VNIVERSITAT DE VALÈNCIA

OPTICAL SOLUTIONS FOR PRESBYOPIA IN THE AGEING EYE:

THE EFFECT OF THE SIZE AND SHAPE OF THE PUPIL.

PROGRAMA DE DOCTORADO EN OPTOMETRÍA Y CIENCIAS DE LA VISIÓN

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Memoria presentada por

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DECLARACIÓN

Ninguna parte de este trabajo ha sido presentada para optar a ningún otro grado ni titulación, ni en esta ni en otra universidad o institución educativa o de investigación.

El Dr. Alejandro Cerviño Expósito, profesor titular de la Universidad de Valencia; el Dr. José Juan Esteve Taboada, personal investigador doctor, y el Dr. Santiago García Lázaro, profesor Ayudante Doctor de la Universidad de Valencia

CERTIFICAN que la presente memoria "OPTICAL SOLUTIONS FOR PRESBYOPIA IN THE AGEING EYE: THE EFFECT OF THE SIZE AND SHAPE OF THE PUPIL", resume el trabajo de investigación llevado a cabo por D. Daniel Monsálvez Romín, bajo su dirección y supervisión, y constituye su Tesis Doctoral 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, firman el presente certificado en Valencia, a julio de dos mil dieciocho.

Fdo. Alejandro Cerviño Expósito

Fdo. Dr. José Juan Esteve Taboada

Fdo. Dr. Santiago García Lázaro

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ACRONYMS

- **BFC(r)**: Best fit circle (radius).
- **BFCirregSD**: Standard deviation of the best fit circle irregularity.
- **CSF**: Contrast sensitivity function.
- **DO**: Distance to the origin.
- **ISO**: International organization for standardization.
- **LDA**: Light Distortion Analyser.
- **LDI**: Light distortion index.
- **MCL(s)**: Multifocal contact lens(es).
- **MIOL(s)**: Multifocal intraocular lens(es).
- **MTF**: Modulation transfer function.
- **OTF**: Optical transfer function.
- **VSOTF**: Visual Strehl ratio in the frequency domain (derived from optical transfer function).

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ANEXO

RESUMEN

La presbicia es la pérdida natural progresiva de la capacidad para enfocar objetos cercanos que se produce con el envejecimiento. Esta capacidad se conoce como acomodación. Esta pérdida generalmente conlleva una reducción de la calidad de vida, razón por la cual su corrección ha sido un asunto de especial interés en los últimos años. En las últimas décadas han surgido en el mercado nuevos métodos de corrección con la intención de mejorar la calidad de vida de la población présbita. Hoy en día, existe una mayor demanda social de tareas que requieren visión funcional en un amplio rango de distancias, como el trabajo con ordenadores o el uso de teléfonos inteligentes. Esto, junto con importantes cambios demográficos, pone un especial valor en la corrección óptima de la presbicia. La población mundial está creciendo cada año debido al aumento de la esperanza de vida general. Esto producirá en el futuro una inversión de la pirámide de población, y es un fenómeno que ya está ocurriendo en todo el mundo. Con esto, se espera que el porcentaje de población présbita alcance altos niveles en el futuro cercano y, por lo tanto, la presbicia se convertirá en un asunto de salud pública mundial.

Hoy en día, existen varias soluciones disponibles para la corrección de la presbicia. Los tratamientos para la presbicia son actualmente correctivos mediante elementos ópticos o métodos quirúrgicos de modificación refractiva. Las soluciones ópticas no son independientes, sino que su eficacia está supeditada a factores físicos, fisiológicos e incluso psicofísicos de los pacientes, dependiendo de la técnica. Entre las soluciones más comúnmente usadas están las gafas, las lentes de contacto (LC) y las lentes intraoculares (LIO). Las gafas proporcionan un método fiable para la corrección de la presbicia, pero su uso se ha asociado a una disminución en la calidad de vida debido a la dependencia del paciente para llevar a cabo actividades cotidianas. La prescripción de LC es un método alternativo para la corrección, aunque informes recientes muestran que las tasas de prescripción son todavía bajas. Esto podría explicarse en parte por la falta de conocimiento clínico por los profesionales de LC y la presencia de un clima de desconfianza debido a las desventajas de los diseños para

la corrección de la presbicia, entre otras razones. Existen varias técnicas para lograr la corrección de la presbicia mediante LC. Estas opciones pueden dividirse principalmente en tres categorías: combinación con corrección en gafas, monovisión y LC multifocales (LCM). En cuanto a las LCM, una de las técnicas más utilizadas, la solución se basa en el principio de formación de imágenes simultáneas. Aquí, las correcciones tanto de lejos como de cerca se colocan dentro del área pupilar simultáneamente en todas las posiciones de mirada. Así, se forman imágenes diferentes al mismo tiempo en la retina. En esta situación, el sistema visual centra la atención en la imagen correspondiente para la distancia de observación deseada e ignora el resto. El objetivo principal de estas correcciones es ampliar el rango de visión funcional. Sin embargo, esto conlleva efectos negativos en el rendimiento visual. Monocularmente, se presenta degradación de la imagen debido a la superposición de diferentes imágenes. Esto puede ocurrir especialmente para visión cercana de objetos con poco contraste y en condiciones de baja iluminación, aunque esto puede mejorar con el tiempo. Malestar y visión deficiente son los principales factores que causan abandono en el uso de LC. Las LIO son otra solución óptica utilizada para la corrección de la presbicia. Las LIO actualmente disponibles se pueden clasificar en dos grupos principales, según su papel dentro del globo ocular: lentes intraoculares fáquicas o pseudofáquicas. Las lentes del primer grupo actúan como ayuda óptica junto con el resto de medios oculares, pero sin extracción del cristalino. El segundo grupo está formado por las LIO que sustituyen la lente natural del ojo, debido principalmente a la formación de cataratas. Las soluciones ópticas actuales pueden usar ambos tipos de lentes. Todos los tipos de LIO multifocales (LIOM) para la presbicia utilizan el principio de formación de imágenes simultáneas, ya sea con tecnologías difractivas o refractivas.

Se han creado múltiples diseños de LCM para tratar de satisfacer las necesidades visuales de la población présbita. Sin embargo, los fabricantes ofrecen a veces información insuficiente, lo que hace difícil evaluar adecuadamente las ventajas y desventajas de un diseño particular. Con el fin de proporcionar más información que puede ser de gran utilidad para los profesionales, se realizan medidas de los perfiles de potencia. Los perfiles de potencia son una poderosa herramienta que podría dar a los profesionales una comprensión más profunda del comportamiento de las lentes y de este modo, se facilitaría la selección de la mejor opción para cada paciente. En esta situación, se podrían aumentar las tasas de prescripción de LCM. Este conocimiento es necesario para lograr una adaptación adecuada. La dependencia pupilar de las LCM de imagen simultánea es conocida y ha sido estudiada por muchos investigadores. Los pacientes présbitas generalmente llevan a cabo sus tareas bajo diferentes niveles de iluminación y, por tanto, con tamaños de pupila diferentes. Además, las pupilas pequeñas se deben considerar como una situación importante y común porque muchas de las actividades se realizan generalmente bajo condiciones fotópicas y esto, junto con la miosis por reflejo acomodativo, conduce a la constricción de la pupila. Además, los pacientes présbitas normalmente presentan tamaños más pequeños de la pupila que la población más joven. El tamaño de la pupila media en pacientes mayores de 60 años se considera entre 3,0 mm (condiciones fotópicas) y 4,5 mm (condiciones mesópicas). Teniendo en cuenta esto, ya que hay un cambio de la distribución de potencia dependiendo de la pupila, es evidente que el comportamiento de estas lentes depende de la pupila de los pacientes. Así, las diferencias en la respuesta pupilar entre los sujetos podrían conducir a comportamientos refractivos diferentes incluso para aquellos con la misma refracción de lejos, adición o exigencias visuales. Por todas estas razones, el tamaño de la pupila tiene un papel significativo al estudiar el funcionamiento de una lente.

En cuanto a las LIOM, la dependencia de la pupila también se ha investigado extensivamente. Varios estudios de evaluación in vitro de LIOM han demostrado la relación entre el tamaño de la pupila y el rendimiento óptico para diversos diseños. Generalmente se evalúa el rendimiento óptico de una lente en su posición centrada. Sin embargo, también es importante tener en cuenta que diversos factores pueden afectar su posición final dentro del ojo, tales como la técnica de implantación, implantación asimétrica, contracción capsular asimétrica, fibrosis de cápsula, ruptura de la cápsula posterior, diálisis zonular, etcétera. Esto resulta en un descentramiento de la lente o en una inclinación. Este desalineamiento respecto al eje visual puede afectar el rendimiento óptico de las lentes. Las LIOM bien centradas con un diseño asférico pretenden mejorar el rendimiento óptico y la sensibilidad al contraste por reducción de la aberración esférica. Sin embargo, el descentramiento puede resultar en una menor función de transferencia óptica.

Una comparación objetiva de las propiedades de formación de imagen de las LIOM, así como de las LCM y su asociación con el tamaño de la pupila, puede ser útil para seleccionar la solución más adecuada para cada paciente. Naturalmente, la dependencia de la pupila siempre se considera en términos del diámetro total de una pupila circular. Sin embargo, debido a condiciones congénitas o adquiridas, la pupila puede no ser circular y puede que haya perdido parte de su funcionalidad. De hecho, cualquier trastorno que físicamente cause daños en los mecanismos del iris o alteraciones en su inervación puede resultar en una pupila con forma irregular. Por ejemplo, el coloboma de iris es una condición que se presenta temprano en la gestación y se asocia con el cierre defectuoso de la fisura óptica. Como resultado, la coroides no está completamente cerrada y así se deforma la pupila. También, las sinequias posteriores se presentan cuando el tejido del iris se adhiere a la cápsula anterior del cristalino dando una forma irregular de la pupila como resultado de un trauma u otras condiciones oculares que implican la inflamación intraocular como uveítis. Un trauma ocular u otros trastornos también pueden llevar a alteraciones de la forma pupilar, como los espasmos musculares que conducen a la midriasis de iris segmentaria. Debe tenerse en cuenta que los ojos con pupilas irregulares debido a enfermedades oculares también pueden presentar una disminución de la visión. Es importante reconocer las anormalidades estructurales del iris con el fin de detectar la causa de la función pupilar (reactividad), forma o tamaño de la pupila anormal. La forma de la pupila y su influencia en el comportamiento de las soluciones ópticas actuales para la corrección de la presbicia no se ha investigado anteriormente. Por lo tanto, si se ha mencionado que el tamaño de la pupila tiene un papel significativo en el rendimiento de soluciones multifocales, se cree que la forma de la pupila también podría tener implicaciones adicionales en su comportamiento óptico incluso en términos de otros factores tales como los efectos de distorsión luminosa.

Aunque las soluciones ópticas multifocales para la presbicia son exitosas para un gran número de personas, también presentan algunas limitaciones. Los candidatos a soluciones multifocales deben aceptar un nivel de compromiso visual potencial, a cambio de una mayor calidad de vida sin dependencia de las gafas. La evaluación de la distorsión luminosa bajo condiciones de baja iluminación se ha convertido en un asunto de especial interés en los últimos años debido al creciente número de LCM, cirugía refractiva corneal y la implantación de LIO. Bajo este concepto, varios fenómenos se incluyen, como la disfotopsia positiva y negativa, deslumbramiento, halos, *starburst*, arcos, etcétera. El término "distorsión luminosa" fue sugerido a fin de incorporar todos estos fenómenos. Estos fenómenos se manifiestan con frecuencia en los pacientes, pero comúnmente se describen como quejas subjetivas. Más allá del uso de cuestionarios subjetivos, hay una necesidad de caracterizar el tamaño y la forma de estas distorsiones de luz. La evaluación de distorsiones luminosas por parte de las soluciones ópticas para la corrección de la presbicia en diferentes condiciones, incluyendo el tamaño de la pupila o la forma, puede ser muy útil para la selección de la mejor solución óptica para el paciente.

El objetivo principal de esta tesis es analizar diferentes soluciones ópticas para la presbicia como una primera evaluación para describir los elementos ópticos y luego ir más allá mediante la evaluación de la influencia de diferentes tamaños y formas de la pupila, ya que la mayoría de los métodos de evaluación actuales sólo han tenido en cuenta una forma circular. Así, este trabajo da especial importancia a aquellas pupilas que no son circulares, y cómo esta característica puede influir en la efectividad de las actuales soluciones ópticas para la presbicia en términos de métricas de calidad de formación de imagen y de distorsión luminosa.

En esta tesis se han utilizado principalmente dos enfoques como métodos generales, los cuales se explican en el **capítulo 3**, titulado “General methods**”**. El primero de ellos hace uso de un dispositivo óptico disponible en el mercado, el dispositivo NIMO TR1504 (Lambda X, Nivelles, Bélgica) y un equipo de laboratorio experimental, el "Light Disturbance Analyser" (LDA) (CEORLab, Universidad de Minho, Gualtar, Braga, Portugal). Sin embargo, una de las principales limitaciones de estos instrumentos es que asumen pupilas circulares. Esta es la razón por la que sólo por medio de simulaciones computacionales (segundo enfoque) ha sido posible evaluar la influencia de la forma de la pupila, ya que los dispositivos ópticos existentes sólo incluyen aberturas circulares. Además, los métodos computacionales permiten desarrollar nuevas métricas a partir de datos producidos por los dispositivos. Para ello, se ha desarrollado software específico. Concretamente, se ha desarrollado un software basado en métodos de óptica de Fourier para las simulaciones y cálculos con diferentes tamaños y formas de pupila. Este software genera un mapa de error de frente de onda a través de la integración acumulativa de un determinado perfil de potencia a lo largo de la dirección radial. Posteriormente, la función pupila se calcula mediante la definición de una máscara pupilar. La función pupila describe el comportamiento de la luz cuando es transmitida a través de un sistema óptico, como una lente o el ojo humano. Esta información se usa para caracterizar elementos ópticos bajo diferentes condiciones. Un segundo software se ha desarrollado para extender las métricas proporcionadas por el instrumento LDA, el cual proporciona un análisis alternativo al del software nativo del instrumento. En este sentido, la información del instrumento se usa para calcular el tamaño de la distorsión por meridianos. Este nuevo ajuste genera nuevas métricas para tener en cuenta los posibles efectos de una pupila con forma no circular.

En el **capítulo 4**, titulado "Assessment of multifocal contact lenses for presbyopia", se da información detallada de nuevos diseños de LCM disponibles en el mercado, lo cual es de crucial interés para los profesionales. Además, se ha analizado el efecto de la forma de la pupila y se discute como un posible factor que afecta el rendimiento óptico de las LCM. Este capítulo se subdivide en la **sección 4.1**, que se titula "In-vitro evaluation of rigid gas permeable multifocal contact lenses with variable multifocal zone", y la **sección 4.2**: "The effect of non-circular shaped pupils on the performance of multifocal contact lenses". Específicamente, en la **sección 4.1**, se analizan un conjunto nuevo de LCM con zona multifocal variable. Estas lentes son rígidas permeables al gas de centro-lejos, disponibles con cinco diámetros de distancia de visión (XS, S, M, L y XL) y dos adiciones diferentes: tipo A (hasta +2,00 D) y tipo B (hasta +2,50 D). La zona multifocal se encuentra en la superficie anterior de la lente, por lo que la superficie posterior se puede diseñar en función de la forma corneal del paciente. Los resultados se presentan en forma de perfiles de potencia. Éstos muestran que la cantidad de adición total alcanzada depende del diámetro de la zona de visión lejana. En otras palabras, cuanto mayor sea el área de visión de lejos, mayor es el radio de la lente para conseguir el mismo nivel de adición. La lente XS proporciona valores más altos de adición en comparación con el diseño de lente XL para una pupila dada. Con esto, los diseños XS y S parecen estar orientados a favorecer la visión cercana. Los diseños L y XL parecen favorecer la visión lejana. Por esta razón, aquellos pacientes exigentes con la visión lejana podrían beneficiarse de los diseños L o XL, y aquellos con alta demanda en tareas de cerca podrían beneficiarse de la XS o S. El diseño M podría ser la mejor solución para aquellos pacientes que tienen necesidades similares entre visión lejana y cercana. En la **sección 4.2**, se considera un enfoque teórico y se implementa mediante simulaciones ópticas para investigar diferentes tamaños y formas pupilares, utilizando perfiles de potencia similares a los obtenidos en el apartado anterior. Específicamente, se consideran un bifocal centro lejos, un perfil de potencia multifocal progresiva, junto con un perfil monofocal. Se utilizan tres pupilas: una circular y dos no circulares (una elíptica y una forma irregular, simulando un efecto de sinequia). Las pupilas fueron definidas dentro de un diámetro máximo de 6 mm. Se han obtenido métricas basadas en la función de extensión del punto (PSF) y la función de transferencia óptica (OTF), así como el diámetro que agrupa el 25% de la luz desde el centro de la PSF (D25) o el cociente visual de Strehl en el dominio de la frecuencia (VSOTF). El parámetro VSOTF se ha utilizado anteriormente para describir el rendimiento visual, ya que muestra una fuerte correlación con métodos subjetivos. Un umbral de 0.12 generalmente se define como el valor VSOTF que corresponde a una agudeza visual en la que aproximadamente la mitad de las personas presentan dificultades al leer (equivalente Snellen 20/32). Se consideran aceptables los valores por encima de 0.12. Los resultados del análisis *through-focus* de la PSF son representados como una valoración cualitativa. Una pupila irregular origina una forma irregular de la PSF. Sin embargo, analizando estas imágenes anteriores, sólo puede hacerse una evaluación cualitativa. Una evaluación cuantitativa es deseable, ya que pueden describir las variaciones numéricamente. Para ello, se introduce el D25. Las diferencias entre pupilas para el parámetro D25 son mayores para el perfil de potencia de la lente bifocal centro lejos. Los resultados para el foco de cerca son similares entre pupilas. Para las pupilas circular y de sinequia, el tamaño de D25 resulta ser más pequeño para cerca que para lejos, mientras que con respecto a la pupila elíptica el tamaño es más pequeño para lejos pero comparable a la visión de cerca. Con respecto a la lente progresiva, todas las pupilas muestran resultados similares en lejos y mejor que la bifocal. Las curvas VSOTF muestran un cambio en la distribución de energía con las diferentes pupilas. En algunos casos, la pupila elíptica y de sinequia dan mejores resultados en cuanto a D25 o VSOTF. Esto es debido a que las pupilas enmascaran una parte del frente de onda, ya que éste se define dentro de la pupila circular de 6 mm. Por ello, el área total dedicada para cada zona óptica y su contribución a cada foco deben ser consideradas. Como conclusión, la forma de la pupila afecta a los parámetros físicos de los perfiles de potencia de las lentes analizadas. Esto significa que la eficacia de las soluciones ópticas para la corrección de la presbicia puede cambiar con pupilas irregulares. Sin embargo, las implicaciones clínicas de estos fenómenos pueden distanciarse de las mediciones físicas, debido a la influencia de otros factores como las aberraciones de frente de onda ocular o el proceso de adaptación neural.

El **capítulo 5**, titulado "Assessment of multifocal intraocular lenses for presbyopia", analiza el comportamiento de LIOM para la corrección de la presbicia. La **sección 5.1** se titula "The effect of non-circular shaped pupils and decentration on the performance of multifocal intraocular lenses". Así como con las LCM, el número de nuevos diseños de LIOM está creciendo y también aumenta el público objetivo. En este capítulo, se analiza el efecto de la forma de la pupila en estas lentes mediante simulaciones ópticas. También es importante evaluar el efecto del descentramiento en el rendimiento de la LIOM, ya que como se mencionó anteriormente, la colocación de la LIO en el saco capsular puede resultar en una posición desalineada.

Dependiendo del diseño de la LIO, algunos estudios han demostrado que el descentramiento puede tener un efecto importante en la calidad óptica proporcionada por la lente. Para este estudio se ha considerado un perfil de potencia de una LIO multifocal anular refractiva con una potencia de lejos de 0.0 D, y aproximadamente +2,50 D de adición. La zona óptica total es de 6 mm de diámetro. Una forma de pupila elíptica se utiliza para el análisis, junto con una circular con propósitos de comparación. De nuevo, se analizan métricas basadas en la PSF y la OTF, como el D25 o el VSOTF. El análisis *through-focus* para el D25 en la posición centrada proporciona resultados similares para ambas pupilas en el foco cercano, mientras que el foco de lejos da valores mayores para la pupila circular. El análisis del descentramiento revela que el foco de cerca se ve más afectado por el descentramiento. En cuanto al VSOTF, se demuestra que el foco cercano se reduce con el aumento del descentramiento para ambas pupilas, mientras que el foco lejano varía más discretamente. La robustez al descentramiento es similar para ambas pupilas para el foco de cerca. Sin embargo, la tolerancia parece ser un poco mejor para la abertura elíptica en la dirección vertical. Como conclusión, la forma de la pupila con descentramiento tiene un impacto en los parámetros físicos que se analizaron. Esto significa que la forma de la pupila puede afectar la eficacia de este tipo de soluciones ópticas para la presbicia. Sin embargo, las implicaciones clínicas de estas variaciones no son directamente extrapolables debido al efecto de otros factores como la contribución del resto de los medios oculares y los procesos neurológicos.

El **capítulo 6** se titula “Clinical evaluation of light distortion with multifocal optical solutions for presbyopia”. En la **sección 6.1**, titulada “Light distortion of soft multifocal contact lenses with different pupil size and shape”, se presenta una evaluación clínica de la distorsión luminosa con diferentes tamaños y forma de la pupila. Como se ha señalado anteriormente, el número de usuarios de LCM ha estado aumentando debido a la creciente popularidad de estas soluciones como una modalidad para corregir la presbicia. La mayoría de los diseños actuales de LCM se basa en la formación de imágenes simultáneas. Sin embargo, este principio puede implicar efectos visuales secundarios, tales como una sensibilidad aumentada al *glare* o la presencia de halos, especialmente bajo condiciones de poca luz debido al mayor tamaño de la pupila. Algunos estudios previos han investigado estos efectos secundarios con LCM. Estos efectos secundarios pueden ser un obstáculo para realizar las tareas diarias, como conducir de noche o con un sol bajo. La gran mayoría de los diseños de LCM de formación de imágenes simultáneas se basan en áreas concéntricas con una zona óptica circular central rodeada por una o más zonas anulares, que producen perfiles de potencia rotacionalmente simétricos. Estos diseños se relacionan bien con la forma de una pupila circular normal, pero el efecto de una pupila no circular y sus implicaciones clínicas no han sido previamente investigados. Este asunto es tratado en esta sección.

Se analizaron un total de 14 ojos de 7 pacientes sanos portadores de LC (3 mujeres y 4 varones) entre 25 y 40 años (media 28,57 ± 8,46 años). El dispositivo LDA ha sido empleado para la caracterización de la distorsión de la luz. Las lentes seleccionadas para el estudio fueron las desechables mensuales Biofinity Multifocal (CooperVision, CA, USA), con diseños "D" y "N" y una adición de +2,50 D. El diseño “D” consiste en un centro para la visión de lejos con un cambio progresivo positivo de potencia hacia la periferia, mientras que el diseño “N” tiene un centro para visión de cerca, con un cambio progresivo negativo. El ojo dominante (DE) de los pacientes llevaba el correspondiente diseño "D" y el ojo no dominante (NDE) el diseño "N". La versión monofocal de estas lentes se incluyó con fines comparativos. Se utilizaron dos pupilas circulares, una de 3 mm (P1) y otra de 5 mm (P2). También, se empleó una forma elíptica de 3 milímetros en la horizontal y 5 mm en la dirección vertical (P3). La aberración esférica y métricas como el índice de distorsión luminosa (LDI), el radio del círculo de mejor ajuste (BFCr) y su correspondiente desviación estándar de irregularidad (BFCirregSD) son analizadas. También se ha calculado la diferencia meridional de la distorsión luminosa entre las direcciones vertical y horizontal.

Como primera aproximación, se realiza una comparación entre las LC monofocales y las correspondientes versiones multifocales. Según los resultados, las LCM inducen un aumento generalizado de LDI (y, por lo tanto, el tamaño de la distorsión) con todo tipo de pupilas. Los mayores valores de LDI se obtienen para el DE, con diferencias más pronunciadas que en el NDE. Específicamente, la mayor diferencia estadísticamente significativa en LDI se obtiene para el DE con P2. El valor de LDI para el DE con P2 y LCM es de 6.09 ± 3.28 (%), el más alto. De hecho, en términos de área total, P2 es la que permite que entre la mayor cantidad de luz.

El análisis del factor pupila revela algunas diferencias significativas. Las mayores diferencias se obtienen para la comparación entre P1 y P2 para el diseño de "D" multifocal, que muestra diferencias en LDI, BFCr y la aberración esférica, con el mayor tamaño de la distorsión para P2. En promedio, la distorsión es mayor con P3 que con P1 para la DE y el NDE. También se realiza un análisis adicional con el fin de comparar las diferencias de tamaño de la distorsión luminosa entre la dirección vertical (M90) y la horizontal (M0), para todas las pupilas, con LCMs. Aunque el tamaño de la distorsión cambia con el tamaño de la pupila o su superficie total, la forma puede ser diferente entre pupilas. Un primer paso es considerar el BFCirregSD. Este parámetro, sin embargo, no muestra diferencias estadísticamente significativas para ninguna comparación por pares. A pesar de ello, la BFCirregSD mayor se obtiene para P3 con el diseño D multifocal. Para confirmar este hecho, se ha llevado a cabo un enfoque más exhaustivo teniendo en cuenta la forma de la pupila no circular, por lo que la diferencia entre M90 y M0 es de especial interés debido a su asociación con los tamaños de abertura máxima y mínima de P3. Este análisis muestra que la forma de la pupila puede tener un impacto en la forma de la distorsión de la luz, ya que la diferencia entre M90 y M0 sólo resulta significativa con P3 para el D diseño multifocal, que proporciona el mayor valor de la diferencia (0.23 grados), de acuerdo con el BFCirregSD más grande anterior. Con respecto al tipo de diseño de las lentes multifocales (D y N), las diferencias sólo resultan ser estadísticamente significativas para la aberración esférica, pero no para las métricas de distorsión luminosa. El coeficiente es más negativo y mayor en módulo para el NDE con mayor tamaño de la abertura. Asimismo, es más positivo y mayor en módulo para el DE con pupila mayor. Como conclusión, se ha demostrado que las LCM aumentan los efectos de distorsión luminosa bajo condiciones de poca luz. Además, el tamaño de la distorsión aumenta con el tamaño de la pupila. Así como el tamaño de la distorsión se asocia con el tamaño de la pupila, parece que la forma de la distorsión también podría estar relacionada con la forma de la pupila.

Como resumen final, el rendimiento de nuevos diseños de LCM en términos del total de adición alcanzada depende del diámetro de la pupila y del área total dedicada para visión lejana. Por esta razón, el tamaño de la pupila de los pacientes, así como sus necesidades visuales, son de crucial importancia. Además, la forma de la pupila afecta a los parámetros físicos derivados de los perfiles de potencia de las diferentes LCM analizadas y también de las LIOM bajo descentramiento. Esto significa que la eficacia de estas soluciones ópticas para la corrección de la presbicia puede cambiar con formas irregulares de pupila. Sin embargo, las implicaciones clínicas de estos fenómenos pueden ser diferentes de las mediciones físicas, debido a la influencia de otros factores como las aberraciones de frente de onda ocular o el proceso de adaptación neural. También, las LCM aumentan los efectos de distorsión luminosa bajo condiciones de poca luz. Además, se incrementó el tamaño de la distorsión con el tamaño de la pupila. Así como el tamaño de la distorsión se asocia con el tamaño de la pupila, parece que la forma de la distorsión también podría ser relacionada con la forma de la pupila.

Por último, es importante destacar la importancia de las herramientas de software computacional para el desarrollo de esta tesis, ya que se ha desarrollado software específico para el modelado óptico incluyendo diferentes tamaños y formas de pupila. Futuras líneas de investigación deben procurar resolver la actual limitación de estos métodos. Nuevos desarrollos de software óptico brindan una herramienta poderosa no sólo para la caracterización de los diseños ya existentes, sino también para predecir el rendimiento óptico de nuevos diseños experimentales.

Esta tesis proporciona un conocimiento más profundo sobre los métodos de corrección existentes. Mirando hacia el futuro, la investigación debería aspirar a alcanzar nuevas soluciones para la corrección o prevención de la presbicia con el fin de preservar una óptima calidad de visión y, por tanto, de vida.

ABSTRACT

Presbyopia is the natural progressive loss of the ability for focusing near objects that occurs with ageing. This ability is known as accommodation. This loss usually means a reduction of the quality of life, which is why its correction has been a matter of special interest in the past years. New correction methods have emerged on the market in the last decades with the intention of improving the quality of life of the presbyopic population. Nowadays, there is an increasingly social demand for tasks that require functional vision at a wider range of distances, such as those using computers or smartphones. This, together with significant demographic changes, places special value on its optimal correction. The global population is increasing every year especially due to the general life expectancy. This will cause an inversion of the actual population pyramid, and it is a phenomenon that is already happening throughout the world. With this, the number of presbyopic population is expected to reach high rates in the near future and presbyopia will become a global public health matter.

Nowadays, several solutions are available for the correction of presbyopia. The treatments for presbyopia are currently corrective by means of optical elements or surgical refractive modification. The optical solutions are not independent, but their effectiveness is subordinated to physical, physiological and even psychophysical factors of the subjects, depending on the technique. Among the most commonly used solutions are spectacle correction, contact lenses (CLs) and intraocular lenses (IOLs). Spectacles provide a reliable method for the correction of presbyopia, its usage has been associated to a decrease in the quality of life due to the patient's dependence to carry out daily life activities. Prescription of CLs is an alternative method to spectacle correction, although recent reports show that the rates of prescription are still low. This might be explained in part by a lack of clinical knowledge by CL fitters and the presence of a climate of mistrust due to the visual compromises of presbyopic designs, among other reasons. There are several approaches to achieve presbyopia correction by means of CLs. These options can be mainly divided into three categories:

combination with spectacle correction, monovision and multifocal CLs (MCLs). As for MCLs, one of the most used approaches is based on the principle of simultaneous image formation. Here, the distance and near powers are placed within the pupillary area simultaneously for every gaze position. Thus, different images are formed at the same time on the retina. In this situation, the visual system centres the attention on the corresponding image for the desired observation distance and ignores the rest. The main aim of these corrections is to extend the range of functional vision. However, this carries with negative effects in visual performance. Image degradation occurs monocularly due to the superimposition of different images. This can especially occur for near objects with low contrast and in low lighting conditions, although it can improve over time. Poor vision and discomfort are the main factors that cause CL wearing discontinuation. IOLs are another widely used optical solution for the correction of presbyopia. Current available IOLs can be classified into two main groups, according to their role inside the eyeball: phakic or pseudophakic IOLs. The lenses of the first group act as supporting elements that are added to the optical system of the eye, but no extraction of the crystalline lens is performed. The second group is formed by those IOLs that replace the natural lens, mainly because of cataract formation. There are presbyopic solutions using both types of lenses. All kinds of multifocal IOLs (MIOLs) for presbyopia use the simultaneous image formation principle, either with refractive or diffractive technologies.

Multiple MCL designs have been manufactured in an attempt to satisfy the visual requirements of the presbyopic population. However, manufacturers sometimes provide insufficient information, which makes difficult to properly evaluate the advantages and disadvantages of a particular design. In order to provide more information that can be highly useful for professionals, measurements of power profiles are performed. Power profiles are a powerful tool that could give practitioners a deeper understanding of the behaviour of the lenses and thus, it would facilitate the selection of the best option for each individual patient. In this situation, the rates of prescribing of MCLs could actually be increased. This knowledge is needed in order to achieve a proper fitting. The pupil dependence of simultaneous image

MCLs is well known and it has been investigated by many researchers. Presbyopic patients usually carry out their tasks under different levels of illumination and thus with different pupil sizes. Besides, small pupils should be considered as an important and common situation because near activities are usually performed under photopic conditions and this, together with the accommodative reflex, leads to pupil constriction. Furthermore, presbyopic patients normally present smaller pupil sizes than younger population. Average pupil size in patients over 60 years is considered to be between 3.0 mm (photopic conditions) and 4.5 mm (mesopic conditions). Considering this, since there is a change of the power distribution depending on the aperture, it seems evident that the performance of these lenses depend on the pupil dynamics of the patients. Thus, differences in the pupillary response among subjects could lead to different refractive power behaviour even for those with the same distance refraction, addition or visual requirements. For all these reasons, the pupil size takes a significant role when studying the performance of a lens.

As for the case of MIOLs, the pupil dependence has also been extensively investigated. Several studies of in-vitro evaluation of MIOLs have shown the relationship between the aperture size and the optical performance for different designs. The optical performance of an IOL is generally assessed at its centred position. However, it is also important to take into account that different factors can affect its final position inside the eye, such as, the implantation technique, asymmetrical implantation, asymmetrical capsular shrinkage, capsule fibrosis, rupture of the posterior capsule or zonular dialysis, etc. This results in decentration of the lens and/or tilt. This misalignment with respect to the visual axis can affect the optical performance of the lenses. Well-centred IOLs with an aspheric design intend to improve optical performance and contrast sensitivity by reducing spherical aberration. However, decentring can result in lower optical transfer function.

Objective comparison of the imaging properties of MIOLs, as well as those of MCLs, and their association with the pupil size can be useful in order to select the most appropriate solution for each patient. Naturally, the pupil dependence is always thought in terms of the total diameter of a circular pupil. However, due to congenital or acquired conditions, the pupil may not be circular and it may have lost part of its functionality. Indeed, any disorder that physically causes any harm in the iris mechanisms or alter the iris innervation can result in an irregular shaped pupil. As an example, the iridal coloboma is a condition which arises early in gestation and it is associated with defective closure of the optic fissure. As a result, the choroid is not completely closed and thus the shape of the pupil is stretched. Also, posterior synechiae are presented when the iridal tissue adheres to the anterior capsule of the lens giving an irregular shape of the pupil as a result of ocular trauma or other ocular conditions that imply intraocular inflammation such as uveitis. Ocular trauma or other disorders may also lead to shape alterations such as muscle spasms that lead to segmental iris mydriasis. It has to be taken into account that eyes with irregular pupils due to ocular conditions can also present a decreased functional vision. It is important to recognize the iris structural abnormalities in order to detect the cause of abnormal pupil size, shape or pupillary function (reactivity). The shape of the pupil and the influence on the behaviour of multifocal optical solutions for presbyopia has not been previously investigated. Thus, if it has been mentioned that the pupil size has a significant role on the performance of multifocal solutions, it is thought that the shape of the pupil might also have additional implications in its optical behaviour even in terms of other limiting factors such as the light distortion effects.

Although multifocal optical solutions for presbyopia are successful for a great number of people, they also present some limitations. Candidates for multifocal solutions need to accept a level of potential visual compromise, in exchange for an increased quality of life without spectacle dependence. The evaluation of night vision disturbances under dim light conditions has become a matter of special interest in the past years due to the increasing number of MCLs, corneal refractive surgery and IOL implantation. Under this concept, several phenomena are included, such as positive and negative dysphotopsia, glare, halos, starburst, arcs, etc. The term “light distortion” was suggested in order to incorporate all these phenomena. These disturbances are frequently reported by patients, but they are commonly described as subjective complaints. Beyond the use of subjective questionnaires, there is a need to characterize the size and shape of these light distortions. The evaluation of light disturbances of optical solutions for the correction of presbyopia under different conditions, including the pupil size or shape, can be very useful for the selection of the patient.

The main goal of this thesis is to analyse existing optical solutions for presbyopia as a first evaluation for describing optical elements and then go further by assessing the influence of different sizes and also shapes of the pupil, since most of the current assessing methods have only taken into account a circular shape. Thus, this work gives special importance to those pupils that are not circular, and how this characteristic may influence the effectiveness of the current optical solutions for presbyopia in terms of image formation quality metrics and the induced light disturbances.

Two main approaches are used as general methods in this thesis, which are explained in **chapter 3,** titled “General Methods”. The first one makes use of a commercially available optical device, the NIMO TR1504 device (Lambda-X, Nivelles, Belgium), and one experimental laboratory equipment, the “Light Disturbance Analyser” (LDA) (CEORLab, University of Minho, Gualtar, Braga, Portugal). However, one of the main limitations of these instruments is that they assume circular apertures. This is the reason why only by means of computational simulations (second approach) it has been possible to assess the influence of the shape of the pupil, since existing optical devices merely include circular apertures. Furthermore, computational methods allow to develop new metrics from data yielded by those devices. For this purpose, specific custom-made software has been developed. Specifically, one software based in Fourier-optics methods has been used for the simulations and calculations with different pupil sizes and shapes. This software generates a wavefront error map via the cumulative integration of a given power profile along the radial direction. Then, the pupil function is calculated with the definition of a pupil mask. The pupil function describes how light is affected when it is transmitted through an optical imaging system, such as a lens or the human eye. This information is used in order to characterize the optical elements under different conditions. A second custom-made software has been used in order to enhance the metrics provided by the LDA instrument for light disturbance characterization. The software makes use of the raw data of the LDA, but it makes an alternative analysis to that of the native software of the instrument. In this case, the information of the instrument is used for the calculation of the distortion at each meridian. This new adjustment generates new metrics in order to take into account the possible effects of the introduction of a non-circular shaped aperture.

In **chapter 4**, which is titled “Assessment of multifocal contact lenses for presbyopia”, detailed information of new commercially available designs is given, which is of crucial interest for practitioners. Additionally, the effect of the pupil shape has been analysed and it is discussed as a possible factor to affect the optical performance of MCLs. This chapter is subdivided in **section 4.1**, which is titled “In-vitro evaluation of rigid gas permeable multifocal contact lenses with variable multifocal zone”, and **section 4.2:** “The effect of non-circular shaped pupils on the performance of multifocal contact lenses”. Specifically, in **section 4.1**, a new set of MCLs with variable multifocal zone is analysed. These lenses are a centre-distance rigid gas permeable lenses that are available with five distance-vision diameters (XS, S, M, L and XL) and two different additions: Type A (up to +2.00 D) and Type B (up to +2.50 D). The multifocal zone is located on the front lens’ surface, so the posterior surface can be designed as a function of the patient’s corneal shape. The results are given in the form of power profiles. It is shown that the amount of total addition achieved depends on the diameter of the distance-vision area. In other words, the bigger the distance vision area, the bigger the radius of the lens in order to get the same level of addition. The XS lens yields higher addition values in comparison with the XL lens design for a given pupil. With this, the XS and S designs seem to be aimed to favour near vision. The L and XL designs seem to favour distance vision. For this reason, patients who demand good distance vision might benefit from the L or XL designs, and those with high demand on near-vision tasks might benefit from the XS or S. The M design could be the best solution for those patients who require the same needs for distance and near vision. In **section 4.2**, theoretical approaches are considered and implemented by means of optical simulations in order to investigate different pupil size and shapes, using power profiles similar to those obtained in the previous section. Specifically, one center-distance bifocal, one progressive multifocal power profiles, together with a monofocal profile, were considered. Three pupils are used: one circular and two non-circular, including one elliptical and one irregular shape. The apertures were defined within a maximum diameter of 6 mm. Metrics based on the point spread function (PSF) and the optical transfer function (OTF) have been obtained, such as the diameter which gathers the 25% of light from the PSF centre (D25) or the visual Strehl ratio in the frequency domain (VSOTF). The VSOTF parameter has been previously used for describing visual performance because it shows a strong correlation with subjective methods. A threshold of 0.12 is usually set as the VSOTF value that corresponds to a visual acuity at which approximately half of the people present difficulties while reading (20/32 Snellen equivalent). Values above 0.12 are considered to be acceptable. The results of the through-focus analysis of the PSF are represented as a qualitative assessment of the light compactness and distribution. An irregular pupil causes an irregular shape of the PSF. However, by analysing these previous images, only a qualitative assessment can be done. A quantitative evaluation is desirable, since it can describe the variations numerically. For this purpose, the D25 is introduced. The D25 differences among pupils are greater for the distance vergence of the centre-distance bifocal profile. The results for near distance are similar for every pupil. For the circular and synechial pupil, the size of D25 is smaller for near than it is for distance vergence, whereas regarding the elliptical pupil the size it is smaller for distance but comparable to near vision. With regards to the centre-distance progressive lens, all pupils show similar results at far and better than those for the bifocal. The VSOTF curves show a change in the energy distribution with different pupil shapes. In some cases, the elliptical and synechial apertures yield better results in terms of compactness (D25) or VSOTF. This is due to the fact that the defined pupils are masking a part of the wavefront, since they were described within the circular 6 mm pupil. For this reason, the total area dedicated for each optical zone and whether it contributes to near or distance foci, should be considered. As a conclusion, the pupil shape affects the physical parameters of the analysed lens power profiles. This means that the effectiveness of the optical solutions for the correction of presbyopia might be altered with irregular pupil shapes. However, the clinical implications of these phenomena might differ from the real physical measurements, due to the influence of additional factors such as ocular wavefront aberrations or the neural adaptation process.

Chapter 5 is titled "Assessment of multifocal intraocular lenses for presbyopia". In **section 5.1**, "The effect of non-circular shaped pupils and decentration on the performance of multifocal intraocular lenses", the analysis is centred on MIOLs. As well as with MCLs, the number of new MIOL designs is growing and the target public is also increasing. In this chapter, the effect of the pupil shape was analysed by means of optical simulations. It is also important to evaluate the effect of decentration on the IOL performance, since as it was previously mentioned, the in-the-bag IOL placement can result in a desalignment. Depending on the IOL design, some studies have shown that decentration can have an important effect on the optical quality provided by the lens. For this study, a power profile of a refractive annular multifocal IOL is considered with a base power of 0.0 D, and approximately +2.50 D of addition. The total optical zone is 6 mm in diameter. An elliptical pupil shape is used for the analysis, together with a circular one for comparison purposes. Again, metrics based on the PSF and the OTF are obtained, such as the D25 or the VSOTF. The through-focus analysis of the D25 for the centred position yields similar results for both pupils at the near focus, whereas the distance focus gives greater values for the circular pupil. The through-decentring analysis reveals that the near focus is more affected with decentring. As for the VSOTF ratio, it is shown that the near focus is reduced with increasing decentring for both pupils, whereas the far focus varies more discreetly. The robustness to decentring seems to be similar for both pupils for the near focus. However, the tolerance seems to be slightly better for the elliptical aperture in the vertical direction. As a conclusion, the pupil shape together with decentring has an impact on the physical metrics that were analysed. This means that the shape of the pupil might affect the effectiveness of this kind of optical solutions for presbyopia. Nevertheless, the clinical implications of these variations are not directly transposable due to the effect of other factors such as the contribution of the rest of the ocular media and the neural processes.

Chapter 6 is titled “Clinical evaluation of light distortion with multifocal optical solutions for presbyopia”. In **section 6.1**, which is titled “Light distortion of soft multifocal contact lenses with different pupil size and shape”, a clinical evaluation of light disturbances is presented. As it has been previously stated, the number of users of MCLs has been rising due to the increasing popularity of these solutions as a modality to correct presbyopia. Most of the current MCLs designs are based on simultaneous image formation. However, this principle can imply visual side effects, such as an augmented sensitivity to disability glare or the presence of haloes, especially under low light conditions due to the increased pupil size. Earlier studies have reported visual such side effects with MCLs. Increased disturbing photic phenomena can be an obstacle to perform everyday tasks, such as night driving or driving with a low sun. The vast majority of the simultaneous image formation designs are based on concentric annular areas with a central circular optical zone surrounded by one or more annular zones, which yield rotationally symmetric power profiles. These designs are well related to the shape of a normal circular pupil, but the effect on non-circular shaped pupils and their clinical implications have not been previously investigated. This topic is discussed in this part.

A total of 14 eyes of 7 healthy contact lens wearer patients (3 females and 4 males) aged from 25 to 40 years (mean 28.57 ± 8.46 years) were analysed. The LDA device has been used for light characterization. The selected lenses for the study were the monthly disposable Biofinity Multifocal (CooperVision, CA, USA), with both “D” and “N” designs, and an addition power of +2.50 D. The D design consists of a centre for distance vision with progressive positive shift towards the periphery, whereas the N design has a centre for near vision with progressive negative shift. The dominant eye (DE) of the patients wore the corresponding “D” design and the fellow non-dominant eye (NDE) the “N” design. The monofocal version of these lenses was included for comparison purposes. Two circular pupils, one of 3 mm (P1) and one of 5 mm (P2) were used. Also, one elliptical shape of 3 mm in the horizontal and 5 mm in the vertical direction was included (P3). In this study, optical spherical aberrations and metrics such as the light disturbance index (LDI), best fit circle radius (BFCr) and its corresponding irregularity standard deviation (BFCirregSD) are analysed. Meridional difference of the light distortion between the vertical and horizontal directions has also been calculated.

As a first approach, a comparison between the monofocal and the corresponding multifocal versions of commercially available lenses is performed. In light of our results, the MCLs induce a generalized increasing of the LDI (and thus, the distortion size) with all kind of pupils. The highest values of LDI are obtained for the DE, with more pronounced differences than the NDE. More specifically, the greatest statistically significant difference in LDI is obtained for the DE with P2. The value of the LDI for the DE with P2 and a MCL was 6.09 ± 3.28 (%), the highest one. Indeed, in terms of total area, P2 is the one that lets the biggest amount of light in.

The analysis of the pupil factor reveals some significant differences. The greatest differences are obtained for the pair comparison including P1 and P2 for the multifocal “D” design, which yielded differences in the LDI, BFCr and the spherical aberration, with greater disturbance size for P2. In average, the disturbance is greater with P3 than with P1 for both the DE and NDE. An additional analysis is performed in order to compare the differences in size of the light disturbance between the vertical (M90) and horizontal directions (M0), for all pupils with MCLs. Although the size of the disturbance changes with the pupil size or its total area, the shape of the disturbance can be different among pupils. A first step is considering the BFCirregSD. This parameter, however, does not show statistically significant differences for any pair comparison. In spite of this, the greatest BFCirregSD is obtained for P3 with the multifocal D design. For confirmation, a more thorough approach has been adopted taking into account the shape of the non-circular pupil, so the difference between M90 and M0 are of special interest due to their association with the maximum and minimum aperture sizes of P3. This analysis shows that the shape of the pupil might have an impact on the shape of the light distortion, since the differences between M90 and M0 only turns out to be significant with P3 for the D multifocal design, which yields the greatest difference value (0.23 degrees), in accordance to the previous greatest BFCirregSD. With regard to the type of design of the multifocal lenses (D and N), the differences are only found to be statistically significant for the spherical aberration, but not for the light disturbance metrics. The coefficient becomes more negative and greater in modulus for the NDE with greater aperture size. Likewise, it is more positive and greater in modulus for the DE with greater pupil. As a conclusion, it has been shown that MCLs increase light disturbance effects under low light conditions. Also, the size of the distortion is increased with pupil size. As well as the size of the distortion is associated with the size of the pupil, it seems that the shape of the distortion might also be related with the shape of the pupil.

In summary, the performance of new progressive centre-distance MCL designs in terms of the total amount of total addition achieved depends on the diameter of the pupil size and the total distance-vision area. For this reason, the pupil size of the patients, as well as their visual needs, are of crucial importance. Besides, the pupil shape affects the physical parameters derived from the analysed lens power profiles of different MCLs, and also of IOLs under decentration. This means that the effectiveness of these optical solutions for the correction of presbyopia might be altered with irregular pupil shapes. Nevertheless, the clinical implications of these phenomena might be different from the real physical measurements, due to the influence of additional factors such as ocular wavefront aberrations or the neural adaptation process. Also, MCLs increase light disturbance effects under low light conditions. Besides, the size of the distortion was increased with pupil size. As well as the size of the distortion is associated with the size of the pupil, it seems that the shape of the distortion might also be related with the shape of the pupil.

Lastly, it is important to highlight the importance of the computing software tools for the development of this thesis, since specific custom-made software was made for optical modelling including different pupil sizes and shapes. Future lines of research should aim to solve the current limitation of this methods. New developments of optical software would provide a powerful tool not only for characterization of already exiting designs, but also for predicting the optical performance of new experimental ones.

This thesis provides a deeper knowledge on existing methods. Looking into the future, investigation should aim to achieve new solutions for the correction or prevention of presbyopia in order to preserve the most optimal quality of vision, and thus, of life.

CHAPTER 1:

INTRODUCTION

1 INTRODUCTION

1.1 PRESBYOPIA: DESCRIPTION AND GLOBAL CONTEXT

Presbyopia is the natural progressive loss of the ability for focusing near objects that occurs with ageing. This ability is known as accommodation. The crystalline lens is the optical element that contributes to the dynamic power variations of the eye in order to focus at different distances. This structure and its optical properties change throughout life (Donaldson et al. 2017). The efficiency of the process of accommodation declines with age, as the crystalline lens loses its elasticity and the activity of the ciliary muscle deteriorates (Glasser and Campbell 1998; Atchison and Smith 2000). This condition starts to be usually expressed sometime around 40 years of age. However, the exact age that near vision correction is needed depends on individual factors such as accommodative ability, distance refraction or ethnicity, among others (Holden et al. 2008). From this moment, the quality of life starts to be reduced (Luo et al. 2008). Presbyopia, as an accommodative dysfunction, has a negative impact causing symptoms such as blurred vision, headache, ocular discomfort and loss of concentration throughout a task (Lossing et al. 2012). For this reason, its correction has been a matter of special interest in the past years. New correction methods have emerged on the market in the last decades with the intention of improving the quality of life of the presbyopic population. Nowadays, there is an increasingly social demand for tasks that require functional vision at a wider range of distances, such as computers or smartphones. This, together with significant demographic changes, places special value on its optimal correction.

According to the 2017 revision of the “World Population Prospects” of the United Nations, which compiles, generates and analyses a wide range of economic, social and environmental data, the global population is increasing every year (World Population Prospects 2017). This is especially due to the general increasing life expectancy, since many countries have experienced a significant reduction in the number of births. As fertility declines and life expectancy rises, the rates of population of a certain age will also rise. This will cause an inversion of the actual population pyramid, and it is a phenomenon that is already happening throughout the world. Nowadays, Europe has the highest percentage of people aged 60 or over (25%), which is expected to reach higher rates in the future (35% by 2050). It is also important to take into account that, although the global population is growing, most of this increase can be attributed to a reduced number of countries. More specifically, the new projections show that, by 2050, half of the world's population growth will be concentrated in just nine countries, amongst which are India or Nigeria.

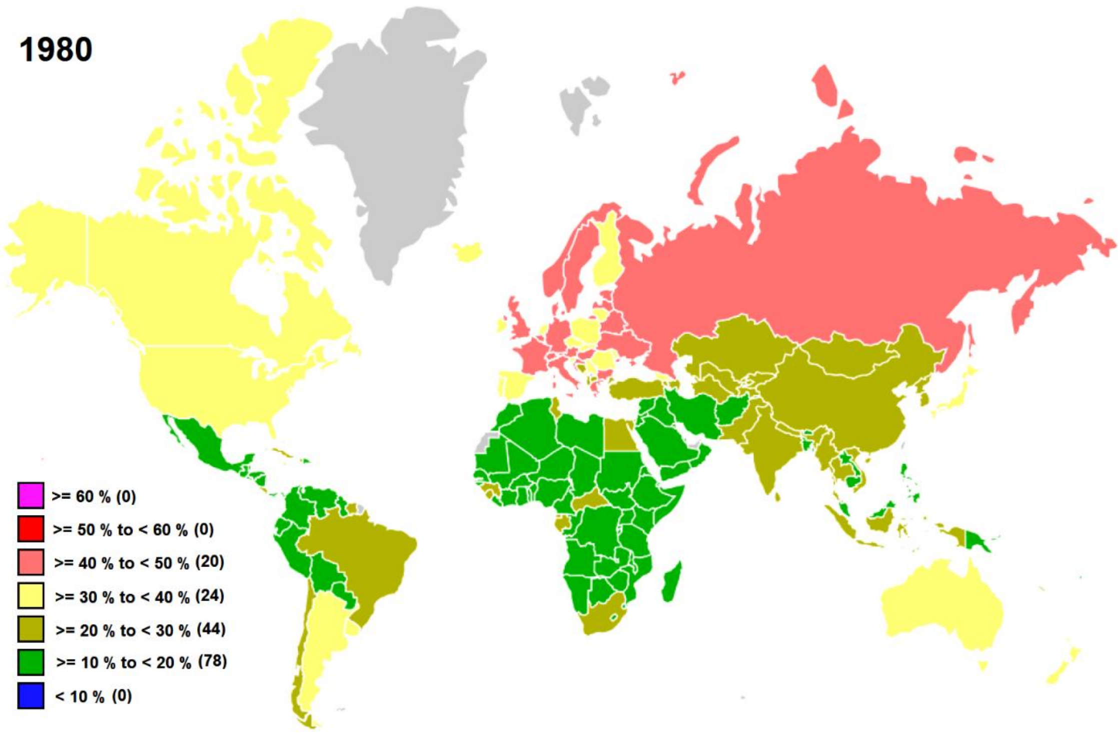

***Figure 1.1**. World map depicting the percentages of people over 40 years in 1980. Map generated from processed data reports from the World Bank international financial institution (Last updated in 2017).*

As it can be directly inferred, the number of presbyopic population is expected to reach high rates in the near future. Then, the socioeconomic status of those countries with the highest growth rates will play a significant role on the treatment of presbyopia and its associated visual impairments. It has been estimated that, among 1,040 million people with presbyopia in the year 2005, approximately half of them did not wear a correction or it was inadequate, preventing them from performing near tasks in the way they needed (Holden et al. 2008).

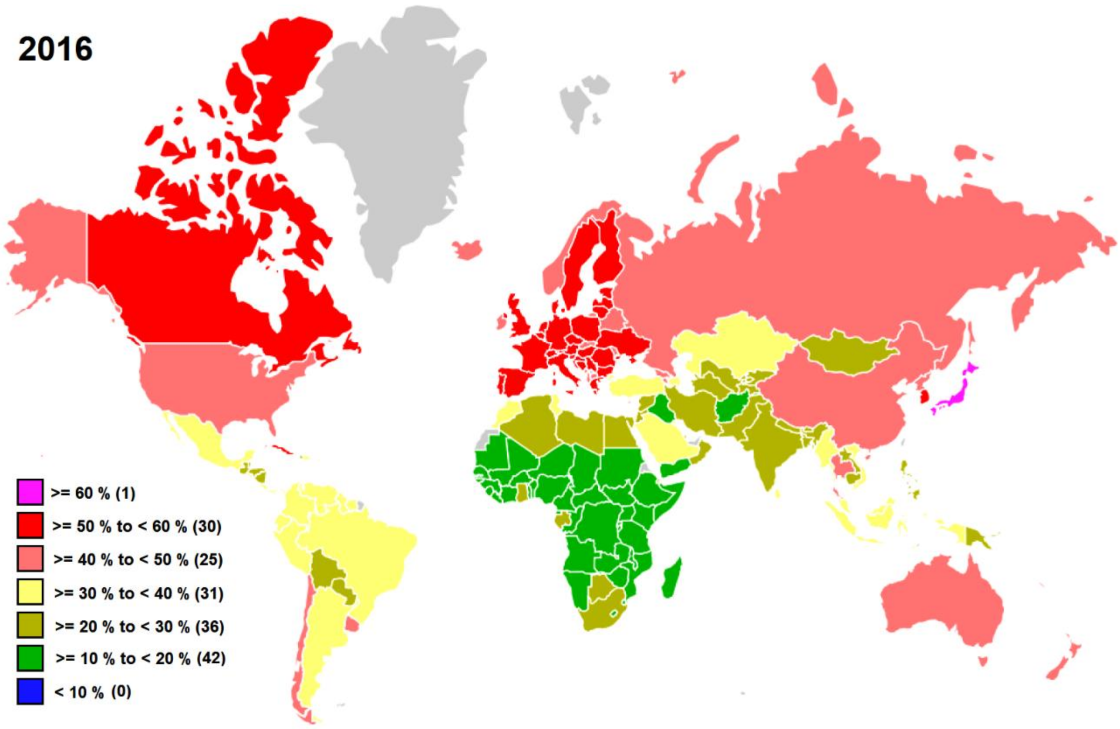

Figure 1.2*. World map depicting the percentages of people over 40 years in 2016. Map generated from processed data reports from the World Bank international financial institution (Last updated in 2017).*

The access to the corrections in developing countries is limited by the reduced number of visual health professionals, the economic difficulties to afford them, and the lack of a public health support (Nirmalan et al. 2006; Uche et al. 2014; Ajibode et al. 2016). Thus, with increasing population, presbyopia will become a global public health matter that needs to be fully considered. As reported by the World Bank, whose official goal is the reduction of poverty, the number of countries with more than a third of their population older than 40 has been significantly increased from 1980 to 2016 (**Figures 1.1** and **1.2**) (World Bank Group 2017). As for the Spanish population, the amount of people aged 40 or older already reached the 55% in 2016, and this percentage is still growing (Cifras de Población (España) 2017).

In the present day, several solutions are available for the correction of presbyopia. Among them, different techniques and approaches can be applied, which will be treated in this section.

Furthermore, the optical solutions are not independent, but their effectiveness is subordinated to physical, physiological and even psychophysical factors of the subjects, depending on the technique. For this reason, factors that may have an impact on the behaviour of such corrections will be discussed.

1.2 OPTICAL SOLUTIONS FOR THE CORRECTION OF PRESBYOPIA

The number of presbyopia correcting options has increased in the past years. The treatments for presbyopia are currently corrective by means of optical elements or surgical refractive modification (Goertz et al. 2014). There is not a pharmaceutical treatment to reverse the ageing process of the lens yet, although it is a field of current research (Renna et al. 2017).

1.2.1 Spectacles

Spectacle correction, which appeared in the 13th century in the western world, is the oldest method and, still nowadays, it is one of the most commonly used. The first prototypes consisted of single-vision (monofocal) lenses for near tasks that were used by monks and students (Callina and Reynolds 2006). In the present day, this solution is known as “reading glasses”. Regarding this option, it is necessary to change the optical correction depending on the observation distance.

Not until the 18th century did bifocal spectacles appeared. This solution held the appropriate correction for distance and near mounted on the same frame, by cutting monofocal lenses in half (Callina and Reynolds 2006). More recent and technologically advanced are the designs based on trifocal or progressive lenses that include a wider correction range of distances. All these elements are known as multifocal solutions.

Although spectacles provide a reliable method for the correction of presbyopia, its usage has been associated to a decrease in the quality of life due to the patient’s dependence to carry out daily life activities (Luo et al. 2008; Goertz et al. 2014). Spectacle correction is limited by eye direction, since clear vision for a given distance is only achieved through a specific area of the lens. Also, the field of view is reduced. Furthermore, optical effects such as the image jump and optical distortions limit the quality of the image, depending on the design (Barbero and Portilla 2016; Rifai and Wahl 2016).

1.2.2 Contact lenses

Prescription of contact lenses (CLs), as an alternative method to spectacles for the correction of presbyopia, has been used since the past century. However, recent reports show that less than the 40% of CLs wearers over 45 years of age are prescribed a presbyopic solution (Morgan and Efron 2009). As it has been suggested, this low rates might be explained in part by a lack of clinical knowledge by CLs fitters and the presence of a climate of mistrust due to the visual compromises of presbyopic designs, among other reasons (Morgan et al. 2011). Nevertheless, since those who already wear CLs before becoming a presbyope often want to keep on using them, growing trends are expected (Bennett 2008; Toshida et al. 2008).

Several studies have reported the habits of prescription by eye care practitioners, but very few ask patients about their preferred option. A recent survey about vision correction preferences showed that presbyopes of all refractive errors selected CLs as the best option when both good vision and comfort can be achieved (Rueff and Bailey 2017). This is a matter of crucial importance, since poor vision and discomfort are the main factors that cause wearing discontinuation (Rueff et al. 2016; Sulley et al. 2017).

There are several approaches to attain presbyopia correction by means of CLs. These options can be mainly divided into three categories: **combination with spectacle correction**, **monovision** and **multifocal** CLs (MCLs) (Toshida et al. 2008; Charman 2014; Pérez-Prados et al. 2017).

1.2.2.1 Combination of monofocal contact lenses and spectacles

The first approach consists of an easy solution for the patient and the practitioner. Monofocal CLs are worn for the correction of distance vision, whereas reading spectacles are used for near or intermediate vision, depending on the visual needs of the patient, at the moment they are required. As it is easy and cheap, it is commonly and widely used (Morgan et al. 2011). However, the spectacle dependence carries with all its associated limitations.

1.2.2.2 Monovision

In monovision, monofocal CLs are used for correction: one eye is optimised for distance and the fellow eye for near vision. This method is also commonly used and according to recent studies the success rates range from 59% to approximately 70% (Evans 2007). In those cases, in which the distance eye is emmetropic, only a single CL would be fitted for near. Historically, the earliest form of monovision came in form of a monocle spectacle lens for near vision, but monovision turned out to be particularly better suited to corrections on the corneal plane, since prismatic effects caused by lens decentration are avoided.

Besides traditional monovision, some modifications can be applied in order to enhance the visual performance at a given distance. Using this concept, *enhanced monovision* makes use of a multifocal CL in one eye and a monofocal in the fellow eye. The distance at which vision is enhanced depends on the visual demands of the patient. If distance vision needs to be reinforced, the corresponding eye will wear a monofocal CL for distance and a multifocal will be fitted in the fellow eye. Otherwise, if enhanced near vision is required, the corresponding eye will be adapted with a monofocal for near. A different approach is known as *modified monovision*, in which both eyes wear multifocal CLs (which are described in the next subsection), but with opposite designs. More specifically, in this case the eye for distance will wear a center-distance multifocal design, whereas the fellow eye is adapted with a center-near model (Efron 2017).

The most common adaptation problems are related to the difficulty to supress the blurred images, specially under low light conditions, or the lack of a third focal length for intermediate distances. Also, the binocular visual function in terms of stereoacuity is penalized with this method with respect to other corrections (Back 1995; Kirschen et al. 1999; Chapman et al. 2010; Fernandes et al. 2013). The impairment is greater the higher the addition power, although many patients do not seem to notice this.

1.2.2.3 Multifocal contact lenses

For many years, monovision was the only available solution for the correction of presbyopia by means of CL, until the first multifocal designs appeared. The multifocality refers to a situation in which more than one single focus is present. In the context of presbyopia correction, MCLs are those lenses whose design includes differentiated areas for each distance correction or present a progressive power shift. Nowadays, this correction method is used more frequently than monovision (Morgan et al. 2011). The success rate of prescribing MCLs ranges from 67% to 83% after three months. However, the rates decrease to approximately 30-40% for long-term wearers (Toshida et al. 2008).

MCLs can be divided into two main groups according to the number of active foci for retinal image formation at a given time: Translating or alternating vision lenses and simultaneous image lenses, which can make use of concentric refractive, aspheric or even diffractive designs (Pérez-Prados et al. 2017).

1.2.2.3.1 Translating or alternating image lenses

This kind of solution consist of a bifocal lens with clearly differentiated areas: a zone for distance vision and a separated area that includes the required addition for near vision. This solution takes benefit from the eye movements. In the primary gaze position, the distance area is the one that is placed before the pupil and contributes to the image formation. For near vision, the eye needs to look down so the lower lid acts a supporting system. In this situation, the lens is apparently pushed up by the lid and the addition area comes before the pupil (Charman 2014). Two main concepts are used for the design of the zones, with variations (**Figure 1.3**). In one of these, a segment is found in the lower side of the lens, which conforms the addition. The other design presents an addition ring at the peripheral area of the lens.

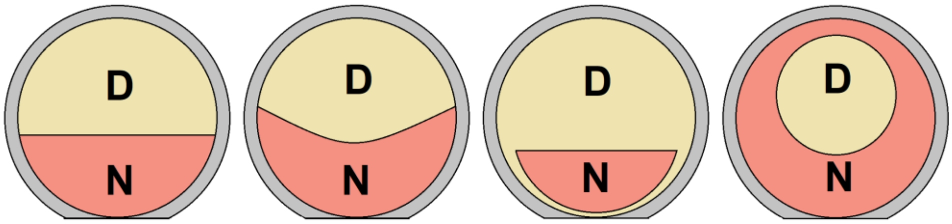

Figure 1.3. *Some of the designs of alternating vision contact lenses. (D: distance zone, N: near zone).*

Most of these designs are found in rigid gas permeable (RGP) materials because they are easier to translate. With alternating lenses, optimal vision at both distances can be theoretically achieved when the appropriate part of the lens is placed over the pupil. For this reason, it is very important to achieve the best stability and position of the lens, since this will have an impact its performance. For this purpose, a ballast prism is used. Factors such as the pupil diameter, the size of the palpebral fissure or the shape, thickness and tension of the lids can alter the correct translation of the lens (Toshida et al. 2008).

1.2.2.3.2 Simultaneous image lenses

These corrections are based on the principle of simultaneous image formation, where distance and near powers are placed within the pupillary area simultaneously for every gaze position. Thus, different images are formed at the same time on the retina. In other words, for a single object, more than one image is formed, one for each dedicated power of the lens. Depending on the object distance, one of these images will be focused, whereas the rest will be defocused. In this situation, the visual system centres the attention on the corresponding image for the desired observation distance and ignores the rest (Pérez-Prados et al. 2017).

The main aim of these corrections is to extend the depth of focus. However, this carries with negative effects in visual performance. Image degradation occurs monocularly due to the superimposition of different images. This can especially occur for near objects with low contrast and in low lighting conditions, although it can improve over time (Pérez-Prados et al. 2017). These CLs are available in RGP, in soft and hybrid (rigid and soft) materials. Although most of the rigid CLs intended for the correction of presbyopia are supported upon the cornea, new scleral lenses for presbyopia are emerging. Most of the designs are mainly refractive, with annular or aspheric lenses. Also, some CLs present a diffractive structure.

The annular designs typically have a central zone for the distance power, surrounded by concentric rings with alternating powers for near and distance. The first available lenses only included a central zone and one single peripheral ring. More recent lenses were designed with more annular zones in order to minimize the effect of the pupil size (**Figure 1.4**), which will be discussed later (Charman and Saunders 1990).

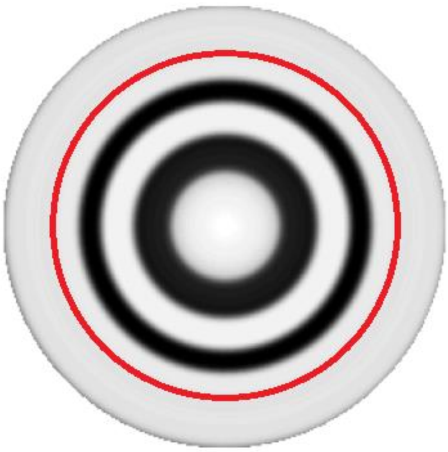

Figure 1.4. *Simultaneous image contact lens: annular design. The central zone gives the distance power. Black concentric rings provide the addition power, and white grey rings distance power. The red circle represents a fictitious pupil.*

On the other hand, aspheric designs have a central circular area for the distance or the near power. The alternative power is achieved by a progressive power shift towards the peripheral area of the lens. As for the centre-distance designs, the less positive power is in the centre and it increases towards the periphery. This design induces controlled positive spherical aberration. On the contrary, in centre-near designs, the highest positive power is in the centre, decreasing its value towards the periphery. This case involves negative spherical aberration. Correct movement and optimal centration are also crucial with these solutions, since a decentred lens can increase optical aberrations and thus cause poorer vision quality (Pérez-Prados et al. 2017). The ratio between the dedicated areas for near or far vision can be different for each design, depending on the working distance requirements (**Figure 1.5**).

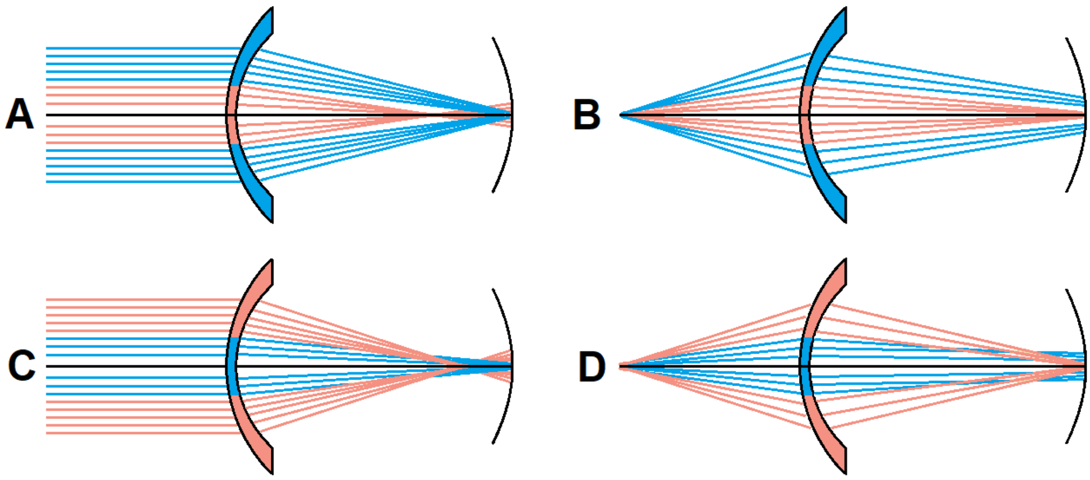

Figure 1.5. *Simultaneous image lenses: aspheric designs. Image formation of a centre-near design for a distant (A) and a near object (B). Image formation of a centre-distance design for a distant (C) and a near object (D).*

Diffractive designs are actually hybrid between a refractive central zone for distance vision and a diffractive echelette structure for near. These lenses provide greater equity between the far and near powers, so they are pupil-independent (Bennett 2008). However, there is a fraction of light that is lost into higher diffraction orders, which do not contribute to the image formation (Pérez-Prados et al. 2017). These designs can present unacceptable comfort and difficulties during the fitting process, besides visual compromise under low lighting conditions. They are not globally marketed.

1.2.3 Intraocular lenses

Intraocular lenses (IOLs) are optical elements that are placed into the eye by surgical methods. The first IOL implantation was performed in 1949 (Apple and Sims 1996). This was a revolutionary method, although IOLs for presbyopia in order to reduce spectacle dependence were not implanted until 1990 (Hoffer and Savini 2014). Current available IOLs can be classified into two main groups, according to their role inside the eyeball: phakic or pseudophakic IOLs. The lenses of the first group act as supporting elements that are added to the optical system of the eye, but no extraction of the crystalline lens is performed. These can be subdivided into anterior-chamber or posterior-chamber lenses, depending on their position in the anterior segment. The second group is formed by those IOLs that replace the natural lens, mainly because of cataract formation. There are presbyopic solutions using both types of lenses. All kinds of multifocal IOLs (MIOLs) for presbyopia use the simultaneous image formation principle, either with refractive or diffractive technologies (Bellucci 2005).

1.2.3.1 Pseudophakic intraocular lenses

As noted earlier, presbyopia is a gradual process that is developed with ageing. However, ageing carries with another potential problem for the lens, normally subsequent to presbyopia: cataracts. In this case, the lens suffers from a denaturation of the proteins, with consequent loss of transparency. This courses with blurred vision, difficulty with night driving or glare symptoms, among others. Although cataracts are more common in older population, they can also be congenital or prematurely acquired (Thompson and Lakhani 2015). At the present, cataracts are the first cause of blindness and worldwide, the only treatment is surgical (Abel 2018). For this reason, there is an urgent need to break barriers to cataract surgery (Batlle et al. 2014).

Although controversial when it first appeared, phacoemulsification and IOL implantation became the state-of-the-art technique in cataract surgery and, nowadays, it is the standard procedure (Raczyńska et al. 2016; Olson 2018). Cataract extraction with IOL implantation is the most common eye surgery performed worldwide in older adults (Bellan 2008). In order to restore vision at different distances, MIOLs in both eyes or pseudophakic monovision has been used (Iida et al. 2011; Alio et al. 2017; Labiris et al. 2017).

Pseudophakic MIOLs are usually classified according to the number of foci that they provide, usually bifocal (distance and near vision) and trifocal designs (distance, intermediate and near vision). The very first prototype consisted in a refractive bifocal lens as a result of slicing in half two different powered monofocal IOLs and gluing the opposite halves together (Hoffer and Savini 2014). This concept is used in current available designs with more modern manufacturing methods. However, the majority of current IOLs consist of annular refractive or, more recent, annular diffractive designs.

Most multifocal IOLs have their design based on the distribution of light between two main foci (bifocal IOLs), for near and distant vision, but there is still lack of intermediate vision (**Figure 1.6**).

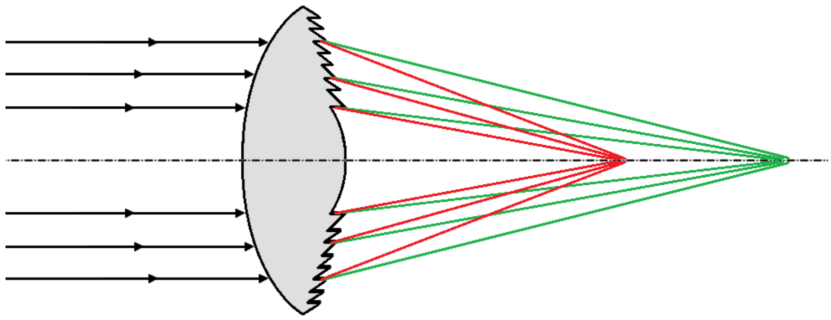

Figure 1.6. *Diffractive bifocal intraocular lens. Light division for distance and near vision (main diffractive orders).*

It has been shown that bifocal lenses with lower addition can improve intermediate vision compared to those of higher addition power (Santhiago et al. 2012). However, this intermediate vision is still limited. The increasingly social demand for tasks that require different working distances motivated the creation of IOL designs capable of providing good vision in a wider range of distances. A first approach consisted in trifocal designs, which split the light into three main foci to cover this intermediate vision (Gatinel and Houbrechts 2013; Mojzis et al. 2014). Nevertheless, the presence of several foci could affect the optical performance of the lens and increase photic phenomena, such as glare or halos, since there is more defocused light present at each focal point (Pieh et al. 2001). Trying to solve such limitations, a new kind of multifocal designs known as extended-depth-of-focus (EDOF) IOLs have emerged in the recent years. Such designs attempt to provide patients with good visual quality over an extended range of vision including far, intermediate and near distances. At the same time, they intend to minimize the photic phenomena in order to reach a distance vision that is comparable to monofocal IOLs.

Other solutions for presbyopia include accommodating IOLs, which are optical elements that produce a dynamic increase of the power of the eye with accommodative effort. These lenses are currently at different stages of development and commercialization (Pepose et al. 2017).

1.2.3.2 Phakic intraocular lenses

More recent advancements in presbyopia correction contemplate implantable phakic MIOLs, intended for patients whose age range from 40 to 55 years, approximately. The surgery in this case is less invasive than a clear lens exchange, which is a procedure that has become more popular in the past years, intended for the same age group that substitutes a noncataractous crystalline lens for a multifocal IOL. The advantage of the procedure with phakic IOLs is the reversibility, whereas clear lens exchange is permanent (Bellucci 2005). The limitations are associated with optical effects such as decreased contrast sensitivity or haloes, together with the typical complications of monofocal phakic IOLs. Posterior chamber phakic IOLs can increase the risk of premature anterior subcapsular cataract formation (Alfonso et al. 2015). Long-term outcomes are needed in order to assess the safety and efficacy of these new lenses (Baïkoff et al. 2004; Pineda et al. 2016).

1.3 POWER PROFILES IN MULTIFOCAL CONTACT LENSES

As it has been described above, multiple MCL designs have been manufactured in an attempt to satisfy the visual requirements of the presbyopic population.

Currently, the majority of MCLs for presbyopia are rotationally symmetric and work under the simultaneous image formation principle. However, manufacturers sometimes provide insufficient information. They usually describe their products only as being centre-near or centre-distance designs, together with the distance power and addition values. This situation of secrecy makes difficult to properly evaluate the advantages and disadvantages of a particular design (Plainis et al. 2013). In order to provide more information that can be highly useful for professionals, measurements of power profiles are performed. A knowledge of power profiles would give practitioners a deeper understanding of the behaviour of the lenses and thus, it would facilitate the selection of the best option for each individual patient. In this situation, the MCL prescription rates could actually be increased (Montés-Micó et al. 2014).

Power profiles are obtained with various methods and techniques (Kollbaum et al. 2008; Joannes et al. 2010; Wagner et al. 2015). It is usually plotted as the radial averaged power as a function of the radial distance from the centre. It is important to know how to interpret the results of the measurements. One of the main questions is to identify the distance and near corrections provided by the lens. Depending on the design, this will be more straightforward or not. For example, for an annular design, there will be two clearly differentiated power values that will be alternating. For an aspheric lens, it is more difficult to define what is really the distance and near powers, since there will not be clearly differentiated powers, but a progressive power shift (**Figure 1.7**). However, methods in order to approximate this in terms of nominal distance and near corrections have been proposed (Plainis et al. 2013; Montés-Micó et al. 2014).

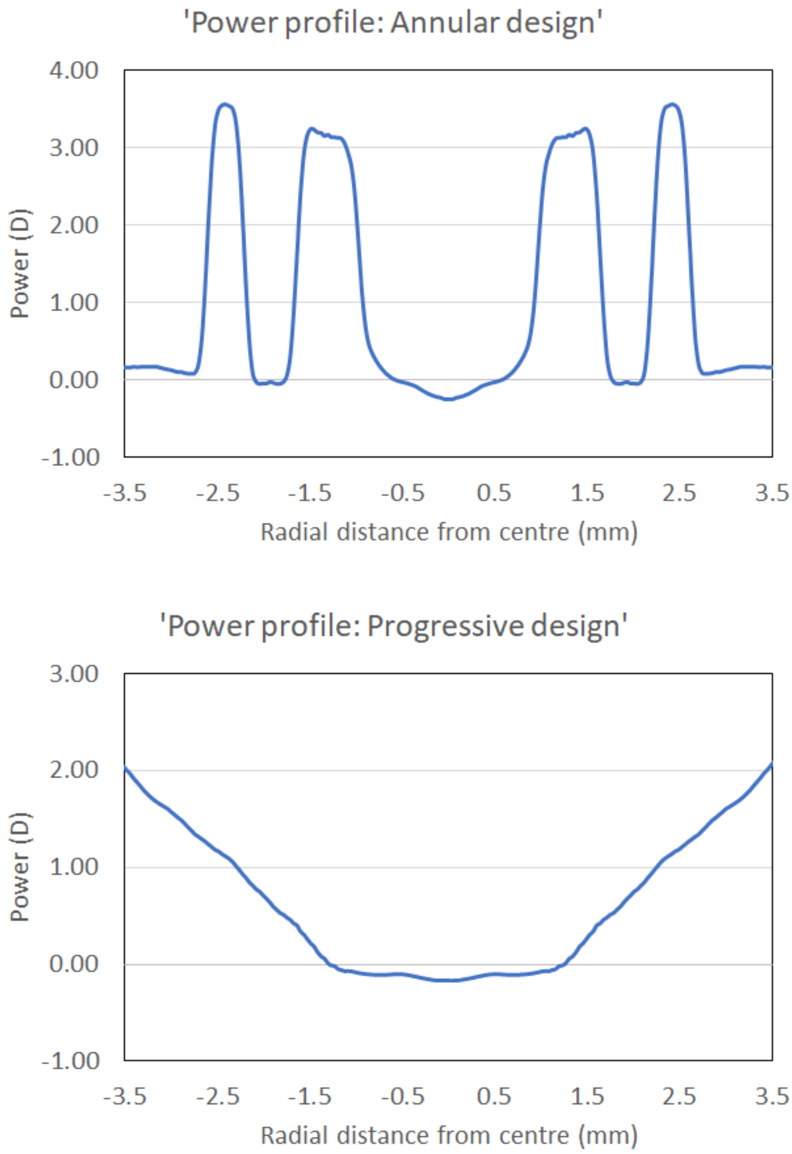

Figure 1.7. *Power profile measurements of different centre-distance designs: annular and aspheric progressive.*

Power profiles describe the distribution and magnitude of the power of a lens, and such information can be used in order to correlate design features with visual performance. Besides, as it is a function of the aperture radius, its performance is easy to associate with the actual pupil size of the patients in order to study the influence of the pupil (Madrid-Costa et al. 2015; Kim et al. 2017).

1.4 INFLUENCE OF THE PUPIL AND CENTRATION IN THE OPTICAL QUALITY OF MULTIFOCAL SOLUTIONS

The knowledge of the optical power distributions within the pupillary area is needed in order to achieve a proper fitting. The pupil dependence of simultaneous image MCLs is well known and it has been investigated by many researchers. Presbyopic patients usually carry out their tasks under different levels of illumination and thus with different pupil sizes. Besides, small pupils should be considered as an important and common situation because near activities are usually performed under photopic conditions and this, together with the accommodative reflex, leads to pupil constriction (Myers and Stark 1990; Koch et al. 1991). Furthermore, presbyopic patients normally present smaller pupil sizes than younger population. Average pupil size in patients over 60 years is considered to be between 3.0 mm (photopic conditions) and 4.5 mm (mesopic conditions) (Koch et al. 1991).

A recent study analysed the power distribution and the proportion of the lens surface of different MCLs designs as a function of the aperture size (Papadatou et al. 2017). Among these, the Acuvue Oasys for presbyopia (Vistakon, Inc., Jacksonville, FL, USA), which consists in concentric aspheric annular zones alternating the distance and near powers. In this design, the centre is dedicated for distance and it is available with different addition powers (low, medium and high). Other lenses that were evaluated include the Fusion 1d Presbyo (Safilens S.R.L., Staranzano, GO, Italy), which presents a power shift towards the periphery of the lens (centre-near design); and the Biofinity multifocal (Cooper Vision, Fairport, NY, USA). This lens is available in centre-near and centre-distance designs and also in different addition powers, but only the centre-near variant was assessed. The high addition Acuvue Oasys was shown to enhance far vision for small aperture sizes. According to their definition, the most equitable distribution between the near and distance powers for this design was reached for an aperture size of approximately 4 mm. Opposite behaviour showed the Fusion 1d

Presbyo and the Biofinity, which enhanced near vision for small aperture sizes, but these lenses also provided a significant percentage for intermediate vision. As for the intermediate vision, the 1d Presbyo dedicates a 15% for a 3 mm aperture diameter, which decreases to 10% for 4 mm in benefit of far vision. The Biofinity multifocal shows the best near vision performance for a 4 mm aperture size, approximately the 60%, whereas the distance power contribution starts to increase from approximately 3.2 mm of aperture diameter. Other studies have also assessed different designs depending on the aperture size (Montés-Micó et al. 2014; Madrid-Costa et al. 2015). The distance correction power can also be chosen as a function of the pupil size and visual requirements. Ring bifocal lenses present less pupil-dependence than the aspheric ones, but the edges of the transitions between far and near powers can increase light scattering, decreasing the optical quality (Madrid-Costa et al. 2015). Some of the MCLs designs have included a spherical aberration component in an attempt to extend the depth of focus. However, if great amounts of aberrations are introduced, a significant loss in the near visual acuity of the patients may occur (Plainis et al. 2013).

Considering all this, since there is a change of the power distribution depending on the aperture, it seems evident that the performance of these lenses depend on the pupil dynamics of the patients. Thus, differences in the pupillary response among patients could lead to different refractive power behaviour of the lenses even for those with the same distance refraction, addition or visual requirements (Madrid-Costa et al. 2015). For all these reasons, the pupil size takes a significant role when studying the performance of a lens. The aperture diameter in multifocal power profiles is often taken as an approximation of the actual pupil size of the patient. Nevertheless, it has to be taken into account that the aperture size of the optical zone that might be considered for analysis and the real pupil are located at different planes. Centration is also important for a correct fitting of a MCL. A proper fitting requires a good centration as well as a careful monitoring of the pupil size. An inadequate centration and movement of the CL on the ocular surface can lead to adaptation and visual problems (Muntz et al. 2015).

As for the case of MIOLs, the pupil dependence has also been extensively investigated. Several studies of in-vitro evaluation of MIOLs have shown the relationship between the aperture size and the optical performance for different designs (Kawamorita and Uozato 2005; Eom et al. 2013; Montés-Micó et al. 2013). Artigas et al. (Artigas et al. 2007) assessed a refractive and two hybrid MIOLs and determined their MTF as a descriptor of the image quality with different pupil sizes. They analyzed the refractive-diffractive monoblock IOL AcrySof ReSTOR SN60D3 (Alcon, Fort Worth, TX, USA), the refractive-diffractive Tecnis ZM900 and the refractive ReZoom NXG (Abbott Medical Optics Inc., Santa Ana, CA, USA). With a pupil diameter of 3.0 mm, the aberration effects became more apparent than with smaller apertures. The best performance for the ReZoom IOL was at 3.5 mm pupil size for distance, with similar near MTF to the other IOLs. As for larger apertures of at least 4.0 mm, the AcrySof ReSTOR SN60D3 yielded the best optical performance in terms of the MTF for distance vision, whereas the Tecnis ZM900 yielded the best near MTF. Alcocer et al. (Ruiz-Alcocer et al. 2014) evaluated the in-vitro optical quality of trifocal diffractive designs as a function of the pupil size. Among their lenses under test, they found that the AT LISA tri 839 MP turned out to be less pupil dependent. Some diffractive designs of MIOLs include a property used in optics known as apodization. Apodization is the variation of the lens properties across the optical zone from the centre to the periphery, which changes the light distribution depending on the pupil size. Specifically, more light is available for the near focus when the pupil is small, whereas it is for distance when the pupil is large. In this scenario, the distant work would be beneficiated in dimmer light conditions, such as night driving, and then reduce glare or halos. The lens design would enhance near vision for near work activity such as reading in bright conditions. Vega et al. (Vega et al. 2011) evaluated the energy distribution between the distance and near focus in a model eye of apodized diffractive lenses with spherical and aspheric designs. They found that the energy efficiency was strongly decreased due to spherical aberration for distance vision. For small pupils, and thus low level of spherical aberration, the aspheric and spherical designs performed similarly.

The optical performance of an IOL is generally assessed at its centred position. However, it is also important to take into account that different factors can affect its final position inside the eye, such as, the implantation technique, asymmetrical implantation, asymmetrical capsular shrinkage, capsule fibrosis, rupture of the posterior capsule or zonular dialysis, etc. (Sauer and Mester 2013; Findl et al. 2015). This results in decentration of the lens and/or tilt. This misalignment with respect to the visual axis can affect the optical performance of the lenses. Well-centred IOLs with an aspheric design intend to improve optical performance and contrast sensitivity by reducing spherical aberration. However, decentring can result in lower optical transfer function because of induced second and third order aberrations such as astigmatism or coma (Altmann et al. 2005). The design of the lens itself plays a main role in its tolerance to decentration.

Objective comparison of the imaging properties of MIOLs, as well as those of MCLs, and their association with the pupil size can be useful in order to select the most appropriate solution for each patient (Pepose et al. 2012), which will be discussed in **section 1.6**. Nevertheless, it has to be taken into account that the in-vitro optical quality evaluation of MCLs or IOLs does not take into account the coupling effect of the lens with the eye or the whole visual system of the patients. Visual performance with these designs postoperatively is also important, considering as well effects such as decentration or tilt.

1.5 IRREGULAR OR NON-CIRCULAR SHAPED PUPILS

Naturally, the pupil dependence is always thought in terms of the total diameter of a circular pupil. However, due to congenital or acquired conditions, the pupil may not be circular and it may have lost part of its functionality. Indeed, any disorder that physically causes any harm in the iris mechanisms or alter the iris innervation can result in an irregular shaped pupil. As an example, the iridal coloboma is a condition which arises early in gestation and it is associated with defective closure of the optic fissure (Karatepe Haşhaş et al. 2017). As a result, the choroid is not completely closed and thus the shape of the pupil is stretched.

Also, posterior synechiae are presented when the iridal tissue adheres to the anterior capsule of the lens giving an irregular shape of the pupil as a result of ocular trauma or other ocular conditions that imply intraocular inflammation such as uveitis (Jakobiec et al. 1977). Ocular trauma or other disorders may also lead to shape alterations such as muscle spasms that lead to segmental iris mydriasis. For example, the Tadpole pupil is a rare condition in which the pupil undergoes sectorial dilation (Thompson et al. 1983).

It has to be taken into account that eyes with irregular pupils due to ocular conditions can also present a decreased functional vision (Agrawal et al. 2010). It is important to recognize the iris structural abnormalities in order to detect the cause of abnormal pupil size, shape or pupillary function (reactivity). **Figure 1.8** shows an example of an irregular shaped pupil.

Figure 1.8. *Coloboma causes an irregular shaped pupil. Image by Kimberly Crandell. URL:*http://www.science20.com/science_motherhood/coloboma_humans_cat_eyes. *[Accessed in June 2018].*

The shape of the pupil and the influence on the behaviour of multifocal optical solutions for presbyopia has not been previously investigated, which is a goal of the present work. Thus, if it has been mentioned that the pupil size has a significant role on the performance of multifocal solutions, it is thought that the shape of the pupil might also have additional implications in its optical behaviour even in terms of other limiting factors such as the light distortion effects.

1.6 VISUAL LIMITING FACTORS OF MULTIFOCAL SOLUTIONS: LIGHT DISTORTION.

Although multifocal optical solutions for presbyopia are successful for a great number of people, they also present some limitations. Candidates for multifocal solutions need to accept a level of potential visual compromise, in exchange for an increased quality of life without spectacle dependence. The evaluation of night vision disturbances under dim light conditions has become a matter of special interest in the past years due to the increasing number of MCLs, corneal refractive surgery and IOL implantation. Under this concept, several phenomena are included, such as positive and negative dysphotopsia, glare, halos, starburst, arcs, etc. These disturbances are not easily distinguishable, and they can have different impacts on the subjective visual quality. The term “light distortion” was suggested in order to incorporate all these phenomena (Klyce 2007).

In fact, whereas the correction of refractive errors with monofocal solutions usually give acceptable visual performance, multifocal solutions can experience reduced contrast sensitivity, ghost images or halos (Wahl et al. 2017). The visual performance is generally assessed in terms of high contrast visual acuity, but this measurement does not serve as a good indicator of vision quality alone. Measurements of the contrast sensitivity function (CSF) can be performed in the presence and absence of glare in order to evaluate the disability glare or describe intraocular scatter. Inhomogeneities in the ocular media that scatter light in the forward direction causes a visual handicap, known as straylight (Łabuz et al. 2016). Straylight and visual acuity are independent aspects, although their importance to quality of vision is comparable. Certainly, some studies have reported increased straylight in patients with a good visual acuity and vice versa (van der Meulen et al. 2012). In a normal eye without any pathologies, approximately 10% of incoming light is scattered. Besides, the light scattering increases with age (van den Berg 1995). An increased straylight can be an obstacle to perform everyday tasks, such as night driving or driving with a low sun. The optical principles used by MCLs or MIOLs that split the light into different foci can imply an augmented sensitivity to disability glare, especially under low light conditions due to the increased pupil size. Indeed, earlier studies have reported an increased sensitivity to glare with MCLs (both RGP and soft CL) (Rajagopalan et al. 2007). It has been a matter of current research whether the design of a lens itself has an impact on the CSF and the disability glare (Garcia-Lazaro et al. 2015; Wahl et al. 2017). In this sense, a recent study evaluated several patients who wore two different designs of the Biofinity multifocal (centre-near and centre-distance) with a distance power of +0.25 D and +2.50 D of addition, and the results were compared to the single vision version (Wahl et al. 2017). They concluded that the area under the measured CSF tested under glare decreased with the MCLs with respect to the spectacle correction. Besides, the centre-distance design yielded greater amounts of disability glare.

With regards the outcomes with MIOLs, many works have assessed the visual performance after the implantation of several designs. As well as with MCLs, dissatisfaction with the outcomes of MIOL implantation has been reported, including decreased visual quality and visual aberrations, glare or halos (Pieh et al. 2001; Ortiz et al. 2008). A retrospective review revealed that, after the surgery, 42% of the evaluated patients had symptoms consistent with photic phenomena, although, in many cases, this was attributed to posterior capsule opacification. It has been suggested that light disturbances are 3.5 times more common with MIOLs than with monofocal IOLs (Woodward et al. 2009). All these effects may be different depending on the design.

These disturbances are frequently reported by patients, but they are commonly described as subjective complaints. Beyond the use of subjective questionnaires, there is a need to characterize the size and shape of these light distortions. Several methods have been used for these purposes. A recent experimental device has been developed by researchers working at the University of Minho, in order to perform measurements of light disturbances. This system has been used in the present work and it will be described in the methods chapter. Different conditions, including the pupil size or shape, can be evaluated. The evaluation of light disturbances of optical solutions for the correction of presbyopia under different conditions can also be very useful for the selection of the patient.

1.7 SUITABILITY OF THE OPTICAL SOLUTIONS: SELECTION OF THE PATIENT.

Each design amongst the available optical corrections for presbyopia has its advantages and disadvantages in terms of providing the optimal vision for a given wearer. It is important to keep in mind that not all the designs affect the same way the visual quality of the patients, depending on the aberrations induced by a given lens and the coupling effect with the inner aberrations of the eye.

In the case of MCLs, the ideal candidates are those young presbyopes with low to moderate additions, who were used to CL correction for distance vision and who need a wide range of vision at different distances. The visual needs of the patients, their occupation and their physiological state are of vital importance and they have to be fully evaluated before choosing the best option. Also, the correct determination of the ocular dominance is crucial for adaptation, mainly in those case where different designs are used on each eye. The motivation of the patients in their day-to-day life, their hobbies or aesthetic reasons can also be important factors for the success. Indeed, the motivation of the patient is essential in order to be constant with the required maintenance of CLs. Alternating image formation rigid MCLs rates of adaptation are actually low, because very specific ocular conditions are required, such as a good position and tonicity of the lids. The position of the lower lid and the pupil size need to allow vision through the distance area at primary gaze position and through the near portion when reading. If the upper lid drags the lens up or the lower lid is too low or flaccid, or the pupil size is too large, the effectiveness of this solution will be compromised (González-Méijome 2011). The state of the ocular surface will also play a significant role in the selection of the correction. As another example, in those cases with a moderate to severe dry eye disease, traditional corneal contact lenses can be contraindicated depending on the global state of the ocular structures, or at least its usage should be controlled more frequently (Pili et al. 2014).

With regards IOLs, an exhaustive evaluation of the ocular structures is needed, such as the anterior chamber, axial length, shape, corneal power, sulcus size, pupil diameter, etc. Especially in the case of anterior chamber phakic IOLs, the anterior chamber configuration is essential for a successful behaviour of the lens. Narrow chambers will present important limitations for the implantation. Pseudophakic IOLs need to be carefully chosen depending on the patient requirements, which is why active listening to the patient's needs is essential in selecting the most appropriate IOL.

The risks of choosing the wrong solutions or an inappropriate method for correction need to be thoroughly considered. For example, in those cases in which the perception of distances plays a significant role in the performace of a task, such as professional drivers or pilots, monovision will not be the most appropriate selection. Choosing the wrong method can cause severe injure or safety issues (Nakagawara and Véronneau 2000). Also, in those patients with a previous history of strabismus or significant phorias, monovision should be taken carefully and keep the anisometropia to small levels up to 1.50 diopters (Pollard et al. 2011). However, in those patients with high near vision requirements, monovision can enhance the performance of their tasks.

Patients need to be properly explained the idea of functional rather than perfect vision, as well as the benefits and weakness of the different options. They should also be warned of the potential presence of halos around point sources of light, as it has been previously described (Braga-Mele et al. 2014). Bad or poor explanation can lead to unreal expectations and might result in frustration and abandonment. The personality of the patients (for example, if they are very perfectionist) should also guide the professional decision. Furthermore, there is a neural component that depends on each patient. This is, the ability of the human brain to supress the blurred images. If there is difficulty to ignore the out-of-focus images, there will also be a reduction of contrast of the in-focus images (Papadatou et al. 2017). If patients have these difficulties and they are not willing to accept the presence of halos that can limit the quality of night vision, they should be excluded.

Lastly, these solutions are not a suitable option for those patients with other ocular conditions that could limit their vision, such as corneal dystrophies or retinal pathologies.

CHAPTER 2:

STRUCTURE, OBJECTIVES AND HYPOTHESIS

2 STRUCTURE, OBJECTIVES AND HYPOTHESIS

The number of presbyopes is increasing every year and it carries with a reduction in the quality of life, which is why the correction of presbyopia is of vital importance. Nowadays, several methods are available, which mainly act as corrective solutions. As the presbyopic population keeps growing, current research is still in quest of the optimal correction method with the minimal impact on the quality of life of subjects.

The main goal of this thesis is to analyse existing optical solutions for presbyopia as a first evaluation for describing optical elements and then go further by assessing the influence of different sizes and shapes of the pupil, since most of the current assessing methods have only taken into account a circular shape. Thus, this work gives special importance to those pupils that are not circular, and how this characteristic may influence the effectiveness of the current optical solutions for presbyopia in terms of image formation quality metrics and the induced light disturbances. Specific software for computational methods has been developed, which is also described in the **third chapter**.

Three main sections conform **chapters four, five and six**. These compile the background, specific methods, results and discussion of the research. The fourth and fifth chapters are focused on the in-vitro assessment of MCLs and MIOLs, respectively, as well as computational calculations with irregular pupil shapes. The sixth chapter incorporates a clinical evaluation of MCLs in low light conditions with non-circular pupils. Finally, **chapter seven** is composed by a general discussion and final conclusions, followed by the future lines of research in **chapter eight**. Additionally, all the references and annexes are congregated at the end of this work.

This thesis shares a deeper knowledge on existing methods. Looking into the future, the final aim is to achieve new solutions for the correction or prevention of presbyopia in order to preserve the most optimal quality of vision, and thus, of life.

HYPOTHESIS

Not only the size, but also the shape of the pupil, have an influence on the optical performance of the existing multifocal solutions for the correction of presbyopia.

CHAPTER 3:

GENERAL METHODS

3 GENERAL METHODS

Two main approaches were used for analysing methods in this thesis. The first one makes use of a commercially available optical device and one experimental laboratory equipment, which are described in **sections 3.1** and **3.2**. However, not only available devices are useful for optical characterization. Besides, they also carry some limitations. This is the reason why only by means of computational simulations it has been possible to assess the influence of the shape of the pupil, since existing optical devices merely include circular apertures. Furthermore, computational methods allow to develop new metrics from data yielded by those devices. This conforms the second assessing approach described in **section 3.3.**

3.1 OPTICAL DEVICES

Nowadays, as it has been previously mentioned, different methods for the correction of presbyopia are available for commercialization. Optical elements which are added to the final optical system of the eye require special attention during their manufacturing process and afterwards for their validation and evaluation. It is important that they are carefully designed and tested following the standard specifications, which are specified by the International Organization for Standardization (ISO). The ISO is a non-governmental organization, founded in 1947, whose purpose is the international regulation of worldwide proprietary, industrial and commercial standards covering manufactured products and technology, as well as healthcare, and so forth. Commercial companies and researchers working at educational Institutions can make use of such devices, one of which will be described next.

3.1.1 NIMO

The NIMO TR1504 device (Lambda-X, Nivelles, Belgium) is useful in order to characterize optically MCLs and IOLs. **Figure 3.1** shows the configuration of this device and its main elements. This optical device is based on a quantitative deflectometry technique (Joannes et al. 2003), that measures light deviations through a combination of the Schlieren principle with a phase-shifting method. This is, the device measures light deviations, from which is possible to calculate the optical power and quality of lenses under test. A backlight source emits green light at 546 nm. Detailed description of the method used to measure the lens power can be found elsewhere (Joannes et al. 2003, 2010). This instrument gives very good reproducibility and accuracy. More specifically, the reproducibility standard deviation to measure the power profile of multifocal lenses is lower than 0.12 D (Domínguez-Vicent et al. 2015).

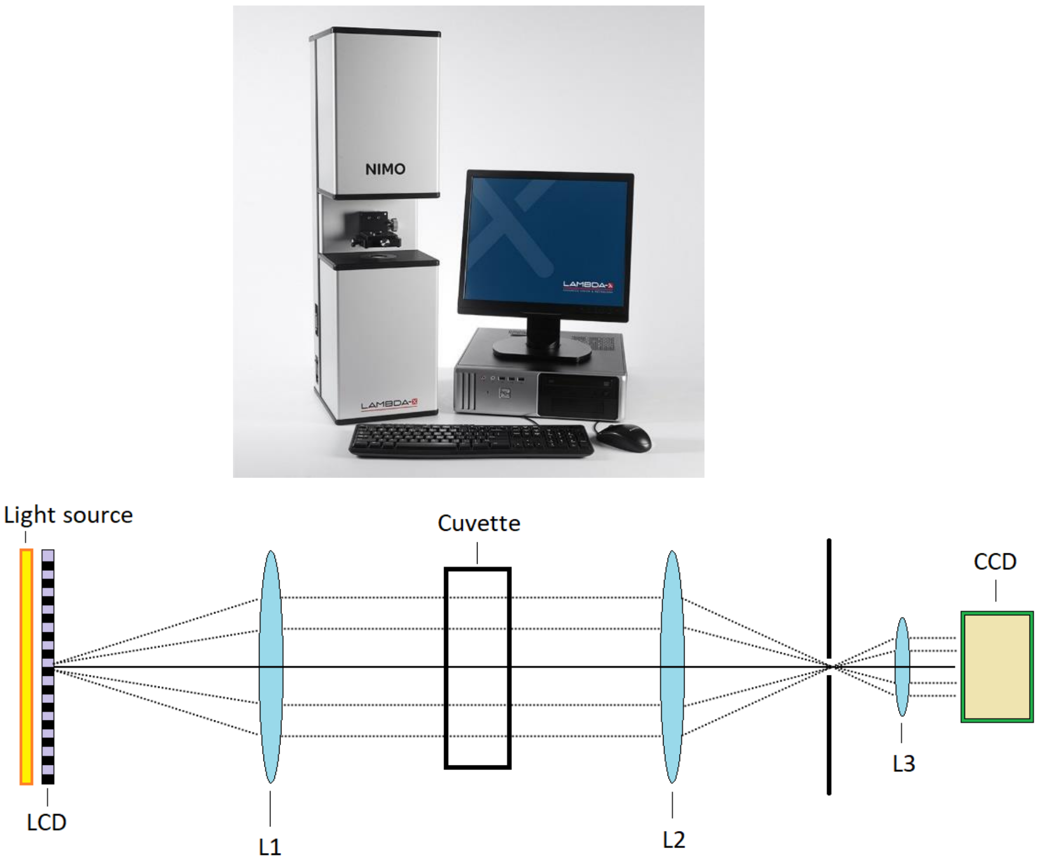

Figure 3.1. *The NIMO TR1504 instrument and the configuration of its elements*

The NIMO provides reliable measurements of lens characteristics such as:

- Lens power, cylinder and axis.
- Wavefront aberration adjustment with Zernike coefficients.
- Radial power maps and power profiles.

In order to perform one measurement and for the software to yield the results, the instrument needs to be calibrated. After this, the lens has to be placed inside the cuvette, which is filled with liquid to allow the measurement, and its centre needs to be aligned within the optical area on the red ring. Certain parameters of the lens need to be specified prior to assessment, such as the material index of refraction, its centre thickness, the back curvature or the optical zone diameter. The refraction index of the liquid in the cuvette also has to be set. Then, the measurement is performed. In the case of MCLs, a ring analysis is shown (**Figure 3.2**), together with the averaged power profile. The averaged power profile displays the radial power averaged on a circumference as a function of the distance to the centre of the lens (**Figure 3.3**).

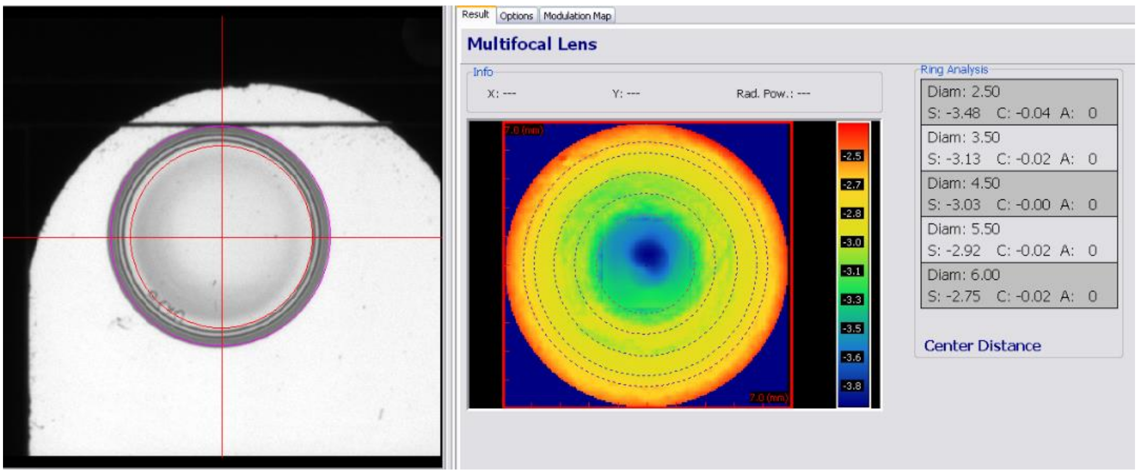

Figure 3.2. *Power map of a rigid gas permeable multifocal contact lens measured with the NIMO TR1504 device.*

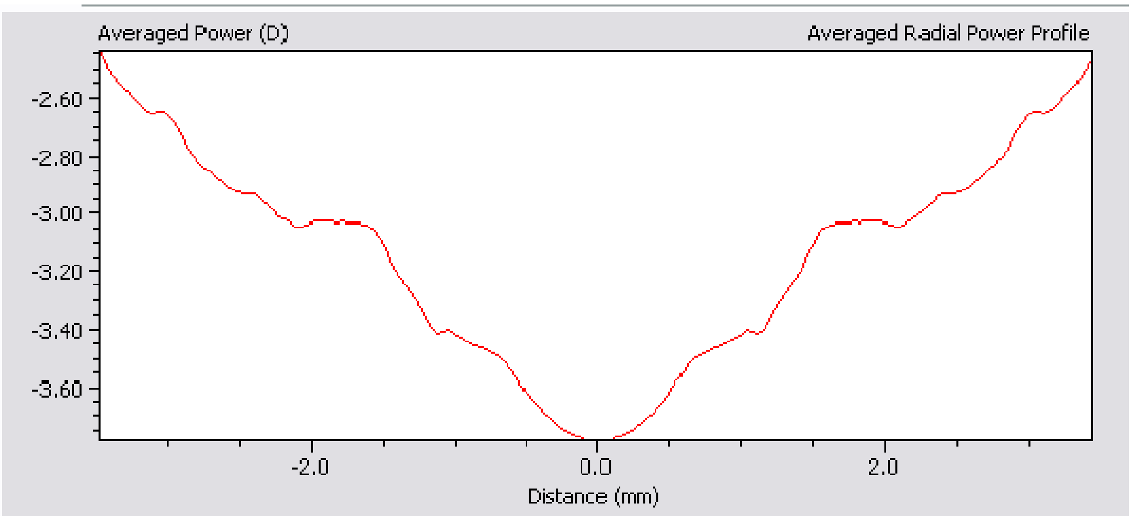

Figure 3.3. *Averaged radial power profile of a rigid gas permeable multifocal contact lens measured with the NIMO TR1504 device.*

3.2 EXPERIMENTAL SYSTEM

3.2.1 Light Disturbance Analyser

The "Light Disturbance Analyser" (LDA) is an experimental device that has been developed by the "Clinical and Experimental Optometry Research Laboratory" (CEORLab, University of Minho, Gualtar, Braga, Portugal). It consists of an electronic black board with a central light source and 240 small light sources surrounding it. This central light is a high-intensity source (up to 3000 cd/m^2), which is responsible for creating the glare condition, whereas the surrounding lights have lower intensity power outputs (up to 6 cd/m^2), which are used as threshold discriminators. The configuration of the board and distribution of the small lights is represented in **Figure 3.4**. Specifically, the peripheral sources are distributed in twenty-four semimeridians with a minimum angular distance of 15 degrees. The calibration and physical description of the light sources have been validated for use in visual assessments. A more detailed description of the instrument components can be found elsewhere (Ferreira-Neves et al. 2015).

Figure 3.4. *Light Disturbance Analyser instrument and the distribution of the central and peripheral light sources.*

The physical display is connected to a computer, which acts as a control unit. The subject that is being evaluated gives feedback to the system through a remote response device. The peripheral stimuli are presented in random order at different semimeridians and at random time intervals ranging from 250 to 750 milliseconds. The measurements can be obtained by using different examination strategies, which include:

- *In-out examination*: The radial light sources turn on sequentially from the centre towards the periphery until they are detected.
- *Out-in examinations*: The radial light sources turn on sequentially from the periphery towards the centre until they are not detected.
- *Subjective examination*: The subject moves the light along a semimeridian until the edge of the light distortion is detected.

For these strategies, the number of exams, different angular distances, velocities of the peripheral stimuli presentation or their intensity can be set prior to analysis. Three evaluations are performed at each semimeridian for each exam, so that the instrument calculates the mean limit of light distortion. If the standard deviation value is greater than 20% of the average, the device repeats the measurement until the standard deviation of the 3 measurements is smaller than 20% of the average. The light distortion can be measured in monocular or binocular conditions in approximately 40 to 60 seconds per exam.

The native software of the instrument provides different metrics for the characterization of the light disturbance (**Figure 3.5**), which are listed below:

- *Distortion area* (DA): it is calculated as the sum of areas of each sector (triangle) formed between each pair of semimeridians under analysis, in mm^2.
- *Light distortion index* (LDI): It is the percentage of the total tested area that is not visible due to visual impairment caused by the light distortion phenomena. Great values of the LDI are interpreted as a poorer ability to discern the surrounding stimuli.

- *Best fit circle radius* (BFC_{Rad}): It is the circle that best fits the shape of the polygon that defines the DA. Its radius is equal to the average length of the distortion along each evaluated semimeridian, expressed in mm.
- *Best fit circle centre coordinates*: These are the Cartesian coordinates (x,y) expressed in mm from the centre.
- *Orientation of best fit circle centre* (BFC_{Orient}): It is the angle of the centre of the BFC from the origin of coordinates, expressed in degrees.
- *DA irregularity* (BFC_{Irreg}): It represents the sum of all the deviations between the actual DA and the BFC outer perimeter for each semimeridian. The addends can be either positive or negative, since the distortion limit can be either in or out the BFC perimeter. It is expressed in mm.
- *Standard deviation of the BFC irregularity* ($BFC_{IrregSD}$): It is the sum of the differences squared and divided by the number of the evaluated semimeridians. Greater values of $BFC_{IrregSD}$ are interpreted as a more irregular distortion. It is expressed in mm.

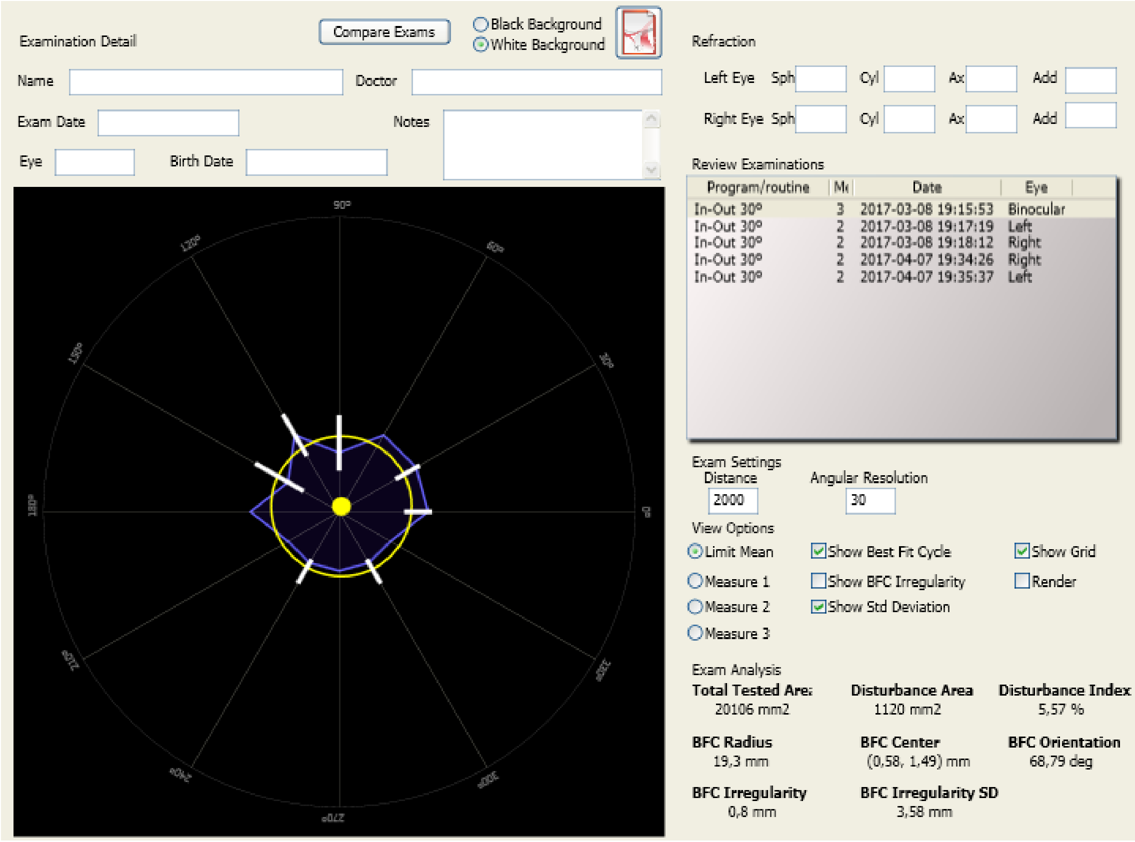

Figure 3.5. *Graphical and numerical characterization of the light distortion results for a given patient measured with the Light Distortion Analyser.*

Additionally, the software creates a rendered simulation of the light distortion condition for a given subject (**Figure 3.6**).

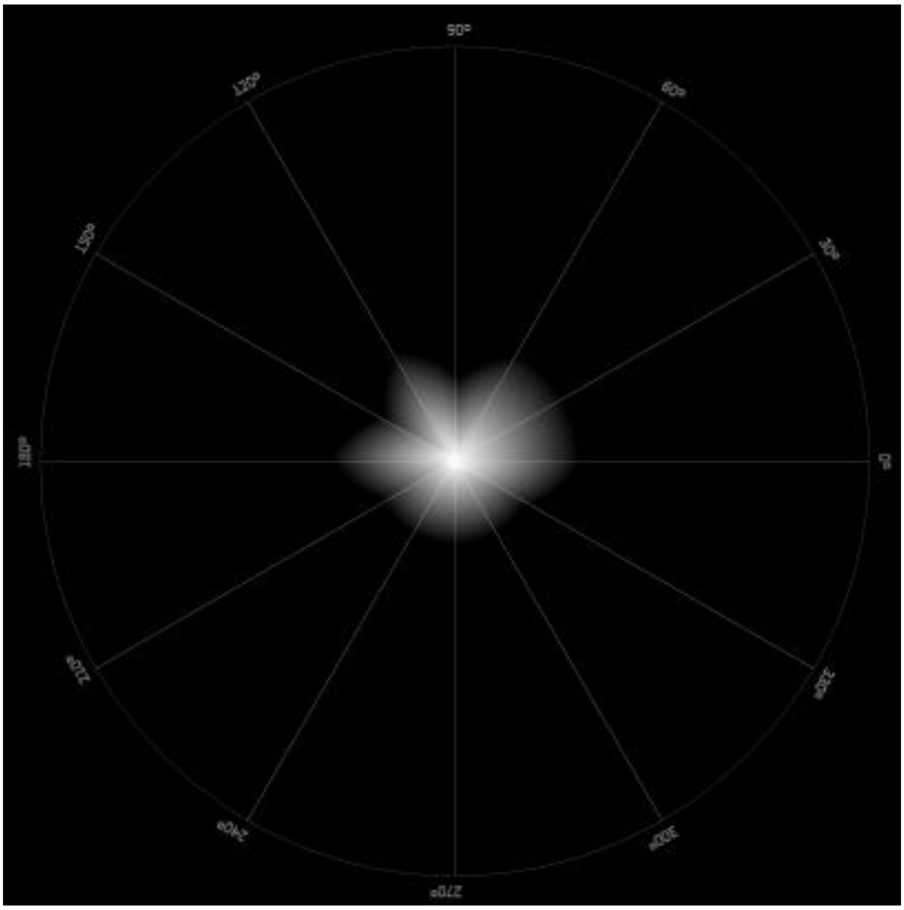

Figure 3.6. *Rendered graphical simulation of the light distortion pattern for a given subject measured with the Light Distortion Analyser.*

This instrument can be extremely useful in order to characterize the light distortion under different conditions, such as the size or shape of the pupil of the subjects, and for those patients wearing different types of multifocal solutions for presbyopia, since they have been proven to increase these effects.

3.3 CUSTOM-MADE SOFTWARE

3.3.1 Light Disturbance Analyser extended software

3.3.1.1 Description

A custom-made software has been developed in MATLAB (Release 2017b, The MathWorks, Inc., Natick, Massachusetts, USA) for extended light disturbance characterization. The software makes use of the raw data of the LDA, but makes an alternative analysis to that of the native software of the instrument, which has been described previously. In this case, the information of the position of those light sources that the patient was able to discern is used for the calculation of the distortion at each meridian. This new adjustment generates new metrics in order to take into account the possible effects of the introduction of a non-circular shaped aperture.

3.3.1.2 Metrics

As it can be observed from **Figure 3.7**, the crosses in each of the dotted lines represent the data points, which have an angular distance of 30 degrees each. These points are used for the calculation of the size of the distortion at each meridian (0, 30, 60, 90, 120 and 150 degrees).

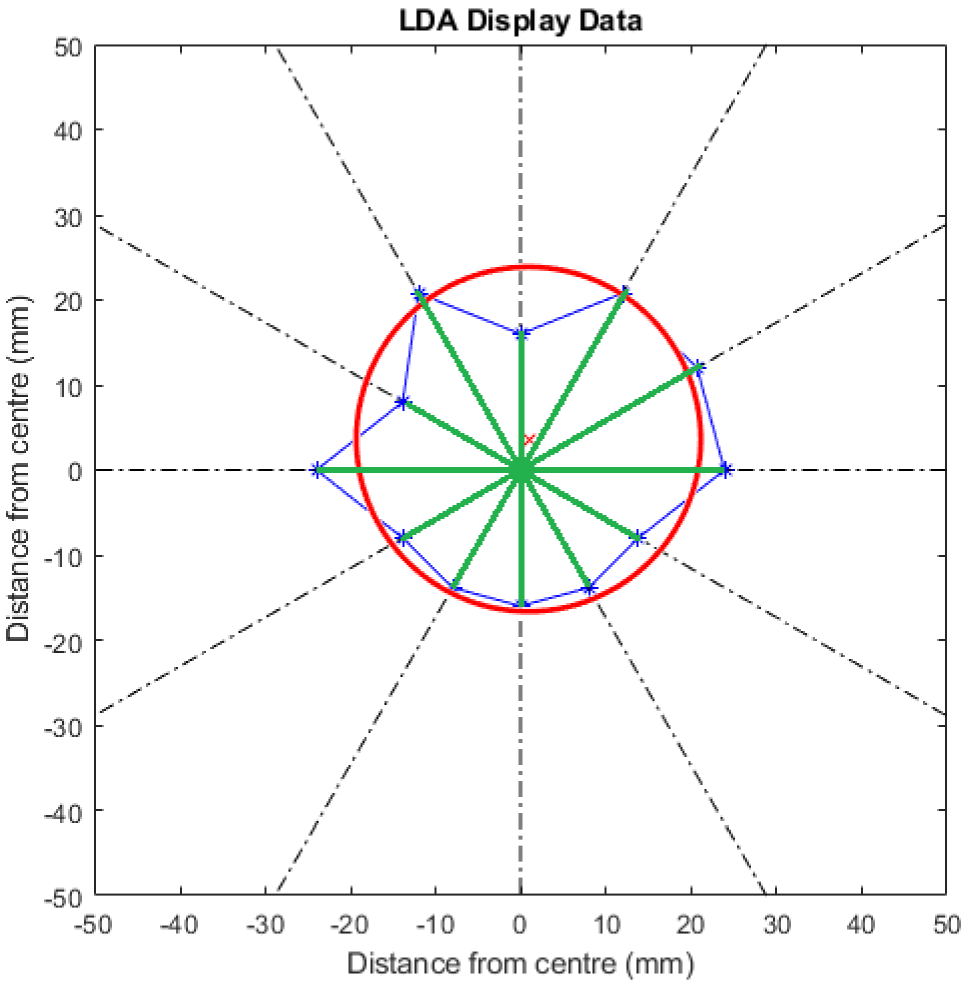

Figure 3.7. *Experimental points and fitting of a circle of the light disturbance for a given patient. The green lines represent the aperture of the light disturbance at each meridian.*

Additionally, two descriptive profiles have been obtained from the data points (**Figure 3.8**). These are the meridional irregularity profile and the meridional distortion profile. The meridional irregularity profile plots the difference in width of the opposite sides of a given meridian. A zero distance means that both sides are equal in size, whereas a negative distance means that the semimeridian value from 0 to 180 degrees is smaller than its corresponding value from 180 to 360 degrees. The meridional distortion profile simply represents the total distortion width for each of the analysed meridians.

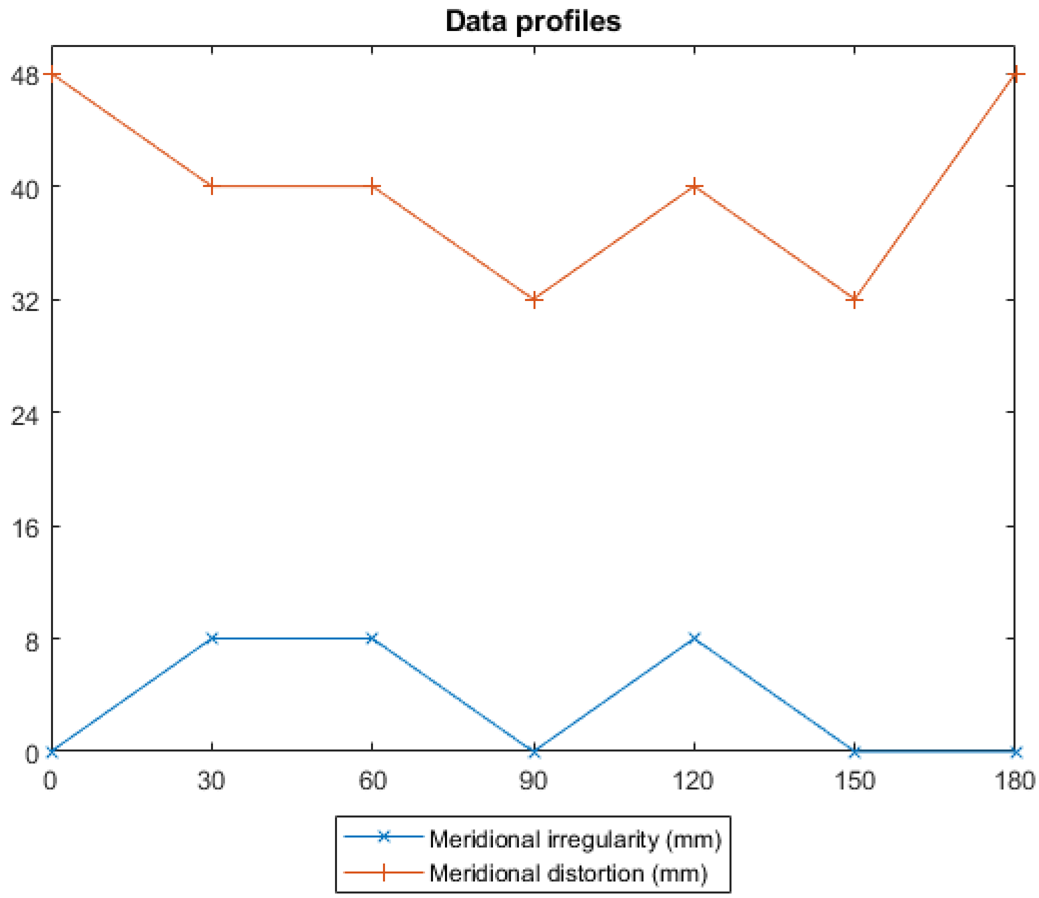

Figure 3.8. *Meridional irregularity and meridional distortion profiles.*

It has to be taken into account that the LDA instrument reference axes are defined with its scale as the patient sees the panel. If these data are going to be associated with other ocular parameters, such as those of the corneal surface or wavefront aberration data, both references need to be the same.

3.3.2 Power profile and wavefront analyser software

3.3.2.1 Description

A custom-made software was developed in MATLAB (Release 2017b). This software is based in Fourier-optics methods and it has been used for the simulations and calculations with different pupil sizes and shapes. The method has been derived from previous studies (Nam et al. 2009a, 2009b) and it has been recently used for similar purposes (Del Águila-Carrasco et al. 2017).

The software generates a wavefront error map W via the cumulative integration of a given power profile along the radial direction r (Eq. 1) (**Figure 3.9**).

$$W\ (r) = \int V(r)\ rdr \text{ (Eq. 1)}$$

where V indicates the power profile as a function of the radial distance.

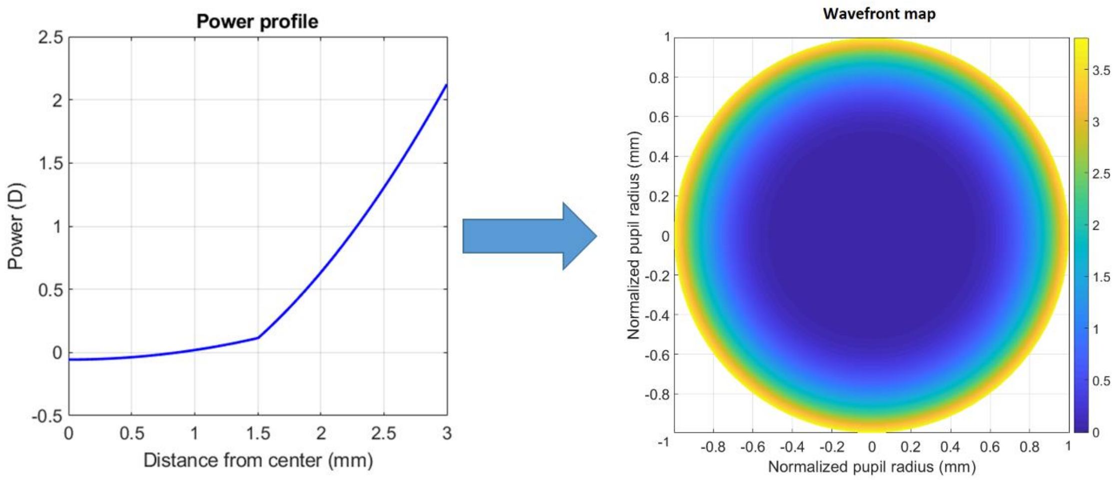

Figure 3.9. *Wavefront map obtained from a given simulated power profile.*

Then, the pupil function is calculated with the definition of a pupil mask. The complex-valued pupil function G describes how light is affected when it is transmitted through an optical imaging system, such as a lens or the human eye. The pupil mask *p(x,y)* is a real-valued function that specifies the amplitude of transmittance of each point of the pupil (*x,y*) (Eq. 2).

$$G(x, y) = p(x, y)\ \exp[\,\frac{i2\pi}{\lambda}(W(x, y)\,]\ \text{(Eq. 2)}$$

The pupil mask can be defined as ones within the pupil area and zeros elsewhere (binary pupil mask), although it may be also defined with variable transmission as a function of the position (apodization) (Watson 2015). This is useful in those cases where the Stiles-Crawford effect wants to be considered. In the case of this work, the optical solutions were analysed independently, so binary pupil masks were used (**Figure 2.10**).

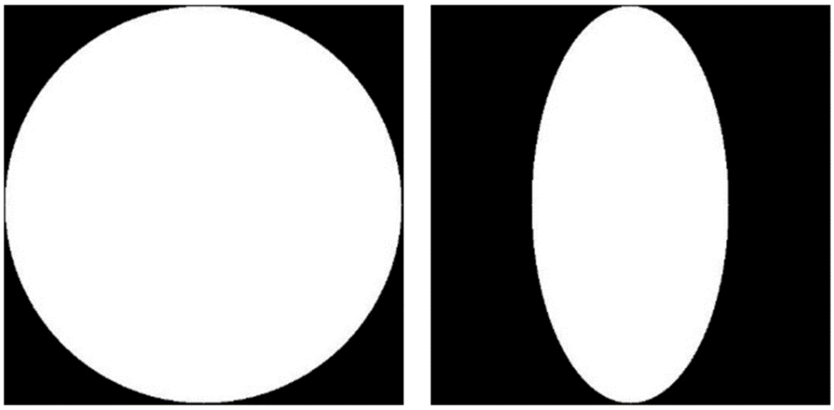

Figure 3.10. *Binary masks of one circular (left) and one elliptical (right) pupil.*

The point spread function or PSF is then given by the squared modulus of the Fourier transform F of the pupil function (Eq. 3).

$$PSF(x, y) = |F[G(x, y)|^2\ \text{(Eq. 3)}$$

The PSF describes the response given by an optical imaging system to a point source or point object. From the PSF, which is defined in the spatial domain, a Fourier transform can be applied in order to convert it to the frequency domain, which decomposes an object into periodic elements. This is how the optical transfer function (OTF) is calculated. The OTF describes how the different spatial frequencies are processed. The modulation transfer function (MTF), which is widely used to characterize optical systems and elements, is the modulus of the OTF. The MTF describes the resolution power of a system (Smith 2007).

Generally, this is the method for a centred lens evaluation. For the decentred positions, a previous step is added. In these cases, a rotationally symmetric power map previously generated from the power profile is decentred in a given direction. Next, the wavefront error map is obtained via the reconstruction of semimeridional integrations as in (Eq. 1), taking the centre of the pupil as the chief ray in order to fulfil the standard axis selection requirements. Finally, the generated wavefront is applied a binary pupil mask corresponding to the given aperture and the software calculates the optical metrics.

3.3.2.2 Metrics

As it has been previously described, the PSF describes the response of a point object whose image is formed through a given optical system, such as the eye, a lens or a set of optical elements. In order to provide a simple understanding of the influence of the pupil shape on the PSF and the variations of the metrics, a system with no optical aberrations will be used as an example for clarification purposes.

Theoretically in terms of geometrical optics, the image of an object point formed by an ideal optical system would be perfectly imaged as a point. However, this is not the way it actually occurs due to the wave nature of light. In this sense, diffraction is caused when light passes through the limits of a given aperture stop. As a result, the light is spread around the ideal perfect image of a point, which yields the diffraction pattern or also named Airy disc in honour of George Biddel Airy, in the case of circular apertures (**Figure 3.11**).

The radius of the Airy Disk depends on the wavelength of light and the size of the aperture, and it is calculated as follows:

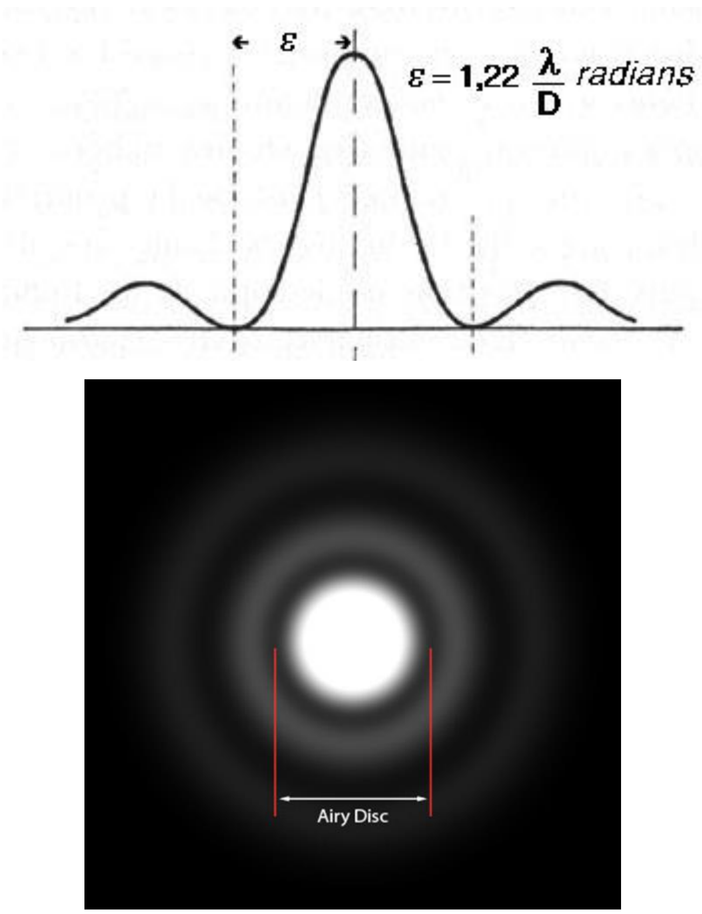

Figure 3.11. *Airy disc pattern and its angular size.*

The Airy disc is the image of a point passing through a diffraction-limited optical system with a circular pupil, that is, its PSF. Several ways can be thought in order to characterize an optical system from its PSF. Up to the present day, different metrics have been proposed which are described in terms of the PSF. Larry N. Thibos et al. (Thibos et al. 2004) presented a useful set of metrics for this purpose. It is worth mentioning parameters such as the diameter 50 (D50), which yields the diameter of a circular area that gathers the 50% of the total energy of light taking as its central value the centre of gravity of those points exceeding a set threshold. Our threshold for the centre calculation for all cases was 0.50, which means that those points greater than half of the peak value were used for locating the centre. Such metric describes the behaviour of an optical system in terms of compactness. However, it ignores the light that falls outside the D50 region, thus ignoring the shape of the PSF tails. The percentage of light can be changed depending on the analysis requirements. In this sense, the D25 metric was defined as the diameter of the circular area gathering the 25% of light for those cases in which there are several foci. Since this metric is based on the PSF peak, which does not have to be located at the origin centre, great amounts of deviation can significantly alter the final image quality, which this metric does not take into account.

Additionally, they also introduced the light-in-the-bucket metric (LIB), which describes the system in terms of contrast. The LIB metric describes the amount of light energy that falls within the limits of a circular area corresponding to the central spot of the Airy disc. These metrics can be presented in two different ways, i.e., as absolute values or as a ratio between the value for an optical system and the value of the diffraction-limited one for a given aperture.

However, when the pupil becomes elliptical we have no longer an Airy disc, but rather an elliptical diffraction pattern. This is because light is diffracted differently across meridians and it is spread more significantly across the direction of the minor radius of the ellipse (**Figure 3.12**).

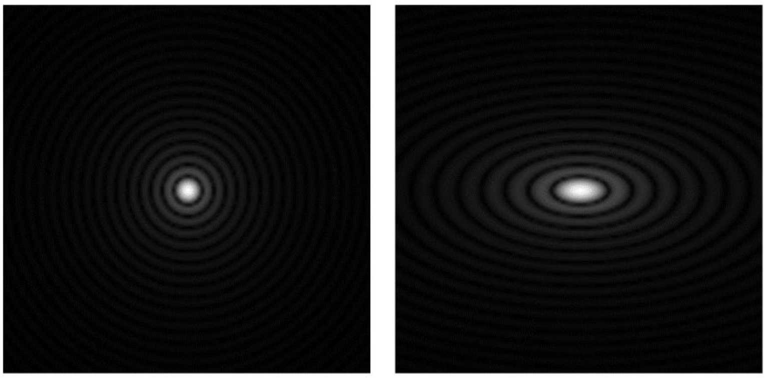

Figure 3.12. *Diffraction-limited PSF for the circular (left) and the elliptical (right) apertures of Figure 3.10.*

Nevertheless, these metrics can still be used but taking its absolute values rather than ratios with respect to the corresponding diffraction-limited system, for comparison between different aperture shapes. This is because the diffraction pattern varies with the pupil shape, thus changing the relativizing parameters. This is an important consideration when comparisons between different pupils are to be done.

Additional metrics such as the visual Strehl ratio computed in the frequency domain (VSOTF) are based on the OTF. The VSOTF computes the ratio of volumes under the OTF and a diffraction-limited OTF, both weighted by the neural contrast sensitivity function (CSFn). This metric has been previously used for describing visual performance since it is well correlated with subjective methods. A threshold of 0.12 has been set as the value that provides acceptable vision, corresponding to a 0.2 logMAR visual acuity (20/32 Snellen equivalent), at which half of the people present some difficulties while reading. Values above 0.12 are considered to be acceptable (Cheng et al. 2004; Marsack et al. 2004). Other metrics of image quality defined either in the spatial or the frequency domain can be found elsewhere (Thibos et al. 2004).

CHAPTER 4:

ASSESSMENT OF MULTIFOCAL CONTACT LENSES FOR PRESBYOPIA

4 ASSESSMENT OF MULTIFOCAL CONTACT LENSES FOR PRESBYOPIA

The number of new MCLs designs has been growing in the past years. New lenses have been released and it is of crucial importance to study the optical performance under different conditions that have been proven to have an impact on their performance, such as the pupil size, as it was previously discussed. In this chapter, detailed information of new commercially available designs will be provided, which is very useful for practitioners. Additionally, the effect of the pupil shape will be analysed and discussed as a possible factor to affect the optical performance of MCLs.

4.1 IN-VITRO EVALUATION OF RIGID GAS PERMEABLE MULTIFOCAL CONTACT LENSES WITH VARIABLE MULTIFOCAL ZONE

4.1.1 Background

Many contact lens wearers need to improve their near vision due to a decline in their accommodative amplitude. In this regard, MCLs are the preferred solution over other corrections with CLs (Efron et al. 2015). Previous studies have reported that the performance of MCLs highly depends on the patient's pupil size, as it has been already introduced. Nevertheless, the pupil diameter has been reported to vary among patients within the same age range (Koch et al. 1991). As a result, not only should MCLs be available with different additions, but also with several sizes of the distance- and near-vision zones to achieve the most customized fit.

Up to the present day, there is a new generation of MCLs with different designs that present a variable multifocal zone with different proportion between distance-and near-vision zones to achieve a customized fit depending on the patient's pupil diameter. These MCLs have a centre-distance design, and they are available with five different distance-zone diameters and two additions. Unfortunately, the nominal distance-vision and addition powers are the only information available regarding the optical power of MCLs.

Since the power profile of MCLs has been demonstrated to report important information that could be used during the fitting process, the aim of the present study was to describe the power profiles of the MCLs as a function of their distance-zone size and assess the effect of the pupil radius on the effective power profile.

The results can help clinicians to choose the proper lens among all these new designs, which optimize the distance/near vision for the patient's pupil diameter and visual tasks requirements. In other words, it is very useful for the selection of the patient.

4.1.2 Methods

A new set of MCLs with variable multifocal zone were analysed (Conoptica MULTILIFE). These lenses are a centre-distance RGP lenses that are available with five distance-vision diameters (XS, S, M, L and XL) and two different additions: Type A (up to +2.00 D) and Type B (up to +2.50 D). The multifocal zone is located on the front lens' surface, so the posterior surface can be designed as a function of the patient's corneal shape.

All the study lenses had the same total diameter (9.60 mm), power (–3.00 D) and material (Boston ES). These parameters were assumed within the tolerance limits stipulated in the ISO 18369-2:2012, for the proper functioning of contact lenses as optical devices. In this study, one lens per each distance-vision diameter and addition was measured.

Measurements and metrics

The NIMO TR1504 device was used in order to yield the power profile measurements (see General Methods section). Once a lens was ready to be evaluated, a measurement of the power profile was taken with an optical aperture of 8.00 mm. After that, the cuvette and contact lens were removed and placed back again in the device in order to obtain up to 10 independent measurements of the power profile. Next, the 10 power profile measurements were averaged out in order to get the mean power profile. This process was repeated for each of the study lenses.

The optical lens power distribution as a function of the aperture radius was described in terms of radial computed colour maps, radial averaged power profiles, addition, and lens portion used for near vision. The computed colour maps were generated as a surface of revolution from the power profile data of each lens provided by the NIMO device by a user script developed in MATLAB. A unique colour map scale was set to all maps for the different designs and addition types so the power characteristics among them are easily comparable.

The radial averaged power profiles were obtained as a function of the distance to the centre, in steps of 0.04 mm. The data on these profiles correspond to the raw measurements taken by the device, which displays the radial power averaged on a circle as a function of the distance to the centre.

The addition along the optical zone was calculated as the subtraction of the power at each point of the power profile and the distance nominal power of the lenses (-3.0 D), from the centre in steps of 0.04 mm. This criterion was selected in order to transform all the power profiles measurements into an addition profile with respect to the same value instead of the central value, which is interpolated and not directly measured by the NIMO.

The last metric was calculated as the ratio between the near-distance vision for a radius up to 3.85 mm in steps of 0.04 mm. For this procedure, the distance vision radius was defined as that whose averaged dioptric power is the nominal power of the lens. The near zone was defined as the part whose averaged dioptric power is more positive than the nominal power of the lens.

4.1.3 Results

The colour radial power maps for the five different designs, for both addition types A and B, are depicted in **Figures 4.1** and **4.2**, respectively. These figures represent the differences in power for each design along a diameter of 8.00 mm. Warm colours indicate more positive powers, whereas cold ones represent more negative values. It can be observed from the figures how cold colours increase their area starting from the XS and following with S, M, L, and XL lenses, indicating the widening of the distance-vision zone and the narrowing of the area dedicated for near-distance vision. This is the general behaviour for every pair comparison between types A and B.

Figure 4.1. *Scaled colour power maps (in dioptres) for XS, S, M, L, and XL designs of type A addition. The axes represent radial distances in mm from the centre.*

Figure 4.2. *Scaled colour power maps (in dioptres) for XS, S, M, L, and XL designs of type B addition. The axes represent radial distances in mm from the centre.*

The power profiles as given by the NIMO are shown in **figures 4.3** and **4.4**, for both types A and B, respectively. The designs XS and S showed similar peripheral curves for the type A addition, whereas the design pairs L and XL showed also similar power profiles towards the periphery for additions Type A and B. From these figures, it can also be observed that further than approximately 1.0 mm from the centre and moving towards the periphery, the XS curves have more positive values than the XL designs.

Figure 4.3. *Radial averaged power as a function of the distance from the centre for XS, S, M, L, and XL designs of type A addition.*

Figure 4.4. *Radial averaged power as a function of the distance from the centre for XS, S, M, L, and XL designs of type B addition.*

Figures 4.5 and **4.6** illustrate the addition achieved as a function of the aperture for the addition Type A and Type B, respectively. On these graphs, the smaller the distance-vision area, the bigger addition within the same aperture.

Figure 4.5. *Addition as a function of the distance from the centre for XS, S, M, L, and XL designs of type A addition.*

Figure 4.6. *Addition as a function of the distance from the centre for XS, S, M, L, and XL designs of type B addition.*

As it was expected, the XS design resulted with the highest addition values compared to the other designs within the same apertures. Generally speaking, the smaller distance-vision area, the smaller aperture is needed to obtain the addition and a higher power can be achieved.

Also, the differences in the distance radius among lenses with different design (XS, S, M, L, or XL) for both addition types can be observed. The radius can be easily identified as the point on the radius axis (distance from centre) at which each curve starts to increase its addition value. As an example, the XL designs have a distance diameter of approximately 5.50 mm, whereas the XS ones have a diameter around 3 mm. In other words, the XS and XL designs showed the smallest and largest aperture needed to get into the near area, respectively.

Lastly, the proportion of the lens used for near vision as a function of the aperture for the Type A (lowest addition) and Type B (largest addition) are shown in **Figures 4.7** and **4.8**, respectively. The near zone was defined as the lens radius whose averaged power is more positive than the nominal power of the lens.

Figure 4.7. *Percentage of dedicated near vision as a function of the distance from the centre for XS, S, M, L, and XL designs of type A addition.*

As it was expected, the smaller the distance vision area, the larger near-vision zone for the same aperture. This is, the XS design showed the largest near-vision area and the XL did with the smallest one for the same aperture. It can be observed that at least more than 50 % of the XS and S designs is used for near-vision, about 40 % is used for near-vision for the M design, and less than 35 % is used for the L and XL designs. However, the L and XL designs showed similar near-vision areas for the same aperture.

Figure 4.8. *Percentage of dedicated near vision as a function of the distance from the centre for XS, S, M, L, and XL designs of type B addition.*

4.1.4 Discussion

The outcomes of this study provide a detailed description of new RGP lenses with variable multifocal zone as a function of the aperture diameter.

The radial colour maps of each lens which are shown in **Figure 4.1** (type A) and **Figure 4.2** (type B) provide a straightforward view of the power profile pattern which could help practitioners to comprehend at a glance how much of the lens area is dedicated for each average power. As it can be observed, the A addition type increases its power towards the periphery in a smoother way than the B type, which is more abrupt, indicating a higher increase of the addition. However, differences in the addition types are more easily visible for those designs of smaller distance vision area. This is due to the fact that the wider the distance vision area, the smaller area is dedicated for near vision, so it is more difficult to achieve higher addition values.

A first criterion to select the contact lens design could be the visual needs required for each patient with regard to distance and near vision. Besides considering the visual needs of the patients, it has to be taken into account that given the design of these MCLs, they are highly pupil dependent. This is why during the fitting process the pupil diameter should be measured at different illumination conditions and at different distances, which nowadays is not commonly used as a part of the fitting protocol. This, together with the knowledge on power profiles, would allow to select the best design which fits the best for a given patient.

From the results of this study, it can be concluded that the XS and S designs seem to be aimed to enhance near vision, meanwhile the L and XL designs seem to enhance distance vision. Generally, patients who demand good distance vision might benefit from the L or XL designs, and those with high demand on near vision tasks might benefit from the XS or S designs. Additionally, the M design could be the best option for those patients who have the same needs for distance and near vision. However, the patient's pupil size takes a main role in the lens selection. For this reason, those patients with larger pupils with high requirements on distance vision, should get L or XL designs.

Otherwise if they need to enhance near vision, lenses with reduced distance area should be considered. Also, since the pupil size adapts to lighting conditions, it seems that another criterion to take into account prior to selecting the lens to fit would be the patient's main task and its conditions for which the lens is needed.

Furthermore, although these results are useful to make a first decision on which lens to adjust, they also provide useful information that could be used as a guide to adjust and make changes during the fitting process. As an example in which a patient wearing an A-S lens has to be refitted with one of the other options because the visual outcomes at close distances are not satisfying, at first one possibility could be thinking of fitting a higher addition type maintaining its design (S). However, if this change turns the tables and makes the patient lack of good distance vision quality for his/her needs, one solution could also be increasing the addition type but also increasing the distance optical diameter and select a B-M design. With this option, the patient would indeed improve the near vision, but not as much as just changing the addition type from A to B, depending on his/her visual demands for each distance. With all these possibilities, together with the provided information in this study, the final fitting should be easily achieved without many changes.

It has to be taken into account that the measurements of the power profile of the study lenses have been obtained with them perfectly centred. However, their actual behaviour differs from this. Factors such as the lens movement and decentration could also influence in the visual performance. Indeed, the behaviour of these rigid MCLs is more affected by the translation than that of soft lenses, which makes the power distribution at the peripheral area become especially significant (Tomlinson and Ridder 1992). This is why not only it is important to select the best distance-area and addition type, but also make a good adjustment between the patient's cornea and the posterior surface of the lens to achieve its correct movement. RGP lenses move more frequently on the corneal surface than soft lenses in order to preserve the corneal physiological integrity and to assure a good lacrimal fluid flow between the back surface of the lens and the cornea (Muntz et al. 2015). This means that the centre of the lens, which is intended for far vision, is more frequently displaced than with soft MCLs. Thus, the near vision area is not always going to contribute as it is shown on the results for a perfectly centred lens. Indeed, the ideal position of the RGP lens for near vision is slightly decentred, since the lower lid pushes it up. This is why the near distance ratio seen in **Figures 4.7** and **4.8** describe the behaviour of the lenses in vitro and in vivo for the distance primary position of gaze, but for the near position of gaze this ratio can be increased. Due to the importance of the lens movement in order to provide good vision at different distances, the corneal topography should be added to the protocol in order to achieve an optimal visual performance with these type of lenses (Donshik et al. 1996; Cardona and Isern 2011).

However, the pupil-dependence of these type of lenses is not as high as that of soft lenses. This is due to the fact that rigid lenses will not require a large pupil size as soft lenses do in order to achieve a good performance at far and near distances, since the lower lid will push up the lens at reading position and it will cover a wider area of the pupil for near distance. For this reason, some patients may get some benefit from rigid lenses when their experience with soft MCLs is not satisfying, due to translation. A smaller dependence of the pupil size with RPG lenses involves a smaller dependence of lighting levels and a better performance throughout the day compared to soft MCLs. As an example, the XS or S designs would increase the ratio of near vision more significantly than the other designs, since their dedicated area for near distance is larger. This is because the push-up of the lower lids would make this area cover a larger part of the patient's pupil. All this said, due to the translation and considering a given pupil size, the differences among the power profile of these lenses do not require of such abrupt changes between the distance and near areas.

The visual quality of the patients adapted with MCLs depends on some other parameters. A lens design can provide good vision quality at some given situations, but not at others, for example, at different illumination conditions. Additionally, a more global vision of the fitting can be done taking into account the binocular performance.

For this, the possibility of fitting two different designs in each eye should be included when the binocular performance is not satisfactory.

Recently, a clinical research assessed the visual performance in early presbyopes wearing different modalities of simultaneous image soft MCLs under difficult lighting conditions, including the effect of glare (Garcia-Lazaro et al. 2015). In this study, the authors analysed the impact on the performance of distance tasks in terms of visual acuity and contrast sensitivity. However, these lenses provide lower visual acuity and contrast sensitivity for high spatial frequencies than monofocal contact lenses. As for the present study, taking into account the different designs of the study lenses, and due to the fact that they provide centre-distance vision, those designs with larger distance area as the L and XL ones (contrarily to soft lenses which most of them provide centre-near vision) may be less affected by difficult lighting conditions in which distance vision is required, such as night driving. In other words, patients with high demands on distance vision under dim light conditions might benefit from the L or XL designs. Nevertheless, further research should be addressed on this subject.

The results of the study show that the pupil size of the patients, as well as their visual needs, are of crucial importance. The information discussed in this study is very useful for a deeper understanding of these multifocal solutions and for the selection of the patient. Indeed, clinicians could benefit from the results obtained in the present study to select the most appropriate lens design that suits with the patient's pupil diameter and visual tasks requirements, among other factors. Understanding the power distribution of MCLs optical designs could increase the rates of successful fittings with this type of lenses.

In this case, the influence of the pupil was thought in terms of a circular shaped aperture. For those pupils that are irregular shaped or non-circular, optical simulations were performed from power profiles based on similar designs in order to study the differences in optical performance. This investigation is discussed in the next section.

4.2 THE EFFECT OF NON-CIRCULAR SHAPED PUPILS ON THE PERFORMANCE OF MULTIFOCAL CONTACT LENSES

4.2.1 Background

Most MCL designs are based on rotationally symmetric profiles to achieve simultaneous vision. Two main concept designs are currently used. One of them consists in areas with power discontinuities from the centre towards the periphery that can mainly provide foci for far and near distances, although some of them include a third focus for intermediate vision (Plainis et al. 2013). The second one makes use of a progressive power shift from the centre towards the periphery, which induces a certain value of spherical aberration (Bakaraju et al. 2010). Both concepts can use the central optical zone of the lens for far or near distance, depending on the user's actual needs.

Pupil dependence of these optical solutions is well known and it has been already discussed. However, this dependence is always considered in terms of the total diameter of a circular pupil. Thus, the efficiency of the optical solution depends on the total diameter of the patient's pupil, as well as the design of the lens itself and the area dedicated for each focus. However, as it was previously introduced, due to congenital or acquired conditions the pupil may not be circular and it may have lost part of its functionality.

Alterations of the normal pupil shape and its function might have an impact on the performance of the lens. In other words, the optical solutions may lose part of their effectiveness when they are used on eyes with irregular pupils. For this reason, the present study was designed as a preamble to investigate the optical quality of optical solutions with irregular shaped pupils. Theoretical approaches were considered and implemented by means of optical simulations.

4.2.2 Methods

Custom-made software based in Fourier-optics methods was developed in MATLAB and used for the simulations and calculations. This software has been already explained and described in detail in **section 3.3.2.** As a brief reminder, the software generates a rotationally symmetric wavefront error map via the cumulative integration of a given lens power profile along its radial direction. Then, it calculates the optical metrics after applying a binary pupil mask.

Pupil shapes.

Three pupil shapes were considered: one circular and two non-circular, including one elliptical and one irregular shape, simulating ocular trauma and iridal synechiae, respectively. All the aperture shapes were generated and defined within a maximum diameter of 6 mm. The elliptical pupil had horizontal and vertical diameters of 3 and 6 mm, respectively. The synechial pupil presented an opaque area on the right side (**Figure 4.9**). The apertures acted as optical masks that limit the light passing through. The wavelength of light for the calculations was 550 nm. The total area for each of these pupils was calculated (**Table 4.1**).

	Area (mm^2)	Monofocal	Center-D Bifocal		Center-D Progressive	
		D	D	N	F	N
Circular	28.27	100%	25%	75%	25%	75%
Elliptical	14.14	100%	50%	50%	50%	50%
Synechial	22.24	100%	24%	76%	24%	76%

Table 4.1. *Total physical area for each pupil and the percentage of dedicated area for the near (N) and the distance (D) focus. They were all defined within a circular aperture of 6 mm.*

Figure 4.9. *The three apertures that were used for the simulations with their corresponding images of the diffraction limited point spread function. The point spread function images are represented in a 10x10 arcmin square.*

Contact lenses power profiles.

One bifocal center-distance and a progressive multifocal center-distance power profiles with approximately +2.25 D addition power were defined over a 6 mm optical zone diameter (**Figure 4.10**). Additionally, a monofocal profile was included for comparison purposes (**Figure 4.11**). The monofocal profile presented a power shift towards the periphery of -0.075 D/mm^2, since an increase of negative power is typically found in some lenses already measured (Plainis et al. 2013; Kim et al. 2017). The centre-distance bifocal power profile presented two differentiated areas: one for distance vision from the centre up to 1.5 mm of radial distance, and one for near vision from 1.5

mm to 3 mm. This bifocal profile also included a negative power shift value of -0.075D/mm^2.

Figure 4.10. *Radial power profiles used for the simulations including one centre-distance bifocal and one centre-distance progressive multifocal designs, with the respective power zones with every pupil. The central yellow area represents distance vision, whereas the peripheral does for near.*

Regarding the centre-distance progressive design, the distance vision was also defined within the central area up to 1.5 mm of radial distance with -0.075 D/mm^2 of negative spherical aberration. As for the area dedicated for near, it ranged from 1.5 mm to 3 mm of radial distance. These simulated profiles have been based on the previous measurements of rigid gas permeable lenses, which yielded similar power distribution (Monsálvez-Romín et al. 2018). All the simulated lenses had an average distance power of 0 D.

Figure 4.11. *Radial power profile of a monofocal lens for comparison purposes.*

Optical quality metrics.

Optical quality metrics were calculated in terms of a through-focus analysis for vergences ranging from +1.00 to -3.00 D in steps of 0.125 D. These vergences were taken as defocus and transformed to Zernike spherical defocus terms for a 6 mm diameter, which were then added to the wavefront of the lens. The PSF was obtained for all cases with each pupil, together with the diffraction limit pattern in order to observe the variations without the influence of the lens aberrations. Numerical metrics were derived from the PSF, such as the D25, which yields the diameter of a circular area that gathers the 25% of the total energy of light. Such metric describes the behaviour of an optical system in terms of compactness. For the special case of the diffraction limit, this percentage was set to 84%. This is because the amount of energy that is gathered around the central core, considering the Airy disc pattern, is approximately 84% regardless of the pupil diameter or the wavelength of light.

The VSOTF was also calculated. This metric has been previously used for describing visual performance since it is well correlated with subjective methods, although we are only dealing with objective assessment in this study as a first-step evaluation. Nevertheless, a threshold of 0.12 was set as the visual Strehl ratio value that provides acceptable vision, corresponding to a 0.2 logMAR visual acuity (20/32 Snellen equivalent), at which half of the people present some difficulties while reading. Values above 0.12 are considered to be acceptable (Cheng et al. 2004; Marsack et al. 2004). It is important to point out that these calculations were normalized by the diffraction-limited system of the ideal circular pupil, in order to observe the relative variations among apertures.

The modulation transfer function for each pupil and lens combination was also represented as radial colour maps at far (0.00 D), intermediate (-1.50 D) and near vergences (-2.25 D). The limits of representation ranged from 0 cycles per degree (cy/deg) up to 60 cy/deg, which is approximately the neural limit (Williams et al. 2004).

Finally, a simulated line of an optotype with white background and black letters corresponding to 0.2 logMAR visual acuity and 100% contrast was also included for the same vergences as those for the modulation transfer function.

4.2.3 Results

The PSFs were generated by means of a through-focus analysis of the performance at different vergences for each combination of pupil and lens design (**Figures 4.12, 4.13** and **4.14**) as a qualitative assessment.

Figure 4.12. *Through-focus analysis representation of the point spread function for the centre-distance bifocal design. Columns represent vergences 0.75 D, 0.00 D, -0.75 D, -1.50 D and -2.25 D, from left to right. Rows represent the apertures: circular, elliptical and synechial pupils, from top to bottom. Each square represents a 20x20 arcmin area.*

Figure 4.13. *Through-focus analysis representation of the point spread function for the centre-distance progressive multifocal design. Columns represent vergences: 0.75 D, 0.00 D, -0.75 D, -1.50 D and -2.25 D, from left to right. Rows represent the apertures: circular, elliptical and synechial pupils, from top to bottom. Each square represents a 20x20 arcmin area.*

The D25 results are shown in Figure **4.15**. The smaller this parameter is, the more compactness of the 25% of the total energy. The centre-distance bifocal (Figure **4.15**, panel A) presents two valleys corresponding to far (0.00 D) and near vergences (-2.25 D). The results for near distance are similar for every pupil. For the circular and synechial pupil, the size of D25 is smaller for near than it is for distance vergence, whereas regarding the elliptical pupil the size is smaller for distance but comparable to near vision. With regards to the centre-distance progressive lens (**Figure 4.15**, panel B), all pupils show similar results at 0.00 D and better than those for the bifocal. This is because the dedicated near focus of the bifocal design has greater impact on its image for the far focus. Since the progressive profile has a smooth power shift according to the positive spherical aberration, the size of the D25 increases with vergence, without appreciating two differentiated valleys. This increase is slower than that for the monofocal design (**Figure 4.15**, panel C), particularly for the circular and synechial pupils. Nevertheless, although the D25 parameter yields similar results in some cases, the shape of the PSFs are different. For the special case of the DL represented in **Figure 4.9**, the diameter of a circular area gathering the 84% of light yielded 0.67, 1.11 and 1.10 arcmin for the circular, elliptical and synechial pupil, respectively.

Figure 4.14. *Through-focus analysis representation of the point spread function for the monofocal design. Columns represent vergences 0.75 D, 0.00 D, -0.75 D, -1.50 D and -2.25 D, from left to right. Rows represent the apertures: circular, elliptical and synechial pupils, from top to bottom. Each square represents a 20x20 arcmin area.*

Figure 4.15. *Through-focus analysis of the diameter of a circular area gathering the 25% of the light distribution (D25) for the centre-distance bifocal (panel A), centre-distance progressive multifocal (panel B) and monofocal (panel C) designs.*

Additionally, **Figure 4.16** shows the VSOTF as a metric that has been associated to subjective methods. On these graphs, the peaks represent the visual Strehl ratio by methods derived from the optical transfer function. The VSOTF for the centre-distance bifocal presented two differentiated peaks, one corresponding to far (0.00 D) and one to near vergence (-2.25 D). In this case (**Figure 4.16**, panel A), the synechial pupil yielded the worst results at far, since the simulated synechia is also covering part of the area for near vision. The circular and synechial pupils showed a greater peak at near vergence, since they present greater area for near vision. The elliptical pupil yielded better distance results, for similar reasons of dedicated areas and the aforementioned effect of the negative spherical aberration. The tolerance limit of 0.12 was exceeded in all cases. The centre-distance progressive multifocal (**Figure 4.16**, panel B) showed only one peak at far distance and a smooth decreasing towards negative vergences. For this profile, also the synechial pupil showed smaller values at far distance. With this design, the VSOTF performed under the limit of 0.12 beyond approximately vergence -0.50 D. As for the monofocal profile with only one peak at 0.00 D, the synechial pupil showed the worst results, whereas the elliptical yielded the highest value.

Figure 4.16. *Through-focus analysis of the visual Strehl ratio in the frequency domain (VSOTF) for the centre-distance bifocal (panel A), centre-distance progressive multifocal (panel B) and monofocal (panel C) designs.*

Figures 4.17 and **4.18** show the MTFs comparison for the multifocal designs for far (0.00 D), intermediate (-1.50 D) and near (-2.25 D) vergences. The bifocal lens (**Figure 4.17**) shows higher MTF values for far and near distances, whereas the progressive multifocal (**Figure 4.18**) yields greater values for distance and intermediate vergences, which is in consonance with previous metrics. **Figure 4.19** displays the simulation of an optotype line (0.2 logMAR and 100% contrast) for the multifocal designs for each considered pupil and confirms the whole preceding analysis.

Figure 4.17. *Two-dimensional modulation transfer function radial colour maps for the centre-distance bifocal design. The centre of the image represents 0 cy/deg. The radial distance is 60 cy/deg. The axes represent the modulation orientation in cy/deg. Rows represent the apertures: circular, elliptical and synechial, from left to right. Columns represent far (0.00 D), intermediate (-1.50 D) and near (-2.25 D) vergences, from top to bottom.*

Figure 4.18. *Two-dimensional modulation transfer function radial colour maps for the centre-distance progressive multifocal design. The centre of the image represents 0 cy/deg. The radial distance is 60 cy/deg. The axes represent the modulation orientation in cy/deg. Columns represent apertures: circular, elliptical and synechial, from left to right. Rows represent far (0.00 D), intermediate (-1.50 D) and near (-2.25 D) vergences, from top to bottom.*

Figure 4.19. *Simulated line of an optotype with white background and black letters corresponding to 0.2 logMAR visual acuity and 100% contrast. Lines were represented for the centre-distance bifocal (first set) and centre-distance progressive multifocal (second set) at far (0.00 D), intermediate (-1.50) and near (-2.25 D) vergences for the circular, elliptical and synechial pupils.*

4.2.4 Discussion

Previous studies have already demonstrated that the size of the pupil on multifocal optical elements is crucial (Madrid-Costa et al. 2015; Papadatou et al. 2017). The present work studied the effect of different pupil shapes on the optical performance of simulated CLs power profiles. The considered apertures acted as binary optical masks for an optical system with no aberrations (diffraction limited) as a first theoretical approach and for specific simulated optical solutions for presbyopia consisting of one centre-distance bifocal and one centre-distance progressive profile. The variations with respect to a normal circular shaped pupil were analysed in order to understand the distribution of light in one elliptical and one irregular pupil at different work distances.

Many MCLs are designed to increase the higher order aberrations in order to provide an increased depth of focus (Benard et al. 2011). As it has been previously mentioned, many MCLs include a determined value of spherical aberration depending on the design. In this study, the effect of the aperture on the PSF was represented and analysed. The results obtained with the simulations proposed here showed that the PSFs of the diffraction limited system with the non-circular shaped pupils of this study expanded (about 65%) compared to the circular aperture that encircles them, as the diameter gathering the 84% of light showed. This was expected since, theoretically, considering a given diameter, the diffraction spatial width increases with decreasing aperture. As an example, in the case of the elliptical pupil, the PSF is wider at the horizontal direction since the aperture at this meridian is smaller. The synechial pupil also showed a similar increase. The synechial aperture provided the most irregular PSF, which is in fact the one that presents narrower and irregular zones.

The shape of the pupil affects image formation (**Figures 4.12, 4.13** and **4.14**). Thus, an irregular pupil causes an irregular shape of the PSF. However, by analysing these previous images, only a qualitative assessment can be done. A quantitative evaluation is desirable, since it can describe the variations numerically. For this purpose, the D25 was introduced. In some cases, the elliptical and synechial apertures yielded better results in terms of compactness or VSOTF. This is due to the fact that the defined pupils are masking a part of the wavefront, since they were described within the circular 6 mm pupil. For this reason, the total area dedicated for each optical zone and whether it contributes to near or distance foci, must be considered (**Figure 4.10**). Indeed, the irregularly shaped pupils altered these percentages. As an example, for the multifocal contact lenses, the circular pupil uses 75% of its area for the near focus, and only 25% for far distance on the centre. These percentages change to 50%-50% respectively, for the elliptical aperture (**Table 4.1**), and a reduction of the total physical area. Besides, the effect of the added negative spherical aberration on the profiles is lower at the centre, which is why the elliptical design gives higher VSOTF and lower D25 values for distance, rather than for near. Similarly, the synechial pupil is masking part of the area dedicated both for distance and near foci, which is why it performs worse than the other two for distance, but better than the elliptical for near because the masked area is smaller for the synechial aperture. The total area of the pupil is also crucial, since a high reduction of the pupil total size would lead to reduced retinal illuminance and thus to lower contrast. This is, the irregularity of the shape of the pupil and its total area would combine to alter the image quality. In the present case, pupils with total areas larger than that of a 3 mm circular pupil were considered.

The masking effect has been used in recent research as a technique aiming to improve the visual quality of human subjects. Bonaque et al. presented an alternative method to correct an aberrated wavefront by changing the amplitude term of the pupil function instead of producing a full phase conjugation (Bonaque-González et al. 2016). In their case, the masking was induced in order to limit the light passing through those regions with strong aberrations. They reported an improvement of 19.8% in their results for highly aberrated eyes with respect to a circular 6 mm pupil. In the present case, the masking is supposed to be naturally acting due to the characteristics of the pupils considered. If the wavefront of the optical solution is thought as the needed correction over a circular pupil in order to achieve simultaneous vision, the masking effect is expected to cut part of this correction off and thus lose effectiveness. The circular pupil preserves the whole induced wavefront for the correction, whereas the non-circular pupils partially do not.

The two-dimensional MTF graphs were included instead of a radial averaged MTF, since the cut-off frequency varies across meridians for non-circular apertures. As an example, for the progressive multifocal design (**Figure 4.18**), the elliptical pupil performs better at 90 degrees of modulation orientation, which is actually the direction of the pupil with the greatest aperture size. The circular pupil showed rotationally symmetric MTF, since the generated wavefront was also rotationally symmetrical, whereas the other two pupils altered this behaviour. This loss of symmetry means that depending on the orientation of the object features, the loss of contrast is different for irregular pupils, which produces an effect similar to astigmatism or other non-rotationally symmetrical higher order aberrations (**Figure 4.19**).

The main purpose of the present study was to theoretically assess the effect of the pupil shape on physical metrics as a preamble to future investigation. Nevertheless, although these changes physically exist, other factors should be taken into account. The limitations of the used method include the calculation of metrics for a single wavelength, thus ignoring the effect of chromatic aberration. Also, we have used contact lenses profiles whose wavefront profiles are rotationally symmetric. The aberrations of the eye have not been considered, since this study only intended to investigate the effect on the performance of optical solutions for the correction of presbyopia with different pupil shapes. However, the aberrations do have an impact on the final image. Taking this consideration into account, the image quality has been shown as optimized for 2-3 mm diameter circular aperture in the human eye (Campbell and Gubish 1966). The calculations of the wavefront for the optical solutions were assumed to be at the pupil plane. It should be considered that both PSF and MTF are very sensitive for high quality optical systems, but the human eye is naturally aberrated and small changes of the PSF or MTF may not have a strong impact on vision, particularly for high frequencies (Bonaque-González et al. 2016). Besides, these simulations do not consider the movement of the lens that produces dynamic changes in the PSF, as well as those dynamic changes of the patient's pupil size. It should be taken into account that in those eyes with irregular pupils as a result of an ocular trauma or ocular conditions, the pupillary function (in terms of amplitude and latency) might also be altered and partially or even totally lost. In this aspect, the variations of the aperture at different distances might differ from those of a normal eye. Thus, the performance of the lens at different distances could be affected. The present study considered a static aperture for the analysis of the performance at different distances. Also, those eyes with irregular pupils may present other visual implications and increased ocular aberrations with respect to a normal eye due to the ocular trauma or inflammation response.

For all these reasons, clinical implications of these phenomena might differ from the real physical results. Neural adaptation, as well as the well-known Stiles-Crawford effect, together with the combination of the inner aberrations of the eye and other visual conditions that coexist with the irregular pupil, can all add up and yield different subjective perception which should be assessed in the future.

CHAPTER 5:

ASSESSMENT OF MULTIFOCAL INTRAOCULAR LENSES FOR PRESBYOPIA

5 ASSESSMENT OF MULTIFOCAL INTRAOCULAR LENSES FOR PRESBYOPIA

As well as with MCLs, the number of new MIOL designs is growing and the target public is also increasing. In this chapter, as in the case of MCLs, the effect of the pupil shape will be analysed by means of optical simulations. It is also important to evaluate the effect of decentration on the IOL performance, since as it was previously mentioned, the in-the-bag IOL placement can result in a desalignment, although IOL centration has been reported to be within the 0.1 to 0.3 mm range (Jung et al. 2000). Depending on the IOL design, some studies have shown that decentration can have an important effect on the optical quality provided by the lens (Altmann et al. 2005).

5.1 THE EFFECT OF NON-CIRCULAR SHAPED PUPILS AND DECENTRATION ON THE PERFORMANCE OF MULTIFOCAL INTRAOCULAR LENSES.

5.1.1 Background

Monofocal IOLs provide an excellent distance vision, but they do not provide spectacle independence. MIOLs aim to reduce the dependence on eyeglasses at different distances after lens extraction for cataract or presbyopic patients, since the correction with eyeglasses has been associated with a reduction in quality of life. As it occurs with MCLs, the vast majority of the MIOL designs are based on rotationally symmetric power profiles, taking into account the shape of the normal circular-shaped pupil. However, due to congenital or acquired conditions, the pupil may not be circular and it may have lost part of its functionality, which was discussed previously. As a reminder, ocular trauma or other disorders may also lead to shape alterations such as muscle spasms that lead to segmental iris mydriasis, giving an elliptical shape of the pupil (Thompson et al. 1983).

Previously, the optical performance of MIOLs in terms of refractive or diffractive technologies and its relationship to pupil size has been investigated, but the pupil shape has not been taken into account. Furthermore, the optical performance of an IOL is generally assessed at its centered position. However, it is also important to take into account that different factors can affect its final position inside the eye, such as the implantation technique, asymmetrical implantation, asymmetrical capsular shrinkage, capsule fibrosis, rupture of the posterior capsule or zonular dialysis, etc (Akkin et al. 1994; Sauer and Mester 2013; Findl et al. 2015). This misalignment may affect the retinal image quality depending on the design (Montés-Micó et al. 2012).

These alterations of the normal pupil shape and the final position in the capsular bag can have an impact on the performance of the lens. In other words, the optical elements may lose part of their effectiveness. The present study was conceived as theoretical approaches to investigate the optical quality of a given refractive MIOL design implanted in eyes with irregular shaped pupils. For these purposes, optical simulations were performed taking into account the influence of the pupil shape and its decentring.

5.1.2 Methods

Custom-made software was developed in MATLAB, which is based in Fourier-optics methods, and it was used for the simulations and calculations. This software has been already explained and described in detail in section **3.3.2**. For the decentered positions, a rotationally symmetric power map previously generated from the power profile is decentred in a given direction. Next, the wavefront error map is obtained via the reconstruction of semimeridional integrations taking the centre of the pupil as the chief ray, in order to fulfil the standard axis selection requirements (Applegate et al.

2000). Finally, a binary pupil mask is applied to the generated wavefront, corresponding to the given aperture, and the software calculates the optical metrics.

Pupil shapes

One circular (5-mm diameter) and one elliptical pupil stretched on its vertical direction were generated (**Figure 5.1**). The circular pupil was included for comparison purposes. The elliptical pupil had horizontal and vertical diameters of 3 and 5 mm, respectively. The apertures acted as optical masks that limit the light passing through. The wavelength of light for the calculations was 550 nm.

Figure 5.1. *Circular and elliptical apertures used for the simulations. The circular aperture is 5 mm in diameter. The elliptical pupil is 3 x 5 mm in diameter. The arrows represent the directions of decentring that have been analysed: horizontal (H) and vertical (V).*

MIOL power profile

One refractive MIOL power profile was considered, based on commercially available designs. The lens profile consists of a centre-distance optical zone with multiple annular areas alternating distance and near vision. The different dedicated zones for both the distance and near foci are shown in **Figure 5.2**. The power profile represented the base power of the lens at 0.0 D, with approximately +2.50 D of addition. The total optical zone was 6 mm in diameter.

Optical quality metrics

Numerical metrics were derived from the point spread function (PSF), such as the D25, which is described in the general methods section. The total amount of light was chosen to be the 25% in order to enhance the discernment between the different foci, since greater values would mask the variations between them. The PSF images were obtained for each pupil at the centred and decentred positions by 0.20 and 0.40 mm and for vergences 0 D (far), -1.25 D (intermediate) and -2.50 D (near).

The (VSOTF) was also included. This parameter has been used for describing visual performance because it shows a strong correlation with subjective methods. A threshold of 0.12 is usually set as the VSOTF value that corresponds to a visual acuity at which approximately half of the people present difficulties while reading (20/32 Snellen equivalent). Values above 0.12 are considered to be acceptable (Cheng et al. 2004; Marsack et al. 2004). It is important to point out that all the VSOTF calculations were normalized by the diffraction limited system for the ideal circular pupil, in order to observe the relative variations among the apertures.

A through-focus analysis for vergences ranging from +1.00 to -3.00 D in steps of 0.125 D was included. These vergences were taken as defocus and transformed to Zernike spherical defocus terms for a 5 mm diameter, which were then added to the wavefront of the lens. Also, through-decentering curves were calculated from 0.00 to 0.40 mm in steps of 0.04 mm and in two directions for each pupil: horizontal and vertical.

Additionally, optical simulations of a specifically designed object target with Snellen E letters have been obtained in order to characterize the lens as an image formation system. These patterns represent horizontally and vertically oriented E letters for visual acuities of 0.6 and 0.8 (12/20 and 16/20 respective Snellen fraction equivalents). The simulations have been included for the centred position and both horizontally and vertically decentred by 0.40 mm.

It has to be taken into account that this study is based on simulations for the characterization of the optical quality of a MIOL, which do not take into account the rest of the ocular aberrations, the Stiles-Crawford effect or the neural processes.

Figure 5.2. *Power profile of a given multifocal refractive annular intraocular lens. The total optical zone diameter is 6 mm. The base power is 0.0 D and the addition value corresponds to approximately +2.50 D.*

5.1.3 Results

The circular and elliptical apertures have been used for the analysis, together with the directions in which the considered lens was simulated to be decentred. Each combination of these apertures and directions has been used for a through-focus and decentring analysis. **Figures 5.3 and 5.4** gather the D25 results. It has to be taken into account that the smaller this parameter is, the more compact the 25% of the total energy is. The through-focus analysis graphs show two main valleys, which are related to the best foci corresponding to vergences 0.0 D and approximately -2.50 D, which corresponds to the lens addition. The through-focus analysis (**Figure 5.3**) for the centred position shows similar results for both pupils at the near focus, whereas the distance focus gives greater values for the circular pupil. However, it has to be pointed out that, even though the D25 parameter is similar for a given situation, the shape of the PSF can be different as it is shown later. With regards decentring, the graphs show that the near focus is more significantly reduced in terms of compactness than the distance focus, for both pupils. The through-decentring analysis (**Figure 5.4**) confirm that the near focus is more affected with decentring for the study lens, since there is a progressive increasing of the D25 parameter. The effect of the direction of decentring also has an impact on the metrics. This is more easily observable the greater the decentring value. In this sense, the elliptical pupil shows more slightly compact results of the PSF for both far and distance foci when the decentring was performed vertically. In this case, the D25 is increased from 1.65 to 3.87 arcmin. On the other hand, the through-decentring curve at far distance show results that remain more stable. The D25 values are significantly greater at intermediate distance with respect to the far and near vergences, suggesting that this lens design does not provide an acceptable intermediate focus.

Figures 5.5 and 5.6 shows the VSOTF results as a metric that been associated with subjective methods. On these graphs, the peaks represent the visual Sthrel ratio. In other words, the greater the peak, the greater the expected visual quality. As it can be observed from the through-focus VSOTF graphs (**Figure 5.5**), the lens yields two clearly differentiated peaks at 0.0 D and approximately -2.50 D. As for the centred position, both pupils show acceptable values greater than 0.12 for both foci, and they behave very similarly in their peak value reached for the near focus. However, the circular pupil yielded lower values, especially at the distance focus. The decentred through-focus charts show that the near focus is reduced with increasing decentring for both pupils, whereas the far focus varies more discreetly. The through-decentring graphs (**Figure 5.6**) give more detailed information about the far, intermediate and near distances for both pupils. As for the far focus, the elliptical pupil yields greater values than the circular, and its tolerance to decentring is shown to be slightly better in the vertical direction. With the circular aperture the VSOTF is reduced by 0.04 (from 0.17 to 0.13) with the maximum decentring value, as well as the horizontal decentring for the elliptical pupil (from 0.22 to 0.18). The vertical decentring for the elliptical aperture only changes by -0.02 for the VSOTF ratio (from 0.22 to 0.20) at far. The intermediate distance analysis confirms the poor quality at this vergence. With regards the near focus, both pupils provide a similar VSOTF and a decreasing trend with decentring. The robustness to decentring seems to be similar for both pupils for the near focus. The reduction is from approximately 0.27 to 0.04, 0.02 and 0.07 for the circular and the elliptical aperture with decentring in the horizontal and vertical directions, respectively. In this case, the values are below the 0.12 limit.

Figure 5.3. *Through-focus comparison curves for the D25 parameter between circular and elliptical (H: horizontal decentring, V: vertical decentring) apertures. The curves are represented for the centred and decentred positions by 0.20 and 0.40 mm.*

Figure 5.4. *Through-decentring comparison curves for the D25 parameter between circular and elliptical (H: horizontal decentring, V: vertical decentring) apertures. The curves are shown for vergences 0.0 D (far), -1.25 D (intermediate) and -2.50 D (near).*

Figure 5.5. *Through-focus comparison curves for the VSOTF parameter between circular and elliptical (H: horizontal decentring, V: vertical decentring) pupils. The curves are represented for the centred and decentred positions by 0.20 and 0.40 mm.*

Figure 5.6. *Through-decentring comparison curves for the VSOTF parameter between circular and elliptical (H: horizontal decentring, V: vertical decentring) pupils. The curves are shown for vergences 0.0 D (far), -1.25 D (intermediate) and -2.50 D (near).*

5.1.4 Discussion

In this study, we developed a theoretical method by means of optical simulations as an approximation to future modelling for predicting the optical quality of IOLs in eyes with irregular shaped pupils. The variations with respect to a normal circular shaped pupil were also analysed in order to understand the differences in behaviour. An annular bifocal refractive IOL design was chosen due to simplicity purposes. Pupil size has been reported to play a key role on the performance of many IOLs, as it has been previously stated. However, no studies have been performed about the effect of the pupil shape. Moreover, it is necessary to take into account that numerous factors, such as asymmetric implantation of the lens, asymmetrical capsular shrinkage, rupture of the posterior capsule, zonular dialysis or capsule fibrosis, can cause IOL decentration, and as a result may diminish retinal-image quality. For this reason, we also simulated the effect of decentration.

The shape of the pupil affected the metrics and the image formation. Additionally, the direction of decentring also had an impact on the metrics for the elliptical pupil. Specifically, the D25 and VSOTF curves showed discrepancy between the horizontal and vertical decentring directions, and this difference was slightly greater with increasing decentring value (**Figures 5.3 to 5.6**). This is because the ratio of the distance/near power distribution for a given decentring value across the pupil is different depending on the decentring direction when the aperture is not circular. Thus, the contribution of each power is altered and one focus is penalized more than the other. As for the circular aperture, the ratio is the same for the same decentring value when the lens is rotationally symmetric, although the local power at each point with horizontal or vertical decentring is different. This is why, although the D25 and VSOTF curves for the circular pupil are the same no matter the direction of decentring, the PSFs are differently oriented but equal in shape (**Figure 5.7**). In the case of the elliptical pupil, since the ratio is different, the orientation of the PSF is different but there is also a slight difference in shape. Also, it is easily observable how the elliptical pupil outperformed the circular especially for the distance focus, whereas the differences between pupils are more discreet for the near focus. This is explained by the masking effect that the elliptical pupil is causing at the borders, not letting light pass through this area as it would happen with the circular aperture. However, the counterpart is that the retinal illuminance would be lower. Then, the final contrast of the image could be affected. The two-dimensional MTF graphs were included in a similar analysis of that of the PSF (**Figure 5.8**). These graphs are of special interest since, for a non-circular aperture as it was previously stated in the case of MCLs, the cut-off frequency differs between the greatest and smallest meridional diameter, which in fact provides a non-symmetrical MTF even for a system without aberrations. A non-symmetrical MTF means that depending on the orientation of the object features, the loss of contrast is different. Object features oriented normally to the dominant direction of the two-dimensional MTF are perceived with higher contrast. The symmetry of the MTF performed best for the centred position for both the distsance and near vergences. Decentring produced a generalized loss of contrast, which was more accused for the near focus. The optical simulations of Snellen E letters depict the effect of the different pupils and their direction of decentring (**Figure 5.9**). Decentring in fact produced a loss of contrast in the images for both pupils especially at the near focus, explained by the previous analysis.

Figure 5.7. *Point spread function comparison between circular and elliptical pupils. The images are shown for the centred position, as well as for decentring values by 0.20 and 0.40 mm. The analysed vergences correspond to 0.0 D (far), -1.25 D (intermediate) and -2.50 D (near). The small pupil images indicate the shape and the direction of decentring for each set of images. The size of the images is 20 arcmin in diameter.*

Figure 5.8. *Two-dimensional modulation transfer function comparison between circular and elliptical pupils. The images are shown for the centred position, as well as for decentring values by 0.20 and 0.40 mm. The analysed vergences correspond to 0.0 D (far), -1.25 D (intermediate) and -2.50 D (near). The small pupil images indicate the shape and the direction of decentring for each set of images. The centre of the image represents 0 cy/deg. The radial distance is 60 cy/deg.*

In line with our results with regard decentring, several IOL designs have been reported to be affected on its optical performance with different methods. Soda and Yaguchi (Soda and Yaguchi 2012) evaluated different types of multifocal IOLs (ReSTOR SA60D3, Alcon; TECNIS Multifocal ZM900, AMO; ReZoom, AMO; SFX-MV1, Hoya). They performed measurements of the MTF with decentration from 0 to 1.0 mm using a simulated eye. The ReSTOR SA60D3 was affected by decentration at near distance. With regard to the TECNIS ZM900, the optical quality started to decrease with increasing decentration. However, for the ReZoom and SFX-MV1, decentration up to 0.75 mm did not cause a significant decrease in quality. These findings show that the design of the lens plays a main role in its tolerance to decentration. Nevertheless, all these designs were analysed with circular apertures, although irregular apertures are also expected to be affected by decentring as in our results.

It is also important to take into account the pupil dynamics effect. Diffractive and hybrid models have been proven to be less affected by pupil diameter (Madrid-Costa et al. 2010). Thus, dynamic changes of the pupil size result in higher ocular aberrations for refractive IOLs. The average pupil size in patients over 60 years are considered to be between 3.0 mm (photopic conditions) and 4.5 mm (mesopic conditions) (Koch et al. 1991). This is applicable for normal round-shaped pupils. In the case of irregular pupils, the behaviour can be different. Multifocal lenses take benefit of the dynamic variations of the pupil with different levels of illumination or the observation distance. It should be taken into consideration that in those eyes with irregular pupils, as a result of an ocular trauma or other ocular conditions, the pupillary function may also be altered and partially or totally lost in terms of amplitude and latency. Also, those eyes with irregular pupils may present other visual implications and increased ocular aberrations with respect to a normal eye due to coexisting alterations. In this study, we considered a static pupil with no variations for every vergence analysis, trying to simulate an altered pupillary function with no dynamic changes.

Figure 5.9. *Simulated images representing horizontally and vertically oriented Snellen E letters corresponding to visual acuities of 0.6 and 0.8 (12/20 and 16/20 respective Snellen fraction equivalents). Images are shown for the centred position, as well as for decentring values by 0.40 mm. The analysed vergences correspond to 0.0 D (far) and -2.50 D (near). The small pupil images indicate the shape and the direction of decentring for each set of images.*

Besides decentring, there is an important consideration that should be added in future studies in order to assess the quality of IOLs. It would be interesting to assess the effect of tilt, since it could also take place during the surgical procedure and it has been reported to affect the optical performance of the lenses (McKelvie et al. 2011). Besides, further studies should be carried out in order to evaluate the coupling effect of different corneal profiles with different aberrations, with the purpose of obtaining clearer conclusions. The limitations of the used method include the calculation of metrics for a single wavelength, thus ignoring the effect of chromatic aberration. Also, the method used a refractive model IOL since conversion to wavefront error maps needed to be calculated from power measurements. However, this method could be used with any wavefront error measurements of more modern designs.

Clinical implications of these phenomena and their correlation with our findings should be more carefully investigated. It has been shown that there are physical changes of the optical quality metrics that depend on the pupil shape and the direction of decentring, although the impact that these variations might have on vision cannot be directly inferred. Besides, small changes of the PSF may not have a strong impact on vision, particularly for high frequencies (Bonaque-González et al. 2016). Neural adaptation, as well as the well-known Stiles-Crawford effect, together with the combination of the corneal and inner aberrations of the eye and other visual conditions that coexist with the irregular pupil, can all combine and yield different subjective perception which should be assessed in future investigation. All these are important considerations although they are beyond the aim of this study, which was to isolate the effect of the shape of the pupil in the optical quality of the IOL at different centration conditions.

CHAPTER 6:

CLINICAL EVALUATION OF LIGHT DISTORTION WITH OPTICAL SOLUTIONS FOR PRESBYOPIA

6 CLINICAL EVALUATION OF LIGHT DISTORTION WITH OPTICAL SOLUTIONS FOR PRESBYOPIA.

6.1 LIGHT DISTORTION OF SOFT MULTIFOCAL CONTACT LENSES WITH DIFFERENT PUPIL SIZES AND SHAPES.

6.1.1 Background

The number of users of MCLs has been rising due to the increasing popularity of these solutions as a modality to correct presbyopia (Morgan et al. 2011). Most of the current MCLs designs are based on simultaneous image formation. In this sense, the optical principle used by these optical solutions is based on the projection of multiple images due to different powers (Pérez-Prados et al. 2017). However, this principle can imply visual side effects, such as an augmented sensitivity to disability glare or the presence of haloes, especially under low light conditions due to the increased pupil size. Earlier studies have reported such visual side effects with MCLs (both RGP and soft MCLs) (Rajagopalan et al. 2007; Wahl et al. 2017). Increased disturbing photic phenomena can be an obstacle to perform everyday tasks, such as night driving or driving with a low sun. This can result in a reduction of the quality of life. Furthermore, these disturbances are not easily distinguishable, and they can have different impacts on the subjective visual quality (Klyce 2007).

The vast majority of the simultaneous image formation designs are based on concentric annular areas with a central circular optical zone surrounded by one or more annular zones, which yield rotationally symmetric power profiles (Bennett 2008; Bradley et al. 2014). These designs are well related to the shape of a normal circular pupil. However, due to congenital or acquired conditions, the pupil may not be circular and it may have lost part of its functionality. Ocular trauma or other disorders may also lead to shape alterations such as muscle spasms that lead to segmental iris mydriasis, giving an elliptical shape of the pupil, as it has been referred to in previous chapters (Thompson et al. 1983).

In the past, the light disturbances effects have been widely investigated for intraocular lenses and refractive surgery (Villa et al. 2007; Salgado-borges et al. 2015; Buckhurst et al. 2017; Escandón-García et al. 2018), but it was not that common for MCLs. Recently, the influence of MCLs on the light distortion effects has become of special interest. In this sense, the optical performance of MCLs in terms of light distortion and its relationship to pupil size has been recently investigated, but the pupil shape has not been taken into account, which will be also discussed in this study.

6.1.2 Methods

A detailed description of the LDA instrument can be found in the methods chapter (**section 3.2.1**). This instrument can be extremely useful in order to characterize the light distortion under different conditions, such as the size or shape of the pupil of the subjects, and for those patients wearing different types of multifocal solutions for presbyopia.

Multifocal contact lenses

The selected lenses for the study were the monthly disposable Biofinity Multifocal and Biofinity single vision, which are made of the same polymer (Omafilcon A, CooperVision, CA, USA). The corresponding single vision or monofocal version was also included in order to compare the light disturbances with respect to the multifocal and thus avoid the possible effects of the material on the distortion. The Biofinity multifocal is available in “D” and “N” designs. The “D” design provides the distance correction at the centre of the lens, whereas the “N” design does so in the periphery while the central area is devoted to the near vision. In this study, an addition power of

+2.50 D was selected for both "D" and "N" designs. Information about the power profiles of these designs can be found elsewhere (Plainis et al. 2013).

Pupils

A total of three pupils were used in order to perform the measurements. Specifically, round pupils of 3 mm (P1) and 5 mm (P2) were used. Also, one non-circular shaped pupil was included, consisting of an aperture of 3 mm in the horizontal and 5 mm in the vertical direction (P3). These pupils were cut by laser and were mounted on a trial frame, which was carefully adjusted. **Figure 6.1** shows the pupil designs that were used for the examination. The material of these pieces (cardboard) avoided internal edge reflections that could alter the results.

Figure 6.1. *Artificial pupils that were used for examination. From left to right, the pupils are 3 mm, 5 mm and 3x5 mm in size.*

Patients

A total of 14 eyes of 7 healthy CL wearer patients (3 females and 4 males) aged 25 to 40 years (mean and standard deviation 29 ± 8 years) were measured. The distance correction of the patients ranged from -1.00 D to +0.50 D (mean spherical equivalent -0.15 ± 0.50 D), and refractive astigmatism was not greater than -1.00 D. In the first visit, the subjects were informed about the details of the study, and a formal consent was obtained after written and verbal explanation of the implications. The patients were asked to sit at a distance of 2 metres away from the LDA instrument. The chair was adjusted so that the height of the central light source was coincident with the height of the eyes of the patient. In this situation, room doors were closed and lights shut down, and only the central light source of the LDA was turned on. The subject had to look at it (both eyes open) and the VIP-300 pupilometer (NeurOptics, CA, USA) was used to measure the natural pupil size under such conditions. This previous step was performed in order to assure that the natural pupil of the patient was greater than the artificial apertures that were going to be placed on the trial frame. The patient was in the dark for about one minute before the exam. If further pupil dilation occurred during the test, this is not expected to affect the measurements as the artificial pupil limits the aperture. Also in this visit, the sensory eye dominance was determined with a positive lens of +2.00 D. This is of special interest in the case of multifocal lenses, so that the dominant eye (DE) wore the corresponding “D” design and the fellow eye (NDE) the “N” design. Patients with still functional accommodation were selected since multifocal lenses are intended to assist and work together with the remaining accommodation of the eye. They are not presbyopes cause the goal of this study was not to assess the performance of the lenses but the influence of the artificial pupil when combined with the lens design. Furthermore, measuring younger eyes ensured ocular media transparency to avoid further confounding effects that might affect light scattering. An anamnesis and ocular examination revealed that the subjects of the study had no ocular abnormality, pupillary dysfunction or systemic condition, no ocular surgery history and they all presented clear intraocular media. Their spherical equivalent was obtained to order the lenses. Their best corrected visual acuity was 20/20 or better.

Measurement protocol

Once the patients were confirmed to be suitable for the study, two more visits in two different days were required, with a minimum of one day to rest in between. In each of these visits, single vision or multifocal lenses were selected for the patient randomly. The patients were given the lenses, put them in and waited for 15 minutes for stabilization before examination. After this, whole eye aberrometry was obtained with the IRX-3 Wavefront Aberrometer (Imagine Eyes, Orsay, France) and the fourth order spherical aberration with the lenses was obtained. Next, the measurements with the LDA were performed. For this purpose, the patients sat on the adjustable chair with the corresponding height as in the first visit. Trial frames were used in order to place the artificial apertures, together with a +0.50 D to compensate for the distance from the LDA (2 metres) to avoid accommodation effects. From this point, the examination was ready to start. The apertures were put on the frame randomly in monocular conditions, alternating also between both eyes. The centre of the artificial apertures was adjusted with respect to the centre of the pupil of the patients. All the measurements were obtained in dark conditions. In this study, the in-out strategy of the LDA has been used, in which the radial light sources turn on sequentially from the centre towards the periphery until detection. The light distortion was evaluated in steps of 30 degrees around 360 degrees. The central light source was set to the 100% of its total intensity in order to create the maximum light distortion effects, whereas the peripheral sources were set to 10% for detection. This percentage was chosen as a significant intensity difference, but not very small that it was hardly detected even under normal conditions.

Light disturbance metrics

The native software of the instrument provides different metrics for the characterization of the light disturbance pattern. The metrics that have been used for this purpose and that will be analysed are the following: Distortion area (DA), Light Distortion Index (LDI), Best fit circle radius (BFCr), Best fit circle irregularity standard deviation (BFCirregSD). Besides, the distance to the origin (DO) has been calculated from the x- and y-coordinates of the centre of the BFC. These metrics are explained in **section 3.2.1**.

Additionally, the custom-made MATLAB software described in **section 3.3.1**. has been used for the calculation of the size of the distortion at each of the orientations that were assessed, named as M0 (horizontal), M30, M60, M90 (vertical), M120 and M150. These parameters were converted to angular size, considering the distances between the test light sources, the distance from the instrument and the nodal points of the eye to be located by 5.6 mm behind the cornea. The meridional angular size has been calculated as the sum of the modulus of each pair of corresponding semimeridians. These metrics are used to observe the dominant direction of the light distortion. The difference between M90 and M0 was also calculated in order to study the effect of the pupil shape. These orientations were selected because they are associated to the maximum and minimum aperture sizes of the elliptical pupil, respectively. **Figure 6.2** shows a graph generated by means of the custom-made software showing the sizes for each meridian.

Figure 6.2. *Light disturbance data points of a given patient. Coloured lines at each meridian correspond to the size of the light disturbance.*

Statistical analysis

The total number of eyes were divided into two samples, DE and NDE. With this, each of the samples consisted of 7 measurements for each dependent variable. The statistical analysis was performed with SPSS software (version 24.0, SPSS Inc., Chicago, IL, USA). Mean and standard deviation were obtained as descriptive parameters. Due to the small number of eyes, assumption of normality could not be achieved for most of the difference scores of the samples. Three sets of pair comparisons were designed related to lens type (single vision or monofocal versus multifocal), pupil, and design of the lens. Thus, for comparisons within the same group of eyes (DE-DE or NDE-NDE), the non-parametric test of Wilcoxon for paired samples was applied, with statistical significance defined as $p<0.05$. In the case the comparisons were performed between groups (DE-NDE), the Mann-Whitney test was used, also with statistical significance defined as $p<0.05$.

6.1.3 Results

Several pair comparisons of interest were selected and classified into three sets according to lens type (single vision or monofocal versus multifocal), type of pupil and multifocal design (D or N). **Tables 6.1 and 6.2** gather all the mean and standard deviation values of all the light disturbance variables and the calculated meridional angular sizes. **Table 6.3** shows the results of spherical aberration for P1 and P2, since P3 is non-circular and a Zernike coefficient cannot be obtained. In table **6.4**, the p-values of the aforementioned analysis are presented. Additionally, **table 6.5** exhibits the differences in angular size between the vertical and horizontal directions and the corresponding p-values of the meridional pair comparisons, that is, M90-M0.

LDI (%)		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	**P1**	3.68 ± 1.45	4.02 ± 0.62
	P2	3.68 ± 0.25	2.91 ± 1.29
	P3	3.98 ± 1.25	3.18 ± 0.86
MULTIFOCAL	**P1**	4.54 ± 2.00	3.91 ± 0.16
	P2	6.09 ± 3.28	4.72 ± 0.92
	P3	5.47 ± 2.20	5.03 ± 1.06
DO (mm)		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	**P1**	0.38 ± 0.30	0.59 ± 0.67
	P2	0.10 ± 0.25	0.55 ± 0.56
	P3	0.93 ± 0.69	0.25 ± 0.36
MULTIFOCAL	**P1**	0.95 ± 0.90	0.19 ± 0.33
	P2	1.47 ± 1.10	1.23 ± 1.14
	P3	1.33 ± 1.07	1.25 ± 0.90

BFCr (mm)		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	**P1**	15.44 ± 3.38	16.37 ± 1.20
	P2	15.71 ± 0.52	13.61 ± 3.51
	P3	16.11 ± 2.50	14.57 ± 1.94
MULTIFOCAL	**P1**	17.16 ± 3.45	16.20 ± 0.34
	P2	19.60 ± 4.77	17.63 ± 1.52
	P3	18.74 ± 3.52	18.19 ± 1.86

BFCIRREGSD (mm)		DOMINANT	NON-DOMINANT
MONOFOCAL	P1	2.43 ± 1.78	1.98 ± 1.39
	P2	0.75 ± 1.31	1.46 ± 1.41
	P3	2.34 ± 1.66	1.65 ± 2.07
MULTIFOCAL	P1	2.29 ± 1.83	0.61 ± 1.04
	P2	2.68 ± 1.44	2.27 ± 1.16
	P3	2.97 ± 2.16	2.20 ± 1.53

Table 6.1. *Mean ± standard deviation of light disturbance parameters: Light disturbance index (LDI), Distance to the origin (DO), Best fit circle radius (BFCr) and Best fir circle irregularity standard deviation (BFCirregSD). The results are shown for both single vision (monofocal) and multifocal contact lenses, for the dominant and non-dominant eyes, and for the three different pupils: 3 mm diameter (P1), 5 mm diameter (P2) and the elliptical pupil of 3x5 mm (P3).*

M0		DOMINANT	NON-DOMINANT
MONOFOCAL	P1	0.82 ± 0.18	0.95 ± 0.16
	P2	0.91 ± 0.00	0.82 ± 0.18
	P3	1.01 0.18	0.82 ± 0.18
MULTIFOCAL	P1	1.08 ± 0.25	0.91 ± 0.00
	P2	1.18 ± 0.33	0.98 ± 0.11
	P3	0.98 ± 0.29	0.98 ± 0.11
M30		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	P1	0.91 ± 0.23	0.91 ± 0.00
	P2	0.85 ± 0.17	0.72 ± 0.21
	P3	0.98 ± 0.22	0.82 ± 0.18
MULTIFOCAL	P1	0.91 ± 0.13	0.95 ± 0.09
	P2	1.04 ± 0.29	0.98 ± 0.11
	P3	1.08 ± 0.17	1.04 ± 0.18
M60		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	P1	0.91 ± 0.29	0.91 ± 0.00
	P2	0.88 ± 0.09	0.82 ± 0.26
	P3	0.95 ± 0.16	0.85 ± 0.17
MULTIFOCAL	P1	0.98 ± 0.17	0.95 ± 0.09
	P2	1.14 ± 0.26	0.98 ± 0.11
	P3	1.14 ± 0.26	1.11 ± 0.16

M90		DOMINANT	NON-DOMINANT
MONOFOCAL	P1	0.95 ± 0.21	1.01 ± 0.18
	P2	0.91 ± 0.00	0.75 ± 0.22
	P3	0.85 ± 0.17	0.88 ± 0.09
MULTIFOCAL	P1	1.01 0.29	0.91 ± 0.00
	P2	1.18 ± 0.24	1.08 ± 0.17
	P3	1.21 ± 0.25	1.08 ± 0.17
M120		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	P1	0.82 ± 0.18	0.88 ± 0.16
	P2	0.91 ± 0.00	0.82 ± 0.18
	P3	0.85 ± 0.11	0.82 ± 0.12
MULTIFOCAL	P1	0.95 ± 0.21	0.91 ± 0.00
	P2	1.11 ± 0.33	0.98 ± 0.11
	P3	1.01 0.26	1.01 0.12
M150		**DOMINANT**	**NON-DOMINANT**
MONOFOCAL	P1	0.88 ± 0.21	0.95 ± 0.09
	P2	0.91 ± 0.00	0.75 ± 0.22
	P3	0.88 ± 0.21	0.82 ± 0.12
MULTIFOCAL	P1	0.95 ± 0.24	0.91 ± 0.00
	P2	1.08 ± 0.25	1.04 ± 0.12
	P3	1.01 ± 0.18	1.01 ± 0.12

Table 6.2. *Mean ± standard deviation of light disturbance angular size across meridians from the horizontal (0 degrees, M0) to 150 degrees (M150), in steps of 30 degrees. The results are shown for both single vision (monofocal) and multifocal contact lenses, for the dominant and non-dominant eyes, and for the three different pupils: 3 mm diameter (P1), 5 mm diameter (P2) and the elliptical pupil of 3x5 mm (P3).*

By lens type, the results showed statistically significant differences. More specifically, the comparison relative to P2 for the DE (P2monofocalDE-P2multifocalDE) yielded differences for the LDI, DO and BFCr and spherical aberration. Indeed, the spherical aberration changed from 0.04 ± 0.05 µm to 0.22 ± 0.11 µm, becoming more positive (**Table 6.3**). According to the NDE, the statistically significant differences were obtained for pair comparison involving pupils P2 and P3. Precisely, the analysis of P2 and P3 (P2monofocalNDE-P2multifocalNDE and P3monofocalNDE-P3monofocalNDE) showed such differences for the LDI and BFCr, but not for P1. In relation to the NDE, the spherical aberration was found to be significantly different for P1 between single vision and multifocal lenses. This value changed towards negative values, from 0.02 ± 0.01 µm to -0.04 ± 0.03 µm (**Table 6.3**). In general, the size of the light disturbance was greater with multifocal than with single vision lenses. As for the meridional analysis in this set of comparisons, the most affected direction was M90, which resulted statistically significantly different between single vision and multifocal lenses for both the DE and NDE with P2 and P3 ($p<0.05$).

Spherical aberration (µm)		DOMINANT	NON-DOMINANT
SINGLE VISION	P1	0.01 ± 0.01	0.02 ± 0.01
	P2	0.04 ± 0.05	0.05 ± 0.07
MULTIFOCAL	P1	0.03 ± 0.03	-0.04 ± 0.03
	P2	0.22 ± 0.11	-0.06 ± 0.16

Table 6.3. *Mean ± standard deviation of spherical aberration coefficients. The results are shown for both single vision and multifocal contact lenses, for the dominant and non-dominant eyes, and for the three different pupils: 3 mm diameter (P1), 5 mm diameter (P2) and the elliptical pupil of 3x5 mm (P3).*

The analysis of the pupil factor (only performed for the MCLs) revealed some significant differences. The greatest differences were obtained for the pair comparison including P1 and P2 for the multifocal dominant design (P1multifocalDE-P2multifocalDE), which yielded differences in the LDI, BFCr and the spherical aberration, with greater disturbance size for P2. The spherical aberration changed from 0.03 ± 0.03 µm to 0.22 ± 0.11 µm. Nevertheless, it is also worth highlighting that comparisons between P1 and P3 yielded limit values for significance ($p=0.05$). Particularly, the LDI regarding the comparisons between P1 and P3 for both the DE and NDE gave limit values, and also did the DO and BFCr but only for the NDE. In average, the disturbance was greater with P3 than with P1 for both the DE and NDE. An additional analysis was performed in order to compare the differences in size of the light disturbance between the vertical and horizontal directions M90 and M0, for all pupils with MCLs. The greatest and only statistically significant difference was obtained for the P3 with the multifocal D design, in which the difference resulted in 0.23 degrees (**Table 6.5**).

With regard to the MCL design (D and N), the differences were only found to be statistically significant for the spherical aberration, but not for the light disturbance metrics. The spherical aberration coefficient in the DE with P1 changed from 0.03 ± 0.03 µm to -0.04 ± 0.03 µm, whereas in the case of P2 it varied from 0.22 ± 0.11 µm to -0.06 ± 0.16 µm for D and N designs, respectively. The coefficient became more negative and greater in modulus for the NDE with greater aperture size. Likewise, it was more positive and greater in modulus for the DE with greater pupil.

Also, a graphical comparison of the different pupil sizes and shape was obtained. **Figures 6.3** and **6.4** depict the box-whisker plots for the pupil comparison among single vision and multifocal groups, corresponding to the evaluated disturbance parameters DO, LDI, BFCr and BFCirregSD. Red lines represent the median values for each of the samples. In **Figure 6.5**, the pupil comparison is shown for the average of the different evaluated directions of the light distortion for the MCLs.

		LDI	DO	BFCr	BFCirreg SD	SA
LT	**P1monofocalDE - P1multifocalDE**	0.29	0.15	0.29	0.93	0.19
	P2monofocalDE - P2multifocalDE	0.03*	0.03*	0.03*	0.05	0.03*
	P3monofocalDE - P3multifocalDE	0.12	0.46	0.12	0.35	-
	P1monofocalNDE - P1multifocalNDE	0.48	0.11	1.00	0.05	0.03*
	P2monofocalNDE - P2multifocalNDE	0.03*	0.08	0.03*	0.35	0.13
	P3monofocalNDE - P3multifocalNDE	0.03*	0.05	0.03*	0.75	-
P	**P1multifocalDE - P2multifocalDE**	0.03*	0.35	0.03*	0.75	0.02*
	P1multifocalDE - P3multifocalDE	0.05	0.25	0.08	0.75	-
	P2multifocalDE - P3multifocalDE	0.46	0.46	0.46	0.6	-
	P1multifocalNDE - P2multifocalNDE	0.07	0.07	0.07	0.07	0.35
	P1multifocalNDE - P3multifocalNDE	0.05	0.05	0.05	0.08	-
	P2multifocalNDE - P3multifocalNDE	0.35	0.92	0.34	0.75	-

MD	**P1multifocalDE - P1multifocalNDE**	0.77	0.09	0.77	0.06	0.03*
	P2multifocalDE - P2multifocalNDE	0.56	0.64	0.52	0.30	0.03*
	P3multifocalDE - P3multifocalNDE	1.00	0.77	0.95	0.33	-

		M0	**M30**	**M60**	**M90**	**M120**	**M150**
LT	**P1monofocalDE - P1multifocalDE**	0.04*	1.00	0.72	0.67	0.20	0.46
	P2monofocalDE - P2multifocalDE	0.07	0.06	0.04*	0.04*	0.10	0.10
	P3monofocalDE - P3multifocalDE	0.66	0.26	0.11	0.03*	0.20	0.20
	P1monofocalNDE - P1multifocalNDE	0.28	0.32	0.32	0.18	1.00	0.32
	P2monofocalNDE - P2multifocalNDE	0.10	0.04*	0.18	0.04*	0.07	0.04*
	P3monofocalNDE - P3multifocalNDE	0.10	0.07	0.04*	0.04*	0.04*	0.07
P	**P1multifocalDE - P2multifocalDE**	0.18	0.10	0.06	0.07	0.07	0.21
	P1multifocalDE - P3multifocalDE	0.18	0.06	0.06	0.14	0.32	0.16
	P2multifocalDE - P3multifocalDE	0.04*	0.71	1.00	0.78	0.41	0.32
	P1multifocalNDE - P2multifocalNDE	0.16	0.56	0.56	0.59	0.16	0.05
	P1multifocalNDE - P3multifocalNDE	0.16	0.18	0.10	0.06	0.08	0.08
	P2multifocalNDE - P3multifocalNDE	1.00	0.32	0.05	1.00	0.32	0.32
MD	**P1multifocalDE - P1multifocalNDE**	0.06	0.59	0.89	0.53	1.00	1.00
	P2multifocalDE - P2multifocalNDE	0.20	0.77	0.90	0.45	0.79	0.61
	P3multifocalDE - P3multifocalNDE	0.42	0.67	0.70	0.31	0.61	0.59

Table 6.4. *Pair comparison p-values of attending to lens type (LT), pupil (P) and multifocal design (MD). Different comparisons include the dominant (DE) and non-dominant (NDE) eyes. Three different pupils are considered: 3 mm diameter (P1), 5 mm diameter (P2) and the elliptical pupil of 3x5 mm (P3). SA: spherical aberration. * Statistically significant differences.*

	DOMINANT	NON-DOMINANT
P1	-0.07 [1.01-1.08] p=0.41	0.00 [0.91-0.91] p=1.00
P2	0.00 [1.18-1.18] p=1.00	0.10 [1.08-0.98] p=0.26
P3	0.23 [1.21-0.98] p=0.02*	0.10 [1.08-0.98] p=0.08

Table 6.5. *Differences in average angular size (degrees) between the vertical and horizontal directions [M90-M0], and the corresponding p-values of the meridional pair comparisons. The results are shown for the multifocal contact lenses, for the dominant and non-dominant designs, and for the three different pupils: 3 mm diameter (P1), 5 mm diameter (P2) and the elliptical pupil of 3x5 mm (P3). * Statistically significant differences.*

Figure 6.3. *Light disturbance parameters (Light distortion index and distance from centre) comparison among single vision (monofocal) and multifocal groups with different pupil sizes and shape. DE: dominant eye. NDE: non-dominant eye. Red lines in the boxes represent the median value. Red crosses represent outlier data.*

Figure 6.4. *Light disturbance parameters (Best fit circle radius and best fir circle irregularity standard deviation) comparison among single vision (monofocal) and multifocal groups with different pupil sizes and shape. DE: dominant eye. NDE: non-dominant eye. Red lines in the boxes represent the median value. Red crosses represent outlier data.*

Figure 6.5. *Meridional angular size comparison of light disturbance with multifocal contact lenses and different pupil sizes and shape. Error bars are not shown for visualization purposes. The standard deviations for each meridian can be found in table 6.2.*

6.1.4 Discussion

In this work, the effect of different pupil sizes and shapes was assessed in terms of the induced light distortion pattern. This is a matter of special interest for those MCLs wearers, who may find their quality of vision compromised. Besides, ocular trauma or other ocular conditions can result in an irregular or a noticeable non-circular shape of the pupil. For this reason, two different designs of MCL were included and the distortion pattern was evaluated with two circular pupils of 3 mm and 5 mm, together with an elliptical shape of 3x5 mm (**Figure 6.1**).

As a first approach, a comparison between the single vision and the multifocal designs (centre distance D and centre near N) of commercially available lenses was performed. In light of our results, the MCLs induced a generalized increasing of the LDI (and thus, the distortion size) with all kind of pupils (**Table 6.1**). The only exception was found for the NDE with P1, however this difference was small and it was not found to be significant, which can be attributed to other factors or data variability due to small sample size. The highest values of LDI were obtained for the DE, with more pronounced differences than the NDE. More specifically, the greatest statistically significant difference in LDI was obtained for the DE with P2. Indeed, in terms of total area, P2 is the one that lets the biggest amount of light in. Considering this, the values of the spherical aberration changed with increasing pupil size (**Table 6.3**). In fact, the biggest difference of spherical aberration between single vision and MCLs was obtained with P2 for the DE, with greater spherical aberration with MCLs. This means that multifocality itself, induced by the optical design of the lenses, causes a greater light disturbance. The BFCr behaved similarly, since the greater the size of the disturbance, the greater the radius of the BFC is. The DO only yielded significant differences for the DE with P2. However, the greatest average value corresponding to the DE with P2 was very small (1.47 mm) with high variability, so this parameter does not seem to be generally significantly affected (**Table 6.1**). With regard to the BFCirregSD, in general, it tended to be greater for MCLs with P2 and P3, although the differences were not statistically significant. Nevertheless, this can be explained by the fact that, as the distortion increases in size with increasing pupil, the interaction with the optical properties of the lens and the ocular inner aberrations is higher, which can result in increased odds of getting differences across meridians. In an attempt to characterize the variability across meridians more thoroughly rather than getting a general indicator (such as the BFCirregSD), the meridians were analysed separately. In this sense, the meridian that was more commonly affected among comparisons between single vision and MCLs was the vertical direction, this is, M90 (aligned with the larger aperture size for the elliptical pupil P3). Certainly, the differences were significant for comparisons with P2 and P3, for both the DE and the NDE (**Table 6.4**). In order to analyse the possible reasons of these results, an important consideration is that the single vision and MCLs of this study were made out of the same polymer. This is motivated by the necessity to control the possible effects of the material on the distortion, since some of them might imply higher dispersion properties than others. By choosing the same materials for the comparison between single vision and MCLs, this factor does not contribute to our findings.

The pupil was also investigated as a possible factor to influence the light disturbance metrics with MCLs. This evaluation considers not only the size of the pupil but also its shape. In terms of LDI and BFCr, the comparison between P1 and P2 for the DE yielded statistically significant differences, with greater values for P2, as well as the spherical aberration. This means that the pupil size plays a significant role on the light distortion size for the D multifocal design. Also, although the differences between P1 and P2 for the NDE were not statistically significant, the distortion was also increased in average (**Table 6.1**). Interestingly, differences between P1 and P3 for both the DE and NDE yielded limit significance values of LDI, whereas differences between P2 and P3 were not high. Nevertheless, although the size of the disturbance changes with the pupil size or its total area, the shape of the disturbance can be different among pupils. A first step is considering the BFCirregSD. This parameter, however, did not show statistically significant differences for any pair comparison. In spite of this, the greatest BFCirregSD was obtained for P3 with the multifocal D design. This result might be anticipated considering that P3 condition represents an elliptical pupil. For confirmation, a more thorough approach was adopted taking into account the shape of the non-circular pupil, so the difference between M90 and M0 are of special interest due to their association with the maximum and minimum aperture sizes of P3. This analysis showed that the shape of the pupil might have an impact on the shape of the light distortion, since the differences between M90 and M0 only turned out to be significant with P3 for the D multifocal design, which yielded the greatest difference value, in accordance to the previous greatest BFCirregSD. The results for the N design did not yield statistically significant differences. However, the p-value for P3 was the lowest, in comparison with the circular pupils P1 and P2 (**Table 6.5**). **Figure 6.5** displays the size of the distortion across meridians, showing the influence of the pupil size and shape. As it can be seen, in general, P1 yields the lowest distortion values for both designs D and N. The differences between P2 and P3 are less marked in size. However, the irregularity between M90 and M0 is easily observable and more noticeable for P3, especially for the D design (**Figure 6.5**).

The comparison analysis between the two different multifocal designs did not yield statistically significant differences in general for the light disturbance parameters. Only the spherical aberration resulted significantly different. In fact, the multifocal D design generated more positive spherical aberration, whereas the N design induced more negative values. This is due to the optical principle that these lenses use in order to achieve multifocality. The D design consists of a centre for distance vision with progressive positive shift towards the periphery, whereas the N design has a centre for near vision with progressive negative shift. It is important to mention that MCLs are often associated to a loss of vision quality compared to single vision lenses (Sha et al. 2016), explained in part by the light disturbances that they produce. Aside from the optical principles that induce optical aberrations in order to achieve multifocality, the combination with ocular media disturbances can also cause decreased quality of vision because light is scattered over the retinal image. In this sense, retinal straylight can lead to vision loss of small detail. Although visual acuity and straylight conform different aspects, both have a significant impact on quality of vision. A recent work

(Łabuz et al. 2016) evaluated the straylight after pupil dilation in wearers of four MCLs by means of a straylightmeter, with the same distance and addition powers (+0.25 D and +2.50 D, respectively). They found that the lowest straylight was found in that MCL with the highest number of optical zones, corresponding to the Acuvue Oasys for Presbyopia with five alternating rings. Interestingly, abrupt changes of the power of the lens could be considered as a potential source of light scattering, although their results showed the opposite. They reported very similar straylight results for lenses with different designs, such as the Proclear Multifocal (Cooper Vision, Fairport, NY) with a progressive power profile, and the Oasys. They already pointed to the material properties of the lenses as a possible cause of straylight differences among designs that should be investigated, since they found that even a greater centre thickness of a given lens (at -3.00 D) yielded better quality measurements than a thinner one.

Light disturbances are especially noticeable under low light conditions, such as those considered in this study. Under these circumstances, the contrast between the light sources and the dark background is maximized. Routine activities that match this condition include but are not limited to night driving. In fact, a questionnaire regarding difficulties while driving revealed that MCLs users were less satisfied with their quality of vision during night-time than daytime driving, particularly regarding light disturbances, glare and haloes (Chu et al. 2009). Indeed, night driving implies different spectral sensitivities (Matesanz et al. 2011; Zele and Cao 2014). These problems are magnified by the fact that under low light conditions, the pupil size is increased and, as it has been shown, larger pupil size is associated with higher optical aberrations and potentially light disturbances. Previous studies have reported results that are in agreement with our findings with respect to the increasing in light distortion with MCLs (Fernandes et al. 2018). Furthermore, they showed that the distortion increased even with single vision lenses in monovision for the NDE, which is corrected for near vision whereas distant objects are defocused. This reinforces that optical aberrations have a significant role on the light disturbances, which are magnified with increasing pupil size. Thus, MCLs with great amounts of spherical aberration (or distance defocus), this is, those progressive with higher addition powers, are more likely to generate significant light disturbances under low light conditions.

No studies regarding irregular shaped pupils have been carried out previously. However, as well as the size of the distortion is associated with the size of the pupil, it seems that the shape of the distortion might also be related with the shape of the pupil, at least with the elliptical shape considered in this study. This might be explained by the fact that different aperture size across meridians would mask differently the areas that induce the optical aberrations, which could alter the shape of the final distortion. However, this pupil condition has been simulated on subjects with normal eyes. It has to be taken into account that an abnormal shape of the pupil could be caused by other ocular conditions that may compromise vision to a greater extent than only affecting the shape of the light disturbance in comparison with normal circular pupils.

The limitations of this study include the following. The greatest limitation is the small sample size, although this investigation conforms a preliminary assessment. Besides, the mean age of the subjects was less than 30. However, this is not a handicap for light disturbance assessment, although dynamic changes of the accommodative status could cause variations on the disturbance. Nevertheless, this can also occur with patients with sufficient remaining functional accommodation, mainly early presbyopes. A possible solution could have been to paralyse accommodation. In any case, this was not necessary because the measurement instrument provides mechanisms in order to strengthen the stability of the light distortion by making sure that the evaluation at each direction does not exceed a certain variability threshold. The counterpart that comes from the instrument is that the distance between the small light sources is fixed, so there is a limit to analyse the differences in light disturbance under different conditions. Another limitation involves the simulated apertures mounted on trial frames, which are placed at a distance of about 15 mm from the actual pupillary plane. Furthermore, the pair comparisons have been performed within groups for both the DE and NDE, or with different samples comparing the DE and NDE. This is not a limitation per se, but it means that only monocularity has been taken into consideration for the analysis. Future studies should consider the effect of binocularity with different pupil sizes and shapes, but it was not treated in this work because of the complexity and additional factors involving binocular neural processes, which was beyond the scope of this study. Some researchers have already referred to the binocular summation effect of the light disturbances, which means that it is diminished binocularly. Nevertheless, it should be studied more carefully in the future. An additional limitation is related to wearing time. In this study, the subjects only wore the lenses during a single visit and the measurements were performed after some minutes. A recent work has been centred on how progressive adaptation after some time wearing MCLs influences these phenomena. Not insignificantly, these findings reveal that the temporal factor seems to have a positive effect, reducing the light disturbances. Additionally, CLs can modify the normal corneal shape and its physiological status, which might affect the quality of vision.

Lastly, the meaning of characterizing the light disturbance with different pupil sizes and shapes under low lighting conditions lies on the importance to generate a deeper knowledge on how MCLs perform. In fact, MCLs users will find themselves under daily-life situations under such conditions that might compromise their visual performance. This will help practitioners in their clinical decisions and researchers for future modelling of new multifocal designs.

CHAPTER 7:

GENERAL CONCLUSIONS

7 GENERAL CONCLUSIONS

- The performance of new progressive centre-distance MCL designs in terms of the total amount of total addition achieved depends on the diameter of the pupil size and the total distance-vision area. For this reason, the pupil size of the patients, as well as their visual needs, are of crucial importance. For this analysis, power profiles are a powerful tool for characterization.

- The pupil shape affects the physical parameters of the analysed lens power profiles of different multifocal contact lens designs. This means that the effectiveness of these optical solutions for the correction of presbyopia might be altered with irregular pupil shapes. However, the clinical implications of these phenomena might differ from the real physical measurements, due to the influence of additional factors such as ocular wavefront aberrations or the neural adaptation process.

- The pupil shape together with decentring have an impact on the physical metrics that have been analysed. This means that the shape of the pupil might affect the effectiveness of IOLs for the correction of presbyopia. Nevertheless, as well as with the case of MCLs the clinical implications of these variations are not directly transposable due to the effect of other factors such as the contribution of the rest of the ocular media and their state to the final image and the neural processes.

- Multifocal contact lenses increase light disturbance effects under low light conditions. Also, the size of the distortion was increased with pupil size. As well as the size of the distortion is associated with the size of the pupil, it seems that the shape of the distortion might also be related with the shape of the pupil.

CHAPTER 8:

FUTURE LINES OF RESEARCH

8 FUTURE LINES OF RESEARCH

- The custom-made software specifically developed for this Thesis constitutes a strong base for optical modelling including different pupil sizes and shapes. Future functions could be developed that include accommodation dynamic changes in combination with the pupil size or shape. Different pupil sizes and shapes could be combined with new optical designs that include two or more optical zones.

- The custom-made software for the analysis of the light disturbances could be enhanced for predicting the distortion size with different MCLs optical designs, considering the coupling effect of the optical aberrations of the eye and those induced by specific lenses, obtained by means of their power profiles.

- New developments of software related to the contents of this Thesis would provide a powerful tool not only for characterization of already exiting designs, but also for predicting the optical performance of new experimental ones.

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Publicaciones y comunicaciones a las que ha dado lugar el trabajo de esta tesis y trabajos relacionados

Publicaciones en revistas científicas de impacto:

Monsálvez-Romín, D.; Domínguez-Vicent, A.; García-Lázaro, S.; Esteve-Taboada, JJ.; and Cerviño, A. Power profiles in multifocal contact lenses with variable multifocal zone. Clin Exp Optom 2018. 101: 57-63. doi:10.1111/cxo.12575

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Domínguez-Vicent A, Esteve-Taboada JJ, Del Águila-Carrasco AJ, Monsálvez-Romin D, Montés-Micó R. In Vitro Optical Quality Comparison of 2 Trifocal Intraocular Lenses and 1 Progressive Multifocal Intraocular Lens. J Cataract Refract Surg. 2016;42(1). doi: 10.1016/j.jcrs.2015.06.040.

Comunicaciones en congresos:

Cerviño A; Monsálvez-Romin D; García-Lázaro S; Esteve-Taboada JJ; Albarrán-Diego C; Pastor F.

Título del trabajo: Wavefront transformation for simulating multifocal implantation in eyes with elliptical
pupils.
Nombre del congreso: XXXIV Congress of the European Society of Cataract & Refractive Surgeons
Tipo evento: Congreso Ámbito geográfico: Internacional
Tipo de participación: Participativo - Ponencia oral (comunicación oral)

Ciudad de celebración: Copenhagen, Dinamarca

Fecha de celebración: 2016

Fecha de finalización: 2016

Monsálvez-Romín D; Ortiz-Herrera C; Domínguez-Vicent A; Esteve-Taboada JJ; Montés-Micó R.

Título del trabajo: Evaluación in vitro de tres lentes intraoculares difractivas correctoras de la presbicia.

Nombre del congreso: 24 Congreso Internacional de Optometría, Contactología y Óptica Oftálmica

OPTOM 2016

Tipo evento: Congreso Ámbito geográfico: Internacional

Tipo de participación: Participativo - Ponencia oral (comunicación oral)

Ciudad de celebración: Madrid, España

Fecha de celebración: 2016

Fecha de finalización: 2016

Trabajos futuros.

Los trabajos futuros para publicar en revistas de impacto están relacionados con la evaluación de la calidad óptica de elementos ópticos para la corrección de la presbicia teniendo en cuenta formas irregulares de la pupila, tal y como se ha tratado en esta tesis en los diferentes estudios que se han llevado a cabo. Se pretende evaluar diseños experimentales y una mejora del software que permita una caracterización más precisa.

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