativa es la corrección de las aberraciones del ojo, con el fin de mejorar la calidad visual de los pacientes. Pero la óptica adaptativa no se limita únicamente a la corrección de las aberraciones oculares, sino que tiene múltiples aplicaciones dentro de este ámbito. Cabe destacar, por ejemplo, su uso para incrementar la resolución de las imágenes registradas *in vivo* de la retina, ampliando en gran medida la información que puede obtenerse de ésta. Otra aplicación de la óptica adaptativa que más atañe a esta Tesis Doctoral es la simulación visual. El simulador visual de óptica adaptativa combina un aberrómetro para medir las aberraciones oculares y un sistema de espejos deformables para corregir y/o inducir patrones de aberraciones predefinidos. Al mismo tiempo, un estímulo visual se proyecta a través del sistema a una micro pantalla. De tal modo, que es posible evaluar la calidad visual de diferentes diseños de lentes intraoculares en diferentes posiciones o diferentes técnicas quirúrgicas mientras se combinan con diferentes perfiles corneales. Gracias a estas posibilidades, podemos analizar las diferencias en la calidad visual entre los diferentes diseños de lentes y/o técnicas quirúrgicas en un mismo paciente sin necesidad de realizar una cirugía.

En el capítulo 2 se evalúa la calidad óptica y visual de lentes intraoculares fáquicas miópicas, específicamente las ICLs, para diferentes potencias refractivas (bajas, medias y altas) y diferentes condiciones de cirugía. Para ello, en primer lugar se miden las aberraciones del frente de onda de las lentes *in vitro* y, a continuación, se emplea un simulador de óptica adaptativa para simular la visión que se obtendría con las diferentes potencias de las ICLs miópicas, tanto para una incisión quirúrgica pequeña como grande.

Los resultados de calidad óptica muestran que las ICLs miópicas presentan aberración esférica negativa, la cual aumenta con la potencia refractiva de la lente; encontrando diferencias significativas en la aberración esférica entre las potencias bajas-medias y las altas. El resto de aberraciones de onda evaluadas (coma, trefoil, tetrafoil y astigmatismo secundario) fueron mínimas. Tras las simulaciones no encontramos diferencias en las medidas de agudeza visual y sensibilidad al contraste entre las ICLs de baja y media potencia, pero pasaron a ser significativas para la ICL de mayor potencia evaluada. Sin embargo, estas pérdidas son compensadas por el efecto de magnificación, lo cual ocurre cuando un paciente miope se somete a la implantación de una ICL. Esto se puede atribuir a mover la corrección refractiva desde el plano de las gafas al ojo. Respecto al efecto de la incisión quirúrgica, encontramos significativamente mejores resultados para la incisión quirúrgica pequeña, ya que cuanto mayor es la incisión más aberraciones son inducidas.

Estos resultados muestran que las ICLs proporcionan una buena calidad óptica y visual, siendo ésta mejor si la incisión quirúrgica es pequeña. Por lo tanto, ante un astigmatismo, los cirujanos deberían preferir implantar una lente tórica a través de una incisión quirúrgica pequeña, en vez de una lente esférica y una incisión quirúrgica mayor para corregir el astigmatismo.

En el capítulo 3, teniendo en cuenta la alta popularidad de otras técnicas de cirugía refractiva corneales, como es el LASIK *(en inglés, Laser in Situ Keratomileusis)*, se comparan ambos procedimientos para la corrección de la miopía. De nuevo, se hizo uso del simulador visual de óptica adaptativa con el fin de simular la visión tras la implantación de una ICL y tras un LASIK a partir de las aberraciones del frente de onda.

Las ICLs mostraron mejores resultados de calidad óptica en ambas métricas analizadas. Respecto a la calidad visual, no se encontraron diferencias para niveles de miopía bajos. Sin embargo, para miopías medias-altas, el efecto de las aberraciones se hace aparente, encontrando diferencias significativas en los resultados de agudeza visual y sensibilidad al contraste entre ambos procedimientos. En cualquiera de los casos, tanto los resultados de calidad óptica como de calidad visual fueron mejores tras la implantación de la ICL. Esto es debido a que el LASIK induce más aberraciones de alto orden, debido a la ablación corneal, que tras la implantación de una ICL.

Ambos procedimientos muestran buena calidad óptica y visual, aunque las ICLs proporcionan mejores resultados, especialmente para miopías medias-altas y pupilas grandes.

En el capítulo 4 se mide y compara dos modelos de ICLs, las convencionales y aquellas que presentan un agujero central, además de analizar como varía el patrón de aberraciones ante descentramientos de la lente tras su implantación. Se miden ambos modelos de ICLs en tres situaciones: centradas y descentradas 0.3 mm y 0.6mm, mediante el instrumento NIMO.

No se encontraron diferencias significativas en los coeficientes de zernike analizados entre los dos modelos de ICLs, en ninguna de las situaciones analizadas. En cuanto a los descentramientos se observó un aumento de la aberración coma, aunque esta no fue visible en las métricas utilizadas para evaluar la calidad óptica.

De modo que los resultados mostraron excelentes y comparables resultados con ambos modelos de ICL evaluados, por lo tanto el agujero central que presentan las lentes no afecta a la calidad óptica de las mismas. Por otro lado, a pesar del incremento de la aberración coma con el descentramiento de las lentes, estos valores fueron clínicamente despreciables y se espera que no tengan ningún efecto en la función visual.

Con el fin de corroborar estos resultados y observar las posibles diferencias al introducir estas lentes en un ojo, en el capítulo 5 se hace uso del simulador visual para simular y comparar la calidad visual de las ICLs convencionales y las ICLs con agujero a diferentes grados de descentramientos.

No se encontraron diferencias estadísticamente significativas en la función visual entre ambos modelos de lentes (con y sin agujero) para ninguna potencia dióptrica evaluada. Los descentramientos evaluados (0.3 y 0.6 mm) no afectaron de manera significativa a la agudeza visual ni a la sensibilidad al contraste, además el descentramiento afectó de la misma forma a ambos modelos de lente evaluados.

Estos resultados afirman los resultados obtenidos en el capítulo anterior, el agujero central que presentan las ICLs, no afectan a la función visual tras su implantación. Por otro lado, este estudio también demuestra la alta tolerancia a los descentramientos de estas lentes, ya que con un desplazamiento horizontal de 0.6mm, la función visual no se vio afectada significativamente.

Una vez caracterizadas y evaluadas las ICLs, para finalizar, el objetivo es encontrar un diseño de ICL que compense la presbicia. En el capítulo 6, se modifica la aberración esférica de las ICLs, haciéndola más negativa y positiva, con el fin de encontrar un valor de aberración esférica idóneo para que no disminuya la calidad visual de los pacientes y a su vez que aumente la profundidad de foco, siendo útil para aquellos pacientes pre-présbitas y présbitas jóvenes, los cuales aún presentan cierto grado de acomodación. Mediante el uso del simulador visual, se simulan las diferentes ICLs con diferentes cantidades de aberración esférica en pacientes jóvenes con la acomodación paralizada y se mide la función visual a diferentes vergencias.

En todas las simulaciones se encontró que un aumento de aberración esférica, tanto positivo como negativo, disminuye la agudeza visual, aunque este decline de agudeza visual solo fue clínicamente significativo cuando el residual de aberración esférica fue negativo y con grandes diámetros pupilares. A su vez, también encontramos que un residual de aberración esférica, tanto positivo como negativo aumenta la profundidad de foco, aunque solo fue clínicamente significativo para altos valores residuales de aberración esférica.

Estos resultados muestran que un residual de aberración esférica negativo disminuye mucho la agudeza visual. Sin embargo un cierto grado de aberración esférica positiva tras la implantación de una ICL mejora la profundidad de foco, ofreciendo aceptables valores de agudeza visual, proporcionando así una ICL para présbitas jóvenes.

Finalmente, en el capítulo 7 se reúnen las conclusiones generales, acorde a lo expuesto en cada capítulo, así como las sugerencias para posibles estudios futuros. Entre estas sugerencias se podría destacar la posibilidad de testear los diferentes diseños de las ICLs para présbitas en pacientes présbitas jóvenes.

Contents

ACRONYMS

ANOVA: Analysis of Variance

BSCVA: Best Spectacle Corrected Visual Acuity

CDVA: Corrected Visual Acuity

CL: Contact Lens

CS: Contrast Sensitivity

D: Diopters

DoF: Depth of Focus

FDA: Food and Drug Administration

FrACT: Freiburg Visual Acuity Test

HOA: Higher Order Aberrations

ICL: Implantable Collamer Lens

IOL: Intraocular Lens

LASIK: Laser in Situ Keratomileusis

logMAR: Logarithm of the minimum angle of resolution

MTF: Modulation Transfer Function

OCT: Ophthalmoscope Coherence Tomography

OTF: Optical Transfer Function

PRK: Photorefractive Keratotomy

PSF: Point Spread Function

RMS: Root-Mean-Square

UDVA: Uncorrected Distance Visual Acuity

VA: Visual Acuity

CHAPTER 1

Introduction

1.1 ADAPTIVE OPTICS

The optical artifacts, such as aberrations, are caused by the medium between the object and the image. When the light passes through the non-homogeneous medium the wavefront is distorted and as a result the image is deteriorated. The adaptive optics is an optical system that is adapted to compensate these optical artifacts, improving the systems' optical quality. The use of adaptive optic systems in order to correct the wavefront aberrations has its origins in astronomy. Babcock (Babcock, 1953) described a system for the compensation of the wavefront distortion that results from atmospheric turbulence (figure 1.1).

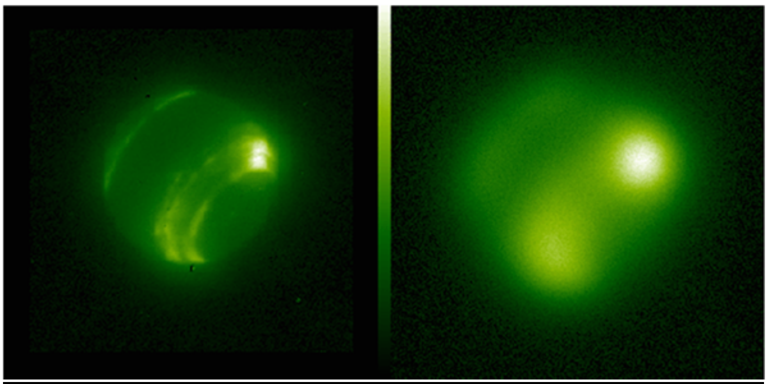

Figure 1.1: Image of Neptune taken with the Keck telescope with adaptive optics (left) and without adaptive optics (right).

Due to the multiple applications of this technique, the adaptive optics systems were widely developed at different fields, such as by the military for imagining satellites and by the biomedicine field, especially in visual optics. The eye as optical system has aberrations that degrade the vision; therefore it was thought that the human eye aberration could be corrected with adaptive optics, providing a high optical quality in normal eyes.

Liang et al. (1997) corrected the ocular wavefront aberration in normal subjects using adaptive optics. They found that the contrast sensitivity (CS) increased when the observers viewed the stimuli through the adaptive optics. They concluded that correcting the higher order aberrations (HOAs) with an adaptive optics device, such as a deformable mirror, or perhaps with a custom contact lens (CL), would provide the greatest visual benefit when the pupil is large or for eyes that have high amounts of aberration. This result spurred the rapid development of wavefront-guided refractive surgery, in which measurements of the eye's wavefront aberration control an excimer laser to correct the eye's static HOAs as well as defocus and astigmatism. The most enthusiastic proponents had hopes that this surgical procedure could improve essentially everyone's vision beyond 20/20. However, there are practical limitations on the visual benefit of correcting HOAs, which will be analyzed throughout the present chapter.

The adaptive optics technology is also use to increase the resolution of retinal imaging, extending the information that can be obtained from the living retina (Liang et al., 1997). It allows the routine examination of single cells in the eye, such as photoreceptors and leukocytes, providing a microscopic view of the retina that could previously only be obtained in excised tissue. The ability to see these structures in vivo provides the opportunity to noninvasively monitor normal retinal function, the progression of retinal disease, and the efficacy of therapies for disease at microscopic spatial scale. Applied to scanning laser ophthalmoscopes, Roorda et al. (2002) presented the first scanning laser ophthalmoscope that uses adaptive optics to measure and correct the HOAs of the human eye. Adaptive optics increases both lateral and axial resolution, permitting axial sectioning of retinal tissue *in vivo*. The instrument is used to visualize photoreceptors (figure 1.2), nerve fibers and flow of white blood cells in retinal capillaries.

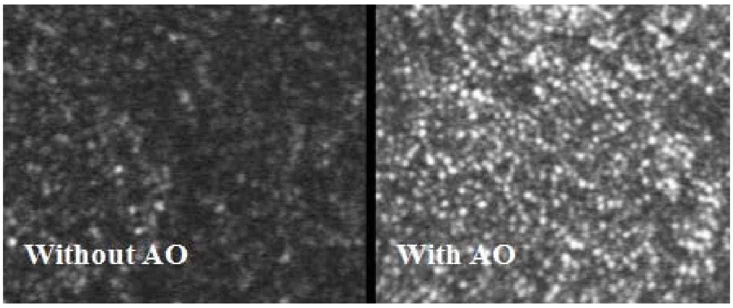

Figure 1.2: The two figures show the same area of retina taken with and without aberration correction with adaptive optics. In this case, the RMS wavefront error was reduced from 0.55 to 0.10 μm (Roorda et al., 2002).

Adaptive optics has also been used in another technique for the registration of other images of the retina, the Optical Coherence Tomography (OCT; figure 1.3). The OCT has become a widely spread technique in the field of visual care.

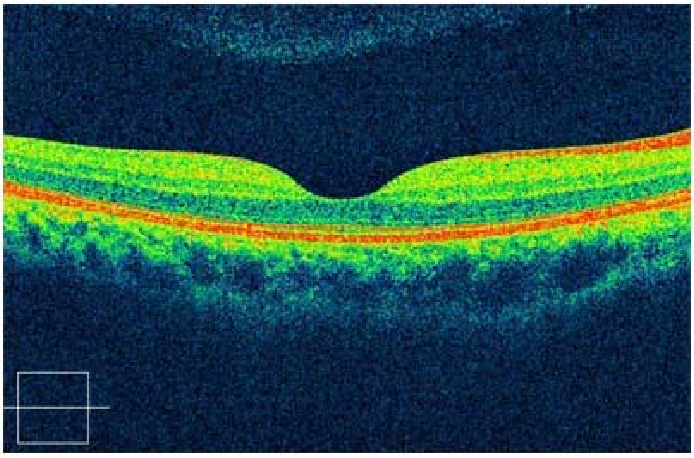

Figure 1.3: OCT image of a normal retina.

On the other hand, within the visual optics field, another important application of adaptive optics is to produce controlled wavefront aberration patterns in the eye, enabling new experiments to better understand the impact of the ocular HOAs on vision. Artal et al. (2004) use the adaptive optics to address the intriguing question of whether the visual system is adapted to the particular pattern of optical aberrations of its own eye. Their outcomes support the hypothesis that the neural visual system is adapted to the eye's particular aberrations. Although, it should be into account the amount of aberration that the neural system can "compensate." Many authors have made use of the adaptive optics technology to simulate different aberration patterns in order to better understand the process of vision. Seeing how each one of the aberrations affects on the retinal image quality, and the interaction between them may increase or decrease visual performance. All these findings will be analyzed throughout the present chapter.

1.2 WAVEFRONT ABERRATIONS

1.2.1 MONOCHROMATIC ABERRATIONS

The image-forming properties of any optical system, in particular the eye, can be described completely by the wavefront aberration. It is defined as the difference between the perfect (spherical) and the actual wavefront for every point over the eye's pupil. Every optical system has a greater or lesser extent degree of aberrations, which causes that the image of an object is not perfect. The human eye as image forming system has aberrations and they play an important role in the degradation of retinal image quality.

1.2.1.1 Definitions

Zernike Polynomials

To describe the ocular wavefront aberrations, are commonly used *Zernike polynomials* (figure 1.4). The Zernike polynomials are a set of functions that are orthogonal over the unit circle. They are useful for describing the shape of an aberrated wavefront in the pupil of an optical system. Several different normalization and numbering schemes for these polynomials are in common use (Thibos et al., 2002a).

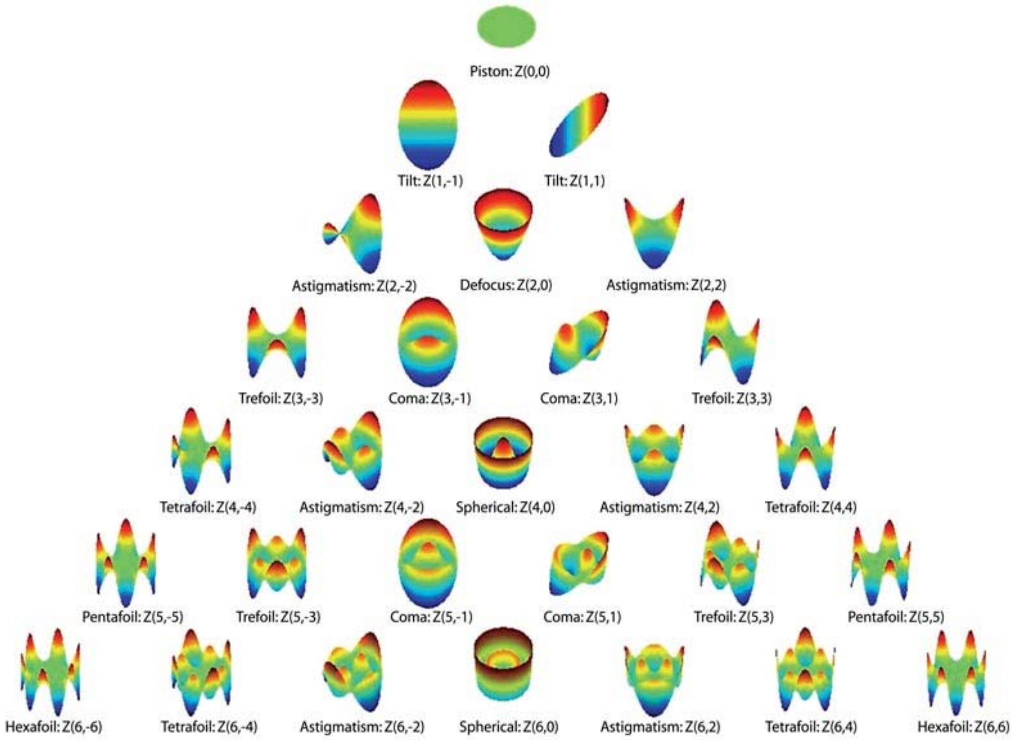

Figure 1.4: Viewing the first 21 Zernike polynomials. Each row corresponds to an order n each column at a rate m, Z(n,m).

Root-Mean-Square (RMS)

For a wave aberrations described using Zernike polynomials, the *Root-Mean-Square (RMS)* wavefront error is defined as the square root of the sum of the squares of a given number of Zernike coefficients.

Point Spread Functions (PSF)

The *Point Spread Function (PSF)* is the image of one point throughout an optical system (figure 1.5). It is calculated as the squared modulus of the Fourier transform of the generalized pupil function. That is, the image of a point of light is not a point, is a spot, called the Airy disk (figure 1.6). Indicates the optical quality of a system, the more strain on a point, lower quality optics.

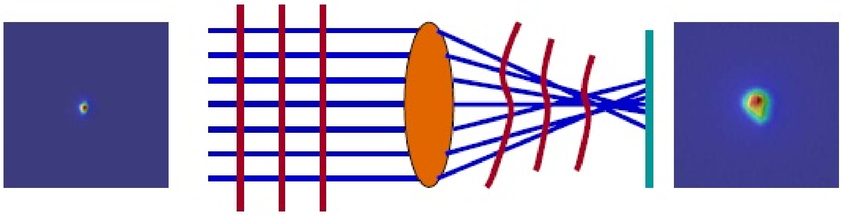

Figure 1.5: Show the image of a point through an aberrated optical system.

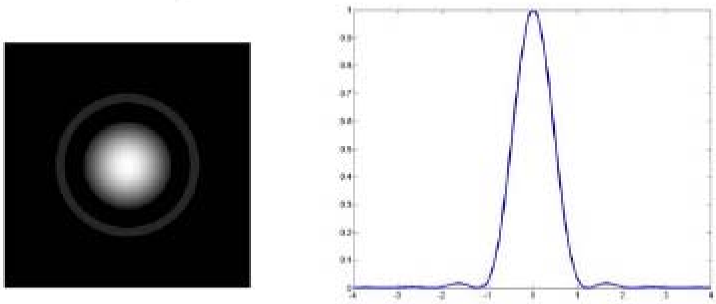

Figure 1.6: The Airy Disc (left) and the PSF only limited by diffraction (right).

Modulation Transfer Function (MTF)

The optical performance of the human eye, as the first step in visual processing, is described by the *Optical Transfer Function (OTF)*, although often only its modulus, i.e., the *Modulation Transfer Function (MTF)*, is used. The MTF (figure 1.7) is transfer function characterizing the proportion of contrast present in the object that is preserved in the image formed by an optical system. It is used to determine the quality of an optical system.

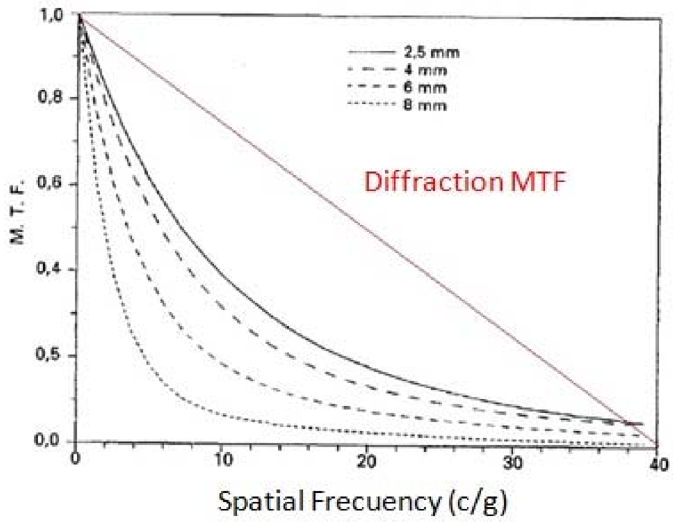

Figure 1.7: MTF limited only by diffraction (ideal) and for different pupil sizes.

Aberrations vary greatly from one individual to another; these variations have been studied by several authors in large populations of normal subjects (Howland and Howland, 1977, Liang and Williams, 1997, Porter et al., 2001, Castejon-Mochon et al., 2002, Thibos et al., 2002b). All authors agree that there is high inter-subject variability, but many aberrations in the left eye were found to be significantly correlated with their counterparts in the right eye. In normal young subject beyond defocus and astigmatism, spherical aberration, coma and trefoil are the most significant aberrations in normal eyes.

Applegate et al. (2002) studied if all aberrations affects equal at CS and visual acuity (VA). They found that for an equal amount of RMS error not all coefficients of the Zernike polynomial induce equivalent losses in high and low contrast VA. Wavefront error concentrated near the center of the pyramid adversely affects VA more than modes near the edge of the pyramid (figure 1.4). Large changes in chart appearance are not reflected in equally large decreases in visual performance (ie, subjects could correctly identify highly aberrated letters). Therefore the VA test would not be enough to reflect a decrease of optical quality, since charts that have a terrible appearance can still be read with uncanny accuracy. When there is relevant visual information, the brain will learn to extract it.

1.2.1.2 Location of Monochromatic Aberrations

In order to find out why the eye is affected by the wavefront aberrations and where the sources of these aberrations in the eye are; the ocular aberrations induced by the anterior surface of the cornea and by the internal optics of the eye had been measured. The aberrations associated with the anterior surface of the cornea can be measured with corneal topography instruments and the aberrations of the complete eye can be measured using a variety of different subjective and objective techniques; being, probably, the most widely used method today, the Hartmann-Shack wavefront sensor. Since we can measure the wavefront aberrations of the whole eye and of the cornea, the relative contributions of the different ocular surfaces to retinal image quality can be evaluated. In particular, the wavefront aberrations of the internal ocular optics are estimated simply by directly subtracting the corneal from the ocular aberration. Figure 1.8 shows a schematic representation of this procedure.

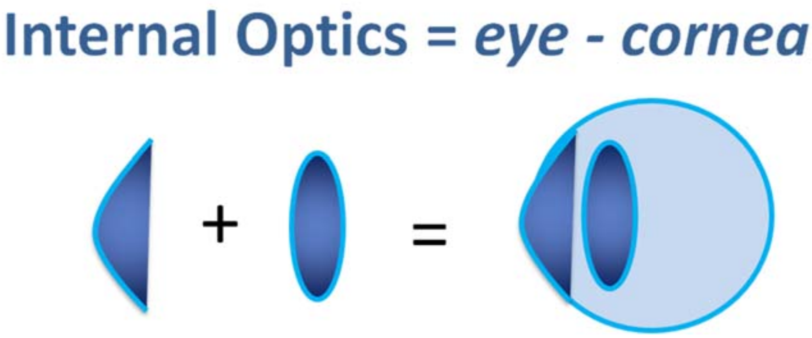

Figure 1.8: Schematic representation of the combination of corneal and ocular wave aberrations to estimate the wave aberration of the internal optics.

The relative contribution of the corneal and the internal optics wavefront aberrations has been evaluated in several studies (Artal and Guirao, 1998, Artal et al., 2001, Artal et al., 2002, He et al., 2003), measuring independently the wavefront aberrations of the anterior surface of the cornea, the complete eye, and internal ocular optics (figure 1.9). All of these studies found that the amount of wavefront aberrations of both, the cornea and internal optics, was larger than for the complete eye. Indicating that the first surface of the cornea and internal optics partially compensate for each other's aberrations and produce an improved retinal image (figure 1.10). Smith et al. (2001)

reported that relaxed crystalline lens has negative spherical aberration, approximately the same level as the positive value of the anterior corneal surface. However, the compensation observed in young eyes was not present for older subjects, due to the ocular optics degradation with age. These finding show that the internal optics may play a significant role in compensating for the corneal aberrations in normal young eyes. Although, this behavior may not be present in every young eye, also depend on the amount of aberrations or the refractive error (He et al., 2003, Salmon and Thibos, 2002).

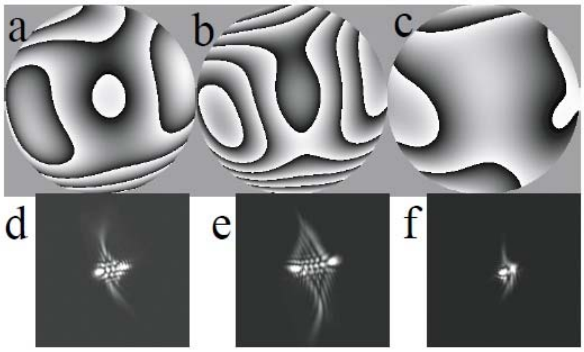

Figure 1.9: **A-C**: Wave-front aberration maps for the cornea (a), the internal optics (b) and the complete eye (c). The pupil diameter was 5.9 mm. **D-F:** Associated PSF calculated at the best image plane from wavefront aberrations panels **A-C** (Artal et al., 2001).

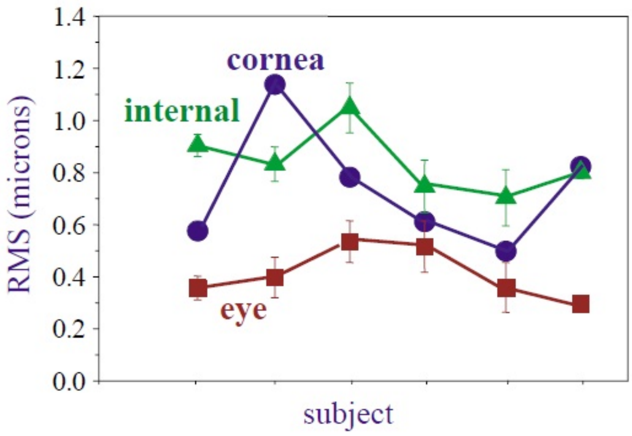

Figure 1.10: RMS of the wave-front aberration of the eye (red squares), the cornea (blue circles), and the internal optics (green triangles) for 6 eyes after defocus was removed (Artal et al., 2001).

Determining the location of the aberrations in the eye has important implications for aberration correction in adaptive optics and also for current clinical procedures, such as wavefront-guided refractive surgery. In normal young subjects, customized ablation should be performed based on the aberrations of the complete eye. If the ablation is based on only the corneal aberrations, the final aberrations of the eye could be larger than before the ablation. Another similar example is after cataract surgery, when an intraocular lens (IOL) is implanted inside the eye replacing the crystalline lens (Artal et al., 2001). These lenses usually have good image quality when measured on an optical bench, but the final optical performance in the implanted eye was typically lower than expected. The reason is that the ideal substitute of the natural lens is not a lens with the best optical performance when is isolated, but one that is designed to compensate for the aberrations of the cornea (figure 1.11). Therefore, IOLs and CLs should ideally be designed with an aberration profile matching that of the cornea or the crystalline lens to maximize the quality of the retinal image.

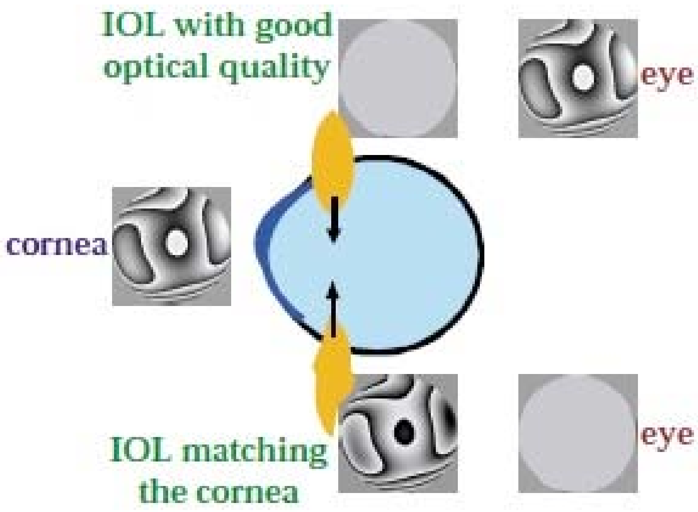

Figure 1.11: Schematic illustration of the effect of the coupling of corneal and IOL aberrations (Artal et al., 2001)

1.2.1.3 Factors that Modify the Aberrations

We must take into account that the optical aberrations in the normal eye depend on many factors and conditions. They vary from individual to individual, with pupil size, age of the subject, accommodation, retinal eccentricity, refractive state, and so forth.

Pupil size

Liang and Williams (1997) reported that the irregular aberrations do not have a large effect on retinal image quality in normal eyes when the pupil is small (3 mm). However, they play a substantial role when the pupil is larger, reducing visual performance and the resolution of images of the living retina. The RMS error for the small pupil lies 3-4 times lower than that for the large pupil of real eyes (figure 1.12). This illustrates the well-known fact that aberrations grow with increasing pupil size (Artal and Navarro, 1994).

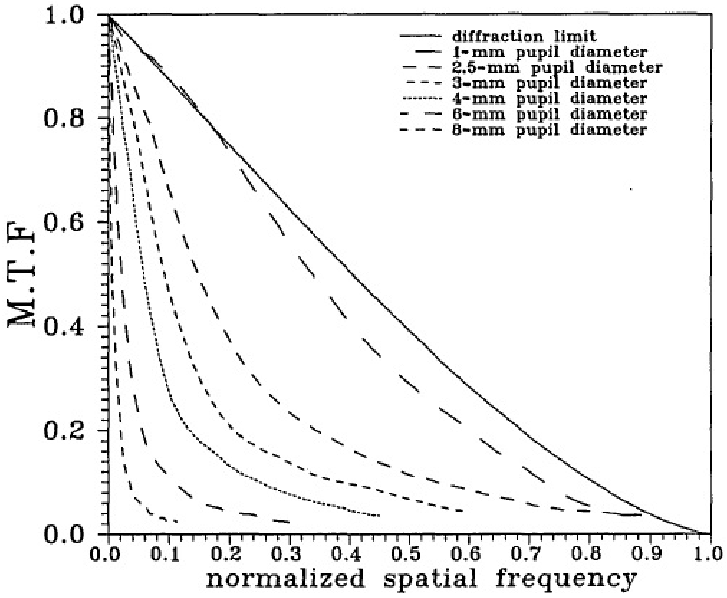

Figure 1.12: Average MTF's for six pupil diameters represented in a normalized spatial-frequency scale. The solid curve corresponds to the diffraction-limited MTF (Artal and Navarro, 1994).

Aging

Elderly eyes typically experience increased light absorption by the ocular media, smaller pupil diameters (senile miosis), and nearly a complete reduction of accommodative capability. Several authors have studied the optical and visual quality in elderly eyes (Artal et al., 1993, Calver et al., 1999, Guirao et al., 1999). Every study agreed that both, optical and visual quality progressively declines with age, showing lower MTF and CS in a group of elderly subjects than for a group of young subjects. This suggests a significant fraction of the loss in spatial vision with age has an optical origin.

Apart from the well-known increase in intraocular scattering, there also appears to be an increment in ocular aberration that causes an additional reduction in the contrast of retinal images. Different factors could contribute to the age-related increment in aberrations, such as changes in the aberrations of the cornea and the lens or their relative contributions. It has been studied that corneal wavefront aberrations are stable with age (Oshika et al., 1999, Guirao et al., 2002, Wang et al., 2003); in contrast the crystalline lens is changing continuously with age, the lens grows, its dimensions, surface curvatures, and refractive index change, altering the lens aberrations. Considering the nature aberration compensation between corneal and crystalline lens; during normal aging, if the crystalline lens aberrations changes while the corneal aberrations not, this balance between the aberration of corneal and internal surfaces will be partially or even completely lost (Artal et al., 2002). Smith et al. (2001) observed that the spherical aberration of the crystalline lens was becoming less negative with aging.

Accommodation

The change in optical aberrations with accommodation can be attributed largely to the changes of the crystalline lens. The crystalline lens shows an increase of the anterior lens curvature centrally and possibly a flattening of the lens peripherally during accommodation. The spherical aberration becomes more negative with the accommodation and changes more than the other HOAs (Lopez-Gil et al., 2008).

Refractive state

It has been reported that myopic subjects have greater RMS values of wavefront aberrations than emmetropic subjects, especially coma aberration. Emmetropic subjects present similar wavefront aberrations to those found for low myopia. Although for larger pupils, the aberration values of the emmetropes is generally slightly smaller than that of the low myopia group. This implies that the optical quality of a highly myopic eye is considerably compromised (Paquin et al., 2002, He et al., 2002).

1.2.2 CHROMATIC ABERRATIONS

In addition to monochromatic aberrations, chromatic aberrations in optical systems arise from chromatic dispersion or the dependence of refractive index on wavelength. Chromatic aberrations are also present in the eye, and these are traditionally divided into *Longitudinal chromatic aberration* and *Transverse chromatic aberration.* The former is the variation of axial power with wavelength. These two types of chromatic aberrations can be understood as the wavelength dependence of the lower order terms of the wavefront aberrations: longitudinal chromatic aberration is the change in focus and transverse chromatic aberration is the change in tip/tilt or prism. Chromatic aberrations limit the actual retinal image quality of the eye since the real world is usually polychromatic and, therefore, its image becomes distorted in the retina in a color-dependent fashion. Furthermore, since adaptive optics systems do not present, in general, the capability for chromatic compensation, chromatic aberrations can reduce the expected benefit of this technology for improved vision.

1.2.2.1 Longitudinal Chromatic Aberration

Longitudinal chromatic aberration is the dependence of the refractive power of the eye with wavelength (the refractive index, and hence the ocular refractive power is higher for short wavelengths). This causes the blue light to behave as myopic and red light as a farsighted (figure 1.13):

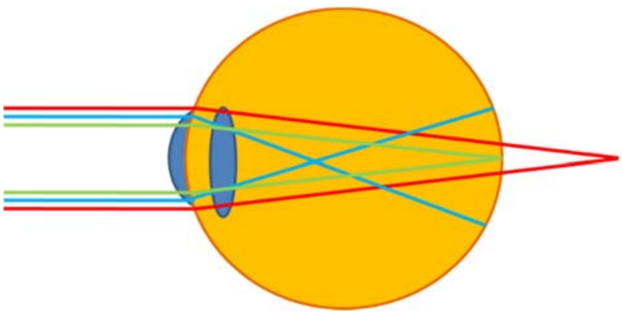

Figure 1.13: Longitudinal chromatic aberration. According to the wavelength, it focuses on different positions on the retina.

Consistently across studies and across subjects, longitudinal chromatic aberration has been found to be around 2D across the visual spectrum, and also agree that the low variability between subjects presented this aberration. Furthermore, this value seems to be stable with the age (Wald and Griffin, 1947, Bedford and Wyszecki, 1957, Charman and Jennings, 1976, Howarth et al., 1988, Marcos et al., 1999).

1.2.2.2 Transverse Chromatic Aberration

Transverse chromatic aberration is the difference in the angular displacement of the retinal image for different wavelengths (figure 1.14). The effect of transverse chromatic aberration is particularly important for decentered pupils (Thibos et al., 1991) and increases with retinal eccentricity.

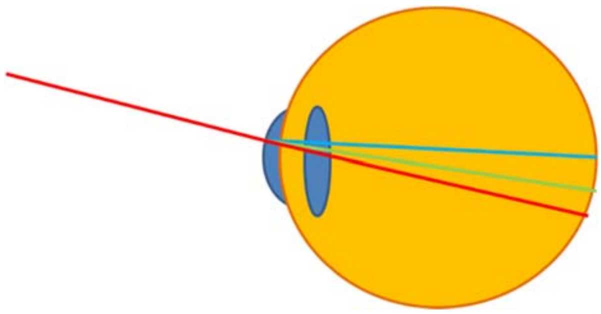

Figure 1.14: Transverse chromatic aberration. According to the wavelength, the image is formed on different positions on the retina.

Whereas the longitudinal chromatic aberration does not show a great variability between subjects, the transverse chromatic aberration is significantly different in amount and direction. The variability could be accounted by individual differences in the position of the fovea with respect to the optical axis, deviations in pupil centration, and different degrees of misalignment of the optical components of the eye. Differences may also arise from differences in the measurement conditions (pupil size, luminance, etc.).

1.3 ADAPTIVE OPTICS SYSTEMS

Wavefront aberrations and diffraction limit VA below the spatial bandwidth imposed by the neural visual system, such as that dictated by the sampling of the photoreceptor mosaic. Conventional corrective methods, such as spectacles, CLs and refractive surgery, improve prism, sphere and cylinder, which correspond to the lower order Zernike aberrations of tilt, defocus, and astigmatism. Image quality in the eye, however, can be significantly increased correcting the ocular aberrations across using, for instance, an adaptive optics system.

Nowadays, adaptive optics systems has been successfully applied to correct both the lower and HOAs in a variety of retinal camera architectures. The adaptive optics systems have also used to improve and asses vision, correcting the ocular wavefront aberrations and controlling the type and amount of aberrations to which the retina is exposed. Specifically, adaptive optics provides a means to directly asses the visual impact of individual types of aberration and allows patients to experience beforehand the predicted visual benefit of invasive surgical procedures, such as refractive surgery.

The first complete adaptive optics system, which successfully corrected the eye's most significant HOAs, was built in the mid- 1990s by Liang and colleagues (1997). The adaptive optics system was employed for retinal imaging and vision testing; which contained a wave-front sensor, which measured the eye's wave aberration, and a deformable mirror, which corrected the wave aberration. Subsequently, numerous authors (Hofer et al., 2001, Fernandez et al., 2002, Yoon and Williams, 2002, Piers et al., 2004, Piers et al., 2007, Perez et al., 2009, Li et al., 2009) also used different kinds of adaptive optics systems to correct the ocular HOAs and to study how different aberration patterns affect the visual performance.

1.3.1 CRX1 ADAPTIVE OPTIC SYSTEM

The adaptive optics visual simulator device (crx1, Imagine Eyes, Orsay, France) has been used to perform the measures and visual simulations of the present thesis.

This adaptive optics system compromises two basic elements: the wavefront sensor and a correcting device. The system optically conjugates the exit pupil plane of the individual with the correcting device, the wavefront sensor and an artificial pupil. The Shack-Hartmann wavefront sensor has a square array of 1024 lenslets. The wavefront aberrations measurements are made at 850 nm. The correcting device is a deformable mirror having 52 independent magnetic actuators used either to partially or totally correct the aberrations up to the fifth order (18 Zernike coefficients) and to add different values of aberrations (up to fourth order).The deformable mirror's surface is controlled with a commercially available program (HASO, Imagine Eyes) which reshapes the deformable mirror from its normally flat surface to the desired shape. The adaptive optics visual simulator also include a Badal system based on a trombone optical configuration, and an internal 800 pixel x 600 pixel black and white microdisplay monitor. The observer viewed visual tests generated on a microdisplay through the adaptive optics system and an artificial pupil (figure 1.15). The experiment's luminance conditions were manually adjustable. The pupil size is artificially adjusted by selecting the diameter of an internal aperture, which is optically conjugated with the eye-pupil plane. Throughout the visual simulation, an eye-tracking system monitors the relative positions of the instrument's optical axis and the subject's pupil. The eye-tracker data are continuously displayed as 2 circular targets in a software window; these graphic circles help maintain the best possible alignment during testing.

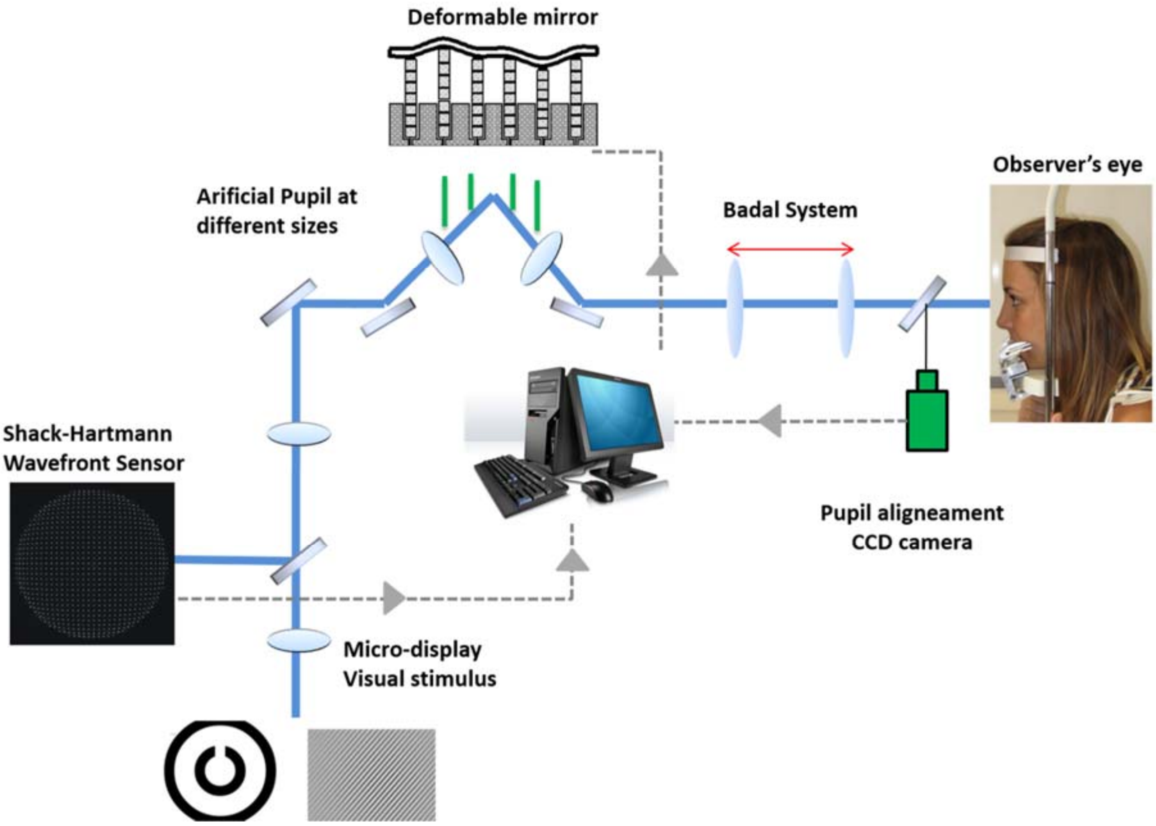

Figure 1.15: Schematic diagram of the crx1 system (Imagine Eyes, Orsay, France) used to measure and correct the eye's aberrations. With the two basic elements: the Shack– Hartmann wavefront sensor and the correcting device (deformable mirror) conjugated to the pupil plane. The visual test generated on a microdisplay was viewed through the deformable mirror and an artificial pupil.

The crx1 allows:

- ✓ Ocular wavefront measurement.
- ✓ Adaptive optics custom-wavefront correction.
- ✓ User-defined adaptive optics wavefront generation.
- ✓ Visual performance assessment through user-defined wavefront aberrations
- ✓ Wavefront assessment of accommodation (range -10/+10 D)

When we measure the ocular wavefront aberrations, the deformable mirror is set to an aberration free shape; and the system performs the function of a wavefront aberrometer, which measures ocular wavefront aberrations as a Zernike polynomial expansion up to the 10th order. Figure 1.16 shows the schematic diagram of the adaptive optics system while wavefront aberrations are being measured.

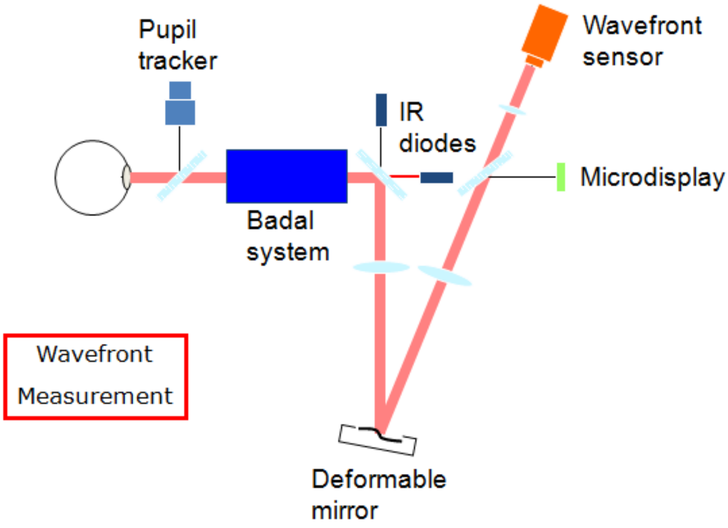

Figure 1.16: Schematic diagram of the adaptive optics system while wavefront aberration are being measured

We can also correct or generate a static (figure 1.17 left) or dynamic wavefront pattern. In order to correct the static ocular wavefront aberration, the deformable mirror should be programmed to reshape itself generating the opposite wavefront pattern of the patient's eye. The adaptive optics visual simulator is able to compensate the wavefront aberrations until 5th order. Then, with the purpose of simulating a static wavefront patter; the operator should define the wavefront pattern desired adjusting the Zernike coefficients until 4th order in the software of the system. The device optically introduces the predefined wavefront using an internal closed-loop system that set the mirror surface to the desired shape and keeps it constant (figure 1.17 right)

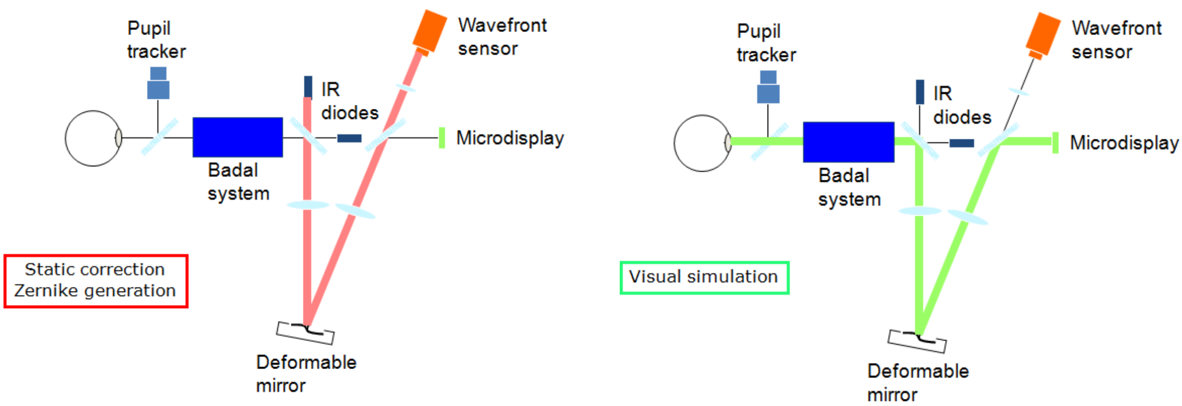

Figure 1.17: Schematic diagram of the adaptive optics system while wavefront aberrations are being corrected/generating (left) and while the visual simulation is happening (right).

Different authors have used the crx1 to correct and simulate different aberration patterns (Rocha et al., 2007b, Legras and Rouger, 2008, Rocha et al., 2009, Rocha et al., 2010, Rouger et al., 2010a, Rouger et al., 2010b, Legras et al., 2012). Legras and Rouger (2008) found that metrics based on wavefront aberration measurements are able to predict the impact of monochromatic aberrations on CS. Rocha et al (2010) corrected the wavefront aberration in highly aberrated eyes showing the great clinically benefit that these kind of patients could benefit when the wavefront aberrations are corrected. Showing the potential advantages of customized refractive surgery, customized CL corrections, and wavefront customized IOL implantation. These authors also studied the changes in visual performance after HOAs correction and different aberration patterns simulations in normal eyes. The studies showed that the visual performance after wavefront aberration correction in normal eyes was statistically significant improved, although not clinically significant for all patients. In addition, this also happened in those subjects with highly aberrated eyes. This could be attributed to a neuroadaption. On the other hand, they also found that a greater amount of aberrations (more RMS), further loss of VA, and aberrations near the center and at the top of the Zernike pyramid (see figure 1.4) decreased VA significantly more than modes near the edge or at the bottom of the pyramid (Rocha et al., 2007b, Rouger et al., 2010a, Rouger et al., 2010b). Nevertheless, the certain amount of wavefront aberrations could have a positive effect on visual performance. Rocha et al. (2009) reported that certain amount of spherical aberration may improve depth of focus (DoF), but we must bear in mind that the visual quality may be compromised.

1.4 VISION CORRECTION APPLICATIONS

Using a visual simulator a patient may experience the vision that will be possible before being subjected to such corneal refractive surgery or intraocular. Can also be considered experimental designs ablation algorithms for laser or intraocular designs, before creating prototypes to implement in order to evaluate the visual quality that can provide different surgical and nonsurgical techniques for the correction of refractive errors. The visual simulator allows the measurement of aberrations in real time without the need of prototypes or performed the surgical technique neither. With this can be analyzed the vision that can provide a kind of solution, analyzing the visual benefits, minimizing risk and evaluation times after treatment. The application of solutions for correction of refractive errors and different solutions for the correction of presbyopic or treatment of eyes with optical distortion, such as keratoconus, are the key to implementing this new technology in patients. Moreover, as we discussed above, these types of systems allow us to know more about what are some of the neural mechanisms of vision. The visual simulator is a technology that can be applied practice and realistic way, in order to obtain best procedures to enhance the visual quality of patients.

1.4.1 CONTACT LENSES

A customized CL is a potential means of correcting the HOAs of the human eye, since they are centered over the cornea, close to the visual axis, and this alignment remains relatively constant in all position of gaze. Initial inspection of the average distribution of HOAs across a typical pre-presbyopic population (Porter et al., 2001) requiring refractive correction shows a distinct deviation from zero for spherical aberration while all other Zernike terms have an average close to zero. This would suggest that an appropriate aspheric correcting surface would reduce the spherical aberration of the eye significantly if it were incorporated into a CL. Although, when eyes are highly aberrated, it is not enough with the aspheric surfaces, so attempts have been made to improve visual performance by correcting the HOAs of the eye using CL manufactured specifically for individual eyes (customized-CL). López-Gil et al. (2002) demonstrated that the CL can be manufactured with sufficient precision and accuracy to reliably generate the amount of aberration desired. The CL was manufactured to induce certain target amounts of pure coma, trefoil or spherical aberration in normal eyes. The results showed a very good agreement between the target, the *ex-vivo* and the *in-vivo* aberrations. The main advantage of the customized-CLs in comparison to customized refractive surgery is its reversibility. In addition, it could be adapted in cases where surgery is not possible or complicated, i.e., keratoconus. However, there are also potential problems that may limit the use of CLs to correct ocular wavefront aberrations, since the flexure, translation, rotation and tear layer may introduce spurious aberrations. The effect of pupil size and accommodation on ocular aberration may cause further difficulties.

1.4.1.1 Customized Contact Lenses in Clinical Practice

Patients with significantly greater levels of ocular HOAs, particularly those with aberrations induced by pathological conditions, such as keratoconus or surgery such a penetrating keratoplasty will benefit in terms of improved retinal image quality with even partial correction of these aberrations. The principal limitations for the ocular wavefront aberration correction by CLs are its translation and rotation with respect to its position. It is feasible to correct HOAs and improve visual performance in pathological or postsurgical eyes. The extent to which eyes within the normal preoperative population can benefit is still to be established and may vary greatly on an individual basis not only by the magnitude of the HOAs present but also in the ability of fitting the lens design in a stable and centered position.

1.4.1.2 Limitations of the Ocular Wavefront Correction with Contact Lenses

The slight changes in the centration and rotation of a lens designed to correct aberrations will significantly reduce the visual benefits experienced by that correction. Guirao et al.(2001) and López-Gil et al. (2009) reported that the Zernike terms rotated from ideal correction could generate lower order aberrations. Hence, a correcting lens with coma will generate astigmatism and defocus when translation; spherical aberration will produce coma, tip and tilt, while defocus or astigmatism will produce only tip and tilt (prism). In general, Zernike terms of higher radial order are less tolerant to translation than lower order radial terms. Clearly the visual benefit of a lens designed to correct both lower and HOAs is depend on repeatable lens translation and rotation following each blink or eye movement.

1.4.2 CORNEAL REFRACTIVE SURGERY

Currently the most common corneal refractive surgeries are Photorefractive Keratotomy (PRK) and LASIK. Initially these procedures are focus on the correction of sphero-cylindrical refractive error. Unfortunately, after this kind of surgeries there is a significant increase of ocular HOAs; especially coma and spherical aberration. Several authors (Marcos et al., 2003, Cano et al., 2004, Gatinel et al., 2010) reported a strong increase of HOAs after corneal laser surgery that is correlated with a significant decrease in quality of vision, especially under mesopic conditions. The most prominent change that takes place with myopic excimer laser surgery is an increase of positive spherical aberration, while hyperopic treatments tend to induce an increase of negative spherical aberration. This significantly HOA increment involves a CS reduction, especially at high frequencies and under mesopic conditions (Montes-Mico et al., 2003, Montes-Mico et al., 2007b, Yamane et al., 2004). The ablation itself, flap creation, corneal biomechanics and other effects of surgery are the potential sources of the HOAs changes after surgery.

Yoon and Williams et al. (2002) showed that adaptive optics facilitated a considerable increase in CS at high spatial frequencies because of correction of monochromatic aberrations. These findings generated a surge of interest in wavefront technology, and its application to customized corneal laser treatment. Only a few years later, wavefront-guided ablation has become widely available for laser vision correction in humans. Thus, it is now routine to measure the optical aberrations of the eye beyond sphere and cylinder with the ultimate goal of achieving an ideal optical correction and improving the quality of the retinal image. In 2002, the FDA approved the first customized, wavefront-guided myopic laser ablation in the United States and multiple proprietary platforms for wavefront-guided ablation are now in use. Along with the rapid development of these systems and the accompanying marketing to both surgeons and patients, there has been a dramatic increase in expectations of what laser vision correction can achieve. However, several limitations persist and the goal of aberration free or “super vision”, at least for most of the patients, is still far from reality. While wavefront-guided treatments are customized in the sense that treatment is directed at patient-specific aberrations, the same treatments not infrequently lead to unpredictable visual outcomes at rates that are similar to conventional ablations attributable to factors such as variability in wound healing and biomechanical factors related to the cornea. Accordingly, a custom treatment does not guarantee a custom outcome for a given patient.

1.4.2.1 Wavefront-guided Refractive Surgery in Clinical Practice

Wavefront-guided refractive surgery has, as a new goal, to correct or at least minimize all optical aberrations of the eye, and consequently to improve or preserve visual performance, especially under scotopic conditions. Several studies (Vongthongsri et al., 2002, Kaiserman et al., 2004, Kim and Chuck, 2008, Keir et al., 2009, Khalifa et al., 2012, D'Arcy et al., 2012, Zhang et al., 2013) have shown that the wavefront-guided customized corneal ablations are safe, effective, and predictable, even in eyes highly aberrated and for large pupil patients. Compared with conventional treatments, wavefront-guided ablations can achieve a reduction in preexisting HOAs and less induction of new HOAs, resulting in improved outcomes with CS and visual symptoms under mesopic and scotopic conditions. Considering that wavefront-guided LASIK does not increase HOAs and does not modify CS compared with preoperative values. It has been reported better option for retreatment than standard LASIK (Castanera et al., 2004, Schwartz et al., 2005, Alio and Montes-Mico, 2006). Wavefront technology is still evolving to address current limitations and to optimize customization of corneal ablations.

1.4.2.2 Limitations of Wavefront-guided Ablation

A major claim to support customized treatment is that it induces less HOAs than conventional treatment. However, some studies demonstrated that the total amount of HOAs is not a reliable predictor of visual performance, since the combination of specific Zernike modes can increase or decrease the visual function for a given level of RMS (Applegate et al., 2003). It remains to be established which specific aberrations or combinations of aberrations are the most critical to decrease or at least maintain unchanged. Just as importantly, it is uncertain whether wavefront-guided ablation can be applied to eliminate specific HOAs or create combinations of aberrations that might improve visual performance. Levy et al. (2005) demonstrated the presence of HOAs in patients with “super-vision” (uncorrected VA better than or equal to 20/15), possibly confirming the beneficial effects of some aberrations or at least no considerable deleterious effect on visual performance.

In addition, several factors tend to limit the success of wavefront-guided treatments and will need to be overcome to optimize clinical results. These factors are:

- *Age-related changes in HOAs*: Wavefront measurements of the eye alter with age because of changes that occur in the lens, cornea, and other structures. Thus, even if an ideal customized ablation were possible, the effects would be unlikely to last because of age-related changes in aberrations.
- *Pupil size*: Constant changes in pupil size as a result of alterations in illumination, accommodation, and convergence affect the levels of HOAs that influence visual performance in an individual eye.
- *Accommodation*: The pattern of HOAs in an individual depends on the state of crystalline lens accommodation. Thus, customized treatments target a static state of HOAs that is not observed during the daily activities of a particular individual.
- *Ocular surface*: The air-tear interface is the most important refractive surface of the eye. Small changes in tear production and distribution, as well as abnormalities of the ocular surface, have a major effect on the aberrations of the eye and will influence the efficacy of customized ablations.
- *Retinal limits*: There is a morphological limitation to visual performance imposed by the ability of photoreceptors to sample the retinal image. Independent of the quality of the optics, there is a biological limitation, which varies somewhat from person to person depending on photoreceptor density and other factors.
- *Neuroplasticity*: Ideally, the targeted correction of wavefront aberrations should also take into account the visual needs and preferences of the individual patient. Cortical adaptation may impose an important limitation since neuroplasticity cannot yet be evaluated efficiently. Thus, it is not possible at the present to determine which aberrations may have been developmentally suppressed by neural processing and which ones are “seen” because they are transmitted to the visual cortex of a particular individual.
- *Postoperative issues, wound healing and biomechanical effects*: The highly accurate mathematical certainties of customized ablations are not as reliably reproduced on living tissues because of the complexity and variability of wound

healing and biomechanical responses. A major limitation hindering the accuracy of customized treatments is the variability of postoperative corneal responses.

Despite of these limitations, even partial correction of abnormalities in highly aberrated eyes that have irregular astigmatism, central islands, decentrations, and other clinical problems could significantly benefit individual patients. Eyes with considerable levels of HOAs are more likely to benefit from customized corneal treatments, especially those with asymmetrical astigmatism, nonorthogonal astigmatism, or spherical aberration.

1.4.3 INTRAOCULAR LENSES

Exist two different kinds of IOLs; those that are used to replace the natural lens of the eye following its removal after development cataract are called pseudophakic IOLs. And the IOLs that are placed in the posterior chamber between the cornea and the crystalline lens in order to correct the refractive error are called phakic IOLs.

1.4.3.1 Pseudophakic intraocular lenses designs

Nowadays cataract surgery is focused not only on restoring VA but also on providing the best possible visual quality. Wavefront-sensor technology has been applied to IOLs designs to provide better image quality and hence better visual performance for patients who have cataract surgery with IOL implantation. As we explain before, both the cornea and natural lens contribute to the total HOAs of the eye; partially compensating each other in a normal young subjects and this balance is progressively lost with age, due to, principally, crystalline lens changes. When the natural lens is removed, obviously, the HOAs will be increased due to the unbalanced effect, and the true corneal aberrations will become apparent. Conventional IOLs designs are spherical. Some new designs use aspheric profiles with negative (aberration-correcting IOLs) or zero spherical aberration values (aberration-free IOLs) to correct or preserve the positive corneal spherical aberration, respectively (figure 1.18). Several IOLs with different degrees of spherical aberration are commercially available; therefore, cataract surgeons can choose the IOL design based on the corneal aberrations of the individual patient.

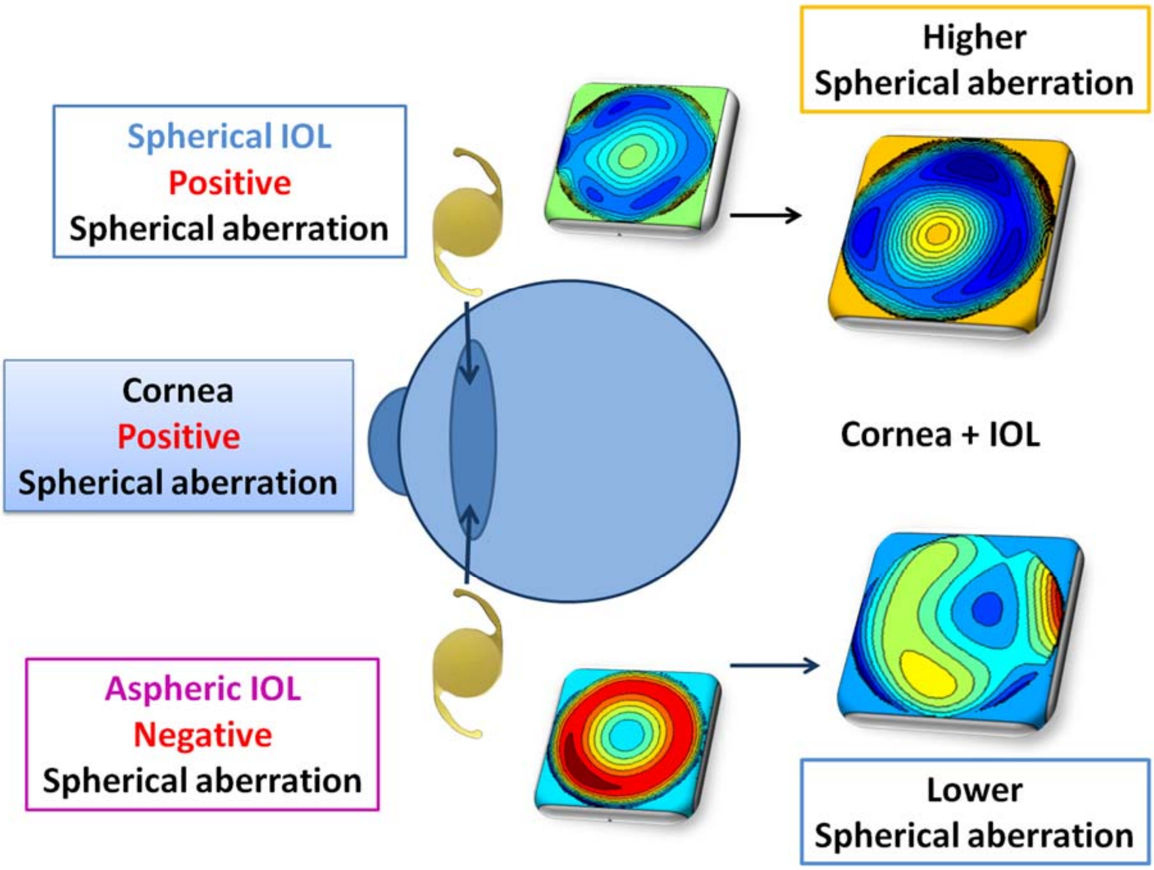

Figure 1.18: Schematic illustration of the effect of the coupling of corneal aberrations and spherical or aspheric IOL.

Aspheric IOLs in Clinical Practice

Several studies have evaluated the optical and visual performance after aspheric and spherical IOL implantation (Kasper et al., 2006, Rocha et al., 2006, Johansson et al., 2007, Rekas et al., 2008, Cadarso et al., 2008, Takmaz et al., 2009, Trueb et al., 2009, Lee et al., 2011). They agreed that the spherical aberration is lower after aspheric IOL implantation than after spherical designs and this effect is greater for higher pupil diameters. Besides, the mesopic CS was better with the aspheric IOLs than with spherical IOLs, but VA values were similar with both IOL designs. Similar VA and CS values were obtained with aspheric IOLs with different amounts of spherical aberration. The aberration-correction IOLs reduced the spherical aberration more after surgery than the aberration-free IOLs, but the aberration-free IOLs showed better DoF, because of this residual of spherical aberration (Marcos et al., 2005, Rocha et al., 2007a).

Limitations of Aspheric IOLs

Theoretically, aspheric IOLs would provide better visual performance than spherical IOLs. However, there are some controversial between studies in terms of whether aspheric IOLs give better performance (Holladay et al., 2002, Dietze and Cox, 2005, Marcos et al., 2005, Marcos et al., 2007, Rocha et al., 2007a, Elkady et al., 2008, Montes-Mico et al., 2009). It is clear the visual advantages of the aspheric IOLs over the spherical IOLs, especially related to bigger pupil sizes. Although, it also found limitations to the benefits of reducing spherical aberration, such as IOL tilt and/or decentration, DoF, and customization to a specific corneal spherical aberration. Several studies have measured HOAs of spherical and aspheric IOLs *in vitro* at different degrees of decentering (Eppig et al., 2009, McKelvie et al., 2011, Madrid-Costa et al., 2012b). They found that the IOL models with lower, or an absence of, negative spherical aberration were most robust to displacement with increased decentration and tilt angle. This could be attributed that with aspheric IOLs decentration asymmetrical 3rd-order aberration increased more than with spherical IOLs (Dietze and Cox, 2005). Recently studies (Madrid-Costa et al., 2012a, Madrid-Costa et al., 2012b, Ruiz-Alcocer et al., 2012b, Ruiz-Alcocer et al., 2012a) have simulated the vision after different designs of IOLs at different degrees of decentering and for different corneal aberration profiles. They found that a slight positive residual spherical aberration could provoke an improvement in the DoF of patients after cataract surgery and this situation will depend not only on the intrinsic design of the IOL (aspheric or spherical) but on the combination of the IOL and the patient's corneal profile. They also reported that in patients with previous myopic LASIK, aberration correcting IOLs should be implanted, in contrast in patients with previous hyperopic LASIK, spherical IOLs were more robust to misalignments. The potential benefits of aspheric IOLs are also limited by inaccurate or absent preoperative measurement of the ocular parameters necessary for IOL power calculation, inaccurate manufacturing, inability to locate the IOL in the correct plane, and surgically induced aberrations (Marcos et al., 2007, Elkady et al., 2008). However, the optical and visual performance of aspheric IOLs is, even in the worst cases, equal to or better than that with spherical IOLs. Surgeons should consider aspheric IOLs for patients and try to customize the asphericity depending on the patient's corneal spherical aberration to obtain the optimum visual performance (Montes-Mico et al., 2009).

1.4.3.2 Phakic intraocular lenses designs

Phakic IOLs are used to correct the refractive error. Despite the use of highly optimized and customized laser treatments such as wavefront-guided, aspheric, and topography-guided ablations, the physical limitations of corneal thickness, curvature, and tissue remodeling limit the indications for a safe corneal refractive procedure. Moreover, the optical quality of the outcomes may not be as good as desired, especially when treating high refractive errors that may require small optical zones, especially in patients with thin corneas and large mesopic pupil sizes. In the absence of contraindications, phakic IOL implantation is the best approach in young patients with moderate to high refractive errors and in those who have a contraindication to a corneal refractive procedure (eg, thin corneas). The insertion of an IOL in a phakic eye should be simple, precise, and reproducible and should produce successful optical results. Advantages are that phakic IOL implantation maintains accommodation and is conceptually reversible (Guell et al., 2010).

Exist three general types of phakic IOLs: angle-supported anterior chamber, iris-claw anterior chamber, and posterior chamber, which are usually fixated in the ciliary sulcus. Each design has its own features, selection criteria, surgical technique, results, and complications. The implantation of phakic IOLs has been demonstrated to be an effective, safe, predictable, and stable procedure to correct moderate and high refractive errors. Complications are rare and are primarily related to the site of implantation.

1.5 PRESBYOPIA

Presbyopia is an age-associated deterioration in the focusing ability of the eye for near objects. It is a normal and expected feature of human visual physiology. There are many age-related changes in different structures of the eye, which have an impact on refraction, retinal image quality, visual performance and presbyopia. The aging eye suffers changes on the cornea and tears film, pupil, crystalline lens, vitreous humor, axial length and ciliary muscle.

- *Cornea and tear film*: Corneal curvature, thickness, and refractive index remain essentially constant, but there is a slow change in corneal astigmatism (Lyle, 1971). The tear production is reduced and evaporation rates are higher in the older eye (Guillon and Maissa, 2010). The light scattering in the cornea increases and the corneal sensitivity and endothelial cell density declines with age (Allen and Vos, 1967, Millodot, 1977, Abib and Barreto Junior, 2001).
- *Pupil (miosis senile):* the pupil diameter under constant lighting conditions reduces progressively with age at all luminance levels (Winn et al., 1994).
- *Crystalline lens:* the lens undergoes a gradual change in its dimensions, surface curvatures, and refractive index distribution due to the progressive addition of new fibers as it ages (Barraquer et al., 2006, Doyle et al., 2013). Because of an increase in optical density the lens also suffer a gradual loss in transmittance.
- *Vitreous humor:* the vitreous gel is gradually replaced by unbound water so that more movement of the vitreous becomes possible. Optically, the effect is that increased number and movement of "floaters" may occur.
- *Axial length:* Grosvenor (1987) proposed that the axial length decreased throughout the adulthood as an emmetropizing mechanism, occurring in harmony with the increase in the refracting power of the eye, which would otherwise cause the refraction of the eye to move in the myopic direction.
- *Ciliary muscle:* the magnitude of ciliary muscle accommodation movement is reduced with increasing age (Croft et al., 2009, Lutjen-Drecoll et al., 2010).

These changes have some effects on the eye, such as changes in refraction, in total ocular aberrations, scattered light, total ocular transmittance and retinal image quality. Presbyopia is also defined as the loss in accommodative amplitude due to the loss in the ability of the lens to change shape. Changes in the behavior of the contractile ciliary muscle accompanied by augmented rigidity of the lens are the most important aspects in the loss of accommodation (figure 1.19). Both lens thickness and trabecular-ciliary process distance were the parameters that showed major alterations with the loss of accommodation in patients of different ages (Benozzi et al., 2013, Croft et al., 2013, Richdale et al., 2013, Charman, 2014).

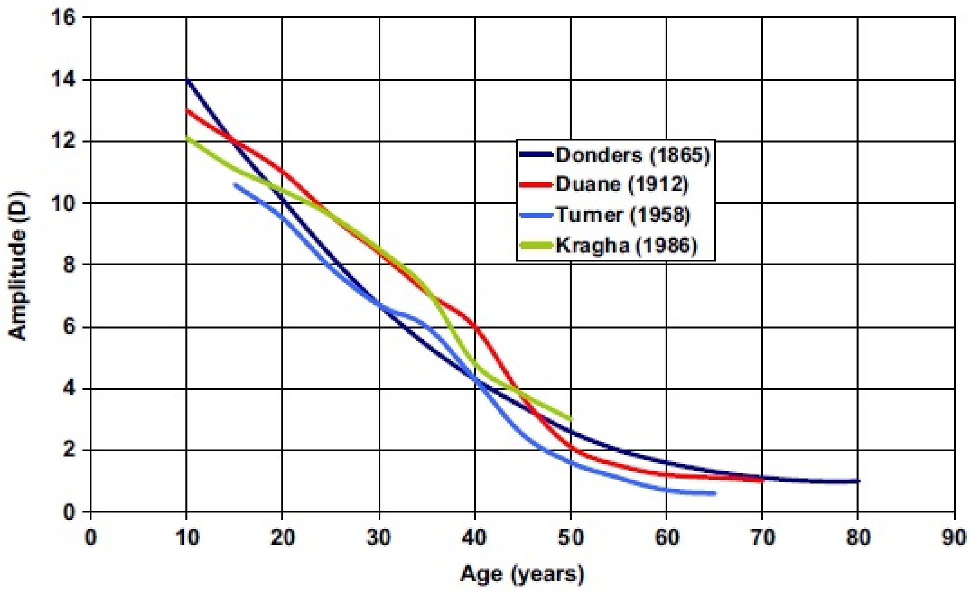

Figure 1.19: The declining amplitude of accommodation with advantage age, as determined by different authors (Charman, 2014 courtesy)

1.5.1 PRESBYOPIA CORRECTION

Many options exist for the correction of presbyopia, including spectacles, CLs, and surgical procedures. Spectacle lenses generally provide better vision quality than alternative methods of correction, such as multifocal CLs and IOLs, which often rely on the creation of multiple images or simultaneous vision. These images overlap on the retina, which a defocused image decreasing the contrast of the image focused for the intended viewing distance. However, the aging population is growing and need better option for near work. Because life expectancy is increasing, a large number of patients will develop presbyopia and cataracts and thus the demand for spectacle-free near vision continues to increase (Goertz et al., 2013). This has resulted in the development of new designs of multifocal CLs and IOLs.

1.5.1.1 Spectacle lenses

Spectacle lenses are relatively simply to prescribe, powers can be modified easily as the visual needs of the patient change, few risk are associated with their use, and many kinds of spectacles are relatively inexpensive. The additional plus power prescribed when correcting presbyopia with spectacle lenses is known as the near addition or add power. It typically ranges from +1.00 to +3.00 D, depending on the residual amplitude of accommodation and vision requirements of the wearer. There are two ways to the correction of presbyopia: *single vision lenses* only for near task and *multifocal lenses* that provide a correction for distance and close vision.

1.5.1.2 Contact lenses

Despite apparent improvements in multifocal CL designs, practitioners are still under-prescribing with respect to the provision of appropriate CLs for the correction of presbyopia. It has reported that the majority of presbyopic CL patients (63%) are still fitted with nonpresbyopic corrections. Simultaneous-image designs represent 29% of all fittings, whereas monovision corrections represent 8% the fitting worldwide (Morgan et al., 2011). It is important to know that successful CL wear by the older patient depends upon more than optical factors alone. Age-dependent ocular changes such as decreased tonus of both upper and lower eyelids, a reduced palpebral aperture, and decreased lacrimal production and tear stability may all influence the success of CL wear. The presbyopia correction throughout CLs could be by *monovision, Altering-image correction and simultaneous-image correction*.

Monovision

Monovision is a popular method for correcting presbyopia, where one eye (usually the dominant eye) is corrected for distance vision and the other for near. Monovision harnesses the capacity of the brain to process the focused retinal image from one eye, while suppressing the other eye's unwanted out-of-focus image. However, this suppression occurs at the expense of stereoacuity. The higher monocular addition is the more pronounced stereoacuity losses are. Monovision success depends on using overlapping DoF of the 2 eyes to achieve reasonable acuity over a range of distance (figure 1.20). Using both positive and negative DoF for each eye allows a minimal difference in powers between the distance and near corrections (Charman, 1980).

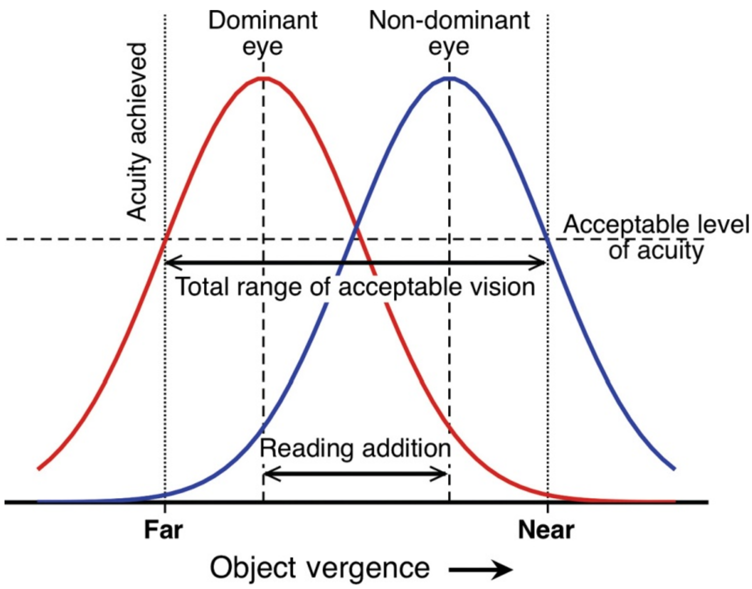

Figure 1.20: The through-focus changes in VA for each eye in monovision, assuming that no accommodation is possible (Charman, 2014).

Alternating-image correction

Alternating-image correction is commonly performed with bifocal CLs, which are manufactured with 2 distinct sectors of different refractive power, one for distance and another for near, placed at the top and bottom of the lens, respectively. They are designed to change position with respect to the pupil when a change is made between distance and near fixations. The intended translation is usually, but not always, in the vertical direction, the orientation of the lens being stabilized by prism or lens truncation. These lenses provide excellent quality of vision for both distance and near visual demands long as a good translation is achieved. Some altering lenses also incorporate a segment for intermediate-vision correction (ie, trifocals). In practice, the effective of altering bifocal CLs is limited by the lens movement. Excessive after blink movement, rotational instability, large pupil diameters, or a near zone located too high can result in the near portion of the lens occupying a significant part of the pupil when distance objects are viewed (Charman, 2014).

Simultaneous-image correction

In simultaneous-image correction, light rays corresponding to (1) both distance and near corrections (bifocal) or (2) distance, near, and intermediate correction (multifocal) are imaged onto the retina. In each case, the retina received both in-focus and out-of-focus stimulus, while suppressing out-of-focus stimuli. The spread of light from the out-of-focus ("unwanted") images impairs the contrast of the focused ("desired") image, resulting in a retinal image of reduced contrast. The contrast losses are dependent on the relative amount of in-focus to out-of-focus light incident onto the retina. This balance varies with the pupil size (Bradley et al., 1993). Performance with simultaneous-image CL designs may also be influenced by the inherent aberrations of the eye, such as spherical aberration (Martin and Roorda, 2003, Bakaraju et al., 2010). As in monovision correction, simultaneous vision correction is based on the principles of blur adaptation, blur tolerance, and suppression of superimposed multiple images on the retina, which occur at cortical level. The effectiveness of any simultaneous images CL design should be evaluated in terms of enhancement that it produces over the natural DoF of the eye (Charman, 2014).

1.5.1.3 Presbyopia surgery

One of the major challenges in refractive surgery over past years has been restoration of near vision in individuals with presbyopia. Currently surgical procedures are based on 3 techniques to restore unaided near and distance vision. They are monovision, one eye corrected for distance and the other for near; multifocality, increasing the DoF, by providing simultaneously distance and near vision; and accommodation, achieving real changes in ocular/lens power. Only accommodating IOL are, in principle, able to provide a dynamic change in the optical power of the eye and hence a real restoration of at least some true accommodation. The remaining techniques compensate presbyopia by inducing monocular or binocular pseudoaccommodation, which can be defined as an artificial accommodative function generated by interfering corneal or intraocular optics. The efficacy of the refractive surgery in presbyopic patients to restore near vision depends on several characteristics of the individual patient such as their biometric parameters, age, and near-vision needs in everyday life. Not all techniques are suitable for any individual patient and not all patients are suitable for any one technique.

Corneal refractive surgery

Corneal pseudoaccommodation can be achieved by means of a corneal multifocal ablation providing focus for distance and simultaneously reducing the near spectacle dependency in presbyopic patients (Telandro, 2004, Becker et al., 2006). This multifocality induces an increase in the DoF that aims to compensate for the loss of accommodation at the crystalline lens. This technique is called ***presbyLASIK***, which uses the principles of LASIK surgery to create a multifocal corneal surface. There are three different ablation profiles to achieve corneal multifocality, transitional multifocality, peripheral presbyLASIK and central presbyLASIK (Alio et al., 2009). The first ablation profile achieved apparently good VA outcomes at near and distance. However, the corneal vertical coma induced to get the multifocality, has a negative effect on the patient's visual quality (Anschutz, 1994). Peripheral presbyLASIK is more common in hyperopic patients, due to the corneal tissue need to be removed in a myopic patient (Pinelli et al., 2008, Epstein and Gurgos, 2009). It had been shown that central presbyLASIK may be used to improve functional near vision in patients with presbyopia (Alio et al., 2006, Illueca et al., 2008). Nevertheless, there are some limitations of presbyLasik, such as the fact of the little high-quality level of scientific evidence for its practice, the dispersion of the techniques and the lack of uniformity of the ablation profiles offered by different excimer laser technologies. Besides, one of the major concerns about multifocality is the reversibility of the procedure. Further studies are necessary to implement the scientific evidence of these techniques (Alio et al., 2009).

Intraocular lenses and cataract cataract surgery

Cataracts occur in elderly patients as a natural result of the ageing process causing a loss of vision. Cataract surgery is the more common surgical procedure in the developed world, whereas cataract is de most common cause of treatable blindness in the developing world. Nowadays, in the developed countries, patients undergoing cataract surgery have high expectations for the postoperative result and want spectacle independence in distance and near vision (Ashwin et al., 2009). When the presbyopia is accompanied by incipient cataract formation, patients who seek presbyopia correction are more often guided toward cataract surgery than to cornea surgery. Even in the presence of a clear crystalline lens, if there is a concomitant refractive error, cataract surgery, rather than corneal surgery, is the procedure of choice. Cataract surgery is then called refractive lens exchange, thus indicating that the procedure is taking place without the presence of a cataract. Modern IOLs designs are now offered for presbyopia (multifocal and accommodative), astigmatism correction (toric) and reduced aberrations (aspheric).

Multifocal IOLs are designed to generate two separate focal points along the optical axis, thereby producing the functional equivalent of accommodation. The aim is to provide good unaided distance and near vision as well as functional intermediate vision. However, there are some side effects of this technology, such as CS losses and photopic problems like glare and halos. To achieve multifocality, these lenses use either the principle of diffraction and/or refraction and they may be divided into three groups: *diffractive, refractive or hybrid multifocal IOLs*.

- *Diffractive multifocal IOLs* generate an interference patterns using multiple diffractive rings with a gradient starting from the center of the IOL to the periphery. These rings serve as a phase grid leading to diffraction of the incoming light and therefore, allow the creation of the two foci independently of the pupil diameter. Height and size of the diffractive steps on the lens are used to separate the distance and near foci (addition) and the percentage of light distribution between foci (figure 1.21). An unwanted side effect is that approximately one-fifth of the light is lost to higher-order foci and aberrations (Alfonso et al., 2007).

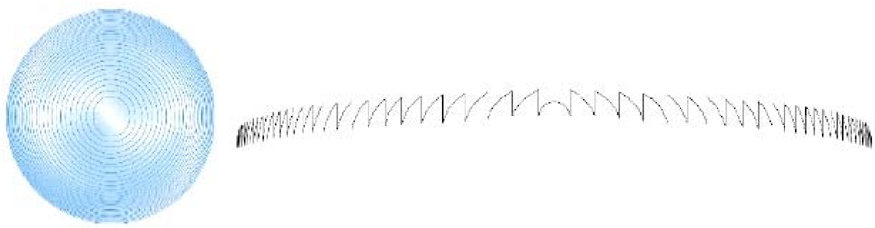

Figure 1.21: Full-optic diffractive multifocal IOL.

- *Refractive multifocal IOLs* have different zonal areas with different refractive powers (figure 1.22). These zones are typically annular in shape around the center of the IOL. Refractive multifocal IOLs normally use a series of zones with near and distance foci, thus being multifocal with 2 main foci. These IOLs are pupil-dependent and, therefore, will perform differently under different light conditions. A typical side effect of this kind of IOLs is halos (Montes-Mico and Alio, 2003, Montes-Mico et al., 2004).

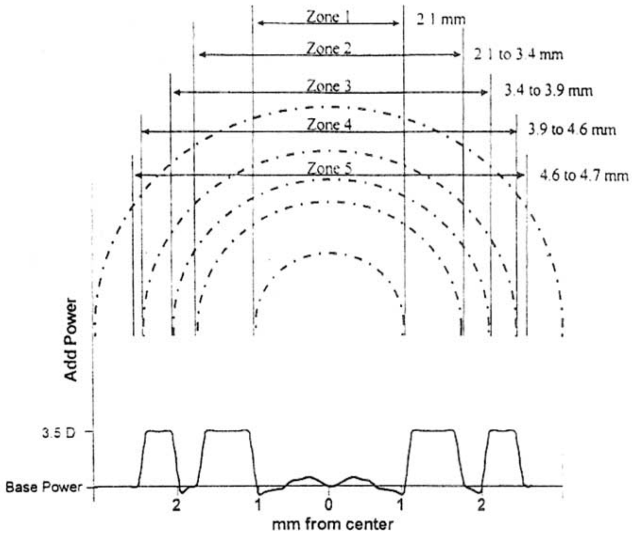

Figure 1.22: Schematic representation of the zonal-progressive multifocal lens design (Montes-Mico et al., 2004).

- *Hybrid multifocal IOLs* combine refractive and diffractive optics to reduce the disadvantages of conventional IOLs with either refractive or diffractive designs (Madrid-Costa et al., 2010).

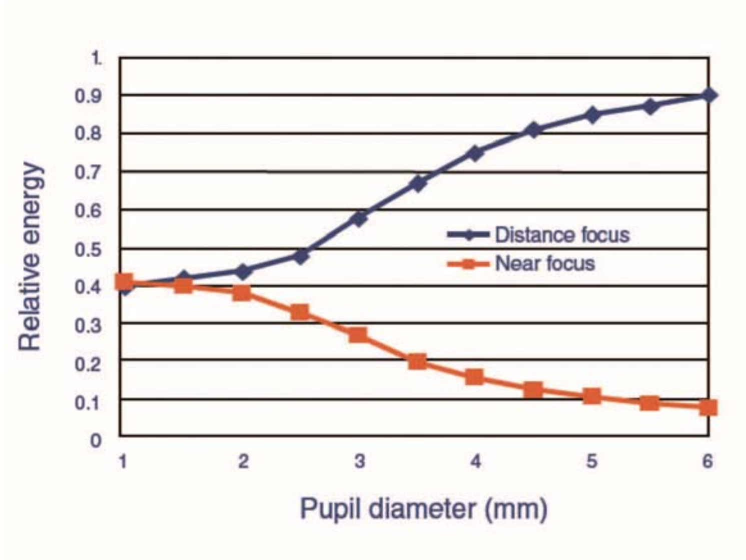

Figure 1.23: Relative energy distribution between foci as a function of the pupil diameter of the hybrid multifocal IOL (Madrid-Costa et al., 2010).

It has been shown (Montes-Mico and Alio, 2003, Montes-Mico et al., 2004, Zelichowska et al., 2008) that multifocal IOLs slightly reduce the CS in comparison with monofocal IOLs. This is due to several factors, such as the division of light energy through 2 focal points (Montes-Mico and Alio, 2003), the straylight (Pieh et al., 2001, Montes-Mico and Alio, 2003, de Vries et al., 2008) and the aberrations produced by the multifocal IOLs (Zeng et al., 2007). Despite of this CS reduction, some studies reported a CS improvement over time, probably due to neural adaptation (Sasaki, 2000, Montes-Mico and Alio, 2003), achieving values like those obtained with monofocal IOLs and within normal values. Near CS was lower than distance CS, because of near focus has a lower percentage of energy. Thus, near vision may be compromised under mesopic conditions, especially with pupil-dependent IOLs. However, near activities are usually performed under photopic conditions, besides the pupil normally shows some constriction at near vision, as a part of the near triad action (Montes-Mico et al., 2004). Regarding VA achieved after multifocal IOL implantation, studies agree that multifocal IOLs provide an improvement at near vision without need an additional correction, (Hutz et al., 2006, Alfonso et al., 2007, Chiam et al., 2007, Zelichowska et al., 2008, Hayashi et al., 2009, Alio et al., 2011b, Alio et al., 2011a). These findings confirm the ability of the multifocal IOLs to provide functional near reading performance, which has a positive effect in the patients' quality-of-life (Javitt et al., 2000, Kohnen et al., 2006, Chiam et al., 2007, Zelichowska et al., 2008, Alio et al., 2011b). Hence, multifocal IOLs improve near and intermediate VA in comparison with monofocal IOLs, without altering distance VA. Comparing the different designs of multifocal IOLs, studies showed that multifocal IOLs with diffractive components provide better near visual performance than monofocal and refractive multifocal IOLs (Hutz et al., 2006, Chiam et al., 2007, Zelichowska et al., 2008, Madrid-Costa et al., 2010, Alio et al., 2011a). Several authors (Dick et al., 1999, Pieh et al., 2001, Montes-Mico and Alio, 2003, de Vries et al., 2008) also reported straylight and others unwanted optic effects, such as glare and halos after multifocal IOL implantation; which were more accused in patients implanted with refractive multifocal IOLs (Chiam et al., 2007, Cervino et al., 2008).

Accommodating IOLs are designed to transmit ciliary muscle contraction into a change of dioptric power of the eye. Currently, there are two design concepts of accommodating IOLs: *single optics and dual optics designs* (Glasser, 2008). Single optics device are based on the optic-shift principle, relying on an anterior movement of the lens optic with ciliary muscle contraction to generate an increase in refractive power, although the precise mechanisms of action do vary between designs. The amount of power change depends on the magnitude of translation and the positive diopters power of the lens. The power change of the translating lens has been increased in a dual-optic design (McLeod, 2006) that combines a more powerful positive lens with a negative lens. The translating positive front optic is combined with a stationary negative rear optic and, because the front optic has a larger dioptric power than the single-optic design, the dual optic could achieve a greater accommodation with the same translation movement than single-optic design (figure 1.24). The single optics design have generally failed, the anterior shift that provide is generally too small and variable to provide clinically useful accommodation (Marchini et al., 2004, Kriechbaum et al., 2005). Clinical studies suggest that rates of posterior capsular opacification are significantly higher in eyes implanted with accommodating IOLs, compared with standard monofocal implants (Sheppard et al., 2010). Current evidence indicates that accommodating IOLs still have a long way to go to provide reliable and large levels of accommodation (Menapace et al., 2007).

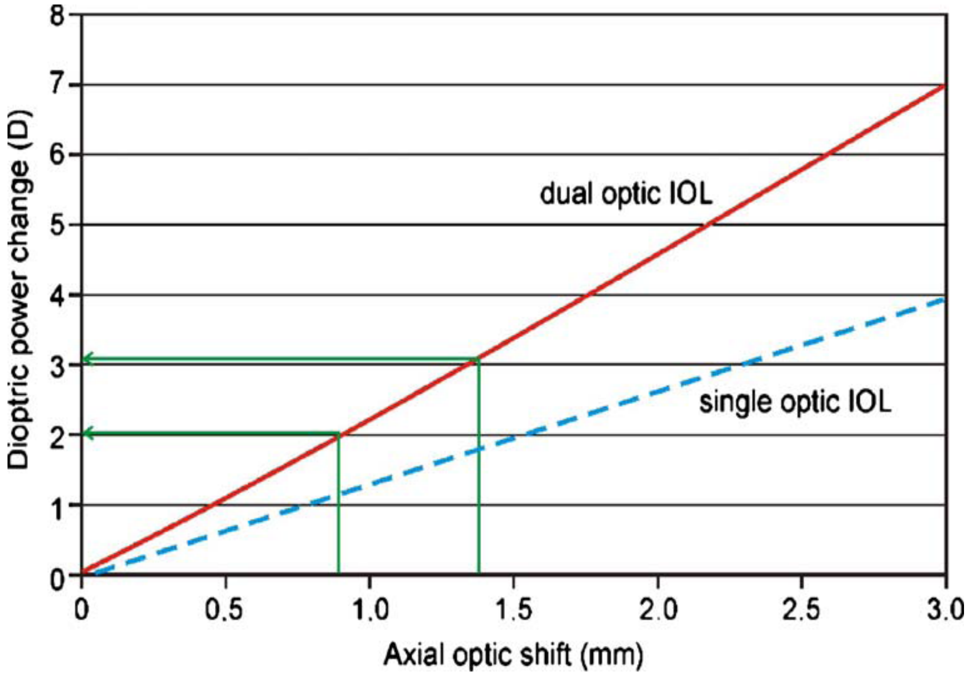

Figure 1.24: Increase in shift-induced dioptric power change.

CHAPTER 2

Optical and Visual Quality of the Visian Implantable Collamer Lens using an Adaptive-Optics Visual Simulator

2.1 INTRODUCTION

There is an increasing number of patients who wish to correct their refractive error by means of refractive surgery. Even though nowadays the most popular option is still LASIK, there are other options available, such as the implantation of phakic IOLs, which is a good alternative when high levels of myopia or hyperopia are to be corrected, since patients with high refractive errors or thin corneas may not be good candidates for LASIK due to the risk for corneal ectasia.

The Visian ICL (STAAR Surgical, Nidau, Switzerland) is a posterior-chamber phakic ICL approved by the United States' FDA for the treatment of moderate to severe myopia. Research studies have shown that the ICL is effective for the correction of myopia (Gonvers et al., 2001, Uusitalo et al., 2002, Sanders et al., 2003, Lackner et al., 2004, Sanders et al., 2004, Pineda-Fernandez et al., 2004, Kamiya et al., 2009, Ieong et al., 2009, Ieong et al., 2010, Alfonso et al., 2011), hyperopia (Davidorf et al., 1998, Pesando et al., 2007), and astigmatism (Alfonso et al., 2010a, Alfonso et al., 2010b). Moreover, other comparative studies (Sanders and Vukich, 2003, Kamiya et al., 2008, Igarashi et al., 2009) concluded that this surgical procedure outperforms LASIK in all measures of safety, efficacy, predictability, and stability, even in eyes with low levels of myopia (Sanders and Vukich, 2006, Sanders, 2007). These results are probably due to the fact that, since ICL treatment does not include any surgical tissue ablation, it induces significantly lower amounts of ocular HOAs than LASIK does (Igarashi et al., 2009).

HOAs could increase after ICL implantation due to the intrinsic properties of the lens (i.e. spherical aberration increases with ICL power) and also depending on the particular type of incision made during the surgical procedure (Kim et al., 2011).

The aim of this study was to evaluate the optical and visual quality provided by ICL of various powers, and the effect of small- and large-incision surgery. For this purpose we used an adaptive-optics system to simulate vision from the ICL's aberration pattern itself. VA for different contrasts, as well as CS were evaluated for 3- and 5-mm pupils.

2.2 PATIENTS AND METHODS

This prospective study was approved by the Institutional Review Board at the university of Valencia-Research Group of Optometry and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from each participant after verbal and written explanation of the nature and possible consequences of the study. The patients gave informed consent to participate in this research.

This study included eleven eyes of eleven individuals, aged 18 to 29 and having all experience in psychophysical experiments. Spherical refractive errors ranged between -2.50 and +1.50 diopters (D) with astigmatism < 0.75 D. They had all clear intraocular media and no known ocular pathology. Wavefront aberrations were measured with natural pupil. The pupil diameter was almost always larger than 5 mm, as the room's light was off during the experiments.

The Visian ICL is a plate-haptic single-piece lens designed to be implanted in the posterior chamber with support on the ciliary sulcus. It is made partly from collamer, a flexible, hydrophilic and biocompatible material. The optic is 6 mm in diameter and the overall size comes in five diameters (11.0, 11.5, 12.0, 12.5, and 13.0 mm). The lens has a central convex–concave optic zone whose diameter ranges from 4.5 to 5.5 mm, depending on the lens' dioptric power. The ICL design has evolved over time; in this particular study we analysed ICL's V4 model.

Adaptive-Optics Visual Simulator

We used the crx1 adaptive-optics system (Imagine Eyes, Orsay, France) explained in chapter 1 (section 1.3.1)

Experimental Procedure

The irx3 Shack-Hartmann wavefront aberrometer (Imagine Eyes, Orsay, France) together with a custom-made wet cell was used to obtain the in vitro wavefront aberration pattern of the type of phakic IOL assessed in this work, the Visian ICL (ICL + wet cell). The aberrations of the wet cell alone were also measured and subtracted from the aberrations of the joint system ICL+ wet cell (Madrid-Costa et al., 2012a, Madrid-Costa et al., 2012b, Ruiz-Alcocer et al., 2012b). Three different ICLs were assessed, having a power of -3, -6 and -15 D, respectively (figure 2.1). Each measurement was repeated 10 times for each lens and the results were computed for both a 3- and a 5-mm pupil diameter.

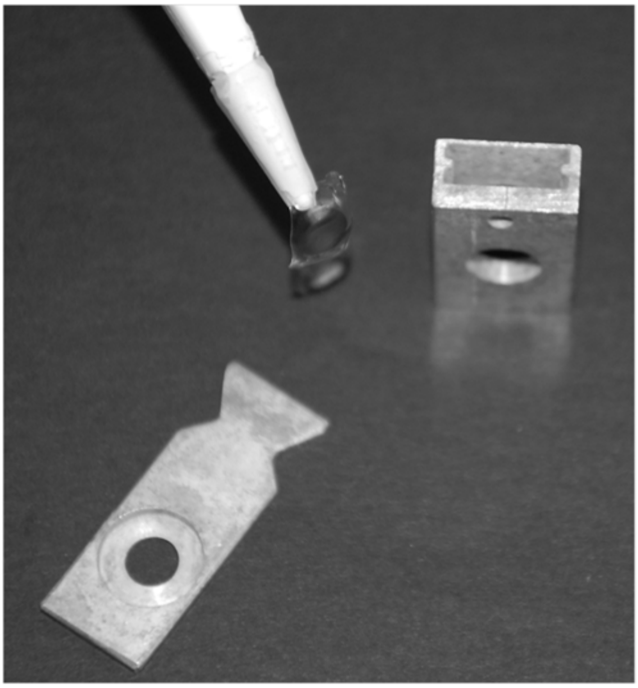

Figure 2.1: ICL in the stand used in the wet-cell.

Once we had obtained each ICL's aberration pattern, the crx1 was programmed to measure and compensate for that particular eye's wavefront error up to the 5th order.

In order to simulate in each individual the vision achieved after ICL implantation, the ICL's wavefront pattern was induced adding also the wavefront pattern of the myopic eye and the HOAs caused by the incision. The natural pupil diameter was monitored for each individual (≥ 5-mm), and the pupil size was controlled using the simulator's artificial pupil. The HOA resulting from a small or a large surgical incision were obtained from the study carried out by Kim et al. (2011). They analysed the eye's HOAs both before and after surgery, when either a small- (< 3.2 mm) or a large corneal incision (3.2 to 4.5 mm) was made. Note that values were adjusted to 3- and 5-mm pupil sizes following the formula developed by Schwiegerling (2002) for the optical and visual simulation analysis.

Optical Quality Evaluation

To evaluate the optical quality of the whole eye (phakic IOL + eye) the MTF, PSF and Strehl's ratio were computed from the wavefront data obtained by the Shack-Hartmann sensor. For the purpose of the present study, the mean one-dimensional MTF was calculated as the average over all orientations of the two-dimensional MTF. All the calculations were performed using a custom-made MATLAB program (Mathworks, Inc., Nantick, MA).

Visual Quality Measurement

High (100%)-, medium (50%)- and low (10%)-contrast VA was measured using the Freiburg Visual Acuity Test (FrACT) software (Bach, 1996) with a white background and luminance of 51 cd/m^2. The acuity threshold was determined by the best-parameter estimation by sequential testing (PEST) procedure (Lieberman and Pentland, 1982) based on 30 presentations. It was an 8-alternative, forced-choice method. The individual's task was to identify the Landolt-C gap position using a keypad. The VA value that was retained was the average of 3 measurements.

The CS was measured for 3 spatial frequencies: 10, 20 and 25 cycles/degree (cpd). Oriented sinusoidal gratings (0^o, 45^o, 90^o and 135^o) were randomly generated and displayed on the micro-display using a 4-alternative, forced-choice method. A modified

PEST testing method based on 30 presentations was used to determine contrast thresholds.

Data Analysis

The analysis of variance (ANOVA) was used to reveal differences between ICL powers. Post-hoc multiple comparison testing was performed using the Holm-Sidak method. A Student t-test for unpaired data was used for the comparison of different incision sizes. Differences were considered to be statistically significant if the P value was below 0.05.

2.3 RESULTS

Optical Quality of the Whole Eye

Figure 2.2 shows the normalized 5-mm pupil MTF for the three ICL powers under analysis and for the small and large incision size. The diffraction-limited MTF has been included for comparison purposes. Similar curves were obtained for the -3D and the -6D ICL for both incision sizes, whereas MTF values were considerably lower for the -15D ICL. In all cases the MTF was worse (i.e., it differed more from the diffraction-limited MTF) for a large than for a small incision. The figure also shows the retinal contrast threshold curve at a retinal illuminance of 500 td.

Figure 2.3 shows the 5-mm-pupil PSF computed for the three powers of ICL and for small and large incision sizes. The PSF was worse for higher ICL powers and larger surgical incision sizes.

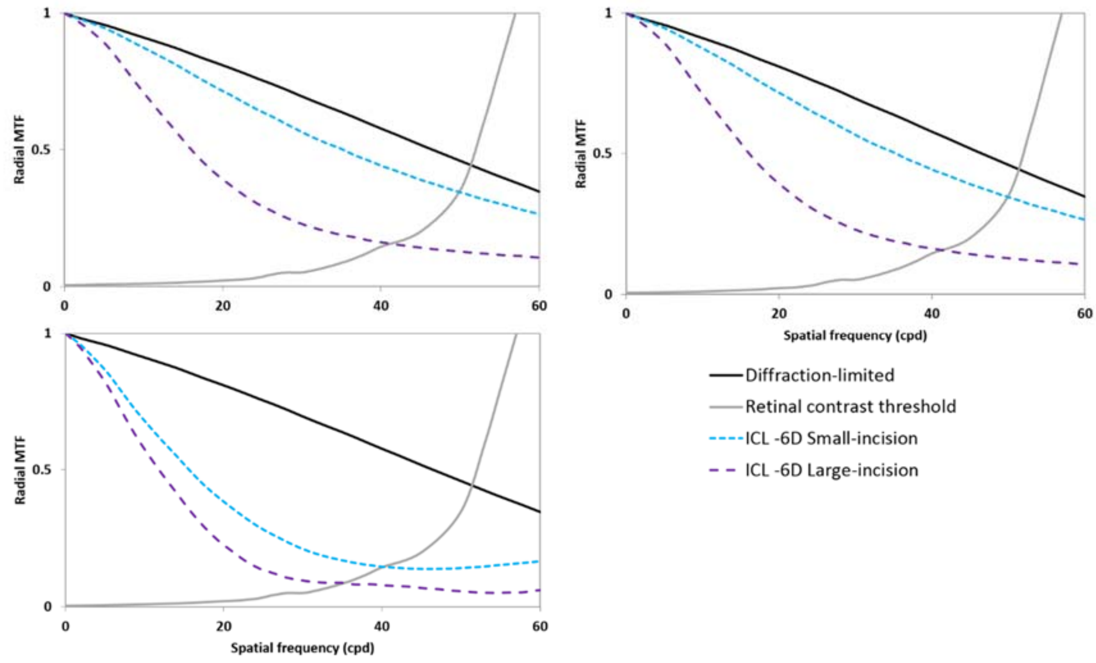

Figure 2.2: MTF of the whole eye (eye + ICL) at 5-mm pupil size. The graphs show the radial projection, averaged over all orientations, of the two-dimensional MTF curve, plotted as a function of the spatial frequency (c/deg), for the three different ICL powers and for small- and large- incision sizes.

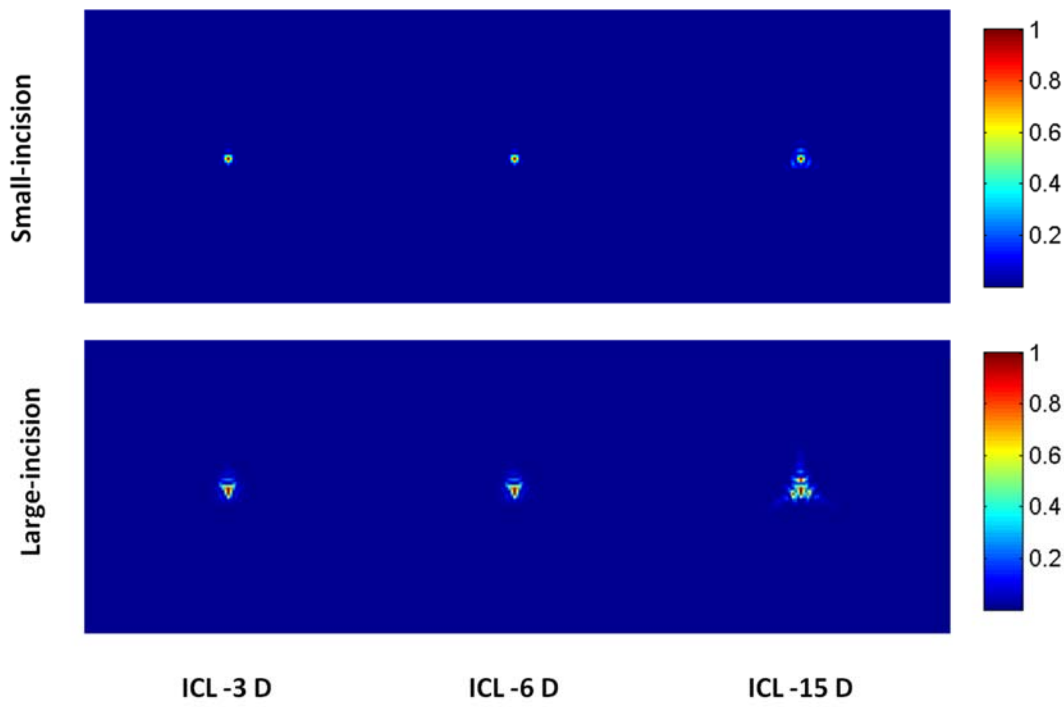

Figure 2.3: PSF of the whole eye (eye + ICL) at 5-mm pupil, for three different ICL powers and for small- and large-incision sizes.

Regarding 5-mm pupil Strehl's ratio values, they were significantly better for a small incision size than for a large incision size, for all powers evaluated: 0.77± 0.05 vs. 0.25 ± 0.08 ($p=0.03$); 0.77 ± 0.06 vs. 0.25 ± 0.06 ($p=0.03$) and 0.39 ± 0.06 vs. 0.12 ± 0.07 ($p=0.01$) for -3D, -6D and -15D ICLs, respectively. Strehl's ratio values for -3D and -6D ICLs are extremely similar, for both incision sizes (0.77 for a large and 0.25 for a small incision size). However, for the -15D ICL Strehl's ratio values decreased in a significant manner for both incision sizes: from 0.77 to 0.39 ($p= 0.006$) for small-incision surgery and from 0.25 to 0.12 ($p=0.009$) for large-incision surgery. The best optical quality was achieved in the case of a small-incision surgery and for -3D and -6D ICLs.

Visual Quality

Figures 2.4 and 2.5 show 3- and 5-mm pupil, respectively, VA results for the three ICL powers and for small and large incision sizes. No statistically significant differences were found in VA between the two incision sizes for a 3-mm pupil, for all ICL powers and contrast values (figure 2.4, $p>0.05$). On the contrary, for a 5-mm pupil, statistically significant differences were found in logMAR VA between small and large incision sizes for all ICL powers and contrast values evaluated (figure 2.5, $p<0.05$). In all cases the VA was better for a small-incision than for a large-incision surgery. Regarding the effect of the ICL power upon visual outcome, we did not find statistically significant differences between ICLs for a 3-mm pupil ($p>0.05$). However, at low contrast we found statistically significant differences in logMAR VA between -3D and -15D ICLs for both incision sizes ($p<0.05$). For a 5 mm pupil no significant differences were observed between -3D and -6D ICLs, but those values did differ significantly from those obtained for the -15D ICL for both incision sizes and contrasts evaluated ($p<0.05$). In all cases the VA obtained with the -15D ICL was worse.

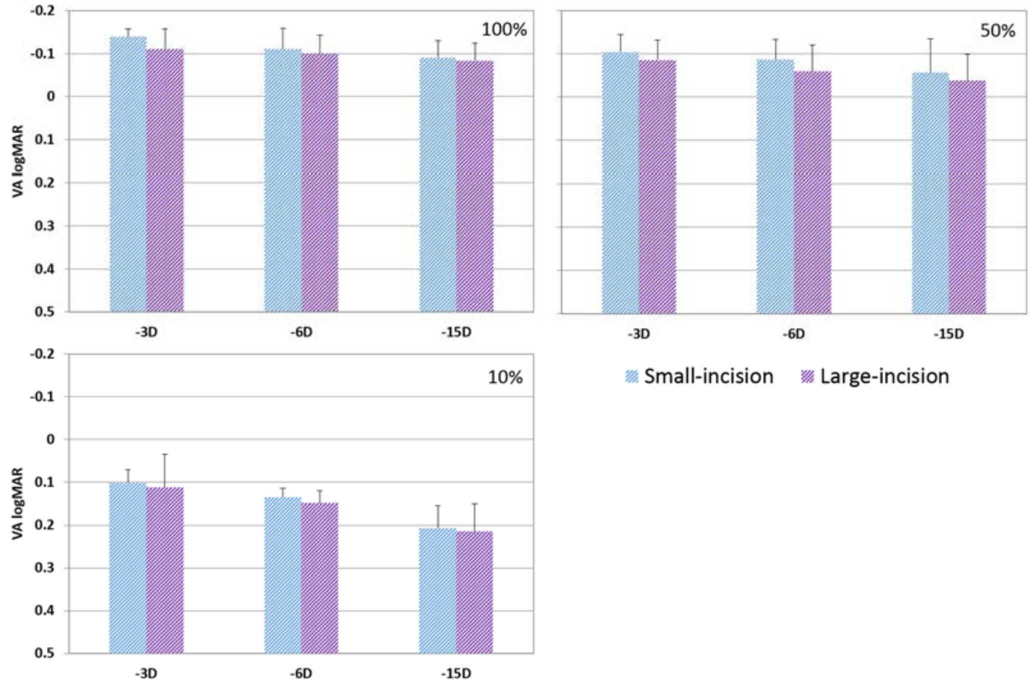

Figure 2.4: VA logMAR for high-, medium- and low-contrast, for three ICL powers (-3, -6 and -15 D) and for small- and large-incisions at 3-mm pupil. Errors bars represent the standard deviation (SD).). (*) Indicates statistically significant differences ($p < 0.05$).

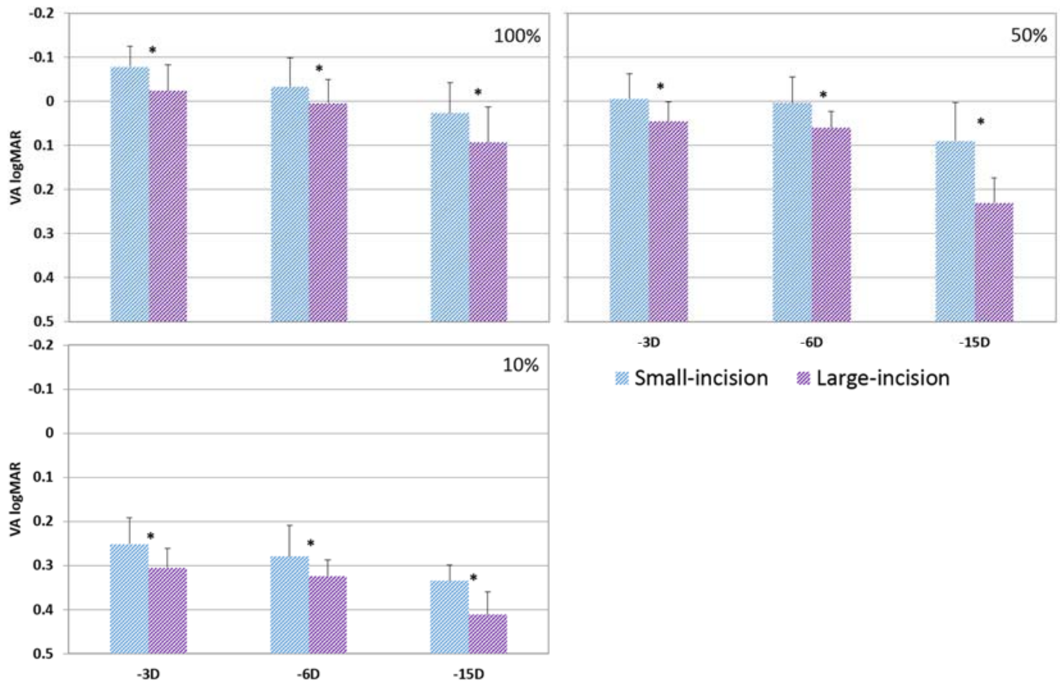

Figure 2.5: VA logMAR for high-, medium- and low-contrast, for three ICL powers (-3, -6 and -15 D) and for small- and large-incisions at 5-mm pupil. Errors bars represent the standard deviation (SD).). (*) Indicates statistically significant differences ($p < 0.05$).

Figures 2.6 and 2.7 show the mean log10 CS values for 3- and 5-mm pupils, respectively. For a 3-mm pupil no statistically significant differences were found between small- and large-incision sizes for all spatial frequencies and ICL powers (p>0.05), except for the case of 25 cpd with the -15D ICL, where better outcomes are attained with a small incision (p=0.016). For a 5-mm pupil statistically significant differences were found for all scenarios (incision sizes, ICL power and all spatial frequencies, p<0.05); in all cases better outcomes were obtained for the small-incision surgery.

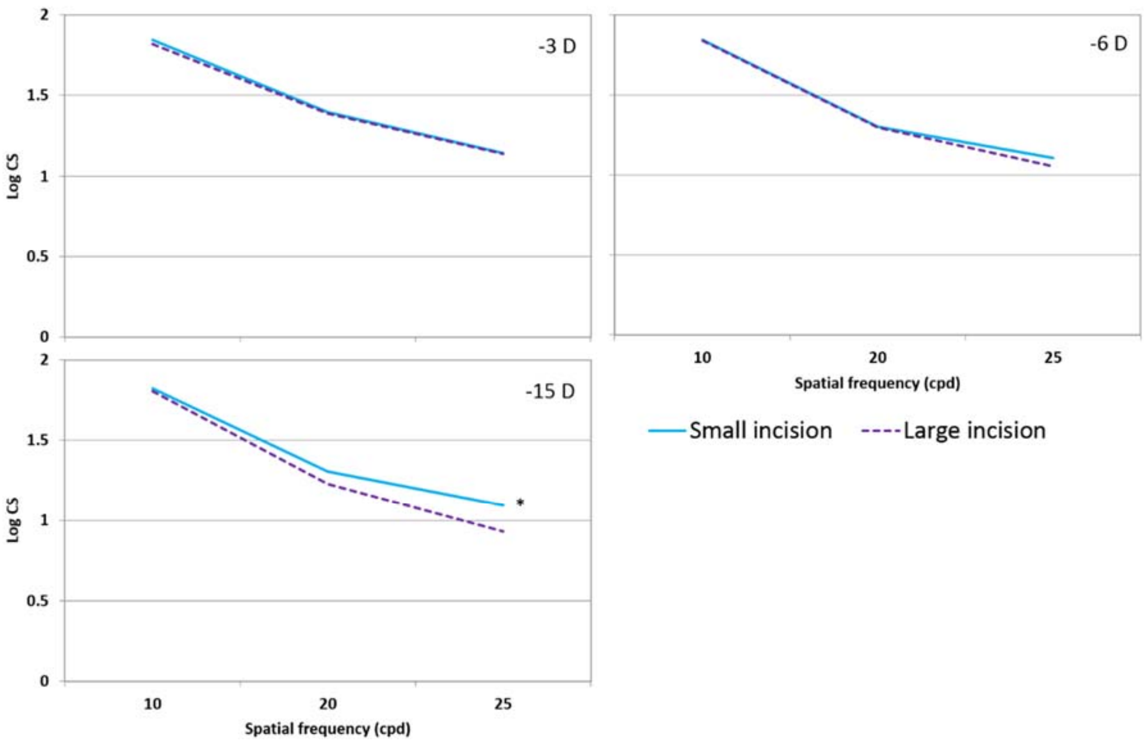

Figure 2.6: Mean log CS for a 3-mm pupil, as a function of spatial frequency (10, 20 and 25 cycles/degree, cpd) for three ICL powers and the two incision sizes under study (*) Indicates statistically significant differences (p < 0.05).

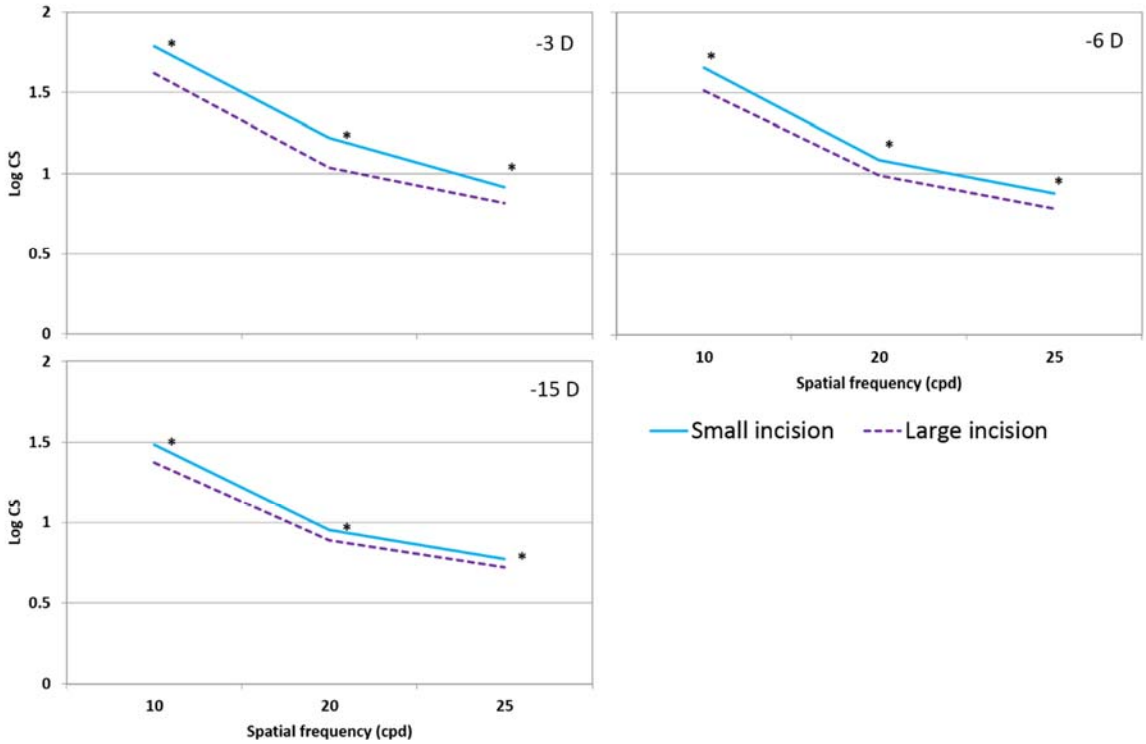

Figure 2.7: Mean log CS for a 5-mm pupil, as a function of spatial frequency (10, 20 and 25 cycles/degree, cpd) for three ICL powers and the two incision sizes under study. (*) Indicates statistically significant differences ($p < 0.05$).

Figure 2.8 was devised to properly compare the effect of ICL power upon CS. This figure shows CS for all ICL powers and both incision sizes, for 3- and 5-mm pupils. For a 3-mm pupil, statistically significant differences were found only between -3D and -15D ICLs for both incision sizes at 20 and 25 cpd ($p<0.05$). On the other hand, for a 5 mm pupil no statistically significant differences were found between -3D and -6D ($p>0.05$), but they did become apparent for the -15D ICL for both incision sizes and all spatial frequencies evaluated ($p<0.05$). In all cases, CS was worse with the -15D ICL.

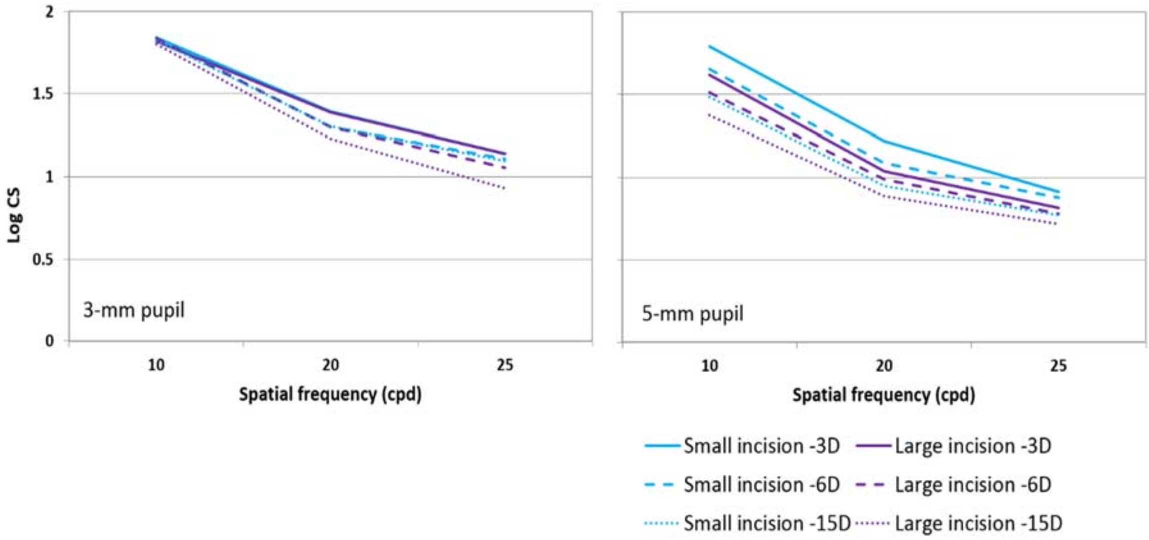

Figure 2.8: Mean log CS plotted as a function of spatial frequency (10, 20 and 25 cycles/degree, cpd) for the three ICL powers and the two incision sizes under study for 3- and 5-mm pupils.

2.4 DISCUSSION

The aim of the present study was to simulate the vision provided by an ICL through different incision sizes, using an adaptive optics visual simulator. This method allows us to assess the patient's visual quality without the need of ICL implantation, analyzing the effect of ICL power and incision size upon the same patient.

Optical Quality

The MTF of an optical system (in this case, eye+ ICL) gives us information about its optical quality. Figure 2.2 showed that for -3D and -6D ICLs and small incision sizes, high-quality MTF curves were obtained, which were close to the diffracted-limited MTF. However, for -3D and -6D ICLs with large incision sizes and -15D ICL for both incision sizes the computed MTF decreased, moving away from the diffracted-limited curve, thus resulting in a lower optical quality.

Regarding the PSF images (see figure 2.3) and the Strehl's ratio values, we can also observe a decline in optical quality for larger incision sizes and higher ICL power (the increase in trefoil due to the large-incision surgery is nicely illustrated in the PSF images). Statistically significant differences were found between both incision sizes for all ICLs powers ($p<0.05$). With regard to the effect of ICL power upon optical quality, we did not find statistically significant differences between -3D and -6D ICLs ($p>0.05$), although they became significant when compared with -15D for both incision sizes ($p<0.05$).

These outcomes are in good agreement with those obtained by Kim et al.(2011). They studied the changes in HOAs induced by the implantation of an ICL in 56 myopic eyes with different sizes of surgical incision, grouped into small (< 3.2 mm) and large (3.2 to 4.5 mm) incisions. For the small-incision group they found a significant change in the Zernike coefficients for trefoil (Z(3,-3)) and spherical aberration, whereas in the large-incision group, in addition to trefoil and spherical aberration, also the RMS of trefoil and total HOAs changed significantly. The change in Zernike coefficient and RMS for trefoil (Z(3,-3)) was significantly greater in the large-incision group than in the small-incision group and the difference in the HOAs change in the 2 groups was borderline significant. Kim et al.(2011) measured three different ICLs (having -5.5D, -16.5D and -19.5D respectively) in a wet chamber using a Shack-Hartmann wavefront sensor. The 3 ICLs had negative spherical aberration and negligible amounts of other types of aberrations. The magnitude of the spherical aberration was higher (i.e., more negative values) in those ICLs having higher power. They concluded that after ICL implantation there is an increase in trefoil and negative spherical aberration, and that these changes may be explained by the effect of the corneal incision and the ICL's negative spherical aberration, respectively. In our study we also measured three different ICL powers (-3, -6 and -15D), and our outcomes were similar to Kim's, who obtained -0.03, -0.21 and -0.19 μm of spherical aberration for the -5.5, -16.5 and -19.5D ICLs, respectively, for a 5.5-mm pupil.

The achromatic retinal contrast threshold values found by Sekiguchi et al.(1993) at a retinal illuminance of 500 td were also included in figure 2.2. This curve suggests that, for an eye having a 5-mm pupil, spatial frequencies up to about 45 cpd should be recognizable, which corresponds to a VA of about 20/13 (visual resolution in white light).

The cut-off frequency for each ICL results from the intersection between the ICL's MTF and the neural curve. The cut-off frequencies for -3D and -6D ICLs are similar, and they are better for a small- (about 45 cpd) than for a large-incision size (about 40 cpd). The -15D ICL's cut-off frequency is the worst: approximately 40 and 35 cpd for small- and large-incision sizes, respectively. In spite of this, visual resolution at these frequencies is good for the -15D ICLs.

Visual Quality

VA values for the 3 mm pupil (see figure 2.4) were good for the three ICL powers, obtaining values above 20/20 at high- and medium-contrast for both incision sizes with no statistically significant differences between them ($p>0.05$). At low-contrast, VA values were favorable too; about 20/25 for the -3D and -6D ICLs, for both incision sizes. However, VA for the -15D ICL was significantly lower ($p<0.05$): about 20/30 for both incision sizes. The effect of increased aberrations with larger incisions (approximately by a factor of 2.6) did not seriously impact VA, since we did not find statically significant differences between the two incision sizes for any of the ICLs powers or contrasts evaluated ($p>0.05$). However, the effect of increased negative spherical aberration with higher ICLs power (a 16-fold increase between a -3D and a -15D ICL) had an impact upon low-contrast VA, resulting in statistically significant differences only between -3D and -15D ICLs for both incision sizes ($p<0.05$). For a 5-mm pupil, VA outcomes were also favorable (see figure 2.5) at high- and medium-contrast for -3 and -6D ICLs, obtaining values around 20/20 for small-incision. These values decreased for -15D ICLs, when the incision surgery was larger and at low contrast. For this pupil size the effect of incision size became apparent, since statistically significant differences were found between both incision sizes for all ICL powers and all contrasts evaluated ($p<0.05$). In relation to the impact of ICL power, no statistically significant differences were observed between -3D and -6D ICLs ($p>0.05$), whereas statistically significant differences were found with the-15D ICL ($p<0.05$).

In terms of CS, the outcomes were also good for a 3 mm pupil, for all three ICL powers and for both incision sizes (see figure 2.6). No statistically significant differences were found between the two incision sizes for all ICLs and spatial frequencies evaluated

($p>0.05$), excepting the case of 25 cpd for the -15D ICL ($p<0.05$). For the 5-mm pupil (see figure 2.7) the outcomes were good for the small-incision scenario, whereas contrast values decreased for the large incision; we found statistically significant differences between both incision sizes for the three ICL powers and for all spatial frequencies evaluated ($p<0.05$). Moreover, the effect of ICL power upon CS was analyzed in figure 2.8: for the 3-mm pupil (left) statistically significant differences were found only between the -3D and -15D ICLs at 20 and 25 cpd, whereas for the 5-mm pupil no statistically significant differences were found between the -3D and -6D ICLs ($p>0.05$), but the -15D ICL curve was significantly different at all spatial frequencies evaluated ($p<0.05$).

Despite the loss of optical and visual quality resulting from the increase of the ICL's power (due to the increase of negative spherical aberration), the impact of spectacle lens magnification upon VA should also be considered (Applegate and Howland, 1993). The relative image magnification that occurs when myopic patients undergo ICL surgery is due to refractive correction moving from the spectacle plane to the eye. For an initial myopic refractive error of about -6D corrected by means of spectacles located at a vertex distance of 14 mm, the spectacle magnification achieved after ICL implantation increases by a factor of approximately 1.1X. In the case of a -15D refractive error that factor is approximately 1.2X. Thus, if no other effects were involved, VA and CS at higher spatial frequencies should improve after myopia surgery, the more the larger the magnitude of the correction. CS at low spatial frequencies is less affected, since the gradient of the CS function is low at those frequencies. Taking these factors into account, VA should improve between 0.05 and 0.10 logMAR, respectively.

The FDA study (Sanders et al., 2003) evaluated the safety and efficacy of ICLs to treat moderate to high myopia. 523 eyes having between 3.00 and 20.00 D of myopia were assessed, and in all of them a V4 model ICL was inserted through a small (3-mm) clear corneal incision. Two years postoperatively, 60.1% of patients had an uncorrected distance visual acuity (UDVA) of 20/20 or better, and 92.5% had 20/40 or better. Kamiya et al.(2009) assessed 56 eyes whose myopic refractive error ranged from -4.00 to -15.25 D. They all underwent V4-model ICL implantation, inserted through a 3 mm clear corneal incision. Four years after surgery the mean logMAR UDVA was -0.03 ± 0.23 logMAR (above 20/20). More recently Alfonso et al.(2011) evaluated the long-term safety and efficacy of ICL implantation to correct myopia. 188 eyes having between -1.50 to -20.00 D of myopia were assessed 5 years postoperatively, and the mean corrected distance visual acuity (CDVA) was 0.83 Snellen decimal (about 20/25). These outcomes are in good agreement with the findings of our study: the differences in terms of VA between these studies and ours was probably due to the measurement method, since they implanted the ICL and then evaluated visual performance, while we have simulated the optical quality that this ICL provides, thus avoiding the effects of the surgical procedure such as ICL decentration or tilt and postoperative complications (Fernandes et al., 2011). They also implanted ICLs having up to 20D, which have a higher level of aberrations and, therefore, lower optical quality.

In most surgeries, the large incision is considered to compensate astigmatism in myopic or hyperopic astigmatic eyes when a spherical ICL is implanted. The outcomes of the present study indicate that the effect of the large-incision surgery could affect the optical and visual quality of patients that undergo this type of surgical approach, especially under larger-pupil-size conditions. Therefore, for a patient with myopic astigmatism, a toric ICL should be considered instead of the spherical model plus a large incision. In this context, several studies (Alfonso et al., 2010a, Alfonso et al., 2010b, Alfonso et al., 2014) revealed a good VA and high stability over 12 months for toric ICLs, showing this as a safe, predictable and effective alternative for the correction of moderate to high astigmatism.

With the use of a visual optic simulator we were able to evaluate the impact upon visual performance of different ICL powers and surgical techniques before the surgical procedure actually takes place. The present study is the first that allows direct comparison of the visual outcome of different ICLs through different incision sizes in the same patient. However, it is fair to bear in mind the intrinsic limitations of our study, such as the surgery effects (although we did consider the impact of the surgical incision), ICL decentration or tilt, which may affect the outcomes reported here. We haven’t considered postoperative complications either (Fernandes et al., 2011), which over time could also affect optical and visual quality.

In summary, ICLs provide good optical and visual quality, better if implanted in small-incision surgical procedures, since the larger the incision size the higher the HOAs that are induced. Eyes with myopic astigmatism should preferably have a toric ICL implanted through small incision instead of a spherical ICL through a large incision. Optical and visual quality also decreases when ICL power increases (due to the rise of negative spherical aberration), but these losses are offset by the effect of spectacle magnification.

CHAPTER 3

Optical and Visual Quality Comparison of Implantable Collamer Lens and Laser in situ Keratomileusis for Myopia using an Adaptive Optics Visual Simulator

3.1 INTRODUCTION

Myopic errors can be corrected by different refractive surgery options. Currently, LASIK is the most popular option to correct myopia, but some patients are not appropriate candidates for this surgery due to thin corneas or high refractive errors among others (Huang and Chen, 2008). An alternative option for these patients that surgeons may consider is the implantation of a phakic IOL. These lenses have been shown to successfully correct myopia allowing correction of the total refractive error without inducing irreversible changes to the corneal contour (Huang et al., 2009).

The Visian ICL is a posterior chamber phakic IOL approved by the United States FDA for myopia correction. Previous studies of the multicenter United States FDA ICL (Sanders et al., 2003, Sanders et al., 2004) and other studies (Alfonso et al., 2011) had shown the safety and effectiveness of the ICL in the correction of moderate to high levels of myopia with 3- (Sanders et al., 2004) and 5-years of follow-up (Alfonso et al., 2011). Outcomes from these studies have demonstrated the viability of the Visian ICL as an alternative to current refractive laser surgical treatment options.

Several studies (Sanders and Vukich, 2003, Tsiklis et al., 2007, Kamiya et al., 2008, Igarashi et al., 2009) reported that ICL implantation is better than LASIK in all measures of safety, efficacy, predictability, and stability, even in eyes with low myopia (Sanders and Vukich, 2006, Sanders, 2007). Mainly, these findings are due to laser ablation required during LASIK surgery making the cornea oblate and increasing HOAs, especially, spherical aberration (Gatinel et al., 2010). In contrast ICL implantation does not require surgical tissue ablation and leaves the central cornea untouched; therefore ICL treatment induces significantly lower ocular HOAs than LASIK offering better retinal image quality (Sarver et al., 2003). An ICL implantation may induce HOAs by the innate optical properties of the lens (i.e. spherical aberration increases with the ICL power) and also due to the incision type during the surgical procedure (Kim et al., 2011). However, up to now there are no studies comparing the visual performance provided by LASIK and ICL for myopia correction on the same eye. Only, Tsiklis et al. (2007) analyzed the differences between ICL implantation in one eye and LASIK in the fellow eye of the same patient. These authors concluded that better quality of vision, stability, and satisfaction score were achieved in the eye with the ICL compared to the eye that had undergone LASIK.

The aim of the present study was to compare the optical and visual quality provided by ICL and LASIK procedures for -3 and -6 D of myopia. For this comparison, an adaptive optics system was used to simulate vision from the ICL's and LASIK's aberration patterns. VA for different contrasts and CS for 3- and 5-mm pupils were evaluated. To our knowledge this is the first study that allows a direct comparison of the visual performance achieved with ICL and LASIK procedures in the same eye.

3.2 PATIENTS AND METHODS

Subjects

Ten individuals, aged from 21 to 30 years and experienced in psychophysical experiments were included in this study. Spherical refractive errors ranged between -3.50 and +0.50 D with astigmatism <0.50 D. They had clear intraocular media and no known ocular pathology. Wavefront aberrations were measured with natural pupil. The pupil diameter was always greater than 5-mm as the room light was off during the experiments.

The tenets of the Declaration of Helsinki were followed. Informed consent was obtained from each participant after verbal and written explanation of the nature and possible consequences of the study. The protocol received institutional review board approval.

Intraocular Lens

The Visian ICL is a plate-haptic single-piece lens designed to be implanted in the posterior chamber with support on the ciliary sulcus. It is made partly from Collamer, a flexible, hydrophilic and biocompatible material. It is 6.0 mm wide and comes in 5 diameters (11.0, 11.5, 12.0, 12.5, and 13.0 mm). The lens has a central convex–concave optic zone with a diameter of 4.5 to 5.5 mm, depending on dioptric power. The ICL design has been modified many times. In this study, we used the ICM V4 model.

Mechanical Microkeratome

The Carriazo-Barraquer mechanical microkeratome (Moria, Antony, France) was used to create the flap (superior hinge). With this microkeratome, the selected plate thickness was 130 µm and the suction ring selected was -1, 0, or +1 as a function of the corneal curvature to achieve a 9.5-mm diameter (Montes-Mico et al., 2007a).

Adaptive Optics Visual Simulator

We used the crx1 adaptive-optics system (Imagine Eyes, Orsay, France) explained in chapter 1 (section 1.3.1).

Experimental Procedure

The way in which the IOLs were characterized can be consulted in chapter 2 (section 2.2). In this study two ICL powers were analysed: -3 and -6 D.

Once we had obtained the aberration pattern of the ICL, we measured the individual eye´s wavefronts using the crx1 visual simulator. The natural pupil diameter was checked for each individual (≥5-mm). The pupil's size was controlled using the simulator artificial pupil. Then, the crx1 was programmed to compensate the eye's wavefront error up to the 5th order. In order to simulate the vision of post-ICL implantation surgery in each individual, the eye's wavefront was measured, it was compensated using the deformable mirror and then the wavefront pattern of the ICL measured was induced adding the wavefront pattern of the myopic eye. The same procedure was followed to simulate the vision post-LASIK surgery, but now the wavefront pattern of the LASIK was induced. The patients' wavefront aberration used where those obtained by Montés-Micó et al. (2007a) with standard LASIK for low (-2.50 to -3.50D) and medium (-5.50 to -6.50D) myopia. Note that these values were adjusted to 3- and 5-mm pupil sizes (Schwiegerling, 2002).

Optical Quality Evaluation

To evaluate the optical quality of both simulated procedures we analyzed the MTF and the PSF. For the purposes of the present study, the mean one-dimensional MTF was calculated as the average over all orientations of the two-dimensional MTF. We have computed these metrics using a custom-made MATLAB program (Mathworks, Inc., Nantick, MA) from the wavefront data obtained from the irx3 Hartmann-Shack sensor.

Visual Quality 0 easurement

VA and CS were measured in the same way that in chapter 2 (section 2.2).

Data Analysis

A Student *t*-test for unpaired data was used for the comparison of different simulated surgical procedures regarding VA and CS. Results are presented as the mean ± SD and statistical significance was set at P <0.05.

3.3 RESULTS

Optical Quality

Figure 3.1 shows the normalized MTF for the ICL and LASIK simulation of -6D at 5-mm pupil. MTF for the diffraction-limited was included for comparison. Note that differences between MTFs come from the HOAs effect. The ICL showed a MTF near of diffraction-limited MTF, but the post-LASIK MTF worsened quite moving away from both curves. The figure also shows the retinal contrast threshold curve at a retinal illuminance of 500 td (Sekiguchi et al., 1993). Figure 3.2 shows the images of the PSF for the ICL and post-LASIK procedures at 5-mm pupil. We may observe the spread of the PSFs corresponding to LASIK surgery compared with the ICL.

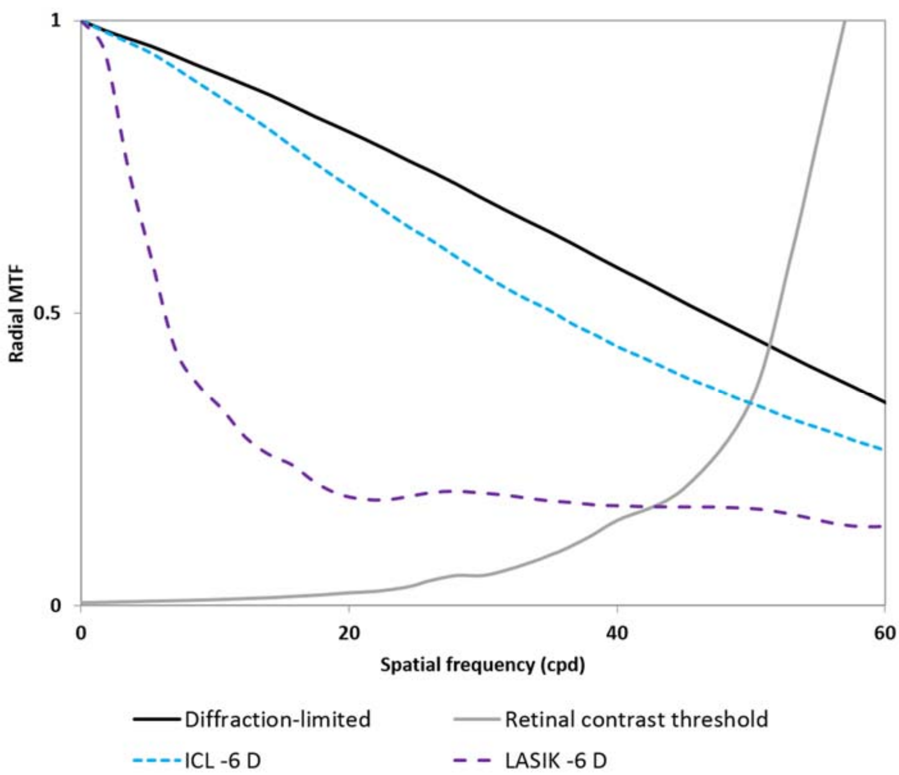

Figure 3.1: Radial projection, averaged over all orientations, of the two-dimensional MTF for 780 nm versus spatial frequency (c/deg) at 5-mm pupil of the eye plus -6D ICL and after -6D LASIK procedure Diffraction-limited curve and retinal contrast threshold curve were included.

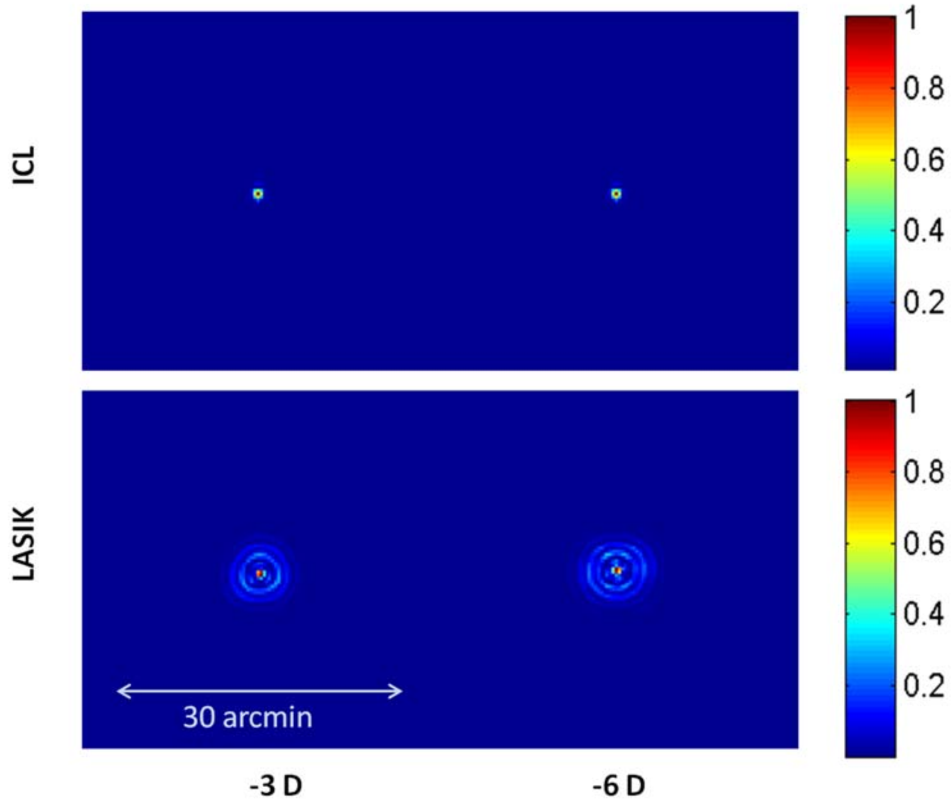

Figure 3.2: PSF at 5-mm pupil of the -3 and -6D ICL and -3 and -6D LASIK.

Visual Quality

Figure 3.3 shows the VA for the -3 (figure 3.3 A and C) and -6 D (figure 3.3 B and D) ICL and LASIK procedures for 3- and 5-mm pupils. Statistically significant differences were found between both procedures for all powers and contrasts evaluated at 3- and 5-mm pupil ($p<0.05$). In all cases the VA was better with the ICL than LASIK.

Figure 3.4 shows the mean log10 CS values for the -3 (figure 3.4 A and C) and -6D (figure 3.4 B and D) ICL and LASIK procedures for 3- and 5-mm pupils. For -3D, there were no statistically significant differences between both procedures at any spatial frequency and pupil evaluated ($p>0.05$). In contrast, for -6D, statistically significant differences were found for all spatial frequencies and pupils ($p<0.05$) showing better outcomes for ICL procedure.

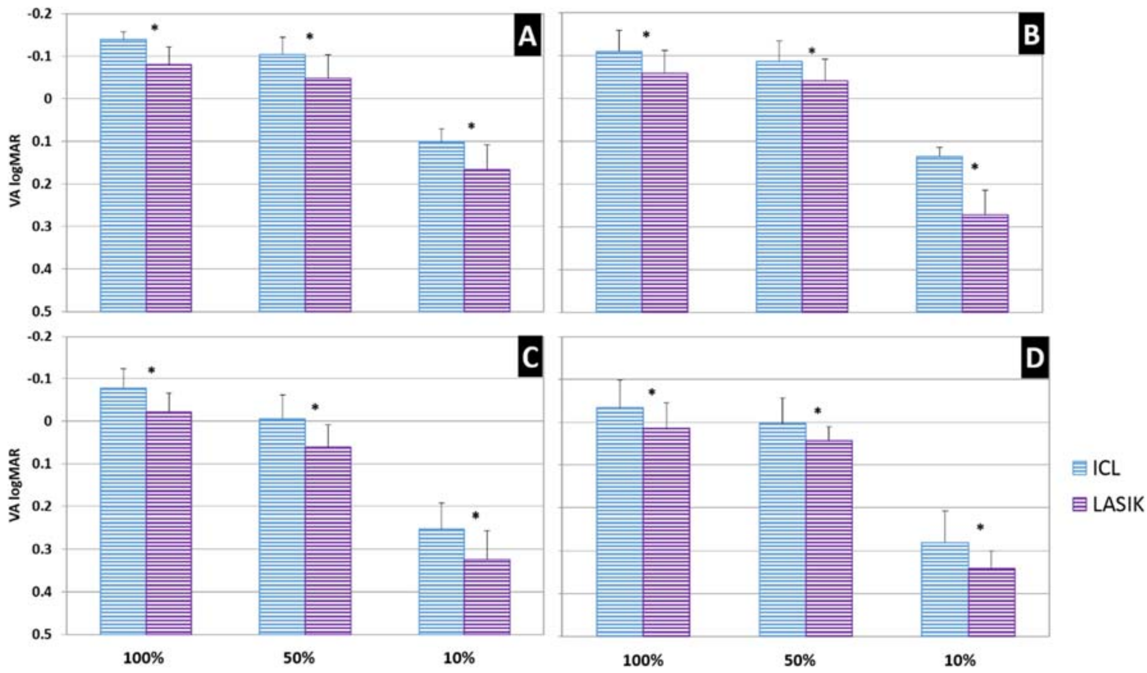

Figure 3.3: VA logMAR and fraction Snellen at high- (100%), medium- (50%) and low- (10%) contrast, with the ICL (black bars) and after LASIK procedure (white bars) for A) -3 D at 3-mm pupil; B) -6 D at 3-mm pupil; C) -3 D at 5-mm pupil; D) -6D at 5-mm pupil. Errors bars represent the standard deviation (SD). (*) Statistically significant differences ($p<0.05$).

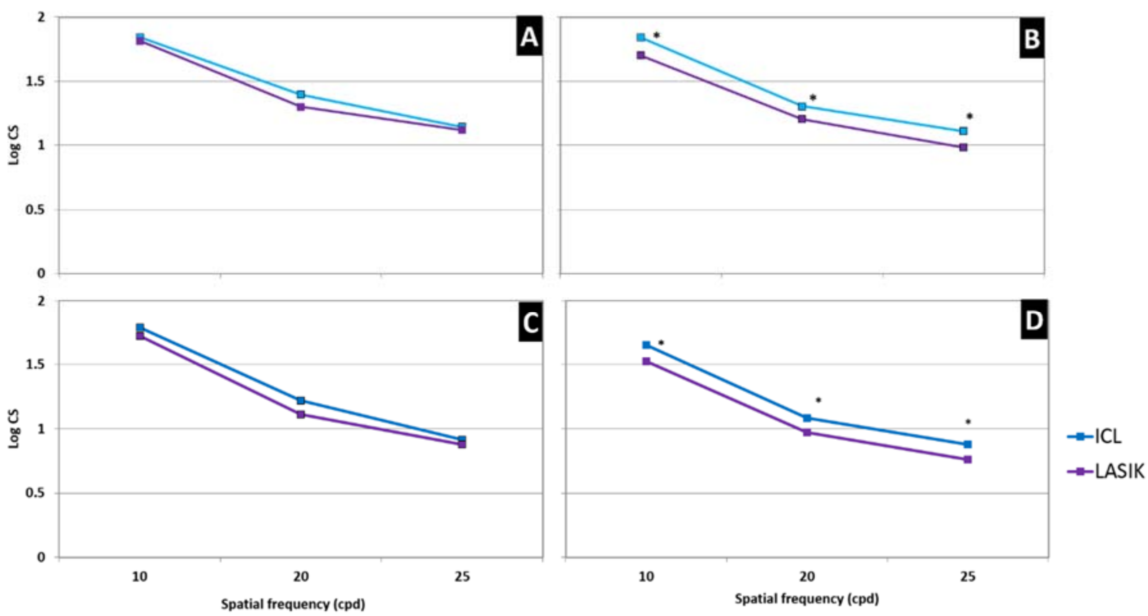

Figure 3.4: Mean log CS at three spatial frequencies: 10, 20 and 25 cycles/degree (cpd) for ICL (black squares) and LASIK procedures (white squares) A) -3 D at 3-mm pupil; B) -6 D at 3-mm pupil; C) -3 D at 5-mm pupil; D) -6D at 5-mm pupil Error bars have been omitted for clarity. (*) Statistically significant differences ($p<0.05$).

3.4 DISCUSSION

The aim of the present study was to compare the optical and visual quality provided by ICL and LASIK procedures using an adaptive optics visual simulator. This method allows us to assess the patient's visual quality without need of ICL or LASIK surgeries, comparing both techniques on the same eye.

Optical Quality

The MTF inform us the optical quality of an optical system and shows how transmits spatial frequencies, being in this case the eye plus the ICL and the eye after LASIK procedure. The -6D ICL showed a good MTF close to the diffracted-limited MTF (see figure 3.1). In contrast, the MTF for -6D LASIK decreased drastically moving away to the diffracted-limited curve and therefore providing a lower optical quality. These results were correlated with the PSF images (see figure 3.2), which spread out more with LASIK procedure than the ICL implantation. These differences in optical quality come from the larger ocular HOAs induced by LASIK surgery compared to the ICL treatment. Therefore, ICL surgery offers better optical quality in relation to that found after LASIK treatment.

Figure 2.1 also includes the achromatic retinal contrast threshold values found by Sekiguchi et al. (1993) at a retinal illuminance of 500 td. This figure suggests that, for an eye with a 5-mm pupil, spatial frequencies up to about 45 cpd should be recognizable, corresponding to about 20/13 (visual resolution in white light). Note that the cut-off frequency for the ICL and LASIK procedures comes from the intersection between these MTFs and the neural curve. The cut-off frequency for the ICL of -6D is about 45 cpd, but the cut-off frequency for the LASIK of -6D is worse, about 40 cpd.

Uozato et al. (2011) obtained the MTFs for different myopic ICL powers using a model eye at various pupil diameters. The outcomes found by these authors for -5D V4 ICL model at 5 mm were quite similar with those obtained in our study. Sarver et al. (2003) compared the image quality due to HOA following LASIK or ICL implantation to correct high myopia. They found that eyes post-LASIK yielded an average three times more spherical aberration and two times more coma than eyes with an ICL implanted. In addition, they represented the two-dimensional PSFs for coma and spherical aberration and the corresponding simulated retinal images. They saw that the PSFs corresponding to the LASIK aberration values were more spread out than for the ICL aberrations values. As expected in the simulated retinal image from the PSFs, blurring in the LASIK images was more apparent than for the corresponding ICL images. In our study, we also found more HOAs after LASIK procedure than ICL implantation, specifically for coma and spherical aberration (note the spread of the PSFs shown in figure 3.2).

Visual Quality

VA values for both procedures evaluated at 3-mm pupil were good, obtaining values above 20/20 at high- and medium-contrasts for -3 and -6D (see figure 3.3 A,B). At low-contrast, VA was highly reduced for both treatments. If we now compare both surgeries, we found statistically significant better VA outcomes for ICL than LASIK both for -3 and -6D and all contrasts evaluated ($p<0.05$). At 5-mm pupil, the VA outcomes for -3 and -6D ICL were about 20/20 at high- and medium-contrasts and about 20/40 for low contrast (see figure 3.3 C,D). These values decreased for LASIK surgery, being statistically significant lower for -3 and -6D and all contrasts evaluated ($p<0.05$).

Previous studies comparing both procedures (Sanders and Vukich, 2003, Sanders and Vukich, 2006, Sanders, 2007, Tsiklis et al., 2007) concluded that eyes that underwent ICL implantation had best spectacle correction visual acuity (BSCVA), UCVA, predictability and stability of refraction compared with eyes that underwent LASIK. Sanders and Vukich et al. (2003) compared the results of LASIK and ICL in the correction of moderate/high myopia in 559 LASIK and 210 ICL eyes between -8 and -12D of myopia. One year postoperatively, the ICL patients demonstrated a large percentage of eyes with 20/20 or better BSCVA (82% LASIK, 90% ICL) and UCVA (36% LASIK and 52% ICL). Tsiklis et al. (2007) compared the long-term results of LASIK in one eye and ICL implantation in the fellow eye of the same patient with high myopia. At 9 years postoperatively, the patient obtained better UCVA, optical quality (less glare and halos), stability of residual errors and satisfaction score in the eye with the ICL compared to the eye treated with LASIK. Sanders and Vukich et al. (2006) also compared the results of

LASIK and ICL in the correction of low myopia (from -4 to -7.88D). They found after 6 months of follow-up a greater proportion of cases seeing 20/20 BSCVA (91% LASIK and 98% ICL) being the UCVA better in the ICL group (57% LASIK and 67% ICL). These outcomes agree with our findings since we reported better optical and visual quality outcomes with the ICL than those found by LASIK. 100% of eyes had a VA of 20/20 or better for both ICL powers. In contrast, 91.6% and 83.3% of eyes had a VA of 20/20 or better for -3 and -6D, respectively, in the LASIK surgery.

The CS outcomes for -3D ICL and LASIK surgeries were good (see figure 3.4 A,C). No statistically significant differences were found between both treatments at 3- and 5- mm pupils and spatial frequencies evaluated ($p>0.05$). However, at -6D, we found statistically significant differences between surgeries for both pupils and all spatial frequencies (see figure 3.4 B,D; $p<0.05$). Note that the HOAs increase for larger ablation LASIK treatments reduces the optical quality of the eye (see -6D LASIK MTF curve in figure 3.1). These CS results correlate with the cut-off frequency obtained for the ICL (45 cpd) and LASIK (40 cpd) surgeries. Montés-Micó et al. (2003) evaluated CS in patients who have undergone LASIK for myopia (-6.40±1.28D). CS was measured 6 months after surgery showing statistically significant lower CS values under mesopic conditions. These authors discussed that low CS for LASIK treatment under mesopic conditions are attributed to the greater amount of HOAs and scatter at large pupil diameters. These explanations are in concordance with our findings of low CS values for LASIK in relation to ICL surgery.

With the use of a visual optics simulator we are able to compare the impact of different surgical techniques on the visual performance of a patient before the surgical procedure. The present study is the first that allows a direct comparison of the visual outcomes of two surgical procedures on the same eye. We have to point out several considerations in our study. Surgeon factor and postoperative changes may affect the visual and optical outcomes of patients submitted to ICL and LASIK surgeries (Sutton and Kim, 2010, Fernandes et al., 2011). However, these are controlled and hence not considered in the present visual simulation experiment.

In summary, both myopic ICL and LASIK procedures provide good optical and visual quality, although ICL potentially provides better outcomes than LASIK surgery, especially for higher refractive errors and pupil sizes. These outcomes are due to LASIK procedure induces higher HOAs than ICL implantation.

CHAPTER 4

Optical Quality Comparison of Conventional and Hole-Visian Implantable Collamer Lens at Different Degrees of Decentering

4.1 INTRODUCTION

The phakic IOL implantation is becoming more popular to correct high and moderate refractive errors. This is due to the phakic IOL implantation leave the central cornea untouched, inducing less HOAs (Perez-Vives et al., 2012, Shin et al., 2012) and showing better optical and visual quality (Sarver et al., 2003, Igarashi et al., 2009, Kamiya et al., 2012, Perez-Vives et al., 2013b) than corneal refractive treatments, in addition it is a reversible surgery. The ICL is a posterior phakic IOL implantation approved by the United States FDA for myopia correction. Several studies have shown the safety and effectiveness of the ICL to correct myopia (Sanders et al., 2003, Sanders et al., 2004), hyperopia (Davidorf et al., 1998, Pesando et al., 2007) and astigmatism (Alfonso et al., 2010a, Alfonso et al., 2010b).

However, cataract development has been noted after ICL implantation (Sanders et al., 2003, Gonvers et al., 2003, Sanchez-Galeana et al., 2003, Sanders et al., 2004, Fernandes et al., 2011). The majority of reported complications after ICL implantation are cataract formation (Fernandes et al., 2011), the FDA studies reported the incidence of secondary cataract was 2.1% within 1 year and 2.7% within 3 years after surgery (Sanders et al., 2003, Sanders et al., 2004).The cause of this complication is likely resulting from direct physical contact between ICL and the crystalline lens or from localized malnutrition causing poor circulation of the aqueous humour (Fujisawa et al., 2007). Therefore, Fujisawa et al. (2007) created a 3-mm central perforation in the ICL in order to improve the aqueous humour circulation, reducing the incidence of cataract formation in porcine eyes (Kawamorita et al., 2012). Shiratani et al. (2008) showed that an ICL with a hole of 1.0 mm in diameter in the center of the optic had no optical effect on vision and it is sufficient to increase the aqueous humour perfusion volume on the anterior surface of the crystalline lens, preventing cataract formation. Uozato et al. (2011) measured *in vitro* the MTFs of conventional ICLs and ICLs with central hole of 0.36 mm for various powers and pupil diameters. They reported that the differences between ICLs with and without hole were small and clinically negligible.

Two peer studies (Shimizu et al., 2012a, Shimizu et al., 2012b) evaluated the visual performance with the Hole ICL implanted, both studies agree that hole ICL showed good results of safety, efficacy, predictability and stability for the correction high to moderate myopic errors and the Hole ICL appears to be equivalent in the induction HOAs and CS function to conventional ICL implantation. In addition, Hole ICL does not require additional peripheral iridotomies and may also reduce the risk of cataract formation. In addition, the effect of decentration was also considered to evaluate how influences it on the HOAs and its effect on the optical quality of these lenses.

The aim of the present study was to compare accurately the optical quality *in vitro* of the conventional ICL and Hole ICL for three powers (-3, -6 and -12D) and evaluate the effect of decentering (0.3 and 0.6 mm) at 3- and 4.5-mm pupils. The PSFs and simulated retinal images, which are related with the visual performance of the patient implanted with these lenses, were computed from wavefront aberrations for each ICL and all conditions of decentering at 4.5-mm pupil.

4.2 MATERIAL AND METHODS

The Visian ICL is a phakic lens made from Collamer, a flexible, hydrophilic and biocompatible material with a plate-haptic design and a central convex/concave optical zone. The ICL lenses are foldable, allowing for posterior chamber injection through a microscopic incision of 3.5 mm or smaller. When properly placed, the ICL should be positioned completely within the posterior chamber between the iris and crystalline lens with support on the ciliary sulcus. In this study we have analyzed the V4b and V4c model for different powers: -3.00, -6.00 and -12.0 D for both models. The V4c model ICL introduces a central hole (diameter 0.36 mm) to increase the aqueous humour perfusion and reduce the risk of secondary cataract formation. The length of the ICLs was 12 mm and the optical diameter was 5.5 mm in all cases.

The Nimo TR0805 instrument (Lambda X, Belgium) was used to analyse and measure wavefront aberrations of the lenses (Joannes et al., 2010). The working principle of the NIMO instrument is based on a Phase Shifting Schlieren technique (Joannes et al., 2003). The principle of Schlieren imaging has been known for some time and is commonly used to visualize variations in density for gas flows. By combining this principle with a phase-shifting method, the Nimo instrument allows the measurement of light beam deviations, which can be used to calculate the power characteristics of the lenses and the wavefront analysis considering 36 Zernike coefficients. This technology has been shown effectively to measure *in vitro* the optical quality of the ICL (Perez-Vives et al., 2013a). In this study, we measured 3 conventional ICLs and three Hole ICLs with the following refractive powers: -3, -6 and -12D. In addition, we evaluated these lenses in three positions: centered, decentered 0.3 mm and decentered 0.6 mm (figure 4.1). Zernike coefficient values were retained as the average of 10 measurements. We analyzed the RMS of total HOAs (third to seventh order), trefoil (Z_3^{-3}; Z_3^{3}), coma (Z_3^{-1}; Z_3^{1}), tetrafoil (Z_4^{-4}; Z_4^{4}), secondary astigmatism (Z_4^{-2}; Z_4^{2}), and spherical aberration (Z_4^{0}) at 3- and 4.5-mm pupils.

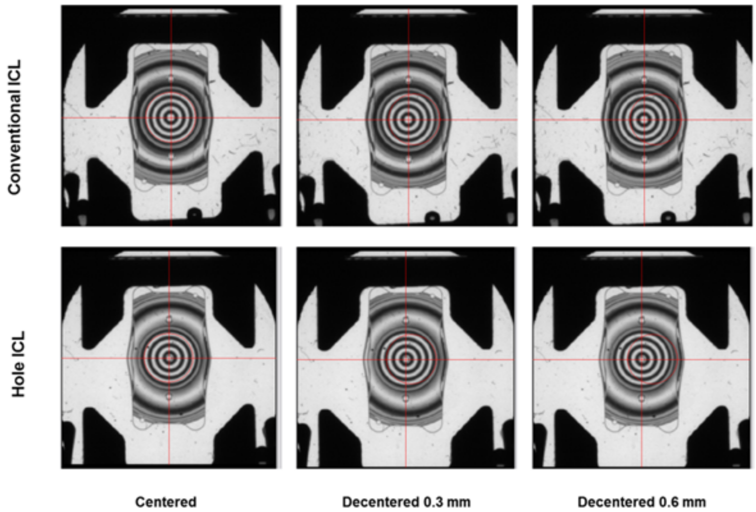

Figure 4.1: Nimo instrument images of the conventional ICL (top images) and Hole ICL (bottom images) at centered position, 0.3 mm and 0.6 mm of decentering.

Data Analysis

The ANOVA was used to disclose differences between both ICL models and different conditions of decentering. Post-hoc multiple comparison testing was performed using the Holm-Sidak method. Differences were considered statistically significant when the P value was less than 0.05.

4.3 RESULTS

Figures 4.2 and 4.3 show bar graphs of the RMS of trefoil (Z_3^{-3}, Z_3^{3}), coma (Z_3^{-1}, Z_3^{1}), tetrafoil (Z_4^{-4}, Z_4^{4}), secondary astigmatism (Z_4^{-2}, Z_4^{2}) and spherical aberration (Z_4^{0}) for each conventional and Hole ICLs and all conditions at 3- and 4.5-mm pupils, respectively. All ICLs evaluated had negative values of spherical aberration, which increases with the ICL power. We did not find statistical significant differences at any Zernike coefficients values RMS evaluated between conventional and Hole ICLs at any ICL powers and for both pupils ($p>0.05$). Regarding the effect of decentering, we only found statistically significant differences in coma aberration between centered position and both degrees of decentering for all ICLs and pupils evaluated ($p<0.05$). Coma aberration increased with ICL decentration, this increment was greater for higher ICL powers and pupil sizes. No statistically significant differences were found in other Zernike coefficients RMS evaluated between centered and decentered positions for any ICLs and pupils evaluated (p>0.05).

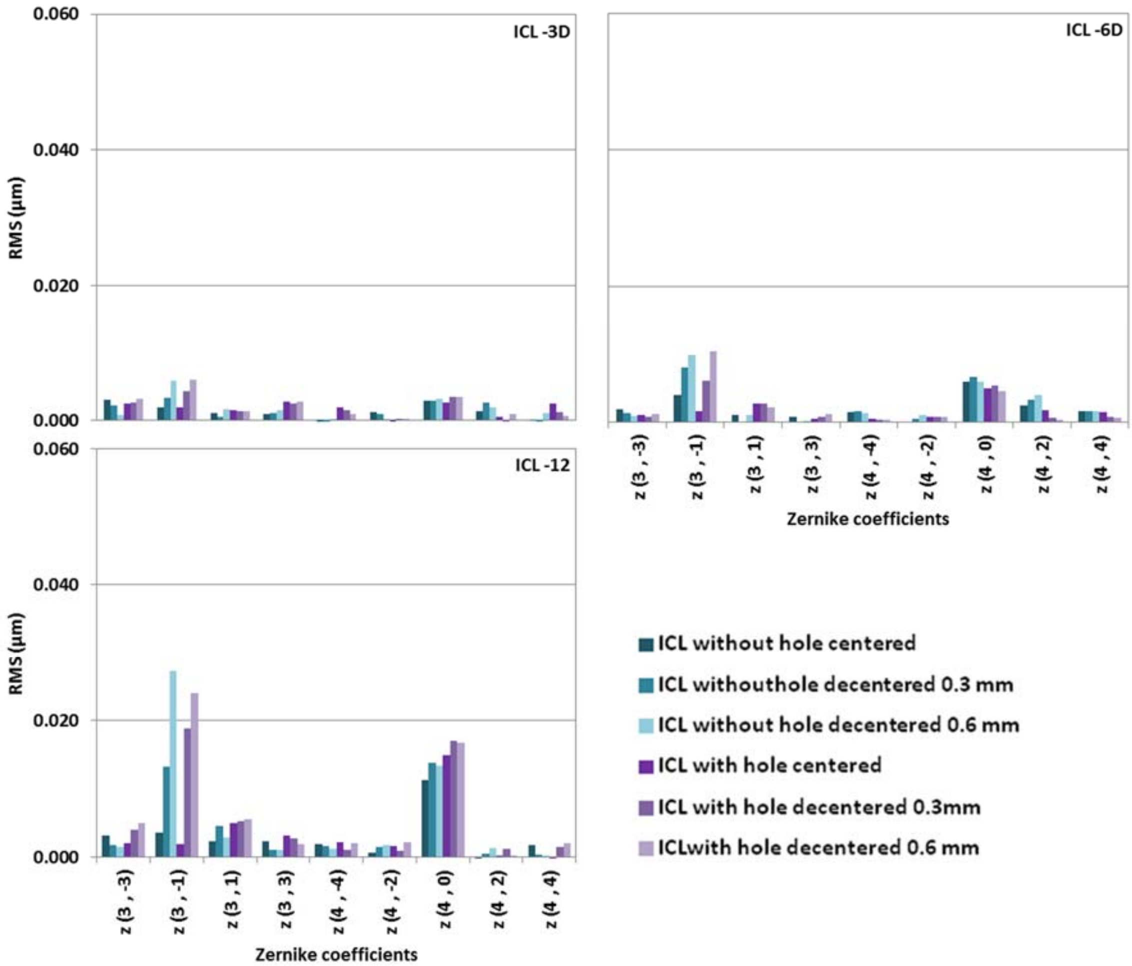

Figure 4.2: RMS of trefoil (Z_3^{-3}; Z_3^{3}), coma (Z_3^{-1}; Z_3^{1}), tetrafoil (Z_4^{-4}; Z_4^{4}), secondary astigmatism (Z_4^{-2}; Z_4^{2}), and spherical aberration (Z_4^{0}) for -3, -6 and -12D of conventional and Hole ICLs at different degrees of decentering at 3-mm pupil.

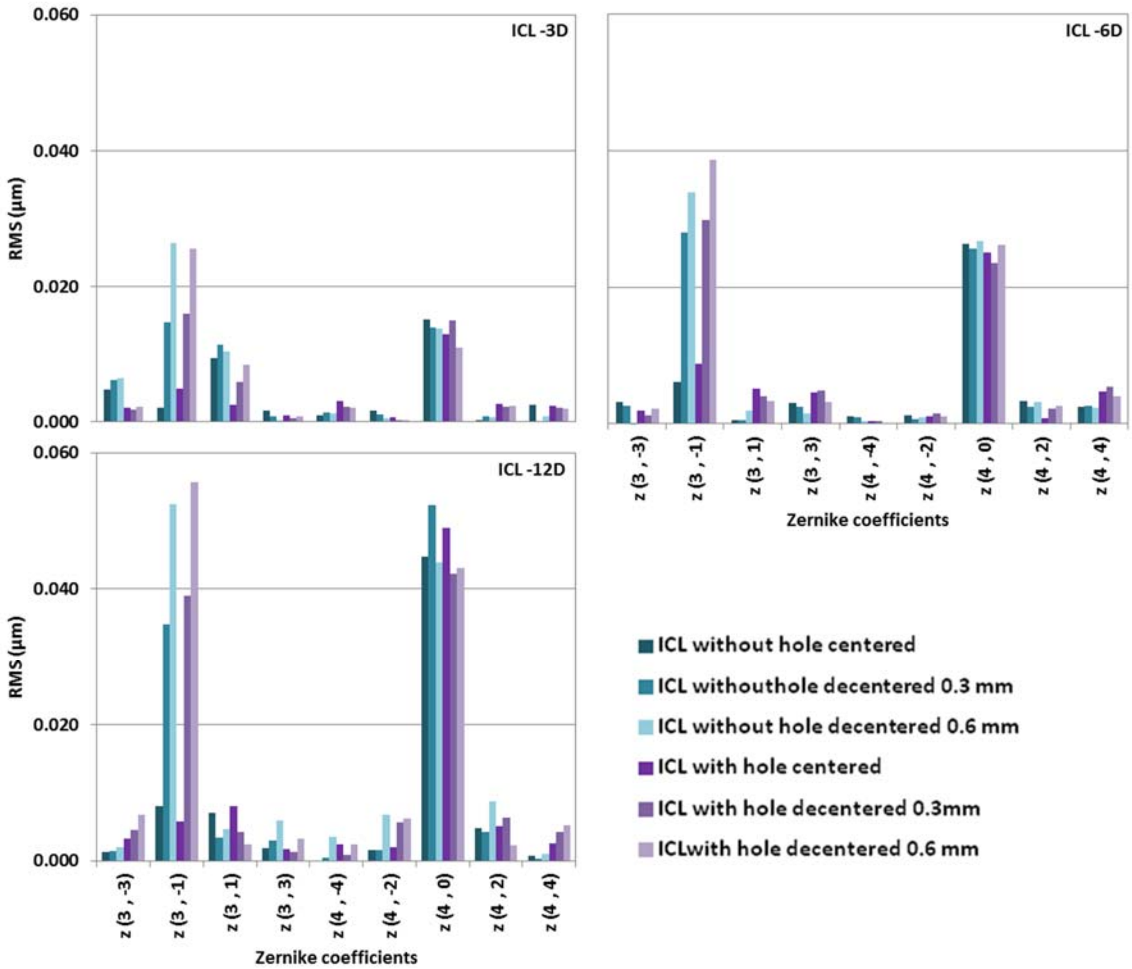

Figure 4.3: RMS of trefoil (Z_3^{-3}; Z_3^3), coma (Z_3^{-1}; Z_3^1), tetrafoil (Z_4^{-4}; Z_4^4), secondary astigmatism (Z_4^{-2}; Z_4^2), and spherical aberration (Z_4^0) for -3 , -6 and -12D of conventional and Hole ICL at different degrees of decentering at 4.5-mm pupil.

Figure 4.4 shows bar graphs of total RMS for each ICL evaluated and all conditions at 3- and 4.5-mm pupil. No statistically significant differences were found between conventional and Hole ICLs at any refractive power and pupil diameter ($p<0.05$). In relation to the effect of decentering on both types of ICLs, for a 3-mm pupil, we found only statistically significant differences between centered and 0.6 mm of decentering for -12D ($p<0.05$). At 4.5-mm pupil, statistically significant differences were found between centered position and 0.6 mm decentering for all ICLs evaluated ($p<0.05$).

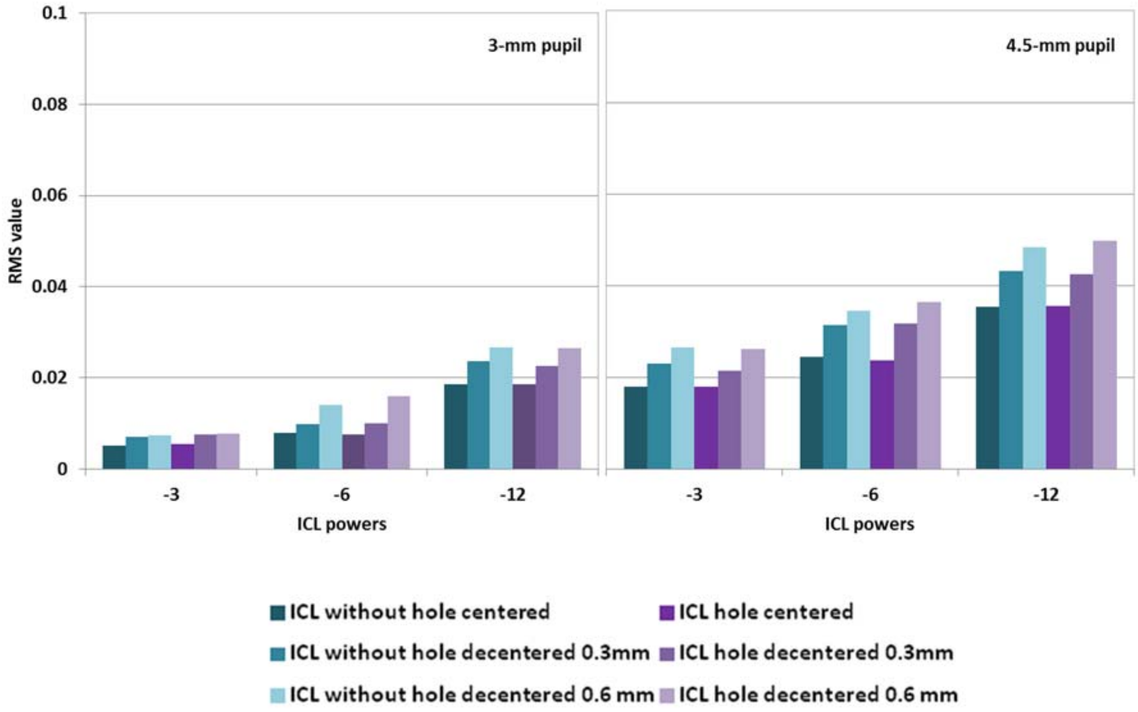

Figure 4.4: RMS of total HOAs (from third to seventh order) for conventional and Hole ICLs at different degrees of decentering for 3- and 4.5-mm pupils.

Figure 4.5 shows the images of PSFs computed from the wavefront aberrations of the ICLs evaluated and for different degrees of decentering at 4.5-mm pupil. The differences between these images were minimal, a slightly greater spread out can be observed at conventional and Hole -12D ICLs in relation to lower power ICLs due to the effect of spherical aberration increment with the refractive power. The corresponding simulated retinal images are shown in figure 4.6, as expected, did not show differences between conventional and Hole ICLs for any refractive power and position.

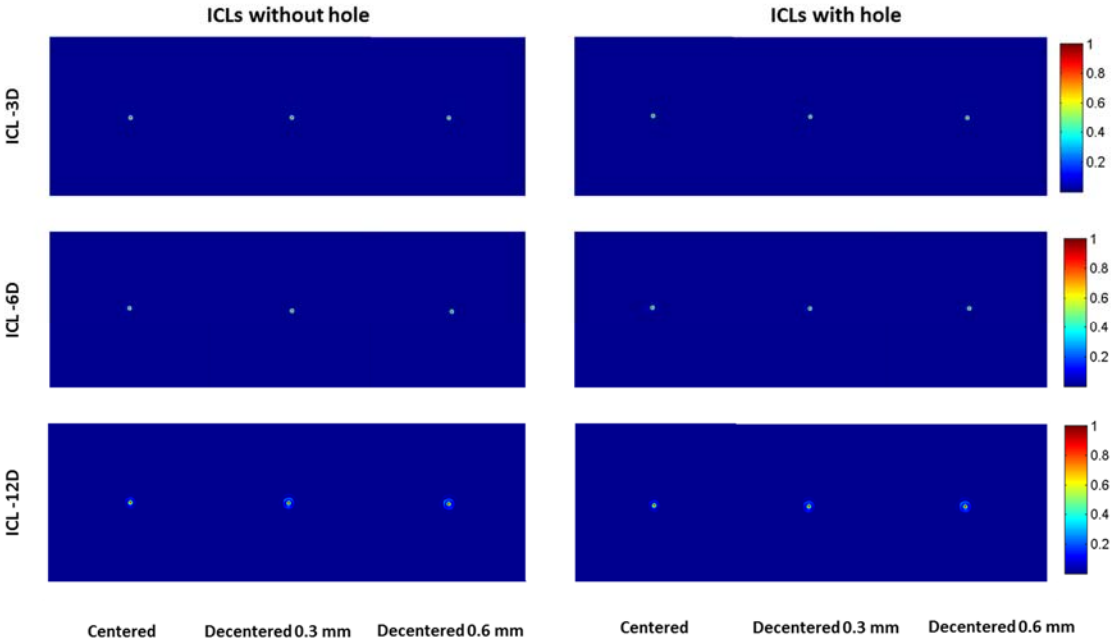

Figure 4.5: PSF computed from the wavefront aberrations at 4.5-mm pupil for -3, -6 and -12D conventional and Hole ICLs at centered position, 0.3 mm and 0.6 mm of decentering.

Figure 4.6: Simulated retinal images computed from the wavefront aberrations at 4.5-mm pupil for -3, -6 and -12D conventional and Hole ICLs at centered position, 0.3 mm and 0.6 mm of decentering.

4.4 DISCUSSION

The aim of the current study was to evaluate the optical quality of the conventional and Hole ICLs at different refractive powers and at different degrees of decentering for 3- and 4.5-mm pupils. This study allows us a direct comparison of the optical quality between conventional and Hole ICLs and analyzes the effect of the ICL decentering on the optical quality.

Effect of the hole on the optical quality

The conventional and Hole ICLs evaluated showed negative values of spherical aberration, which increased with the ICL power, and negligible amounts of other aberrations in the centered position. This agrees with other studies (Kim et al., 2011, Perez-Vives et al., 2013a, Perez-Vives et al., 2013c) that measured conventional myopic ICLs *in vitro* and found negative values of spherical aberration and low values of other aberrations. We did not find statistical significant differences between conventional and Hole ICLs for any Zernike coefficients evaluated, any decentering position and both pupils ($p>0.05$; see figures 4.2 and 4.3). The total RMS increases when the refractive power increases due to the spherical aberration increment (Kim et al., 2011, Perez-Vives et al., 2013a, Perez-Vives et al., 2013c), but no statistically significant differences were found in total RMS between conventional and Hole ICLs for any ICL power evaluated ($p>0.05$; see figure 4.4). No comparison with other studies is possible since no studies have previously analyzed the wavefront aberrations of the Hole ICL.

In addition, conventional and Hole ICLs had similar PSFs and simulated retinal images (see figure 4.5 and 4.6). We cannot appreciate differences between them, since both ICL models showed similar wavefront aberrations values without differences between them at any refractive power evaluated. In these images we can also see the effect of spherical aberration increment for both types of lenses at the highest refractive power analyzed (-12D) at 4.5-mm pupil. Note a little spread out in the PSFs images and the slightly blur in simulated retinal images. Recently, Pérez-Vives et al. (2013a) measured the wavefront aberrations *in vitro* of the ICLs for low/medium- (-3, -6 and -9D) and high-powers (-12 and -15D) and for two pupil diameters (3- and 4.5-mm). They found that the negative spherical aberration increases with ICL power being related with its innate optical properties. At 3-mm pupil, no statistically significant differences were found between ICL powers for any Zernike coefficients evaluated, although it became significant at 4.5-mm pupil between low/medium- and high-power ICLs. They concluded that the spherical aberration increment is clinically negligible to affect the visual quality of a patient after its implantation. In addition, in another study (Perez-Vives et al., 2013c), these authors evaluated the visual quality for different powers (-3, -6 and -15D) and sizes of incision surgery using an adaptive optics visual simulator. They found a slightly decrease in visual quality for -15D ICL at 4.5-mm pupil because of the rise of negative spherical aberration, but these losses are offset by the effect of spectacle magnification.

Two previous studies evaluated the optical quality of the Hole ICL, one using mathematically software analysis (Shiratani et al., 2008) and other measuring *in vitro* its MTFs (Uozato et al., 2011). Shiratani et al. (2008) obtained the MTFs using ZEMAX optical simulation software, they found that an ICL with a central hole (diameter 1.0 mm) was similar to an ICL without hole. Uozato et al. (2011) showed, using an *in vitro* optical simulation model to measure the Line Spread Function, that the differences in MTF between an ICL with a 0.36 mm central hole at various ICL powers and a conventional ICL were small. Both studies agree with our outcomes that the differences between two ICL models are minimal and clinically negligible.

Other studies (Shimizu et al., 2012a, Shimizu et al., 2012b) have evaluated the Hole ICL after its implantation for moderate to high myopia. Shimizu and colleagues (2012a) evaluated 20 eyes of 20 patients with spherical equivalents of -7.36±2.13 D who underwent Hole ICL implantation. The UCVA was -0.20 logMAR (20/12) and all measures of safety, efficacy, predictability and stability were favourable at 6 months after surgery. No significant rise in intraocular pressure or a secondary cataract formation were observed in any case during 6 months. More recently, Shimizu et al.(2012b) compared postoperative visual performance in patients who underwent conventional ICL in one eye and Hole ICL in the other eye to correct moderate to high myopia. They evaluated 58 eyes of 29 patients with spherical equivalents of -7.55±2.09 D. Ocular HOAs and CS function were measured before and 3 months after surgery at 4- and 6-mm pupil. They concluded that Hole ICL implantation induces similar HOAs and an equivalent CS function than conventional ICL implantation. These studies also agree with our *in vitro* outcomes that the Hole ICL induces similar HOAs than conventional ICL providing high and similar optical quality. Our simulated retinal images of both models are directly comparable and hence no differences in visual performance are expected as reported by Shimizu et al. (2012b) in real patients.

Effect of Implantable Collamer Lens decentering on the optical quality

In the present study, we also evaluated the effect of the ICL decentration on HOAs. We have found that ICL decentration induces coma aberration, which is greater when the ICL power and pupil size increase. Statistically significant differences were found in coma aberration between centered and both degrees of decentering for all ICLs and pupils evaluated ($p<0.05$; see figure 4.2 and 4.3). The maximums increments of coma aberration were 0.02 and 0.05 µm at 3- and 4.5-mm pupils, respectively. These increments affected the total RMS of the lenses evaluated (see figure 4.4) being statistically significant different for the largest decentration and the highest refractive power and pupils. This effect is expected considering that a displacement of a lens with spherical aberration generates coma aberration (Lopez-Gil et al., 1998, Guirao et al., 2001, Lopez-Gil et al., 2009).

The PSFs and simulated retinal images showed low influence of coma aberration increment since we cannot appreciate the visible differences between centered and decentered ICL positions (see figures 4.5 and 4.6). Rocha et al. (2007b) measured the changes in VA induced by individual Zernike ocular aberrations (defocus, astigmatism, coma, trefoil and spherical aberration) of various RMS magnitudes (0.1, 0.3 and 0.9 µm) at 5-mm pupil. Focusing on the coma aberration, they found that the coma aberration of 0.1 µm does not affect the VA, aberrations up to 0.3 µm induces significant losses in VA. The value of 0.1 µm of coma aberration corresponds to 0.025 and 0.072 µm at 3- and 4.5-mm pupils, respectively. Hereby, the increment of coma found in our study due to the ICL decentering (the maximum value found were 0.02 and 0.05 µm at 3- and 4.5-mm, respectively) is expected to not affect the visual quality of a patient implanted with the lens.

Tahzib et al.(2008) found, in eyes implanted with an Artiflex phakic IOL, a mean lens decentration of 0.24±0.12 mm with a maximum decentration of 0.5 mm. They measured in these patients the wavefront aberration and concluded that there was a significant correlation between lens decentration and postoperative spherical and coma aberrations. No clinical data exist about the amount that ICLs may be decentered when implanted. In this study we only simulated the ICL decentration up to 0.6 mm since greater decentrations may have other implications and changes in the vault of the lens besides affecting the optical and visual quality. Probably, higher ICL decentration would involve a second surgery to reposition the ICL.

The present study only evaluated the optical quality of the ICLs themselves, regardless the ocular wavefront aberrations. We have to take into account that ICLs should be implanted, so the characteristics of the patients' eye could affect the final visual quality. Further studies will include visual simulations, adding ocular wavefront aberrations to analyze how affect the hole and different decentrations on visual performance.

In conclusion, our study shows good and comparable optical quality of conventional and Hole ICLs for all ICL powers evaluated. ICL decentering affects the same manner both ICLs models evaluated. Although coma aberration increased with ICL decentering these values were clinically negligible and have not a significant effect on the visual performance.

CHAPTER 5

Visual Quality Comparison of Conventional and Hole-Visian Implantable Collamer Lens at Different Degrees of Decentering

5.1 INTRODUCTION

The ICL is a posterior phakic IOL approved by the United States FDA for myopia correction. Several studies have shown the safety and effectiveness of the ICL to correct myopia (Sanders et al., 2003, Sanders et al., 2004) hyperopia (Davidorf et al., 1998, Pesando et al., 2007) and astigmatism (Alfonso et al., 2010a, Alfonso et al., 2010b). However several complications have been reported (Fernandes et al., 2011). Complications include increased intraocular pressure (Sanchez-Galeana et al., 2002), endothelial cells loss (Edelhauser et al., 2004), pupillary block (Bylsma et al., 2002), pigment dispersion (Brandt et al., 2001), glaucoma (Brandt et al., 2001, Bylsma et al., 2002, Sanchez-Galeana et al., 2002) and anterior subcapsular cataract (Lackner et al., 2004, Sanchez-Galeana et al., 2003, Sanders, 2008, Alfonso et al., 2010c). Anterior subcapsular opacities results from surgical trauma or continuous ICL and crystalline lens contact because of insufficient vaulting (Sanchez-Galeana et al., 2003, Lackner et al., 2004, Sanders, 2008, Alfonso et al., 2010c). On the other hand, Fujisawa et al. (2007) reported that another cause of secondary cataract formation may be the poor circulation of the aqueous humour that induces an ICL implantation.

In order to reduce some complications and disadvantages, the ICL designs have undergone different improvements. The latest model is V4c Visian ICL, which have been designed with a central hole of 0.36 mm to improve the aqueous humour circulation (Kawamorita et al., 2012) and eliminates the need to perform neodymium:YAG

(Nd:YAG) iridotomy or peripheral iridectomy before ICL implantation. Shiratani et al. (2008) showed that an ICL with a hole of 1.0 mm in diameter in the center of the optic did not degrade the performance of the ICL compared to the conventional version and it is sufficient to increase the aqueous humour perfusion volume on the anterior surface of the crystalline lens, preventing cataract formation. Pérez-Vives et al. (2013d) compared the optical quality of conventional and Hole ICLs, measured *in vitro*, at different degrees of decentering. They found comparable optical quality between both designs of ICLs, without statistical differences between them. The effect of decentering equally affects both conventional and Hole ICLs. Shimizu et al. (2012a, 2012b) evaluated the visual performance with the Hole ICL implanted. They showed good outcomes of safety efficacy, predictability and stability for the correction high to moderate myopic.

The aim of the present study was to compare the visual performance provided by conventional ICL and Hole ICL for three powers (3-, -6 and -12 D) and evaluate the effect of decentering (0.3 and 0.6 mm) on the visual performance. For this purpose we used an adaptive-optics system to simulate vision from the ICL's aberration pattern itself. VA for different contrast and CS were evaluated for 3- and 4.5-mm pupils.

5.2 MATERIAL AND METHODS

This study included fifteen eyes of fifteen individuals, aged 21 to 28 and having all experience in psychophysical experiments. Spherical refractive errors ranged between -1.50 and +0.25 D with astigmatism < 0.25 D. They had all clear intraocular media and no known ocular pathology. Wavefront aberrations were measured with natural pupil. The pupil diameter was almost always larger than 4.5 mm, as the room's light was off during the experiments.

The Visian ICL is a phakic lens made from Collamer, a flexible, hydrophilic and biocompatible material with a plate-haptic design and a central convex/concave optical zone. The ICL lenses are foldable, allowing for posterior chamber injection through a microscopic incision of 3.5 mm or smaller. When properly placed, the ICL should be positioned completely within the posterior chamber between the iris and crystalline lens with support on the ciliary sulcus. In this study we have analyzed the V4b and V4c ICL models for different powers: -3.00, -6.00 and -12.0 D for both models. The V4c model ICL introduces a central hole (diameter 0.36 mm) to increase the aqueous humour perfusion and reduce the risk of secondary cataract formation. The length of the ICLs was 12 mm and the optical diameter was 5.5 mm in all cases.

Adaptive-Optics Visual Simulator

We used the crx1 adaptive-optics system (Imagine Eyes, Orsay, France) explained in chapter 1 (section 1.3.1).

Experimental Procedure

The crx1 was programmed to measure and compensate for that particular eye's wavefront error up to the 5th order. In order to simulate in each individual the vision achieved after ICL implantation, the ICL's wavefront pattern was induced adding also the wavefront pattern of the myopic eye. The natural pupil diameter was monitored for each individual (≥ 4.5-mm), and the pupil size was controlled using the simulator's artificial pupil. The HOAs of both models of ICLs were obtained from the study carried out by Pérez-Vives et al. (2013d). They measured the HOAs and analysed the optical quality of ICLs with and without central hole at different degrees of decentering (centered and decentered 0.3 and 0.6-mm).

Visual Quality Measurement

VA and CS were measured in the same way that in chapter 2 (section 2.2).

Data Analysis

The ANOVA was used to disclose differences between both ICL models and different conditions of decentering. Post-hoc multiple comparison testing was performed using the Holm-Sidak method. Differences were considered statistically significant when the P value was less than 0.05.

5.3 RESULTS

Figures 5.1 and 5.2 show high-, medium- and low-contrast VA outcomes for -3, -6 and -12D conventional and Hole ICLs for centered, 0.3 and 0.6 mm decentered positions at 3- and 4.5-mm pupils, respectively. We did not find statistically significant differences in VA values between conventional and Hole ICLs at any ICL powers, decentered position and for both pupils (p>0.05). Regarding the effect of decentering, no statistically significant differences were found between centered and decentered positions for any ICL powers and pupils evaluated (p>0.05).

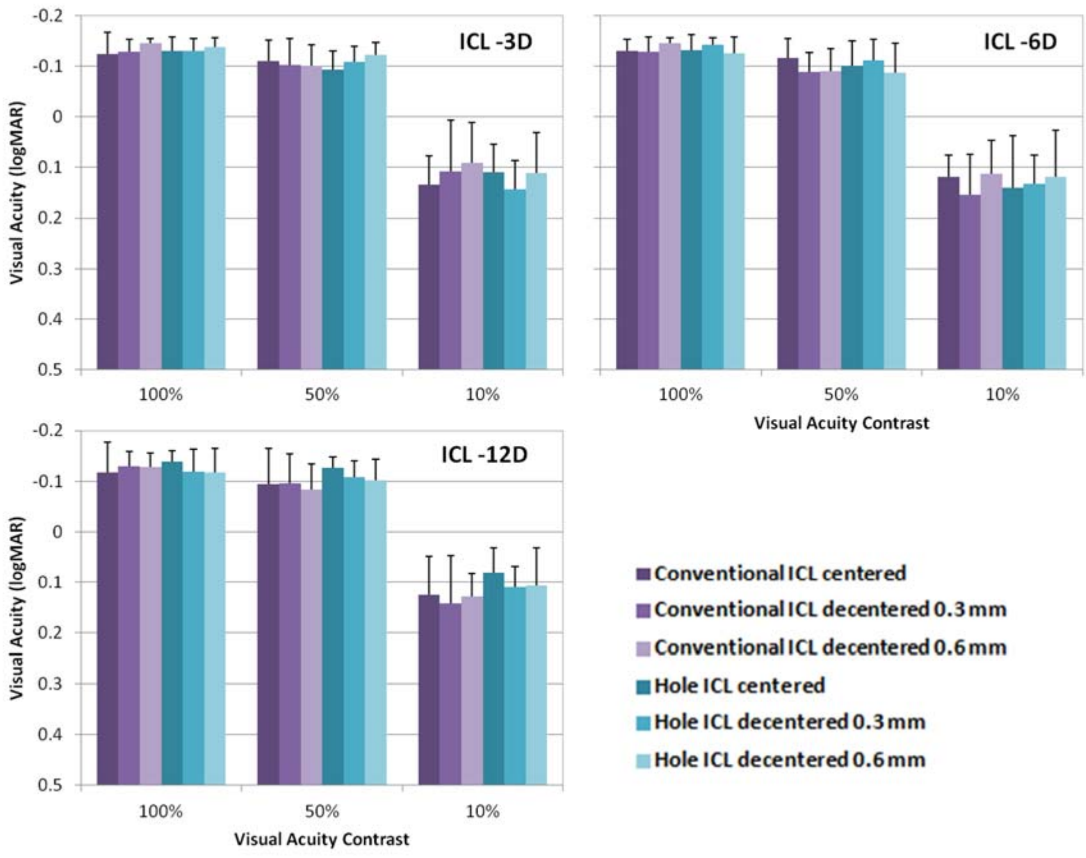

Figure 5.1: VA logMAR at high (100%), medium (50%) and low (10%) contrast, for -, -6 and -12D of conventional and Hole ICL at different degrees of decentering at 3-mm pupil.

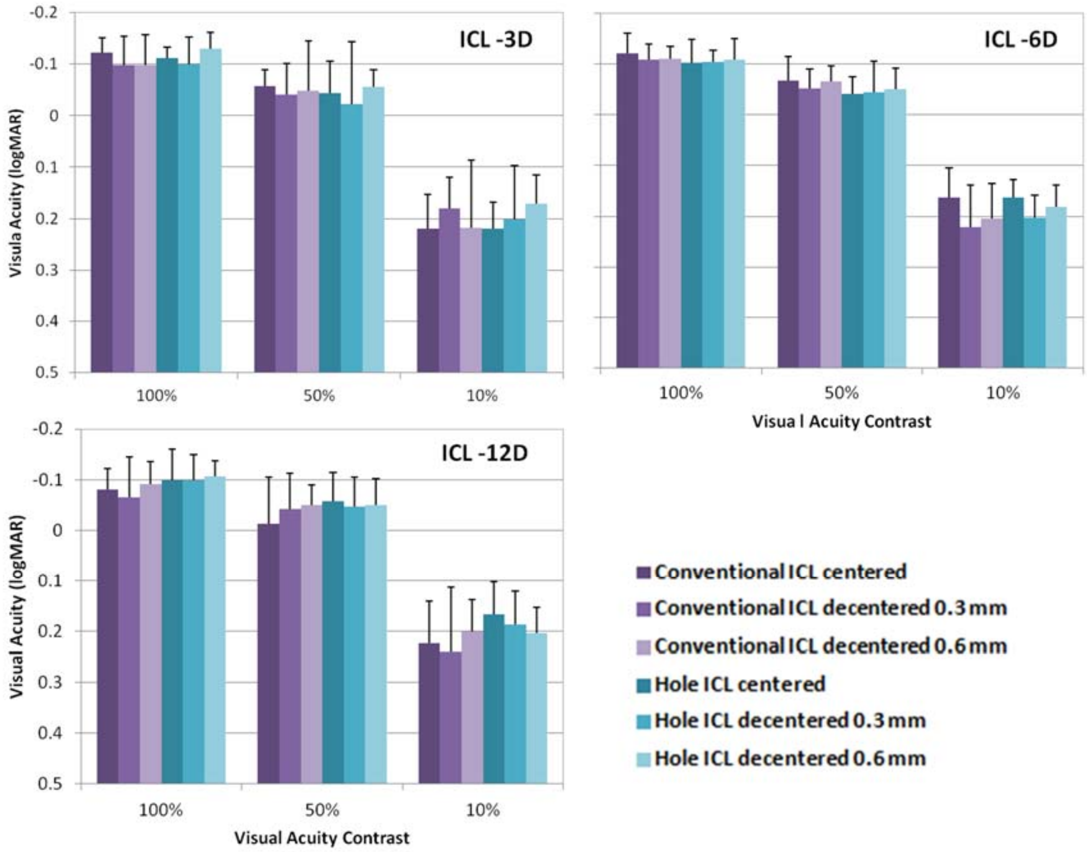

Figure 5.2: VA logMAR at high (100%), medium (50%) and low (10%) contrast, for -3, -6 and -12D of conventional and Hole ICL at different degrees of decentering at 4.5-mm pupil.

Figures 5.3 and 5.4 show the mean log10 CS values for -3, -6 and -12D conventional and Hole ICLs for centered, 0.3 and 0.6 mm decentered positions at 3- and 4.5-mm pupils, respectively. No statistically significant differences were found in CS values between conventional and Hole ICLs at any refractive power, decentered positions and pupil sizes ($p>0.05$). In relation to the effect of decentering on both types of ICLs, we did not find statistically significant between centered and decentered positions for any ICL powers and pupils evaluated ($p>0.05$).

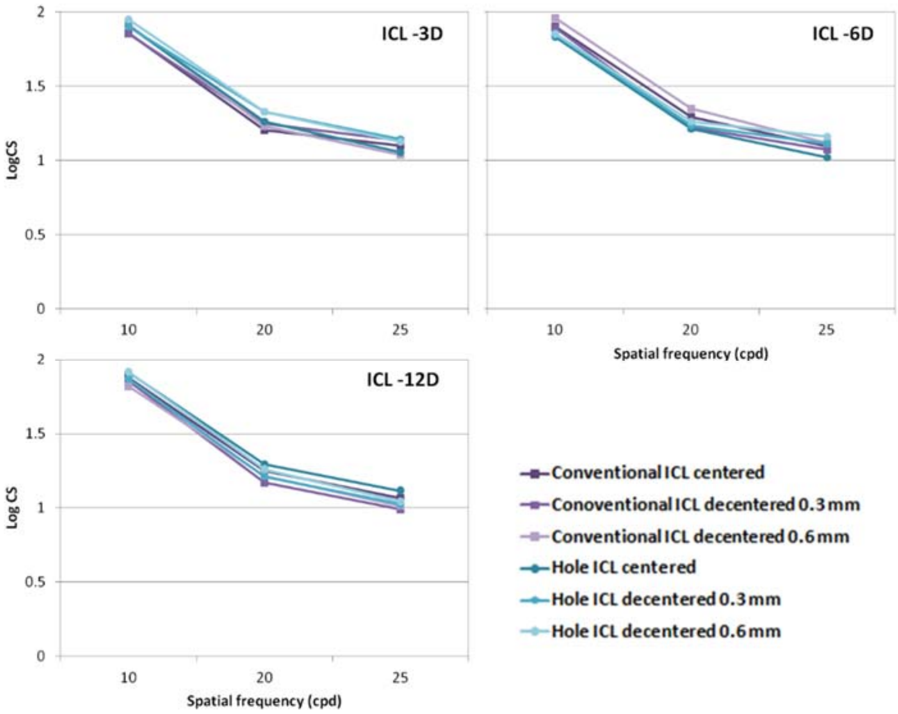

Figure 5.3: Mean log CS plotted as a function of spatial frequency (10, 20 and 25 cpd) for -3, -6 and -12D of conventional and Hole ICL at different degrees of decentering at 3-mm pupil.

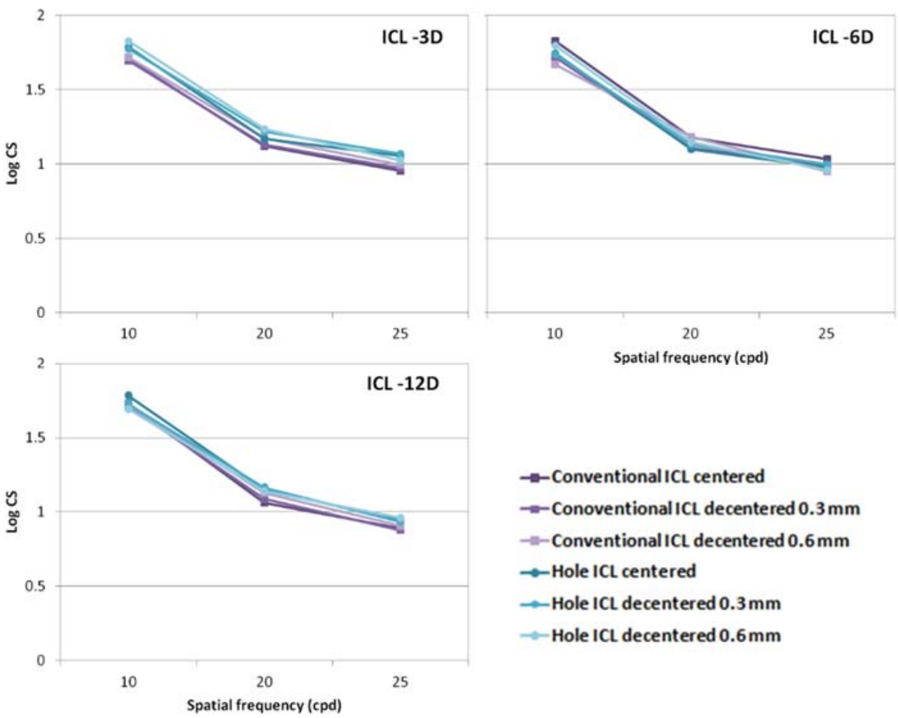

Figure 5.4: : Mean log CS plotted as a function of spatial frequency (10, 20 and 25 cpd) for -3, -6 and -12D of conventional and Hole ICL at different degrees of decentering at 4.5-mm pupil.

5.4 DISCUSSION

The aim of the present study was to simulate and compare the vision provided by a conventional and Hole ICLs at different refractive powers and at different degrees of decentering. This method allows us to evaluate and compare the patient's visual quality without the need of ICL implantation, analyzing the effect of ICL model and ICL decentering effect.

Effect of the hole on the optical quality

VA values achieved with conventional and Hole ICLs at different degrees of decentering and for both pupils were good, obtaining values above 20/20 at high- and medium contrast for all ICL powers. At low contrast, VA values were favorable too, about 20/30 for all powers of conventional and Hole ICLs, at different degrees of decentering and for both pupils. No statistically significant differences were found between conventional and Hole ICLs at any ICL power, any decentering position and both pupils ($p>0.05$; see figures 5.1 and 5.2). These outcomes agree with those obtained by Shimizu et al. (2012a). They analyzed the early outcomes of 20 eyes of 20 patients implanted with Hole ICL to correct moderate and high myopia (mean spherical equivalent -7.36±2.13 D). They found that the mean uncorrected VA was -0.20 logMAR and 100% of eyes had uncorrected VA of 20/20 or better 6 months after surgery.

In terms of CS, for conventional and Hole ICLs the CS function was good and comparable, we did not find statistically significant differences between conventional and Hole ICLs at different degrees of decentering and both pupils ($p>0.05$; see figure 5.3 and 5.4). Shimizu et al. (2012b) compared postoperative visual performance after Hole ICL implantation in one eye and conventional ICL implantation in the other eye to correct moderate and high myopia (mean spherical equivalent -7.55±2.09 D). They evaluated the HOAs and photopic and mesopic CS function 3 months after surgery at 4- and 6-mm pupils. They concluded that after the Hole ICL implantation, the postoperative area under the log CS function was equivalent to that after conventional ICL implantation under photopic and mesopic conditions. Besides, Hole ICL implantation induced similar HOAs than conventional ICL implantation. This studio also agrees with our simulating outcomes that Hole ICL implantation provided similar outcomes in CS than conventional ICL implantation in real patients.

Pérez-Vives et al. (2013d) measured the HOAs of conventional and Hole ICLs *in vitro* at different degrees of decentering for 3- and 4.5-mm pupil. They did not find statistically significant differences in any Zernike coefficient terms evaluated between conventional and Hole ICLs for any ICL powers and pupil sizes. Moreover, they also evaluated the PSF and simulated retinal images of ICLs calculated from the ICLs' wavefront aberrations. They did not find differences in the PSF and simulated retinal images, since both ICL models showed similar wavefront aberrations values without differences between them at any refractive power evaluated. These outcomes also show that the differences between both ICL models are minimal and clinically negligible.

Effect of ICL decentering on the optical quality

The effect of the ICL decentration on visual performance was also evaluated in the present study. We found that VA values at centered, 0.3 and 0.6 mm decentered were good and comparable for both pupils and all ICL powers, without statistically significant differences between them ($p>0.05$; see figures 5.1 and 5.2). Regarding to the CS outcomes, the effect of decentering neither affected the CS values, we did not find statistically significant differences in CS results between centered and decentered positions ($p>0.05$;figures 5.3 and 5.4). Moreover, ICL decentering affects the same manner both ICL models.

Pérez-Vives et al. (2013d) found that ICL decentration induced coma aberration, which was greater when the ICL power and pupil size increased; statistically significant differences were found in coma aberration between centered and both degrees of decentering for all ICLs and pupils evaluated. Although, they found the PSFs and simulated retinal images showed low influence of coma aberration increment since they could not appreciate the visible differences between centered and decentered ICL positions. Therefore, they concluded the increment of coma, due to the ICL decentering, was expected to not affect the visual quality of a patient implanted with the lens, since these increments were less than 0.025 and 0.072 µm at 3- and 4.5-mm pupils. These changes in coma RMS values do not affect the visual performance (Rocha et al., 2007b). The present study confirms this fact; although the ICLs have been implanted in an eye, the coma increment when the ICL is decentered does not affect the visual performance.

The visual simulator allows us evaluate the impact of different IOLs and different conditions on visual performance before the surgical procedure takes place. However, we must take into account several limitations of our study, such as the surgery effects, ICL tilt or other postoperative complications (Fernandes et al., 2011), which may affect the outcomes reported here.

In summary, the outcomes of the present study show that conventional and Hole ICLs provide good and comparable visual performance for all powers and pupils sizes evaluated. Moreover, ICL decentering affects the same manner both ICL models evaluated. The ICL decentering did not have any effect on the visual performance, like Pérez-Vives et al. (Perez-Vives et al., 2013d) predicted in their study.

CHAPTER 6

Implantable Collamer Lens for Presbyopia

6.1 INTRODUCTION

The Visian Implantable Collamer Lens is a posterior chamber Phakic IOL approved by the United States FDA for myopia correction. Several studies have demonstrated the safety, efficacy and predictability of its implantation in eyes with moderate and high myopia (Sanders et al., 2003, Lackner et al., 2004, Sanders et al., 2004, Kamiya et al., 2009, Alfonso et al., 2011), hyperopia (Davidorf et al., 1998, Pesando et al., 2007) and astigmatism (Alfonso et al., 2010a, Alfonso et al., 2010b). The best candidates for the Visian ICL are between the ages of 21 and 45, since the ICL does not include the correction of the presbyopia.

These lenses show low levels of HOAs and negative low-values of spherical aberration (Kim et al., 2011, Perez-Vives et al., 2012), therefore the ICL implantation show good visual function (Perez-Vives et al., 2013c). However, spherical aberration induces multiple focal points on the focal axis of an optical system and these points may contribute to increase the DoF (Rocha et al., 2009, Benard et al., 2010, Benard et al., 2011, Ruiz-Alcocer et al., 2012a). It is important that there is an acceptable compromise between the DoF and visual quality, since high levels of spherical aberration decreases the visual function (Li et al., 2009). Rocha et al.(2009) found a maximum DoF of approximately 2.0 D with 0.6 μm of spherical aberration and became smaller when the aberration was increased to 0.9 μm. Benard and colleagues (2010, 2011) in their both studies evaluated the DoF with spherical aberration values of ±0.3 μm and ±0.6 μm. In all cases they found an increase of DoF.

The aim of the present study was to find out the ideal ICL's spherical aberration value, which produces a DoF increment without disrupting the VA. In order to obtain an ICL for presbyopic patients and extend the age of the best candidates until, at least, 55 years old. For this purpose, an adaptive optics system was used to simulate the vision after different ICL experimental prototypes implantation, in which the spherical aberration values were changed. The VA for different contrast and DoF were evaluated for 3- and 4.5-mm pupil. To our Knowledge, this is the first study that allows us to evaluate different ICL experimental prototypes in the same patient without needing the surgery.

6.2 MATERIALS AND METHODS

Subjects

Ten eyes of ten patients, aged from 20 to 35 years and experienced in psychophysical experiments were included in this study. Spherical refractive errors ranged between -2.00 and +0.50 D with astigmatism <1.00D. They had clear intraocular media and no known ocular pathology. Approximately 30 min before experimental measurements, three drops of cyclopentolate hydrochloride 0.5% were instilled to paralyze their accommodation.

The tenets of the Declaration of Helsinki were followed. Informed consent was obtained from each participant after verbal and written explanation of the nature and possible consequences of the study. The protocol received institutional review board approval.

Intraocular Lens

The Visian ICL is a phakic lens made from Collamer, a flexible, hydrophilic and biocompatible material. The ICL lenses are foldable, allowing for posterior chamber injection through a microscopic incision of 3.5 mm or smaller. When properly placed, the

ICL should be positioned completely within the posterior chamber between the iris and crystalline lens with support on the ciliary sulcus. It is 6.0 mm wide and comes in 5 diameters (11.0, 11.5, 12.0, 12.5, and 13.0 mm). The lens has a central convex–concave optic zone with a diameter of 4.5 to 5.5 mm, depending on dioptric power. The ICL design has been modified many times. In this study, we used the ICM V4b model.

Apparatus

We used the crx1 adaptive-optics system (Imagine Eyes, Orsay, France) explained in chapter 1 (section 1.3.1) and the Nimo TR0805 instrument (Lambda X, Belgium) explained in chapter 4 (section 4.2).

Aberrations patterns

In the present study, we simulated the vision after -3.00 and -6.00 D ICLs implantation. In order to find the ICL's spherical aberration value that increases the DoF without deteriorating the VA; we created 4 ICL experimental prototypes, in which the spherical aberration has been changed according to previous studies that analyzed the relationship between the spherical aberration and DoF (Rocha et al., 2009, Benard et al., 2010, Benard et al., 2011, Ruiz-Alcocer et al., 2012a). Rocha et al.(2009) reported a maximum DoF of approximately 2.00 D with 0.6 μm of spherical aberration at 6-mm pupil. Benard et al.(2010, 2011) found that the addition of ±0.3 and ±0.6 μm of spherical aberration increases DoF around 30% and 45%, respectively in one study and 45% and 64%, respectively in the another study at 6-mm pupil. Thereby, the ICL prototypes were calculated to get a whole spherical aberration (Eye + ICL) of ±0.3 or ±0.6 μm (values for 6-mm pupil). The ICL experimental prototypes simulated were:

Eye + ICL (-3/-6 D) + SA1= +0.3 μm (6-mm pupil)

Eye + ICL (-3/-6 D) + SA2= -0.3 μm (6-mm pupil)

Eye + ICL (-3/-6 D) + SA3= +0.6 μm (6-mm pupil)

Eye + ICL (-3/-6 D) + SA4= -0.6 μm (6-mm pupil)

The ocular HOAs were selected of the middle-age eye, around 35 to 50 years (Lopez-Gil et al., 2008). These four ICL prototypes were computed for -3.00 and -6.00 D ICLs at 3- and 4.5-mm pupils.

Experimental Procedure

The crx1 was programmed to measure and compensate for a particular eye's wavefront error up to the 5th order. Afterwards, we introduced in the crx1 each ICL prototypes aberrations defined previously in order to simulate the vision achieved after ICL implantation whose spherical aberration has been changed. The visual simulation were done for 3- and 4.5-mm pupils. The pupil size was controlled using the simulator's artificial pupil.

Visual Quality Measurement

VA was measured in the same way that in chapter 2 (section 2.2).

Depth of Focus

For measuring the defocus curves, the target was moved from -5.00 to +2.50 D in 0.25 D steps with the built-in Badal system and in all vergences the VA was measured monoculary using FrACT software. The magnitude of the DoF depends on how it is defined, and for our study, we used the criterion that DoF is the range focusing error which the VA does not decrease below 0.1 logMAR (20/25 Snellen equivalent) (Ogle and Schwartz, 1959, Tucker and Charman, 1975, Ruiz-Alcocer et al., 2012a).

Data Analysis

A Student *t*-test for unpaired data was used to reveal differences in VA and DoF between normal ICLs and different ICLs' experimental prototypes simulated. Results are presented as the mean ± SD and statistical significance was set at $P < 0.05$.

6.3 RESULTS

Visual Acuity

Figure 6.1 and 6.2 show the high-, medium- and low- contrast VA outcomes for -3.00 and -6.00 D ICLs, respectively, and for ICL prototypes simulated at 3- and 4.5-mm pupils. At 3-mm pupil, there were not statistical significant differences in VA between normal ICLs and different ICL prototypes (p>0.05); except for -6D ICL + SA4 at 50% VA contrast (p<0.05). In contrast, at 4.5-mm pupil, statistical significant differences in VA were found between normal ICLs and all ICL prototypes (p<0.05); except for -3 D ICL + SA3 at 100% VA contrast, for -3D ICL + SA1 at 10% contrast and for -6D ICL + SA4 at 50% VA contrast (p<0.05). In all cases VA achieved with normal ICLs was better than with ICL prototypes evaluated.

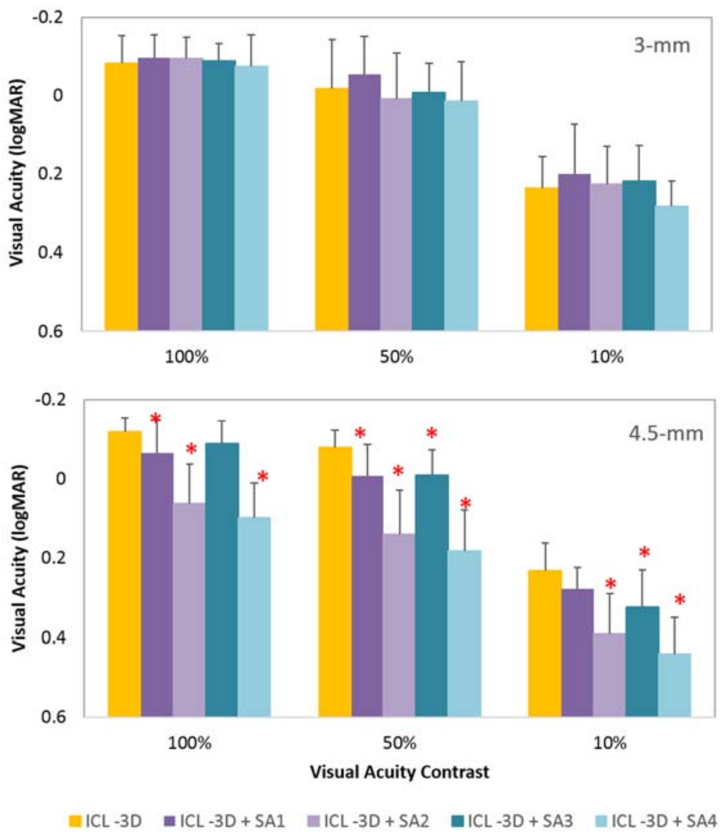

Figure 6.1: VA logMAR at high contrast (100%), medium contrast (50%) and low contrast (10%) for -3 D ICL and all -3 D ICL prototypes evaluated at 3- and 4.5-mm pupils. Error bars represent the standard deviation (SD). * indicates statistically significant differences (p<0.05).

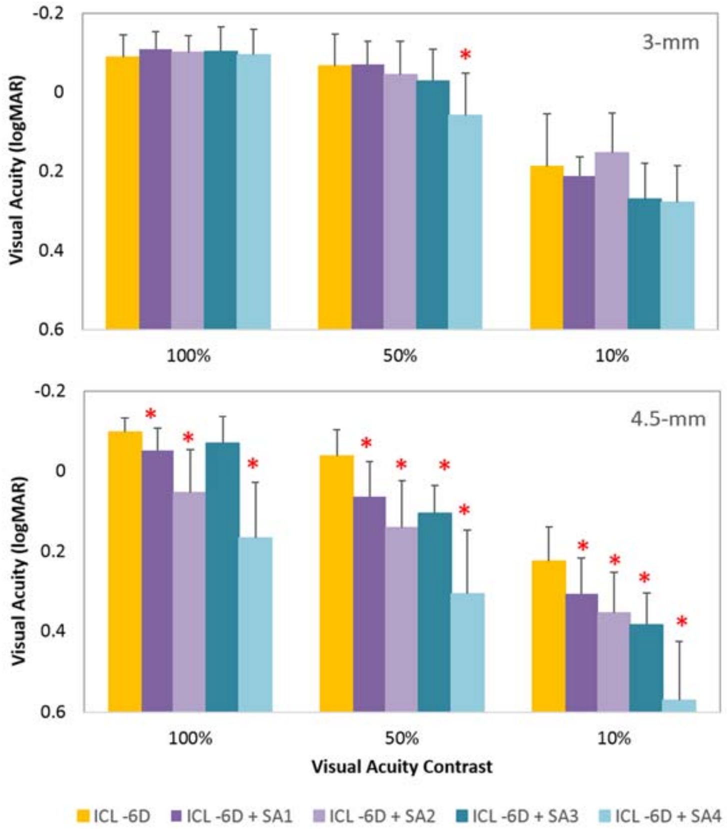

Figure 6.2: VA logMAR at high contrast (100%), medium contrast (50%) and low contrast (10%) for -6 D ICL and all -6 D ICL prototypes evaluated at 3- and 4.5-mm pupils. Error bars represent the standard deviation (SD). * indicates statistically significant differences ($p<0.05$).

Depth of Focus

Figure 6.3 shows the defocus curves for -3.00, -6.00 D ICLs and ICL prototypes at 3- and 4.5-mm pupils. Tables 1 and 2 show the DoF expressed in diopters for -3.00 and -6.00 D ICLs, respectively, and for ICL prototypes at 3- and 4.5-mm pupil sizes. For -3D ICL + SA1, SA2, SA3 and SA4 increased DoF by 28%, 47%, 57% and 62%, respectively, at 3-mm pupil. There were statistically significant differences in DoF between normal -3.00 D ICL and all -3D ICL prototypes ($p<0.05$); except for -3D ICL + SA1 ($p>0.05$). At 4.5-mm pupil, for -3D ICL + SA1, SA2, SA3 and SA4 increased DoF by 1.5%, 16%, 32% and 36%, respectively. Finding statistically significant differences between normal -3.00 D ICL and -3D ICL + SA3 and SA4 ($p<0.05$). For -6D ICL + SA1, SA2, SA3 and SA4 increased DoF by 4.9%, 19.5%, 65% and 60%, respectively, at 3-mm pupil. At 4.5

mm pupil, for -6D ICL + SA1, SA2, SA3 and SA4 increased DoF by 16.2%, 32.5%, 66% and 55%, respectively. Statistical significant differences between normal -6.00 D ICL and -6D ICL + SA3 and SA4 at 3- and 4.5-mm pupil ($p<0.05$) were found. In all cases the DoF was greater when the spherical aberration increased.

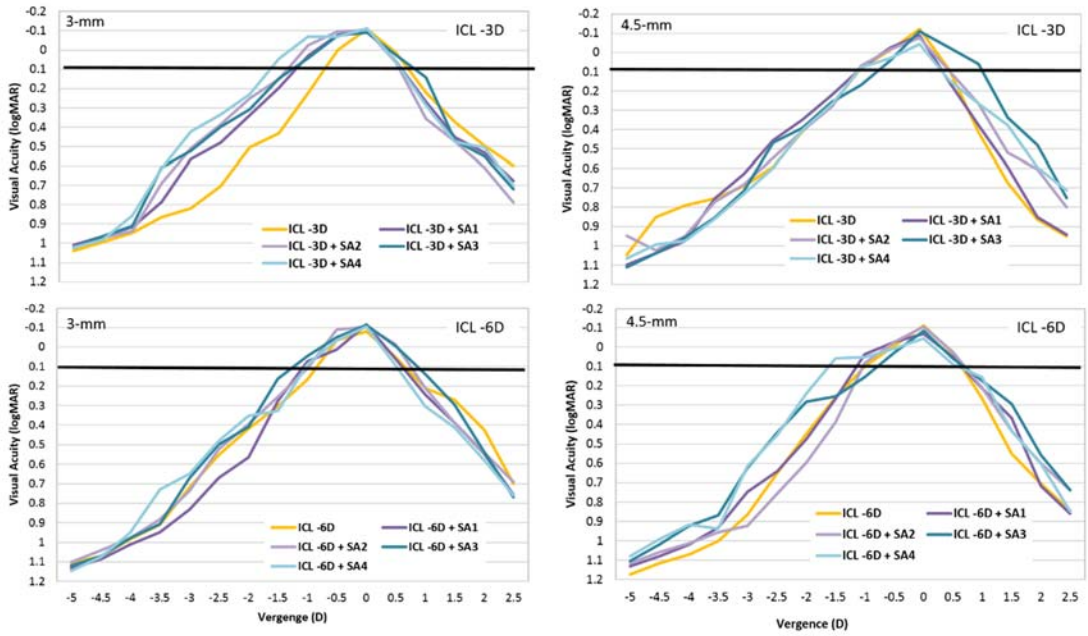

Figure 6.3: Mean high-contrast VA logMAR as a function of the lens defocus (D) with each of four ICL prototypes studies for -3D ICL at 3-mm pupil, -3D ICL at 4.5-mm pupil, -6D ICL at 3-mm pupil and -6D at 4.5-mm pupil.

DEPTH OF FOCUS (D)

	Normal ICL	-3D ICL + SA1	-3D ICL + SA2	-3D ICL + SA3	-3D ICL + SA4
3-MM	1.36±0.69	1.75±0.52	2.00±0.76*	2.14±0.62*	2.21±0.81*
4.5-MM	1.36±0.38	1.38±0.49	1.58±0.35	1.79±0.76*	1.86±0.56*

**: Statistically significant differences regarding normal ICL.*

Table 6.1: DoF values for -3D ICL and with different spherical aberration values at 3- and 4.5-mm pupil sizes.

DEPTH OF FOCUS (D)

	Normal ICL	-6D ICL + SA1	-6D ICL + SA2	-6D ICL + SA3	-6D ICL + SA4
3-MM	1.43±0.61	1.50±0.82	1.71±0.81	2.36±0.38*	2.29±0.39*
4.5-MM	1.29±0.39	1.50±0.41*	1.71±0.49	2.14±0.56*	2.00±0.58*

**: Statistically significant differences regarding normal ICL.*

Table 6.2: DoF values for -6D ICL and with different spherical aberration values at 3- and 4.5-mm pupil sizes.

6.4 DISCUSSION

The aim of the present study was to simulate and evaluate the vision and the DoF after ICL implantation, changing the ICLs' spherical aberration values. This method allow us to find out an ICL's spherical aberration value, which produces a DoF increment without disrupting the VA.

Visual Acuity

VA values achieved with -3.00 and -6.00 D ICLs were excellent at 3- and 4.5-mm pupils, obtaining values above 20/20 at high- and medium-contrast (see figures 6.1 and 6.2). At 3-mm pupil, all ICL prototypes achieved VA values above 20/20 at high- and medium-contrast; except for -6D ICL + SA4 at 50% VA contrast, which slightly decreased around 20/25. Besides, the VA at 10% contrast did not change significantly. However, at 4.5-mm pupil, the effect of aberration became apparent, thereby when the ICLs' spherical aberration values were changed the VA obtained decreased. Although the VA decreased significantly, the ICL prototypes whose spherical aberration was positive, achieve VA values greater than 20/20. Thus, the effect of negative spherical aberration on VA was larger than that of positive spherical aberration. Li et al. (2009) also found a significantly VA decreased when ±0.2 and ±0.3 μm of spherical aberration at 6-mm pupil were induced. Being the effect of positive spherical aberration on VA less than that of negative spherical aberration. Other previous studies (Rocha et al., 2007b, Rouger et al., 2010b) also evaluated the changes in VA by individual Zernike ocular aberrations by different magnitudes using an adaptive optics visual simulator. They found significantly VA losses when the spherical aberration was ±0.3 μm or greater at 5-mm pupil.

Depth of Focus

At 3-mm pupil, the DoF increased significantly 0.64, 0.78 and 0.85 D for -3D ICL + SA2, SA3 and SA4, respectively, compared with -3.00 D ICL. At 4.5-mm pupil, the DoF increased significantly 0.43 and 0.50 D for -3D ICL + SA3 and SA4, respectively, compared with -3.00 D ICL (see table 6.1). Comparing with -6.00 D ICL, the DoF increased significantly 0.93 and 0.86 D, at 3-mm pupil, and 0.85 and 0.71 D, at 4.5-mm pupil, for -6D ICL + SA3 and SA4, respectively (see table 6.2). The DoF increase was independent of the sign of the added spherical aberration. The maximum DoF increment was 2.36 D, it was achieved with the ICL prototype that contained the higher spherical aberration value at 3-mm pupil. Rocha et al. (Rocha et al., 2009) also found a maximum of approximately 2.00D with 0.6 μm of spherical aberration and became smaller when the spherical aberration was increased to 0.9 μm. Besides, they also reported that the DoF was not dependent of the sign of the spherical aberration. Benard et al. (Benard et al., 2010) found that the DoF increased by 30% and 45% when 0.3 and 0.6 μm, respectively, of spherical aberration were added. They suggested that the subjective DoF increased more when 4th-order spherical aberration and 6th-order spherical aberration of opposite signs were added (Benard et al., 2011, Yi et al., 2011). Legras et al. (2012) reported that the DoF increased by 0.61 and 0.71 D when 0.3 and 0.6 μm of spherical aberration were simulated, respectively at 6-mm pupil. They also observed that the DoF decreased when the pupil size increased. Some differences between the outcomes of the previous studies and those obtained in the present study are mainly due to the criterion that defines the DoF, some authors (Rocha et al., 2009, Benard et al., 2010, Benard et al., 2011, Yi et al.,

2011) used 0.4 logMAR target compared with our 0.1 logMAR; differences in pupil diameter and the effect of the presence of other wavefront aberrations (Applegate et al., 2003).

Other previous studies (Rocha et al., 2007a, Ruiz-Alcocer et al., 2012a) have also evaluated the DoF after IOL implantation. They reported that slight residual amount of positive spherical aberration that comes from the IOL and the cornea offers a good compromise between distance VA and DoF. Although, extreme values of residual positive spherical aberration provoke a disruption in the balance of spherical aberration and DoF due to the VA decreases at all vergences, resulting in a decrease in DoF as well. It should also be noted that negative residual spherical aberration significantly decreases VA and the DoF when these values are compared with similar values of the opposite sign. These outcomes also agree with those found in the present study.

Visual simulator allow us to evaluate experimental IOLs designs before creating prototypes to implement in order to evaluate the visual quality that can provide different IOLs designs for the correction of refractive errors. However, we must take into account several limitations of the present study, such as the surgery effects, ICL tilt or other postoperative complications and the variability of ocular wavefront aberrations of the population, which may affect the outcomes reported here. Future studies will include visual simulations with different ICL prototypes evaluated in presbyopic patients in order to prove the benefits of these ICL designs.

In conclusion, the outcomes of the present study suggest that with a certain value of spherical aberration, the ICLs could be useful for young presbyopic patients, providing around 2D of DoF and excellent VA values.

CHAPTER 7

Conclusions and Further Studies

In the present PhD thesis we have analysed and characterized the ICLs *in vitro* and then we have simulated the vision after their implantation. The ICLs have been studied for different refractive powers, at several pupil diameters, for different surgical conditions, such as the implantation through a large- and small-incision. The ICLs also have been compared with other refractive surgeries, like LASIK procedure at different levels of myopia. Different ICL designs, conventional and Hole-ICLs, have been evaluated and compared for several refractive powers and at different degrees of decentering. Once, we were familiarized with the adaptive optics thechnology and we had the ICLs characterized and profundly studied; we changed the aberration pattern of the ICLs in order to create an ICL for presbyopic patients. The main conclusions of these studies were:

- The myopic ICLs measured *in vitro* show excellent optical quality. Although they have a slightly residual of negative spherical aberration, it could be beneficial after its implantation, because of the compensation with the slightly residual of positive spherical aberrtion that shows normal eyes.
- The negative spherical aberration of the myopic ICLs increases with the ICL power, affecting the visual outcomes with high refractive powers. Although these losses are offset by the effect of the spectacle magnification.
- Eyes with myopic astigmatism should be preferably implant a toric ICL through a small incision instead of a spherical ICL through a large incision.

- ICL surgery provides better optical and visual quality results than LASIK procedure, especially for higher refractive errors and pupil sizes.
- The central hole that presents some ICLs does not have any effect on their own optical quality and neither on the visual performance after its implantation. Showing comparable outcomes with the previous ICL designs without central hole.
- Both conventional and hole ICLs have high tolerance to decentrations. Althought the coma aberration increases with the ICL decentering, these values are not clinically significant and do not affect the visual performance.
- The ICLs could be useful for young presbyopic patientes changing the spherical aberration to a certain value, which may provide good VA values and around 2.00 of DoF.

With the use of visual simulator we are able to evaluate the impact upon the visual performance of different surgical techniques before the surgical procedure actually takes place. Furthermore, we can also create an experimental design and evaluate the visual benefits before creating prototypes or performing the surgery. The visual simulator is a useful tool to evaluate and compare controllably different surgical procedures and enhanced or create new experimental designs for correcting presbyopia.

The conclusions of the different studies of this Thesis can establish the basis for future research lines and potential studies, such as:

1. Measure the HOAs of hyperopic and toric ICLs and simulate the vision after their implantation.
2. Compare the ICL implantation with other phakic IOL designs.
3. Compare the ICL procedure with other refractive surgeries.
4. Simulate the vision after ICL implantation through different corneal profiles, such as irregular corneas as occur in keratoconus.
5. Increase the sample for presbyopic ICL experimental design study and perform the CS test.
6. Test the presbyopic ICL experimental design in young presbyopic patients with the visual simulator.

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APPENDIX A

Publications from the Thesis

This Thesis has resulted in the following peer-reviewed publications:

1. Optical and visual quality of the Visian Implantable Collamer Lens using an adaptive optics visual simulator. *American Journal of Ophthalmology* 2013; 155(3): 499-507. Impact Factor: 3.631. Position: 4/58. Ophthalmology Section of the Journal Citation Report.

2. Optical and visual quality comparison of Implantable Collamer Lens and laser in situ keratomiulesis for myopia using an adaptive optics visual simulator. *European Journal of Ophthalmology* 2013; 23(1): 39-46. Impact Factor: 0.912. Position: 45/58. Ophthalmology Section of the Journal Citation Report.

3. Optical quality comparison of conventional and Hole-Implantable Collamer lens at different degrees of decentering. *American Journal of Ophthalmology* 2013; 156(1): 69-76. Impact Factor: 3.631. Position: 4/58. Ophthalmology Section of the Journal Citation Report.

4. Visual quality comparison of conventional and Hole-Visian Implantable Collamer lens at different degrees of decentering. *British Journal of Ophthalmology* 2014; 98(1): 59-64. Impact Factor: 2.809 Position: 10/58. Ophthalmology Section of the Journal Citation Report.

5. Implantable Collamer lens for Presbyopia. *Journal Cataract Refract Surgery* 2014 (submitted). Impact Factor: 2.552 Position: 15/58. Ophthalmology Section of the Journal Citation Report.