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ANALYSIS AND CORRECTION OF CORNEAL ASTIGMATISM IN MODERN PSEUDOPHAKIA

By

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A thesis submitted to Plymouth University in partial fulfilment for the degree of

DOCTOR OF PHILOSOPHY

Health and Human Sciences Doctoral Training Centre

2015

Abstract

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Toric intraocular lenses (IOLs) are designed to reduce spectacle dependency by correcting corneal astigmatism at the time of surgery. However, these IOLs are reliant on the accurate prediction of post-operative corneal astigmatism through reliable ocular biometry and the accurate calculation of surgically induced astigmatism.

In the thesis the repeatability of assessing corneal curvature was assessed using six commercially available keratometers. The results question the validity of corneal biometry and infer that much of the apparent change in corneal shape usually associated with surgically induced astigmatism may be due to measurement error. The use of the oblique cross cylinder formulae for the calculation of post-operative corneal curvature was also investigated. This formula is incorporated into all commercially available toric IOL calculators and is utilised in every toric IOL implantation. The results from this thesis indicate that the formula is not applicable to the human cornea and that the use of the calculator does not increase the effectivity of the toric correction.

Furthermore, the thesis queries the assumption that post-operative corneal astigmatism is directly proportional to post-operative refractive error. The disparity between both the magnitude and axis of astigmatism measured by keratometry and manifest refraction in a pseudophakic population was investigated. The axis measurements in particular showed very poor agreement; far outside an acceptable level of misalignment, significantly decreasing the effective correction provided if the lens was aligned with the keratometry readings. Inclusion of the posterior corneal curvature and thickness, along with a smaller chord length may lead to a more accurate assessment of corneal power. Despite the difficulty in providing an effective toric IOL correction, it was found that the correction of corneal astigmatism at the time of cataract surgery might decrease the risks of falls. Uncorrected astigmatism and cataract both cause a reduction in stability when stepping oven an obstacle, which is one of the most common causes of trips and falls in the elderly population.

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List of Abbreviations

ATR	Against the rule astigmatism – the steepest meridian is horizontal
Axis	The orientation of the steepest corneal meridian
CCI	Clear corneal incision
COM	Centre of Mass
IOL	intra ocular lens
IOLM	IOLMaster
J_0	Vector representing the power of corneal astigmatism along the 0 and 90 direction.
J_{45}	Vector representing the power of corneal astigmatism in the oblique direction.
JERK	A function of the time derivative of the acceleration and is a measure of dynamic stability.
MR	Manifest refraction
MSE	Mean Spherical Equivalent
OBL	Oblique astigmatism (neither horizontal or vertical)
OPD scan	Optical Pathway Device scanner (Nidek)
SIA	surgically induced astigmatism
V1	Visit 1
V2	Visit 2
V3	Visit 3
VA	Visual Acuity: measurement of the best-corrected central vision
Vision	Unaided vision as measure on a chart
WTR	With the rule astigmatism – steepest meridian is vertical

To my parents, who lead the way.

Acknowledgements

I would like to begin my acknowledgements with a huge thank you to the School technicians: Abby Pearce, Adam Carter and Julie Soane for their tireless assistance in all my projects.

Another key team who shall not go unmentioned are the many dedicated ophthalmic nurses, health care assistants, administrators, technicians, optometrist and ophthalmologists working in the REI. They all helped make way for the bulk of my research during 2014. In particular, I want to say thanks to Steve from ophthalmic imaging, Kim, Chris, Faith and Chris from pre-operative assessments and Dr Dave Adams and Professor Nabil Habib for their constant support and encouragement. I will remember my time at the hospital fondly.

I am also grateful to Plymouth University for sponsoring my PhD and allowing me this great opportunity.

Furthermore, I am indebted all my supervisors; Dr Phillip Buckhurst, Dr Hetal Buckhurst, Dr Gary Shum and Professor Christine Purlsow, for their guidance and expertise throughout this time (not only with the thesis). Special mention must be made to James Buckhurst whose tacit contribution at the end was nonetheless important

I have to say a massive thank you to the Optometry department and all my PAHC PhD buddies including Nicola Szostec, Elle Compton and Esther Fox. Your support (and Percy Pigs) made the process much, much more enjoyable. Meanwhile, Daniela Oehring can take credit for any statistical knowledge gained through this period. I appreciate the patience to all my family and friends have show in my many absences and late arrivals due to urgent deadlines and a heavy workload. A particular thanks needs to go to my parents and sympathetic siblings who stepped in as CV gurus, ace editors and a sympathetic ear when time was tight and nerves were fraught. A special mention must also goes out to Dr Steph Mroczkowska who literally ran the length of my PhD with me, in wind, rain or shine.

Saving the best for last, I want to not only thank but also ask for the forgiveness from my steadfast partner in crime; my husband Rich. I am sorry to have dragged you though this, but am so glad you were with me every step of the way. This is for you and, yes, we can share the title.

Authors Declaration

At no time during the registration for the degree of Doctor of Philosophy has the author been registered for any other University Award without prior agreement of the graduate committee. Work submitted for this research degree at Plymouth University has not formed part of any other degree either at Plymouth University or at another establishment. This programme involved two university based and one hospital based study to collect data. All studies were lead and completed by the author. Relevant national and international scientific seminars and conferences were regularly attended at which work was often presented; and papers presented for publication.

Publications and Presentations:

1. **Buckhurst, P., Buckhurst, H. & Hamer, C.** (2013) Assessment of ciliary muscle morphology using a new Fourier domain swept source anterior chamber optical coherence tomographer *Investigative Ophthalmology and Visual Science. E-Abstract 3035.*
2. **Hamer, C., Buckhurst, H., Purslow, C. & Buckhurst P.** (2013) Agreement and reproducibility across 6 instruments for measuring keratometry *Proceedings of the British Congress of Optometry and Vision*
3. **Hamer, C., Habib, N., Buckhurst, H., Purslow, C.** & **Buckhurst P.** (2014) Surgically-induced corneal astigmatism measurement error *Proceedings of the XXXII Congress of the European Society of Cataract and Refractive Surgeons*
4. **Buckhurst, P., Hamer, C., Buckhurst, H., Purslow, C.** & **Habib, N**. (2014). Improving the reliability and repeatability of corneal curvature assessment through image analysis of topographic maps and the compensation of torsion *Proceedings of the XXXII Congress of the European Society of Cataract and Refractive Surgeons*
5. **Hamer, C., Habib, N., Buckhurst, H., Purslow, C.** & **Buckhurst P.** (2014) Can we improve the accuracy of Cataract Surgery *Proceedings of the 40th Hospital Optometrists Annual Conference*
6. **Hamer, C., Habib, N., Buckhurst, H., Purslow, C.** & **Buckhurst P.** (2015) Corneal curvature for Toric IOLs *Proceeding of the British Society of Refractive Surgery Conference.*
7. **Hamer, C., Habib, N., Buckhurst, H., Purslow, C.** & **Buckhurst P** (2015) Do toric IOL calculators accurately predict the shift in orientation of the steepest corneal meridian following cataract surgery? *Investigative Ophthalmology and Visual Science. E-Abstract 3035.*
8. **Buckhurst P, Hamer, C., Habib, N., Buckhurst, H.,** & **Purslow, C** (2015) The relationship between corneal astigmatism and refractive astigmatic error in pseudophakic eyes. *Investigative Ophthalmology and Visual Science. E-Abstract 3035.*
9. **Hamer, C., Habib, N., Buckhurst, H., Purslow, C.** & **Buckhurst P** (2015) Investigating the effect of clear corneal incision in the principal meridians of the cornea *Proceedings of the XXXIII Congress of the European Society of Cataract and Refractive Surgeons*
10. **Buckhurst P, Hamer, C., Habib, N., Buckhurst, H.,** & **Purslow, C** (2015) The relationship between peripheral and paracentral astigmatism and refractive astigmatic error in pseudophakic eyes. *Proceedings of the XXXIII Congress of the European Society of Cataract and Refractive Surgeons.*

11. **Hamer, C., Habib, N., Buckhurst, H., Shum, G., Purslow, C.** & **Buckhurst P** (In Press) Comparison of reliability and repeatability of corneal curvature assessment with 6 keratometers. *Clinical and Experimental Optometry.*
12. **Hamer, C., Habib, N., Buckhurst, H., Shum, G., Bunn, L., Marsden, J., Purslow, C.** & **Buckhurst P (**Under review**)** The Effect of Astigmatic Distortion and Simulated Cataract on Standing Balance (In review) *Journal of Cataract and Refractive Surgery.*

Word count of main thesis: 53,175.

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Chapter 1 Introduction

Cataract surgery is one of the most commonly performed surgeries in the world (Allen et al. 2006) (AgeUK 2012). In the UK alone around 300,000 surgeries are performed within the NHS each year (Gray et al. 2010). During cataract surgery, the aged natural crystalline lens is removed and a new artificial intraocular lens (IOL) is implanted in its place. The IOL is required to replace the refractive power previously provided by the crystalline lens; modern IOLs are now designed not just to maintain but also to improve vision. Surgical technology and techniques have evolved and improved extensively in modern times. The desired goals of both surgeons and patients are to achieve emmetropia or 'spectacle-free' vision post-operatively rather than just maintain the original refractive error (Agresta et al. 2012). Advancement in both IOL power calculations and methods used to measure ocular biometry have resulted in improved accuracy in determining the IOL power required to correct the pre-surgical refractive error (Verhulst et al. 2001). A benchmark for the NHS if the biometry guidelines are followed correctly is to have 97% patients within 1.00 dioptres of 'emmetropia' (optimal vision) (Gale et al. 2007; Ophthalmologists 2010). Yet, there are still some sources of inaccuracy within the surgical procedure; the surgically induced post-operative corneal shape changes can limit the visual outcomes and contribute to post-surgical refractive error (Hill 2008). The reduction in surgical incision size has significantly reduced the amount of shape change that occurs to the cornea (Hayashi et al. 1995; Pfleger et al. 1996; Moon et al. 2007; Masket et al. 2009; Dewey et al. 2014). Nevertheless, it is widely established that even with small and micro incisions there is some change in corneal shape (Hayashi et al. 1995; Hill 2008; Wei et al. 2012). What is not known is precisely what impact the position of the pre-surgical principal maximum and minimum curvatures (meridians) relative to the incision site has on the post-surgical corneal meridian positions.

Hitherto, the assumptions used to predict post-surgical corneal alterations have taken into account a dioptric power change but only assumed the meridian positional change (Hill 2008). As such, there is currently insufficient research to determine the exact effect of a surgical incision on the shape of the cornea and what factors involved affect the visual outcome post-surgically. With the increasing popularity of more complex IOLs designed to correct more complex prescriptions such as astigmatism, this information is vital to improve post-operative visual outcomes.

1.1 The Anterior Eye and Astigmatism

1.1.1 Cornea

Averaging in diameter of 11.7 mm horizontally and 10.6 mm vertically, the cornea constitutes one sixth of the external ocular surface. The cornea is a largely avascular transparent structure and is responsible for two thirds of the eye's refractive power (approximately 42 dioptres) (Lens et al. 1999). The corneal surface is aspheric, gradually flattening towards the periphery. The transparency of the cornea is the result of highly organised and regular structure of the fibrils (Oyster 1999).

The cornea and limbus mostly consist of collagen: a fibrous protein that is homogeneous in structure. Collagen is characteristically made up of three chains of amino acids that form a helix spiral around one another. The helices in a single molecule form thin strands that can join with other molecules forming the longer collagen fibrils varying in length and diameter (Oyster 1999). Corneal fibrils are arranged in a highly regular pattern and can be seen as the banding or striation in electron microscopy. The collagen in the cornea (and sclera) is embedded and surrounded with complex structures called proteoglycans, which are core proteins with glycosaminoglycans (GAGs) bound to them. The GAGs are important to corneal structure as they create spacing and attract water to create a gel around the collagen fibrils (Lens et al. 1999). Maintaining space around the collagen fibrils helps preserve the corneal transparency, however the amount of water must also be controlled (Oyster 1999). The structure is generally kept in a relatively dehydrated state, this contributes to its transparency, if it was to become hydrated the cornea will become opaque (Lens et al. 1999).

X-ray diffraction patterns have been analysed to determine the structure of the corneal fibrils in vitro. Most of the fibrils are in orthogonal alignment in the central cornea area until 1.5 mm from the limbus where they bend 45 degrees in a 2.5 mm space to merge with a peak produced by the circumcorneal annulus (Meek et al. 1999). The annulus is located 1.0 mm from the limbus in the sclera. The annulus is smaller in the superior region (1.5 mm) than inferior region (2.0 mm). There is a variation in the angular spread from 46-73 degrees, smaller spread at superior/inferior points and widest between these two- it appears symmetrical about the inferior-superior axis (Meek et al. 1999). Astigmatism may cause an interruption to the fibril arrangement due to the irregularity of the corneal shape (Meek et al. 1999). Also using X Ray diffraction, Boote et al (2003) found that the pre-pupillary regional fibres were much more closely packed than that of the peripheral fibres. This is thought to help bolster the corneal strength in the more curved and thinner central region.

1.1.1.1.1 Layers of the Cornea

Traditionally the cornea is considered to have 5 layers: the Epithelium, Bowman's Layer, the Stroma, Decement's Membrane and the Endothelium. However, in 2013 a new layer was proposed called Dua's Layer: located between the stroma and Decement's membrane (Dua et al. 2013). Recognition and identification of this new layer can assist in cornea surgeries, such as deep anterior laminar keratoplasty (DALK). Dua's layer is tougher than the Decement's membrane (DM) and, providing it is not split from the DM, it will provide more resilience during the procedure (Dua et al. 2013; Zaki et al. 2015). However, the definition of Dua's layer has not yet been confirmed as many consider it part of the stroma rather than a separate layer (Jester et al. 2013; McKee et al. 2014).

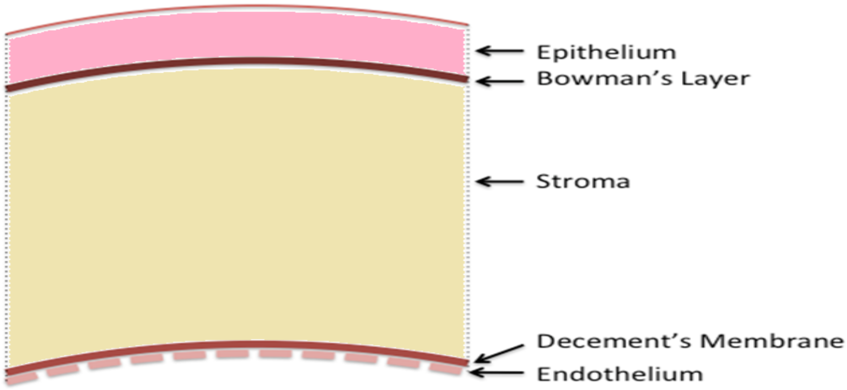

Figure 1.1: Image of the traditional 5 layers of the cornea

1.1.1.1.2 Epithelium

The corneal epithelium is a continuation of the conjunctiva and acts as a shield from injury for the stroma. It has rapid regenerating cell development and does not scar once healed. The epithelium completely replaces itself once a week. It is made up of three layers of cell types; basal, wing and flattened epithelial cells. The basal cells are responsible for mitosis and when new cell are produced they migrate upwards to become wing cells then move up to the anterior surface to be flattened cells. The anterior flattened cells excrete mucin to help bond with the tear film (Lens et al. 1999).

1.1.1.1.3 Bowman's Layer

Bowman's Layer was previously known as 'Bowman's Membrane' but investigation into its structure led to it being changed to a 'Layer' instead (Oyster

1999). It acts to protect the stroma by creating a barrier to external microorganisms. It is made up of collagen fibrils that do not appear to have the same order of the stroma or epithelium. It has been suggested that the fibril ends curve upwards from the stroma and interweave together. It is also notably free from fibroblasts, unlike the stroma (Lens et al. 1999).

1.1.1.1.4 Stroma

The Stroma is the thickest layer of the cornea at 90% of the tissue. The collagen fibres form lamellae, which have a precise regular structure: each lamellae are positioned at 90 degrees to one another without any interweaving. The regular structure contributes to the clarity of the cornea. There are also fibroblasts and keratocytes present in this layer. The keratocytes are flattened stromal cells with long extensions, these work to aid in the healing process and engulf foreign particles. Lymphocytes and macrophages are present and involved in the inflammatory process (Lens et al. 1999).

1.1.1.1.5 Descement's Membrane

This layer is posterior to the stroma and the main role it plays is to act as the basement membrane to the endothelium and protect the more posterior structures of the eye from any cells and vessels passing through from the anterior layers. This is a thin layer of fine collagen fibres that are arranged in a hexagonal pattern. It also extends beyond the scleral spur and can be seen in some slit lamp examinations (Lens et al. 1999).

1.1.1.1.6 Endothelium

This layer is made up of a single layer of polygonal flattened cells interlocking in a honeycomb pattern. One of the most important roles of this layer is the production of an ion pump that moves water from the cornea into the aqueous. It is the key to the dehydrated state of the cornea and vital for corneal transparency (Oyster 1999). Each of the cells has 3 million small pumps, moving water and nutrients through the cornea. Babies are born with around 4500 cells per mm2 (around 500, 000 cells in total)(Efron 2010). Unlike the epithelium, it cannot regenerate at all and any cells lost are permanent, the density of cells slowly reduces between birth and 50 years old, where little difference is seen(Wilson et al. 1982). The remaining cells to spread out to cover the space if possible (Lens et al. 1999; Bourne 2003). Corneal graft patients survive with as little as 500 cells per mm2 (Lass et al. 2013) so there is a considerable reserve to maintain corneal transparency in most people.

1.1.2 Astigmatism

Astigmatism is the term used to describe an eye, which has two principal meridians of differing power (Bennett et al. 1998). The literal definition can be broken down to an eye that lacks a single point of focus. '***A***' is means *lacking*, ‘***stigma’*** comes from the Greek meaning *a point* and ‘***-ism’*** describes a state or condition (Benjamin et al. 2007).

The eye’s optical system is made of the combined power of the lens and the cornea. If this optical system is not spherical, it results in astigmatism (Bennett et al. 1998).

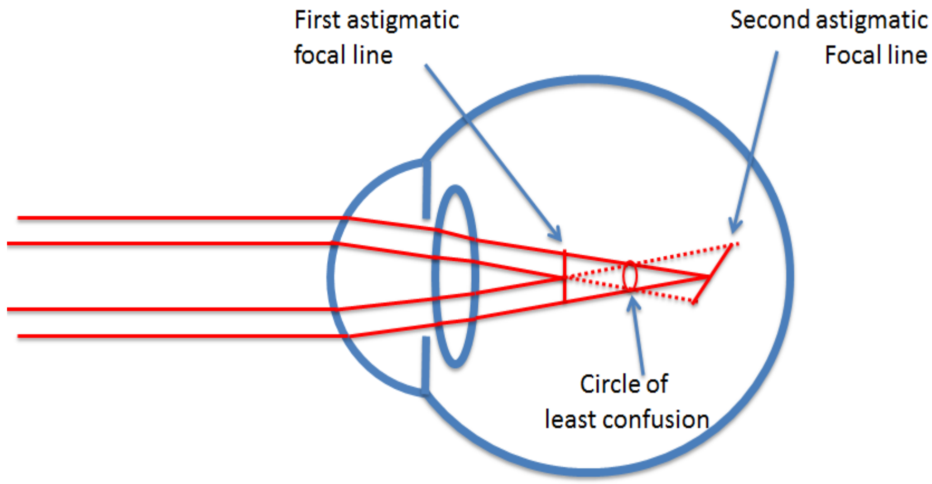

Figure 1.2: Ray diagram of an astigmatic eye

Astigmatism is categorised into three different groups: with the rule, against the rule and oblique astigmatism. Each type of astigmatism affects vision differently.

1.1.2.1 With the Rule Astigmatism (WTR)

The most powerful meridian is vertical (90 ± 20°) and the flat meridian is horizontal. The unaided vision is generally better with this type compared to equal amounts of against the rule or oblique astigmatism (Benjamin et al. 2007).

1.1.2.2 Against the Rule Astigmatism (ATR)

The most powerful meridian is horizontal (180 ± 20°) and the flat meridian is vertical (Benjamin et al. 2007). This can result in poorer unaided vision than with-the-rule and some tasks such as reading can be quite problematic without correction (Wolffsohn et al. 2011).

1.1.2.3 Oblique Astigmatism

The most powerful meridian is orientated obliquely, neither vertical nor horizontal. There is more variance in the vision in this category. Generally, it is worse than with the rule astigmatism but not necessarily than against the rule astigmatism (Benjamin et al. 2007; Wolffsohn et al. 2011).

1.1.2.4 Prevalence

Generally, it has been found that the average corneal astigmatism in the pre-surgical cataract population is roughly 1.00 DC (Hoffer 1980; Riley et al. 2001; Vitale et al. 2008; Ferrer-Blasco et al. 2009; He et al. 2009; Hoffmann et al. 2010; Knox Cartwright et al. 2010; Sherwin et al. 2011). The prevalence of significant astigmatism (classed as ≥1.50 Dioptres of astigmatism) has been found to be between 16 and 22% (Table 1.1) (Hoffer 1980; Ninn-Pederson 1992; Vitale et al.

2008; Ferrer-Blasco et al. 2009; He et al. 2009; Hoffmann et al. 2010; Knox Cartwright et al. 2010; Nangia et al. 2010; Khan et al. 2011; Sherwin et al. 2011).

Nangia et al found that the prevalence of astigmatism is lower in populations with lower levels of education and near work such as rural India (Nangia et al. 2010).

Generally, there is an increase in the prevalence of against the rule astigmatism with age (Gudmundsdottir et al. 2005; Vitale et al. 2008; Hoffmann et al. 2010). This is attributed to a general steepening of the cornea along the vertical meridian, increasing the ATR astigmatism of the cornea that may be attributed to the change in eyelid tension anterior surface (Hayashi et al. 1995; Gudmundsdottir et al. 2005). As the crystalline lens is always ATR, the increase in corneal ATR, increases rather than cancels out the overall astigmatism of the eye (Bennett et al. 1998). Guzowski et al (2003) found that not only was there a shift towards against the rule astigmatism but there was also a decrease of oblique astigmatism in the older population (Guzowski et al. 2003).

Author	Where?	Corneal or Total	N eyes	N subjects	Method/ Device used	Mean astigmatism	>1.00DC (%)	>1.50DC (%)	> 2.00DC (%)
Cartwright et al (2008)	UK database	Corneal	25,548 unpaired	25,548	IOL Master	1.04 ±0.79	40	21	11%
Ferrer-Blasco et al (2009)	Uni Valencia, Spain	Corneal	4,540	2,415	RM-KR-8800 (Topcon)	0.90 ±0.93	29.1	22.22	8.63
He et at (2009)	China	Total	1,269	1,269	Autorefractor	48.3% over 0.75DC	-	-	-
Hoffer (1980)	CA, USA	Corneal	7,500	-	Biometry	1.00 ±0.10	33.1	19.1	11
Hoffman et al (2010)	Eye-surgery hospital, Germany	Corneal	23,239	23,239	IOL Master	0.98 ±0.78D	36.05	16	8
Khan et al (2011)	British Hospital	Corneal	1,230	746	IOL Master	1.03 ±0.728	40.41	20.5	9.69
Nangia et al (2010)	Rural India (hospital)	Total	9,405	4,711	Autorefractor / subjective	0.29 ±0.6	-	-	-
Ninn-Peterson el al (1992)	Swedish hospital	Corneal	5,554	5,554	-	-	~40	~ 20	~ 10-12%
Riley et al (2001)	Auckland Hosp, NZ	Corneal	502	488	Manual Keratometry (Topcon?)	0.9 ±0.8	43 (≥1.00DC)	-	-
Sherwin et al (2011)	Norfolk Island, South Pacific	Total	1293	477	Subjective	-	24.1	4.1 (≤1.50DC)	-
Vitale et al (2008)	USA	Total	14213	14213?	National Survey	-	< 40's = 23.1 >40's = 27.6	-	-

Table 1.1: Table displaying reported prevalence of astigmatism in the population.

1.1.2.5 Correcting Astigmatism

Astigmatism reduces unaided vision. As the amount of uncorrected astigmatism increases, the visual acuity decreases (Peters 1961). Measured subjectively, most subjects felt some tasks e.g. driving, reading, viewing a mobile phone or VDU became more difficult without correction (Wolffsohn et al. 2011). Wolffsohn and colleagues (2011) found that uncorrected astigmatism as low as a 1-dioptre correction to improve visual quality for tasks such as those mentioned above.

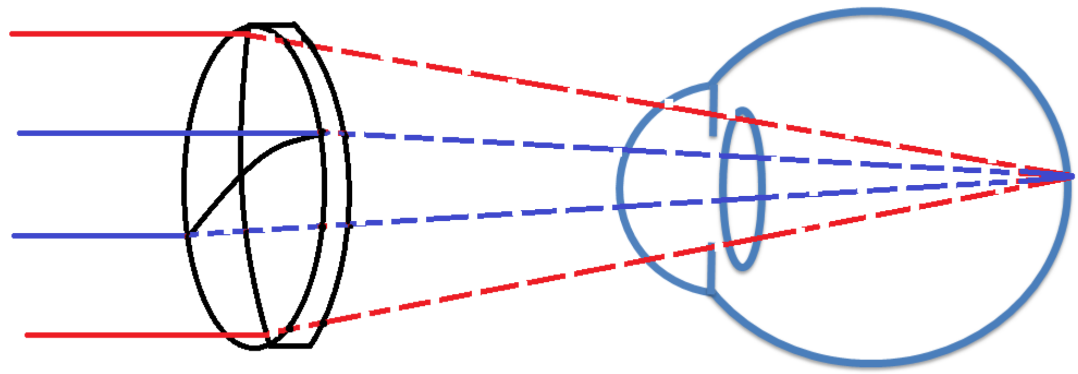

Figure 1.3: Ray diagram of the correction of astigmatic eye with a toric lens

The correction of astigmatism is traditionally achieved with the use of toric spectacle lenses. In order to correct the astigmatic surface, a correcting lens surface must also have varying powers in two principal meridians. A toric surface has two perpendicular principal radii of curvature. This allows a toric lens of specific orthogonal principal powers (curvatures) to be aligned with the principal meridians of the astigmatic eye, correcting the refractive error (Jalie 1984).

1.1.2.6 Distortion and Aniseikonia in the Correction of Astigmatism

There are some problems with the correction of astigmatism. The corrections for astigmatism used can sometimes result in distortion or aniseikonia.

1.1.3 Distortion

Distortion occurs as a result of changing magnification across an image. In the case of toric spectacle lenses, the different radii of curvatures each produce a different amount of magnification across the image (Guyton 1977). This can distort the image, altering straight lines and the orientation of some objects. Usually, adults in particular are more susceptible to this change and are poorer at adapting. This includes a high sensitivity a change in position and rotation of the lens, away from the previous correction position. With poor adaptation to the distortion, some patients will have as many problems with their correction as without (Guyton 1977).

It has been found that this problem can be reduced with reduction of the back vertex distance and by putting the correction at the entrance pupil (Guyton 1977). The entrance pupil is a virtual image of the pupil produced by the cornea and aqueous, which sits roughly 0.3 mm in front of the actual pupil (Srivannaboon et al. 2007). If the toric correction is placed at the corneal or lens plane with an IOL, rather than at the spectacle plane with glasses, then the distortion is reduced (Guyton 1977).

1.1.4 Keratometry: Assessing Corneal Curvature

The term keratometry means measurement of the cornea, however most keratometers only measure the anterior surface corneal curvature (Tunnacliffe 1997). Keratometers are principally used in contact lens fitting but also can be used to determine corneal power in cataract and refractive surgery. The use is important in cataract surgery pre-surgical assessments, as it is important to know what power of IOL, in combination with the cornea, will attain the best visual outcomes for the patient. Moreover, keratometers can be used to aid in the diagnosis of some corneal dystrophies and disorders such as keratoconus (Bennett et al. 1998; Wolffsohn 2008).

1.1.4.1 Basic Principal of Keratometry

Keratometry is based on the principals of reflection; making use of the first purkinje image that is reflected from the tear film, covering the anterior surface of the cornea (Tunnacliffe 1997; Bennett et al. 1998; Gutmark et al. 2010). An object of known size is projected onto the centre of the corneal anterior surface from a fixed distance and the reflected image size is measured. The radius of curvature can then be calculated with the known distance and image size (Bennett et al. 1991).

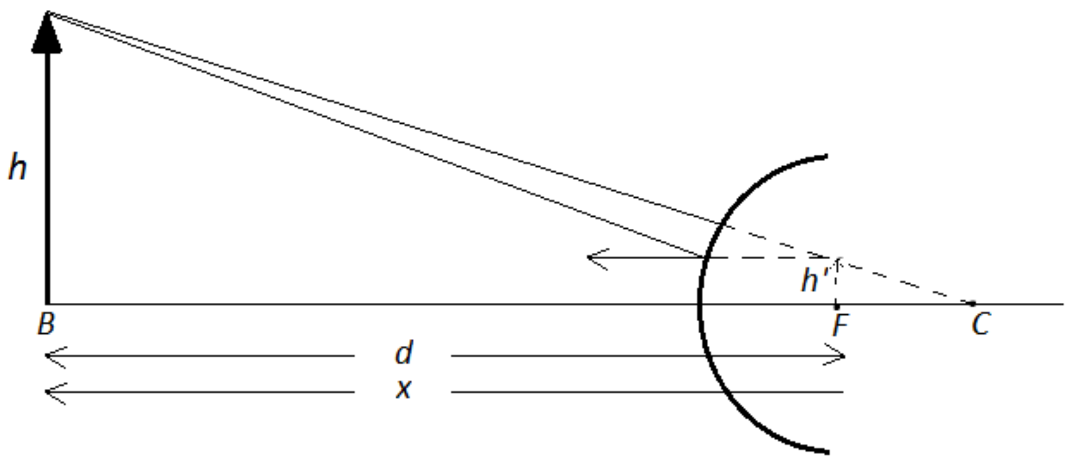

Figure 1.4: Ray diagram depicting the basic keratometry equation

The basic keratometric radius equation (Equation 1.1) is derived by using the radius of curvature of a convex mirror (Equation 1.2) along with Newton's magnification formula (Equation 1.3). It is given that in a keratometer, the distance –*x* is approximately equal to the distance *d*.

$$r = 2\frac{h\prime}{h}d$$ *Equation 1.1*

$$f = \frac{r}{2}$$ *Equation 1.2*

$$m = \frac{h\prime}{h} = -\frac{f}{x}$$ *Equation 1.3*

If a telescope is incorporated, image h can be reflected to form h'' which is can be observed by the viewer. In this design, the distance and therefore magnification is fixed so a constant of the objective lens magnification can be produced (Equation 1.4).

$$m_o = \frac{h''}{h'}$$ *Equation 1.4*

Initial designs had problems with accuracy as head and eye movements made it difficult to use the scale to assess the moving image. Image doubling was introduced to help overcome this. One example of how this has been implemented is using a prism over half the objective lens area. The doubled images are moved until they are just touching, the displacement required to do this equals the height of the image (Bennett et al. 1991; Tunnacliffe 1993; Bennett et al. 1998).

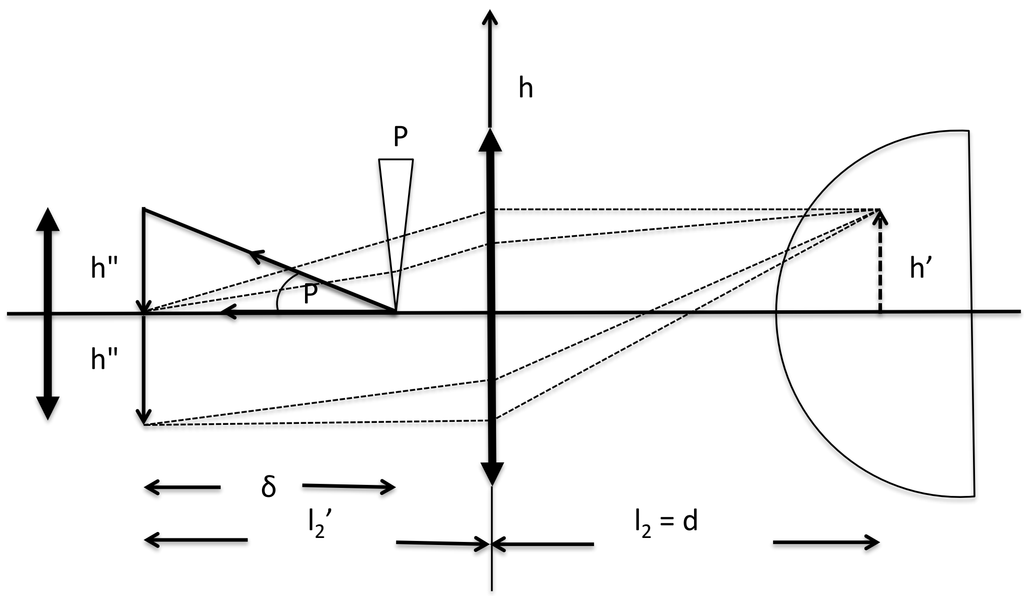

Figure 1.5: Ray diagram depicting the doubling of the mires induced by a prism.

Given that $h'' = -P\delta$ and that h'' is known for small angle (with the degrees in radians) then $m_o h' = -P\delta$. This allows the derivation of the equation for a doubled image keratometer (Equation 1.5).

$$r = -2\frac{P\delta}{m_o h}d$$ *Equation 1.5*

The displacement of the images y when touching is then equal to h''. The corneal power can be calculated using the radius measured with the keratometer. However, given that the instrument only measures the anterior surface the power of the cornea is derived from an adjusted refractive index is used (Tunnacliffe 1997) This is called the keratometric refractive index and varies depending upon the manufacturer, Haag Streit and Bausch and Lomb use 1.3375, American Optical use 1.336 and Zeiss use 1.332 (Gutmark et al. 2010)

1.1.4.2 Development of Keratometry

In the late 1700's, scientists began developing instruments that could measure corneal curvature, these were required to investigate the source of accommodation, with the theory that the cornea was changing shape, not the crystalline lens (Gutmark et al. 2010). The instruments were originally termed ophthalmometers and later re-named keratometers (Bennett et al. 1998). In 1779, Ramsden and Home produced one of the first keratometers that measured a doubled image (Gutmark et al. 2010). In the development of the original designs, some inspiration was found from the astronomers, as many were looking to measure the radius of planets and the sun with similar contraptions. In 1779, Ramsden borrowed the idea of doubling image size from the astronomer Savary, who was trying to measure the curvature of the sun, he had created a doubled image using displacement to get an exact measurement (Gutmark et al. 2010). In 1881, Emil Javal and Halmar August Schiøtz designed the first keratometer for use in clinical practice outside of the laboratory (Tunnacliffe 1997). They used candles to illuminate the mires (objects) from the front and allowed rotation of the instrument to measure corneal curvature at different axial positions.

1.1.4.3 Modern Design Principles

Although keratometers continued to be based on the same basic principles, some adaptations in methods of doubling and projecting the mires allowed improvements and variations in the instrument designs.

There are two main ways of doubling the image and aligning the image:

1. Fixed doubling, variable mires. The first is to fix the doubling apparatus and vary the mire location, the instrument position is changed to measure each principal meridian of astigmatism. The Javal Schiøtz design is an example of this.
2. Fixed mire position, variable doubling. This also allows the instrument to measure the corneal astigmatism from just one position. The Bausch and Lomb design is based on this.

Another important factor to consider is that traditional keratometry was designed to only measure the steep central corneal region: Most measurements are over a central diameter of 2.2 to 3.5 mm (Srivannaboon et al. 2007). This area is measured because the cornea begins to flatten with a gradual increase in the radius of curvature from the 4mm apex outwards (Tunnacliffe 1997).

1.1.4.3.1 Two-Position

A Javal Schiøtz is a two–position, fixed doubling, and variable mires keratometer. It is named after Emil Javal and Halmar August Schiøtz who designed this keratometer for clinical use in 1881 (Tunnacliffe 1997). The illuminated mires are projected onto the eye. The Wollaston prism used in this design is a beam splitter that produces two equally intense images (Bennett et al. 1998). The mires used in this design are almost unchanged since the original design, comprising of orange and green mires (Figure 1.10). Overlap of the mires appears yellow (Tunnacliffe 1997; Bennett et al. 1998). Each step in the orange mire represents one dioptre. It allows the measurement of astigmatism by projecting the mires from an arc, when the mires are aligned with a principal meridian of astigmatism the black lines running through the mires line up, if it is not on a principal meridian, the mires appear out of alignment (Tunnacliffe 1997). The Javal Schiøtz was one of the first keratometers to be developed and produced for use in practice. It is used to measure corneal curvature over a central area of 3.4 mm (Benjamin et al. 2007): this is a large area compared to many other modern counterparts (Visser et al. 2012).

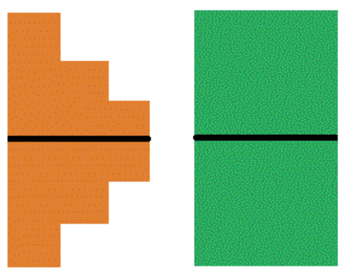

Figure 1.6: Javal Schiøtz mires

1.1.4.3.2 One-Position

The Bausch and Lomb design is a one position, variable doubling, fixed mire position, first produced in 1932 by Bausch and Lomb. This design has four apertures allowing light into the telescope used. The top and bottom apertures form an axial image of the mires that appears single when the instrument is at the correct distance (ensuring that *d* is a constant). These form the bottom right mire (Figure 1.11), the left and right apertures are part of the variable doubling system with orthogonally placed doubling prisms. Light passing through the right aperture also passes through a base out (horizontal) prism; light passing through the left aperture also passes through a base up (vertical) prism. Each prism has now doubled the image of the mire, the former has a horizontal split in the image and the latter splits the image vertically (Tunnacliffe 1997; Bennett et al. 1998).

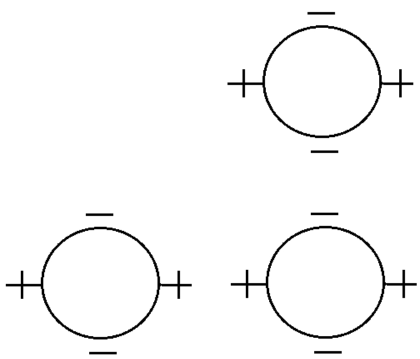

Figure 1.7: Bausch and Lomb mires

Similar to the Javal Schiøtz, the images will not align correctly until the instrument is rotated to the orientation of the corneal principal meridians. However, as the mires have a vertical and horizontal split, it allows measurement of the orthogonal principal cornea meridians in a single position (Tunnacliffe 1997; Bennett et al. 1998).

1.1.4.4 Errors in Keratometry

It is generally accepted that Keratometry has various sources of error due to the fundamental assumptions upon which it is based. These are thought to cause an error of around ±0.05mm (Tunnacliffe 1997):

1. Different working distances are required for each image in an astigmatic cornea: the steeper meridian will produce an image closer to the cornea than the flatter cornea. If the instrument is not adjusted and focused for each meridian, then one of the meridians will be measured inaccurately (Tunnacliffe 1997).
2. A poorly focused eyepiece: If the accommodation induced by instrument myopia is not controlled, then the radius will be underestimated (Benjamin et al. 2007).
3. The assumption that the cornea is uniformly spherical: the corneal curvature varies with the distance from the centre, flattening towards the periphery (Benjamin et al. 2007). The small central area predicts an incorrect overall radius.

1.1.4.5 <u>Topography</u>

Topography is another method of assessing the corneal curvature. It utilises the principals of reflection, similar to traditional keratometry but allows the opportunity of measuring a wider area of corneal curvature (Tunnacliffe 1997; Benjamin et al. 2007).

The first example of this technique was developed in 1880. Antonio Placido developed a method of studying the corneal surface with concentric rings of light. The Placido disc was developed from this to project the image of an illuminated set of concentric rings onto the corneal surface. Devices using this design are termed keratoscopes (Benjamin et al. 2007) (Srivannaboon et al. 2007).

Figure 1.8: Placido Disc

Until the invention of computer analysing systems, this method could only be used to qualitatively measure the curvature. In the 1890's Gullstrand began the development of algorithms that would allow quantitative analysis of the imaging using a photokeratoscope that imaged the reflection (Benjamin et al. 2007). Further development did not occur until improvement of computer processing and video technology that could analyse several thousand points across the reflected image (Benjamin et al. 2007). More importantly, the reduction in production costs for this technology allowed the machines to become available for use in clinical practice (Bennett et al. 1998).

The results are displayed as colour-coded topographic maps that could be used in practice however the quality of the maps can be affected by poor quality or irregularities in the tear film as it relies upon this to be a smooth refracting surface (Srivannaboon et al. 2007). Some instruments produce multiple maps describing different features in addition to the sagittal power including the elevation, tangential power, the eccentricity and tear film quality.

The increase in demand for this method of analysis came about due to the increasing prevalence and interest in refractive surgery that required quantitative analysis of the cornea as a whole (Benjamin et al. 2007).

1.1.4.5.1 Modern Keratoscope Design Principles

In basic terms, the curvature is determined by analysing the size of the rings and the darker gaps between them; larger gaps between the rings indicate a steeper curvature and vice versa (Srivannaboon et al. 2007).

In most keratoscopes, a video image of the rings is taken, the angular size of each point on the rings is measured and the surface is reconstructed using each point. The values can then be converted to a radius of curvature or dioptric power using an index similar to the traditional keratometers. Lastly, this is displayed as the colour topographic map by referencing each point's elevation in reference to a known spherical or ellipsoid surface (Benjamin et al. 2007).

1.1.4.5.2 Keratometry readings

Although shape analysis is performed for the whole cornea in topography, generally the curvature values given are 'simulated' (sim-K) over the central area (usually 3mm) with two orthogonal axes, 90 degrees apart. This sim-K metric is designed to be interchangeable with the traditional methods of keratometry (Wolffsohn 2008).

1.1.4.5.3 Scheimpflug Technique

The Scheimpflug technique captures cross sections of the anterior eye using a camera and orthogonal slit beam. The rotating Scheimpflug camera accumulates up to 100 images and produces a 3D model of the cornea. This allows measurement of both the anterior and posterior structures, as seen in the Pentacam (*Oculus Optikerate GmbH, Weltzer, Germany*) keratometry measurements (Dubbelman et al. 2002; Wolffsohn 2008). A particular advantage of this technique is that it allows assessment of the radius of curvature of the anterior and posterior corneal surface as well as the thickness of the cornea (Dubbelman et al. 2002; Elbaz et al. 2007). This allows the simultaneous assessment of the corneal shape, power, thickness, eccentricity, the anterior chamber depth and anterior chamber angle.

1.1.4.5.4 Slit-scanning topography

Another alternative method of corneal assessment is slit-scanning topography. Instruments such as the Orbscan II (*Orbtek, Salt-Lke City, UT, USA*) scan the anterior surface, assessing the elevation of the cornea to determine the curvature and power. It uses orthogonal scans as opposed to radial scans to assess the corneal shape. It is less influenced by the tear film and has been found to have good agreement with the manual keratometry (Leyland 2004) and the combined Placido disc- scheimpflug systems (Guilbert et al. 2012).

1.1.5 The Crystalline Lens

The crystalline lens is a biconvex lens accounting for 1/3 (approximately 20 dioptres) of the eye's total refractive power (Bennett et al. 1998). In medical terms, the word phakic refers to the crystalline lens. An eye with the lens present is referred to as a phakic eye, an aphakic eye has no lens and a pseudophakic eye has an artificial lens (Lens et al. 1999). It is the only variable optical structure of the eye, providing accommodation by changing shape to alter the optical power (Oyster 1999).

The lens is made up of 90% proteins, the highest concentration found in human tissue. It is a mixture of soluble (hydrophilic) and insoluble (hydrophobic) proteins, the majority being soluble. Crystallin proteins are part of this soluble group and these cells are responsible for the special properties of the lens. The crystallins are packed together in a dense uniform pattern and this structure is responsible for the lens transparency. The lens cells are permanent with the first-born cells still present in adult life (Oyster 1999). The stability of these cells also allows maintenance of the transparency and flexibility of the lens (Oyster 1999).

The crystalline lens is formed from the lens substance (nucleus and cortex) surrounded by a single layer of epithelium cells and enclosed in collagenous capsule that has elastic properties (Lens et al. 1999). The lens is suspended between the vitreous and aqueous of the anterior chamber by zonule fibres attached to the ciliary body. The zonules are inelastic microfibrils that insert into the capsule near the lens equator (Koretz et al. 1997).

The lens cells form long thin fibres and like an onion, the lens is made up of many layers around a central core (the nucleus). The crystalline lens is a spheroid structure and continues to grow throughout life developing new outermost layers around over time. This means that the central nucleus of the lens is the oldest part and the cortex surrounding is the youngest (Smith et al. 1998).

As part of its role in the optical refraction system, the lens is principally involved in accommodation; allowing the eye to focus at different distances e.g. from far to near (Koretz et al. 1997). The shape of the lens changes, altering the refractive power in order to form an image at the back of the eye for objects viewed at varying distances. The closer the object viewed, the more the lens has to increase its refractive power, in order to focus the divergent light rays entering the eye onto the retina at the back of the eye. When looking at a distance object the lens is held in position as a thin lens by the tension of the zonule fibres pulling on the elasticated capsular bag. When looking at a near object, the ciliary body muscles contract, releasing the zonular fibre tension, allowing the elasticated lens capsule to become more spherical. The optical or refractive power of the lens is increased allowing the eye to focus divergent rays of light coming from a near object (Glasser et al. ; Oyster 1999).

The posterior surface of the crystalline lens is in contact with the vitreous at the patellar fossa, a bowl shaped depression of the anterior surface. The vitreous cannot be compressed due to the high water content, therefore the lens cannot move backwards when accommodating, so most of the shape change occurs anteriorly (Oyster 1999).

In order for the crystalline lens to refract light and focus an image on the retina it requires a very high refractive index (approximately 1.400) because it must be higher than that of the aqueous (1.336) and vitreous (1.336) surrounding it (Oyster 1999; Smith 2003). The capsule refractive index is thought to almost match that of the vitreous so will have negligible refractive effect (Smith 2003). It has long been established that the lens has a gradient index across the structure, not a uniform one, in order to more accurately refract peripheral rays when forming a single image on the retina (Smith et al. 1998; Oyster 1999; Smith 2003).

The continual development of the crystalline lens and production of cells causes changes throughout life (Glasser et al. 1998). The lens increases in diameter and rigidity with age, and there is also an increase in lens curvature, focal length and spherical aberrations (Glasser et al. 1998). All of these changes result in a decrease of accommodation in an individual.

1.1.6 Cataracts

Cataract is the term used to describe a crystalline lens that has developed opacity within the lens capsule or any part of the structure (Kanski 2003). It can cause visual impairment through loss of contrast, duller perception of colour and in some cases increase in short-sightedness (Steinert 2010). Cataracts are the most common cause of blindness in the world despite the availability of treatment with a routine operation in developed countries, such as the UK (Allen et al. 2006). Cataracts mostly affect the ageing population, with the average age for cataract surgery in the UK being 76 years old (Gray et al. 2010). It is thought that 42% of all Britons over the age of 75 years will develop significant cataracts (AgeUK 2012).

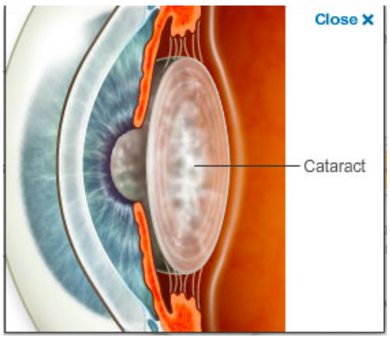

Figure 1.9: Cataract (image courtesy of NHS choices)

1.1.7 Causes of Cataracts

Most cataracts are attributed to a natural ageing process. It is reported that 42% of people over 75 will develop cataracts and the population over 75 is predicted to double in the next 30 years(AgeUK 2012). It could be inferred that the number of cataract sufferers in this age group may double with this. Nonetheless, it has been found that some dietary and lifestyle habits may reduce or increase the likelihood or rate of onset of cataracts (Seddon et al. 1995). Kanthan and colleagues (2010) found both heavy drinkers and those who abstain from alcohol were at higher risk of cataracts than those with moderate consumption of around 1-2 drinks a day. Additionally, a link has been found between smoking and increased risk of nuclear cataracts as well as earlier onset and surgical intervention needed compared to those who have never smoked (Tan et al. 2008).

Other causes include ocular trauma, metabolic changes such as diabetes, severe diarrhoea, drug side effects (e.g. steroids) and exposure to some radiations such as those seen in microwaves and infra-red light (Rink 1987). Links have also been found between UV exposure and increased incidence of cataracts (Zigman et al. 1979; Cheng 1989).

The nucleus has been found to be sensitive to some nutritional deficiencies; protein, vitamin A, thiamine and riboflavin can protect against the onset of nuclear cataracts if consumed in the necessary amounts (Cumming et al. 2000).

Another reason for lens changes is due to the ageing process, the ratio of insoluble cells increases greatly with age; it is thought that some of the soluble cells become insoluble. This is linked with the opacification process that is seen in cataract development (Oyster 1999).

1.1.7.1 Classification

The three most common types of cataracts are nuclear, cortical and sub-capsular. They are generally classified by the location of and density of the opacity. The most commonly used classification system is the LOCS (lens opacities classification system) III (Chylack et al. 1993). Another method of classification is the Oxford classification that classifies the cataract by severity and presence of various features within the lens including spokes, retro dots, brunescence and posterior sub-capsular opacity (Sparrow et al. 1986).

1.1.7.1.1 Nuclear Cataract

The most commonly occurring age-related cataract is the nuclear sclerotic cataract (Steinert 2010). The continuous growth of lens fibres throughout life, compresses together forming a larger and less pliable structure. The lens proteins then aggregate and release pigment. This decreases the transparency of the lens and causes the nucleus to appear yellow or even brown with excess pigmentation.

Protein changes in the cytoplasm scatters the light and it appears as opacification of the lens (Steinert 2010).

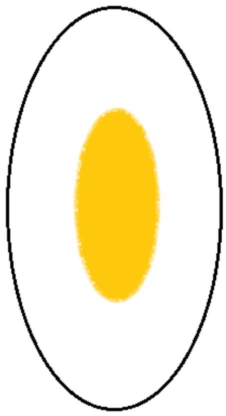

Figure 1.10: Nuclear cataract

1.1.7.1.2 Cortical cataract

Cortical cataracts occur due to fluid clefts forming which result in plaque spokes. Eosinophillic fluid accumulates between the lens cells, displacing and degradating bordering cells. If left, globules of protein released from the cells can build up to replace the cortex and form a morgagnian cataract. In other cases deposits of crystals made up from lipids, cholesterol or calcium can form in the deep cortex. This results in a characteristic 'Christmas tree cataract' as seen in myoptonic dystrophy (Steinert 2010).

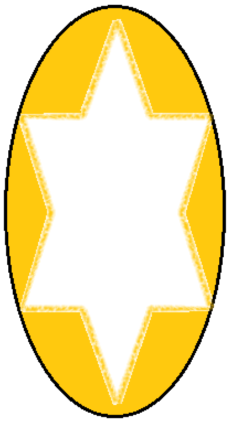

Figure 1.11: Cortical cataract

1.1.7.1.3 Posterior Subcapsular Cataract

Posterior subcapsular cataracts are caused by proliferation of peripheral lens epithelium cells. These migrate towards the back of the lens, enlarge and appear as plaques in front of the posterior surface. Formation of this type of cataract can be associated with certain medications such as corticosteroids or injury (Steinert 2010).

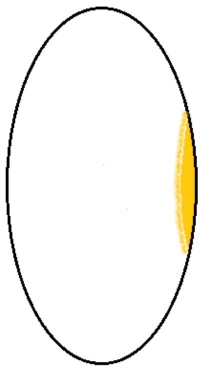

Figure 1.12: Posterior Sub-capsular Cataract

1.2 Cataract Surgery

1.2.1 History

Cataract removal or surgery has existed in some form or another for around 3000 years. Primitive methods of surgery included the crude methods of couching that was later evolved and replaced in the developed world by extraction techniques. Objects used for cataract surgery have been found in Greece dating back between 1000 and 2000 B.C. and it also thought to have occurred in both ancient Egypt and Greece as well as in Roman times (Pesudovs et al. 2001; Blomstedt 2014).

1.2.1.1 Couching

This method describes the dislodging of a mature cataract from the zonule fibres and moving the opacity away from the central vision. Initially this was carried out with a blunt object that would hit or probe the eye hard enough to dislodge the lens from the aged and weakened zonules (Bellan 2008). Later, it developed into the use of a sharp needle-like object that would pierce the eye and break the zonules to dislodge the lens (Bellan 2008). This technique was standard until around the 19th century when other techniques were developed. Nevertheless, couching still occurs in some of the more rural and less developed countries such as Yemen; carried out by travelling traditional healers and 'quacks' (Bamashmus 2010). Unfortunately, this technique carries a high risk of blindness through secondary complications such as retinal detachment, corneal opacity and panuveitis and has been shown to be a significant cause for ocular morbidity (Bamashmus 2010).

1.2.1.2 Early Extraction

Although couching remained the dominant technique for cataracts until 1750 AD, there has been evidence of the earliest methods of extraction that first reported to have occurred in India by Sushrata in 800 B.C (Grzybowski et al. 2014). Although it was originally thought to be the primitive method of couching, further investigation found that the description more closely matched that of an extracapsular extraction. The description included opening of the capsular bag and an attempt at removing the lens (Roy et al. 1975). Other attempts at extraction were not reported until around 1750 in Paris, this technique removed the lens as a whole through a very large corneal incision and was associated with a various infections and mortalities (Bellan 2008). Later development of sutures and alternative locations of incisions such as the formation of scleral tunnels began to emerge with lower infection rates as the methods evolved over the next two centuries (Jampel 1999).

1.2.1.3 Intracapsular versus Extracapsular Extraction

There are two main methods of cataract extraction: intracapsular extraction and extracapsular extraction. Jacques Daviel introduced cataract extraction to France in 1753 and the technique was developed throughout the 19th and 20th century (Hildreth 1952). Both techniques benefited greatly from the introduction of anaesthesia, introduced by Koller in the late 19th century, coming in the form of cocaine eye drops (Goerig et al. 2012).

1.2.1.3.1 Intracapsular Cataract Extraction (ICCE)

This is the removal of both the lens and capsular bag, which involves separating the capsule from the zonule fibres completely and had the advantage of removing the possibility of posterior capsular opacification (PCO). However, it also holds the risk of posterior subluxation of the lens into the vitreous, leading to severe complications (Pesudovs et al. 2001).

1.2.1.3.2 Extracapsular Cataract Extraction (ECCE)

This is the removal of the lens from within the capsular bag, leaving the elastic capsular bag in place and acting as a barrier to the posterior chamber. It became a less popular technique by the early 20th century until the appearance of intraocular lenses that were much more successful when implanted into the vacated capsular bag (Apple 2000; Bellan 2008).

1.2.1.4 Aphakia After Cataract Surgery

Until the introduction of IOLs in the mid to late 20th century, patients were left aphakic after the surgery. This meant that they were left with a significant hypermetropic (longsighted) refractive error (around 15-20 Dioptres). The main way to correct this was through the use of spectacles. Nonetheless, the high prescriptions required caused many problems; the high plus power caused significant magnification and this caused a reduction in the visual field for the patient. In addition to this, the corrections would be bulky and heavy leading to uncomfortable spectacles if worn all day. Contact lenses offered an alternative option but as most wearers were elderly, there were a lot of problems with handling and tolerating the lenses (Apple 2000; Pesudovs et al. 2001).

1.3 Intraocular Lenses, IOLs

The introduction of intraocular lenses (IOLs) was a long awaited solution to the problem of aphakia. Harold Ridley was the pioneer of the IOLs, implanting the first IOL on the 29th November 1949. The IOL was 8.35 mm in diameter, shaped like the crystalline lens and weighed 112mg. Despite successful posterior capsular bag placement and wound closure, the visual outcome was not a success: the lens induced -18D of myopia for the patient (Apple 2000; Hoffer 2010; Lindstrom 2010).

Ridley credits the inspiration of the idea to a medical student who asked why there was no replacement lens for the one being removed when observing one of his a cataract extractions (Apple 2000). It took nearly 40 years of development and research to bring Harold Ridley's initial idea of a posterior chamber IOLs sitting in the capsular bag into a successful reality (Lindstrom 2010).

Ridley's initial implantations had a significant level of post-surgical complications including dislocation. It was due to this that other surgeons began to look for an alternative site for insertion of the lens (Lindstrom 2010).

Baron first proposed the anterior chamber IOL. He produced a solid plastic lens that sat in the anterior chamber, in contact with the corneal endothelium. This design caused many problems including corneal decompensation, inflammation and secondary glaucoma due to the position of the IOL in respect to the cornea and anterior angle (Hoffer 2010). Strampelli, Choyce and Scharf redesigned the anterior chamber IOL to give clearance from both the cornea and anterior chamber angle. Dannheim introduced the idea of closed loop haptics and Barraquer cut part of the loops to introduce an open loop haptic that would later form the basis of the modern day posterior chamber IOL designs (Hoffer 2010).

Choyce, who had worked closely with Ridley, produced many different anterior chamber IOLs and was the first to achieve Food and Drug Administration (FDA) approval following adaptations to the Strampelli design (Hoffer 2010). Binkhorst, was another key player in the IOL development, and it was he who first coined the term Pseudophakia in the late 1950's (Hoffer 2010). He was a great believer in using Iris clip IOL designs and saw some improvement in success when he implanted these after ECCE surgery making use of the capsular bag as another structure to stabilise the IOL with. Dislocation of his IOLs usually resulted in the IOL sitting fully in the capsular bag (Apple 2000).

By the 1980's, extracapsular extraction with implantation of the IOL in to the capsular bag had risen in popularity once again (Rosen et al. 2013). Binkhorst among others felt that this would help stabilise the IOL position and decrease post-operative complications (Apple 2000). John Pearce was the first to produce an IOL specifically designed for implantation in the posterior chamber. It was tripod in design with two feet in the bag and one sutured to the iris (Rosen et al. 2013). Others soon followed suit such as Shearing with J type haptic designs to increase stability. It was Anis who produced the first fully in the bag design with a double closed looped haptic and Arnott who produced a one-piece Poly(methyl methacrylate) (PMMA) IOL also to sit inside the capsular bag (Apple 2000).

Foldable IOLs began to appear in the early 1980's with Epstein producing the first silicon foldable IOL to be placed in the capsular bag. In California, USA, Mazzacco began implanting a silicon plate haptic foldable IOL through a 3.5 mm incision following phacoemulsification (Hoffer 2010). However, there were initial problems adapting to the new technique as the IOL needed to be placed within an intact capsular bag with a circular capsularhexis (introduced by Fercho) as stipulated by the FDA (Hoffer 2010).

New materials including acrylic polymers both hydrophobic and hydrophilic have been used for foldable IOLs as well as silicon elastomers as their properties allow them to be folded at room temperature for insertion through smaller incisions (Steinert 2010).

1.4 Modern IOLs

In a phakic eye, the cornea produces positive spherical aberration and the crystalline lens causes negative spherical aberration. In a youthful eye these aberrations largely cancel each other out (Steinert 2010). With age, the lens increases in positive spherical aberrations (Glasser et al. 1999). When an eye is made pseudophakic, it is important to consider this correction of spherical aberration

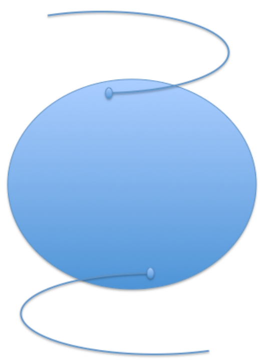

Figure 1.13: Open-loop haptic IOL

1.5 Spherical IOLs

Traditional monofocal IOLs incorporate spherical optics and hence increase in positive spherical aberrations (SA) of the eye. The positive SA of this design coupled with the positive SA of the cornea results in a loss of optical quality, especially with increased pupil (aperture) size (Eppig et al. 2009). However, this IOL type is less sensitive to tilt and decentration as other aspheric designs and the optics are not affected in these instances (Eppig et al. 2009). In the earlier IOLs with poor stability, this may have been a benefit of the design. Another additional benefit is that the increase in spherical aberrations increases the depth of focus.

1.5.1 Aspheric IOLs

The advent of laser surgery dramatically increased knowledge of sophisticated optics and optical systems including the measurement and detection of aberrations and quality of vision (Steinert 2010). This increase in understanding allowed development of IOLs that could be designed to reduce aberrations and increase the optical quality. However, one disadvantage of aspheric IOL design is that they limit the depth of focus in comparison to spherical lenses. Aspheric IOLs were designed to limit and control aberrations produced by the IOLs with some designs aimed at reducing the overall aberrations in the eye to improve the vision even more (Steinert 2010).

A normal cornea is thought to produce an average of +0.27 μRMS (root mean square) SA and the lenticular SA averages at -0.27 μRMS (Lindstrom2000).

1.5.1.1 Aberration Correcting IOLs

Aspheric IOLs can be produced to create negative spherical aberrations, designed to cancel out the positive spherical aberrations produced by the cornea and improve the vision post-operatively for the patient. The Tecnis *Z9000* IOL (Advanced Medical Optics) is aberration-free IOLs. It is designed to produce -0.277 μRMS of negative spherical aberrations to cancel out the positive spherical aberrations of the cornea. They have been found to produce superior mesopic vision with good self-reported improvement in night-time driving from patients (Denoyer et al. 2009). This type is highly sensitive to decentration and can increase other higher order aberrations such as 'Coma' with incorrect positioning (Montés-Micó et al. 2009). The value of Spherical aberrations varies with IOL design and may over or under-correct depending on the correction offered by the lens and the individual's magnitude of corneal spherical aberration.

1.5.1.2 Aberration Neutral IOLs

These IOLs are designed to be more robust against the effects of decentration, with a continuous power profile across the surface and to reduce the aberrations produced by a typical spherical IOL. This leaves the positive aberrations from the cornea uncorrected but not increased (Montés-Micó et al. 2009). This can be an advantage in an eye with atypical amounts of corneal SA as the aberration correcting IOLs could be over correcting the SA. The SofPort Advanced Optics IOL (Bausch and Lomb) is an example of this type. It is found to perform well in mesopic conditions and near vision in comparison to both spherical and aberration control IOLs and displacement is not as debilitating as aberration control lenses (Denoyer et al. 2009). It should also be noted that positive spherical aberrations in the ocular system can aid near vision and may be a benefit to the patient.

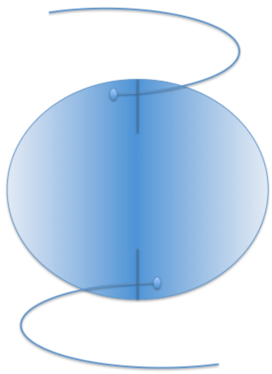

Figure 1.14: Open looped haptic toric IOL with markings

1.6 Toric IOLs

Toric IOLs (Figure 1.14) have been designed to correct astigmatism and have been shown to provide increased spectacle independence for distance tasks (Agresta et al. 2012; Mencucci et al. 2013; Hirnschall et al. 2014). For a toric IOL to be effective, the principal meridians of the IOL need to be aligned with the post-operative principal meridians of the cornea. If a toric IOL is not aligned with the steepest meridian of the cornea, this can lead to an under correction of the refractive error. If the toric IOL is placed 30 degrees from the required axis, the astigmatism correction is reduced to nothing. Small amounts of misalignment can cause a significant loss in visual acuity (Sanders et al. 1992; Felipe et al. 2011).

Aspheric toric IOLs have also been introduced successfully and demonstrated good optical correction of both astigmatism as well as spherical aberrations (Scialdone et al. 2013).

1.7 Multifocals

The Monofocal IOLs (spherical, aspherical and toric) have been designed to correct the distance vision. Implantation of these lens designs will not correct the near vision at all. Patients will require some form of optical correction for all near work e.g. spectacles. Multifocal IOLs are designed to create at least two focal points for the eye to allow a correction of both distance and near vision. There are multiple different designs available, including toric multifocal designs. Implantation of a multifocal lens lead to high numbers of subjects reporting no need for spectacles and improved near vision (Packer et al. 2010; Calladine et al. 2012; Gil et al. 2012; de Vries et al. 2013).

1.7.1 Refractive

This design includes one or more concentric circles of power in the lens to create two or more images at difference distances. Despite high levels of success with these levels and improvement of near and distance acuity reported by the patients, there are a number of side affects associated with this design. Most multifocal IOLs can induce halos and glare (de Vries et al. 2013), refractive multifocal often cause more photic phenomena than diffractive lenses (Cillino et al. 2008).

Figure 1.15: Refractive multifocal IOL

1.7.2 Diffractive

This design utilises the principals of diffraction rather than refraction. Light detracting at a boundary of an optical zone creates an interference pattern and separates the light, the separation of the optical zone rings (boundaries) will determine how much the light splits and the difference in focal length. Again, there has been high success with this type in creating a correction for different viewing distance. However, the design commonly increases aberrations and is also known to decrease the image contrast for the patient (Braga-Mele et al. 2014).

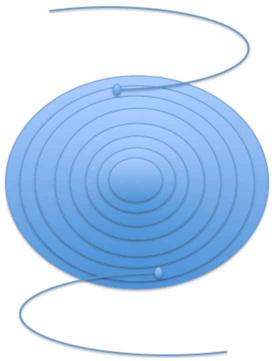

Figure 1.16: Diffractive multifocal IOL

1.7.3 Sectorial

Sectorial designs are not rotationally symmetrical with one segment of near vision on the lens. This design can produce good distance and near vision but some are subject to increased levels of coma aberrations and sensitive to decentration (Alio et al. 2011).

Figure 1.17: Sectorial multifocal IOL

1.8 Toric Multifocal IOLS

Toric multifocal IOLs have been designed to provide correction for corneal astigmatism as well as near and distance vision correction. These lenses use of the above forms (refraction, diffraction or sectorial) in combination with a toric correction and have had some success in the correction of moderate astigmatism in combination with a distance near correction (Shimoda et al. 2014) (Alio et al. 2011; Garzon et al. 2015; Hayashi et al. 2015).

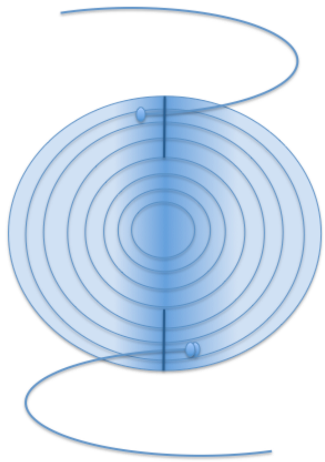

Figure 1.18: Diffractive toric multifocal IOL

1.9 Surgical Incisions

In order to remove the cataract it is necessary to create at least one incision into the anterior chamber of the eye.

1.9.1 Surgically Induced Astigmatism

The corneal incisions made during cataract surgery can alter the shape of the cornea (Shepherd 1989; Buzard et al. 1991; Steinert et al. 1991; Hayashi et al. 1995; Alio et al. 2005). This change in cornea shape is termed surgically induced astigmatism (SIA). It is generally accepted that an incision will cause a flattening effect to meridian on which it sits (Tejedor et al. 2005; Hirnschall et al. 2014) (Table 1.2).

1.9.2 Changes in Surgical Incisions

Different size, shape, location and orientation of the surgical incision alter the post-surgical outcomes that are associated with the surgery (Kershner 1997; Linebarger et al. 1999; Alio et al. 2005; Reddy et al. 2007; Wei et al. 2012).

1.9.2.1 Limbal incision

This incision is made at the limbal region of the cornea. A large 180° limbal incision was carried out in ICCE surgeries to allow both the lens and capsular bag to be removed as a whole (Linebarger et al. 1999). This incision resulted in a long recovery time, a high risk of complications and a highly astigmatic cornea (Steinert 2010). After the introduction of posterior chamber IOLs, the ECCE increased in popularity and the incisions became smaller, around 10-11mm in length (Linebarger1999). This was sufficient to remove the nucleus whole and insert a rigid PMMA IOL (Steinert 2010).

Author	Eyes	N	Incision Size (mm)	Location	SIA (D)	Follow Up
Chang et al (2015)	605	357	2.75	S	~0.65	3 month
		248	2.2		~0.50	3 months
Febbraro et al (2015)	190	61	3	S WTW	0.38±47	1 month
				ATW	0.38±47	
		66	2.2	WTW	0.05±0.45	
				ATW	0.16±0.34	
		63	1.8	WTW	0.04±0.39	
				ATW	0.16±0.29	
Ofir et al (2015)	70	49	2.8	steepest meridian	0.49±0.29	8.65±2.4 weeks
Nemeth et al (2014)	88	88	2.4	83-139°	0.50 ±0.28	1 month
Ozyol & Ozyol (2014)	45	45	2.2	SN	0.39	3 months
				S	0.22	
				ST	0.17	
				T	0.28	
Klamann et al (2013)	129	129	2.75	steepest meridian	0.51±0.34	4 weeks
			2.2		0.54±0.49	
			1.8		0.34±0.29	
Luo et al (2012)	120	120	3	T	0.65	3 months
			2.2		0.35	
			1.8		0.25	
Musanovic et al 2012	60	30	3	??	0.85±0.63	1 month
		30	2.2		0.85±0.72	
Yoon et al (2012)	60	30	3	N	0.62	3 months
				T	0.53	
Wei et al (2012)	18	36	3.5	T	1.11± 0.82	3 months
			2.5		0.84± 0.63	
Alio et al (2011)	27	21	~2.7	Steepest meridian	2.49 ±0.91	6 months
Gobin et al (2011)	<1D astig	42	2.8	T	0.06	3 months
	>1D astig	34			0.09	
Visser et al (2011)	67	45	2.2	Superior	0.19 ± 0.78	6 months
				Temporal	0.40 ± 0.60	
Masket et al 2009	44	22	3	?	0.35±0.21	6 weeks
		22	2.2		0.67±0..48	
Moon, et al, 2007	98	121	2.5	T	1.00 ±0.05	3 years

Table 1.2: Recent reports of surgically induced astigmatism using micro-incisions. (S= superior, T = temporal, WTW = with the wound change, ATW = against the wound change.)

1.9.2.2 Phacoemulsification

Charles D Kelman is responsible for the revolutionary introduction of phacoemulsification to cataract surgery. The technique was developed to remove cataracts through an incision as small as 2-3 mm by fragmenting the lens inside the eye before removal (Pandey et al. 2004). This technique used ultrasonic energy to break up the cataract nucleus and cortex into small parts and then aspirate them (Bellan 2008). By being able to break up the cataract before removal, the gateway was opened for much smaller incisions being made to carry out the surgery (Pesudovs et al. 2001; Bellan 2008; Steinert 2010). The first operation with phacoemulsification was carried out in 1967 on a painful red eye that was to be enucleated (Linebarger et al. 1999). Kelvin then went on to develop and refine the instrument and technology and to stabilise hand piece (Linebarger et al. 1999). This technique was not used routinely until the late 1980's (Pesudovs et al. 2001). At this point, the final incision was determined by size and type of IOL that is to be inserted.

1.9.2.3 Scleral Tunnel Incisions

Moving the incision anteriorly from the limbus and entering the anterior chamber through a scleral tunnel was designed to help stabilise intraocular pressure and prevent iris prolapse (Alpar 1985; Linebarger et al. 1999). It also allowed quicker recovery in comparison with limbal incisions (Steinert 2010). Consequently, the sutures used with this incision tend to induce a moderate level of astigmatism immediately after surgery. Though this can be temporary and the astigmatism can reduce again after the sutures have been removed. A partial depth incision is made into the sclera through the conjunctiva, cauterising blood vessels where necessary, a tunnel or pocket incision is then made through the corneal into the anterior chamber (Alpar 1985). Careful planning and pre-placement of the sutures at the beginning of surgery helped to minimise the pull and torque of the sutures that induces astigmatism (Alpar 1985). The choice of the wound site, often moving it to a temporal position to avoid gravity and lid interference that prevented wound healing, improved the outcome. Smaller tunnel incisions (<5mm) can heal without sutures, reducing the surgical effect further (Dam-Johansen et al. 1997).

1.9.2.4 Clear Corneal Incisions

This is the most commonly used incision in modern surgeries, teamed with phacoemulsification and foldable IOL implants. Initially there was some confusion in the classification of an incision as limbal or clear cornea, and the two were often confused. One definition is that a limbal incision is made within the limbal arcades or conjunctival vessels and a clear corneal is created beyond these (Steinert 2010). The corneal fibrils change direction and arrangement at the limbal arcades (Meek et al. 1999; Boote et al. 2003), which may alter the healing response. Small clear corneal incisions are self-healing and don't require sutures (Linebarger et al. 1999). However, with the increase in popularity of this type of incision, there has been an increase in some post-operative complications such as endophlamitis infections. According to Mamalis et al, the increased rate of infections may be due to lack of wound suturing (Mamalis et al. 2008).

1.9.2.5 Effect of Size of Incisions

With the introduction of phacoemulsification and foldable IOLs, incision size could be reduced. Where a sub 4 mm incision is used, it has been advised that sutures are not necessary (Dam-Johansen et al. 1997; Linebarger et al. 1999).

The smaller the incision made, the less SIA that is induced with the incision (Samuelson et al. 1991; Hayashi et al. 1995; Wei et al. 2012) Hayashi found that with an allowable limit of 0.5DC of astigmatism, there was almost no change in corneal shape post-surgically (Hayashi et al. 1995). Other studies by groups led by Ofir, Wei, Hill and Change found between 0.40 and 0.80D of SIA using micro-incisions (<3mm) (Hill 2008; Chang et al. 2012; Wei et al. 2012; Ofir et al. 2015). Wei and colleagues found that although there was no significant difference between 3.5 and 2.5 mm incisions, the smallest incision was the most stable post-surgically (Wei et al. 2012). Even with these small changes in corneal shape, it is important to take SIA into account to allow improved prediction of the post-surgical results (Hill 2008).

1.9.2.6 Effect of Location of Incision

The location of the surgical incision is an important factor in the outcome of the surgery as SIA varies with the location (Wirbelauer et al. 1997; Tejedor et al. 2005). It is now widely accepted that temporal incisions have been shown to induce the least amount of SIA; the most is induced with superior incisions and is likely to increase against the rule astigmatism (Mendivil 1996) (Wong et al. 1994; Tejedor et al. 2005). A nasal incision will have a greater SIA than the temporal but less than superior (Tejedor et al. 2005). Superior incisions are thought to cause a larger SIA due to the shorter distance between the incision site and corneal apex as the cornea is approximately 1mm shorter in the vertical meridian when compared to the horizontal meridian (Ozyol et al. 2012).

During cataract surgery, there are several incision strategies that can be adopted to reduce corneal astigmatism. The most common method is to place a clear corneal incision on the steepest corneal axis (Wirbelauer et al. 1997; Ozyol et al. 2012) with the aim of creating a flattening effect along this axis. It has been reported that the choice of incision site can be determined by the amount of pre-existing astigmatism and flattening effect required (Tejedor et al. 2005). For example, if there is at least 1.50 dioptres of astigmatism with steep axis at 90 degrees then a superior incision is recommended. Despite the apparent advantages regarding on-axis incisions, the site of choice for most ophthalmologists is on the temporal side (Leaming 2004; Pick et al. 2008).

Careful planning of the placement and size of the incision or addition of extra incisions is sometimes used to control astigmatism in the surgery.

1.9.2.6.1 Limbal relaxing incisions (LRI)

Partial thickness incisions can be used to try and reduce corneal astigmatism. They are made independently of the corneal incisions used for the surgery and are placed to flatten the cornea where needed. A nomogram is used to determine the position/axis and thickness of the incision required (Ouchi et al. 2009). However, this technique relies upon a predictable healing response. The surgeon must carefully consider the location of the incision for the insertion of the IOL as this may cancel out the effect of the LRI (Ouchi et al. 2009). The advent and use of femtosecond lasers make this easier to control (Trikha et al. 2013; Kohnen 2014; Chan et al. 2015).

1.9.2.6.2 Paired opposite clear corneal incisions (Paired OCCIs)

This type is thought to provide a predictable correction for pre-existing corneal astigmatism during cataract surgery (Khokhar et al. 2006). A second incision can be made along the same axis but on the opposite side of the cornea (paired opposite incisions) to create a greater flattening effect and reduce higher levels of astigmatism (Khokhar et al. 2006). This technique also relies upon a predictable and uniform corneal healing response.

1.9.3 Toric IOL Calculators

Hill reports that when implanting a toric IOL, the SIA (surgically induced astigmatism) must be taken into account to determine the toric IOL position and power. It was proposed that SIA needed to be taken into account during pre-surgical planning in order to achieve optimal visual outcomes (Hill 2008). The predicted post operative corneal astigmatic power can be calculated using commercially available toric IOL calculators such as the Alcon Acrysof Toric IOL calculator (http://www.acrysoftoriccalculator.com/Calculator.aspx, accessed November 2015).

The Alcon Acrysof calculator uses the oblique cylindrical lens formula to predict the post-surgical axis and power that will need to be corrected by the toric IOL. It predicts that the steepest axis of the corneal astigmatism will move post-surgically unless the incision is placed on axis. This is based on the assumption that the SIA caused by the incision, combined with the pre-surgical astigmatism will act similarly to the combination of two cylindrical or toric ophthalmic lenses. These oblique cylinder calculations were derived to calculate the resultant power of two thin toric lenses held together (Holladay et al. 2001).

If a corneal incision is placed obliquely to the steepest corneal meridian then the calculator will predict a post-operative shift of the meridian. This facility allows the surgeon to place the principal meridians of the toric IOL in accordance with the predicted post-operative steep corneal meridian rather than the original pre-surgical meridian (Hill 2008). Although there has been extensive research in the dioptric power change to the cornea, to date no studies have been conducted to determine if this change in corneal meridian takes place. Furthermore, the toric calculator is based upon thin toric lens assumptions and it is unknown if the cornea and incision act like two thin toric lenses in contact.

1.10 Vision and Mobility in uncorrected Astigmatism

1.10.1 Prevalence of Falls

One third of people over the age of 65 fall each year in the UK (approx. 3 million). Hip fractures alone can cost up to £28,000 per patient, not including the ambulance fee (£115 per call out). Each year hip fractures (mostly caused by a fall) cost around £2 billion. Many people never fully recover their mobility and independence. It is also estimated that one in five patients dies within 3 months of the fall despite treatment (AgeUK 2012). Most falls occur during routine tasks or walking, 50% occur within the home. Tripping over an object has been observed to be the most common cause of falls (Robinovitch et al. 2013). Although vestibular reflexes, decreased muscle strength, decreased standing balance is included, vision is commonly mentioned as a large contributing factor into co-ordinating balance, planning movements and maintaining balance. Visually impaired older people are more likely to fall than sighted peers (Dhital et al. 2010).

1.10.2 Vision

There are multiple risk factors that can contribute to falling, rarely is it due to one single cause. There are conflicting articles on the significance of visual acuity reduction on the risk of falls, but there seems to be some agreement that it makes the subject more likely to fall. In many of the cases, the visual impairment could be prevented with a change in glasses or cataract surgery. Visual acuity alone is not enough to determine the visual impairment (Abdelhafiz et al. 2003). There is no defined range or reduction that is significant (Black et al. 2005). Contrast sensitivity and visual fields seem to have the biggest impact on hip fractures (Dhital et al. 2010) (Abdelhafiz et al. 2003).

1.10.3 Intervention: Cataract Surgery

There is conflicting evidence on the reduction of falls associated with cataract surgery intervention. It appears that earlier intervention of cataract surgery can be used to reduce the risks of falling in certain groups of the elderly population, especially to those with more than 4 medications a day, who use a walking appliance and have a previous history of falls (Brannan et al. 2003). In a large study of Medline data in America, it was shown that there is a reduction in the incidence of hip fractures after cataract surgery. The conclusion was that earlier surgical intervention could reduce the incidence of hip fractures and save money (Tseng et al. 2012). In contrast to this, a study carried out by McGwin Jr et al

(2006) followed a group of elderly patients with cataracts over 1 year (half elected not to have surgery) and found that surgical intervention made no difference to the rate of falls. However, the follow up of 1 year may have meant that increased risk of falling with age cancelled out any effect of cataract removal (McGwin Jr et al. 2006).

1.10.4 Pseudophakia and Uncorrected Astigmatism

NHS patients with significant corneal astigmatism will likely undergo routine surgery with no adjustments for this type of refractive error. A spherical or aspherical monocular IOL will be implanted with a standard incision, which leaves the astigmatism uncorrected post-surgically. This uncorrected refractive error can reduce acuity, Peters found a line reduction for each step of 0.50DC (Peters 1961). The remaining uncorrected astigmatism can also impede various tasks including: reading, using the computer and viewing a mobile phone (Wolffsohn et al. 2011).

Our vision plays an important part of our locomotion and gait, and is used to continually to adapt both to our surroundings (Patla 1997; Patla 1998). If a refractive error is left uncorrected, it can be assumed that there will be an impact on stability and mobility. When monofocal IOLs are implanted in to an astigmatic eye, it results in a significant refractive error that has been shown to cause problems with some tasks (Wolffsohn et al. 2011). To correct the refractive error, a spectacle or contact lens correction will need to be worn, increasing the need for spectacles for these patients. In addition to this, correction of astigmatism with toroidal lenses has been shown to induce distortion and visual problems (Guyton 1977). Furthermore, induced oblique astigmatism has been shown to alter foot placement when stepping up onto a raised surface (Johnson et al. 2013).

Nevertheless, the evidence of the effect of cataracts on walking and balance is conflicting (Supuk et al. 2013). The role of vision in mobility and balance is complex and not fully understood (Guerraz et al. 2008) and can change depending upon the body health and age. For example, there is a suggestion that changes in foot placement occur due to age in general (Foster et al. 2015) therefore changes seen in cataract patients are difficult to distinguish from those expected due to the normal aging process.

1.11 Conclusion

Cataract surgery has now improved to such an extent that most patients and surgeons seek distance vision correction as well as removal of the cataractous lens (Gale et al. 2007; Alio et al. 2014). In order to do this the surgeon must be able to accurately assess the cornea, predict the impact of the surgical incisions and determine the refractive error of the eye that can be corrected by IOL. In the case of residual astigmatism due to the corneal shape, it is even more imperative to accurately assess the principal meridians so that a lens or relaxing incisions can create the most effective correction. However there are many sources of error and assumptions about the corneal shape made that have not been fully investigated despite the potential impact on the visual outcome after surgery. A better understanding of the corneal response is necessary.

Precise keratometry is key for the assessment of the corneal shape to determine the astigmatism, the assessment of SIA and the prediction of post-operative astigmatism with toric IOL calculators. There are various instruments available to assess keratometry, but it is unclear which is the best choice for most accurate and repeatable assessment of the cornea. There is no gold standard and it is unknown if they are interchangeable in the hospital environment in which they are often used.

The effect of any instrument error on the calculation of SIA has also not been previously investigated and it has been assumed that it is negligible and the full amount of change (the difference between visits) is reported. However the modern micro- incisions used currently cause so little change that the contribution of the error may be much more significant now. Additionally the use of Cartesian vectors to assess the change may also cause erroneous results in comparison to other methods suggested e.g. Polar method and little has been investigate in this area.

The toric IOL calculators have been produced to increase the accuracy of toric IOL implantation. These calculator methods are based on optical lens equations (the cross-cyl formulae) and have not previously been validate for application to the pre-operative cornea and predicted SIA to see if the change in cornea shape is predictable despite their widespread use.

To achieve emmetropia for the whole population, toric IOLs need to be used for around 20% surgeries (Ferrer-Blasco et al. 2009). In order to provide the most accurate correction of the eye, the surgeon must be able to predict the post-operative astigmatism, which is assumed to fully correspond with the cornea astigmatism. There is well-established linear relationship that has been previously reported to describe this relationship. Nevertheless, there has been little to no assessment of the accuracy of the axis and magnitude as separate aspects of the corneal curvature assessment. Most of the previous work has used magnitude alone or vectors. The accuracy and repeatability of the axis in particular has been neglected despite the necessity of accurate assessment and alignment with toric IOLs for most effective correction.

The improvements in cataract surgery have vastly improved the lives of many people. The benefits of cataract removal have been proposed to benefit mobility and balance in addition to general vision tasks such as reading. The evidence gathered so far has been conflicting and the effect has yet to be fully determined. However, the methods of assessment have been limited to questionnaires and standing balance and this may have limited the accuracy and sensitivity of the data collection. Direct assessment of balance, especially during mobility tasks may allow a more detailed assessment of the changes seen due to reduced vision from both cataracts. Furthermore, the difference in correction for astigmatic patients has not been assessed to determine whether toric IOLs can be more beneficial than spherical lenses in daily life and could reduce falls.

Aims of the Thesis:

- To determine the repeatability and reproducibility of the measurement of corneal astigmatism.
- To assess the relationship between ocular refractive astigmatism and corneal astigmatic error.
- Examine the methods of calculating surgically induced astigmatism.
- To examine the validity of using an oblique cross cylinder formula for predicting post operative astigmatic error.
- To develop a novel method of testing changes in mobility and postural stability induced by reduced vision.
- Determine the effect of form deprivation and loss of contrast sensitivity on mobility and postural stability tasks.

Chapter 2 Comparison of Reliability and Repeatability of Corneal Curvature Assessment with Six Keratometers

2.1 Introduction

2.1.1 Background

The cornea is responsible for ⅔ of the total optical power of the eye and hence the accurate assessment of corneal curvature prior to cataract surgery is vital for achieving optimal refractive outcomes. Until recently, the accuracy of determining both corneal astigmatic power and axis has not been as crucial for instrumentation used in pre-cataract surgery measurements, since spherical intraocular lens (IOL) power determination is based on average corneal curvature.

Cataract surgery has evolved into a precise refractive procedure and there is now an increased demand from both patients and surgeons for the correction of astigmatism at the time of surgery. Consequently, reliably identifying and assessing the principal corneal meridians of curvature (power) is now an essential requirement. Correction of corneal astigmatism at the time of surgery can be achieved via manipulation of corneal curvature or through the implantation of toric IOLs (Buckhurst et al. 2010). Limbal relaxing incisions have a flattening effect on the cornea and are used to reduce astigmatism at the corneal plane. However, the refractive outcomes following this procedure can be variable given that the technique is dependent on a predictable healing response (Muller-Jensen et al. 1999; Ouchi et al. 2009; Buckhurst et al. 2010).

2.1.2 Keratometry

Numerous instruments are commercially available for the assessment of corneal curvature and the measurements made by these instruments are widely considered to be interchangeable (Read et al. 2009; Visser et al. 2012; Whang et al. 2012). Yet, given that the optical principles behind these instruments differ, it is likely that inherent differences among devices exist when assessing corneal power. Furthermore, in much of the published literature examining the validity and repeatability of these instruments, the emphasis has been on the mean spherical curvature alone, ignoring the accuracy of the astigmatic orientation and magnitude. A recent trend given the popularity of toric IOLs, is to examine corneal curvature through vector analysis (Santodomingo-Rubido et al. 2002; Srivannaboon et al. 2012; Whang et al. 2012; Magar et al. 2013; Hoffmann et al. 2014; Srivannaboon et al. 2015) as this provides a more detailed and relevant assessment of corneal power (Alpins 2001; Alpins et al. 2004).

Modern topographers and auto-keratometers still utilize the reflection principals and measure the anterior surface via reflection from the tear film. In topography, the whole corneal surface is used as a convex mirror and the reflection of a known light source and diameter (most commonly a Placido disc) are analysed.

Topographers analyse the whole corneal surface, although in order to provide readings that are interchangeable with traditional keratometry, ‘simulated Ks’ are produced over a smaller central area (usually 3mm) producing two principal meridians (minimum and maximum curvature) (Whang et al. 2012).

Scheimpflug imaging determines corneal curvature through the assessment of corneal sections. A corneal section is created by placing a camera at an angle to a slit beam of light projected onto the cornea. Multiple images are then taken while rotating the camera 360 degrees. A 3D image of the cornea can be created, allowing the assessment of both the anterior and posterior surfaces (Dubbelman et al. 2002; Elbaz et al. 2007).

2.1.3 Aim

The aim of this study was to assess the variability, reliability and agreement of corneal curvature measurements quantified as mean spherical equivalent (MSE) and corneal astigmatism determined using a range of commercially available devices.

2.2 Methods and Materials

2.2.1 Subjects

This was a prospective study examining one hundred eyes of one hundred adult subjects (32 males, 68 females). The mean age was 36.0 ± 11.4 years (range 19 - 57 years). All subjects were recruited from the Plymouth University staff and student population by the principal investigator (CH). Data collection occurred between April and July 2013.

2.2.1.1 Inclusion Criteria

- Aged 18 and over
- Healthy corneas.
- Able to give informed consent

2.2.1.2 Exclusion Criteria

- Previous refractive or other corneal surgery
- RGP contact lens wear, as a cause of corneal warpage (Wilson et al. 1990)
- Corneal dystrophies or other abnormal corneal pathology that would affect the accuracy of the reading (Roh et al. 2015)

Soft contact lenses wearers were asked not to wear their contact lenses on the day of assessment with at least 12 hours elapsed since the last wear to reduce the influence of the contact lens on the corneal shape.

2.2.1.3 Sample size calculation

The size of the subject group was determined with an alpha level of 0.05 and a power of 80% confidence. Multiple sample size test calculations were carried out with the G*Power 3 (Heinrich Heine Universität, Düsseldorf, Germany) programme to determine the size with the assumption of a moderate effect size advised by Cohen's table comparison of paired means (effect size 0.50), correlation (effect size 0.30) and ANOVA analysis (effect size 0.25). A minimum sample size of 84 was required to satisfy power requirements across these analyses (Prajapati et al. 2010). Therefore, 100 volunteers were recruited to allow for dropouts or exclusion of some subjects throughout the study. For the selection of the subgroup a minimum of 22 subjects were needed to compare the two observers: 30 subjects were recruited to allow for any loss throughout the study.

2.2.1.4 Ethical Approval

All procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by the Plymouth University Ethics committee (Ref 12/13-111 on 3rd April 2013).

2.2.2 Methods

All 100 subjects attended two assessment sessions, separated by at least 24 hours. At each visit, corneal curvature was recorded with six instruments, in a randomised order. Each instrument was calibrated at the beginning and at set intervals through the study. Single not multiple readings were not taken by the observers to replicate procedure in a routine clinical setting. The observer was masked to the readings as 5 out of the 6 instruments were automatic and the investigator could not influence the readings.

2.2.3 Instrumentation

2.2.3.1 Javal-Schiøtz

Keratometry utilizes the principles of reflection; the corneal surface and tear film act as a convex mirror, which reflect the image of an object at a given distance. The curvature of the cornea is then determined through analysis of the resultant image. Keratometry assumes a spherical corneal shape and is highly dependent on a stable tear film (Bennett et al. 1991). The Javal-Schiøtz is a two –position, fixed doubling, manual keratometer and calculates the central corneal curvature over a 3.4 mm diameter area (Bennett et al. 1991).

2.2.3.2 IOLMaster 500 (Carl Zeiss Meditec Inc., Jena, Germany)

The IOLMaster utilizes automated keratometry for the assessment of corneal curvature. It projects 6 spots in a hexagonal pattern of light onto the corneal/tear film at a diameter less than 2.3 mm. The separation of the opposite pairs of lights is measured objectively by the instrument's internal software. In the case of an astigmatic cornea, the curvature is calculated from three, fixed position meridians (Santodomingo-Rubido et al. 2002).

2.2.3.3 Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany)

The *Pentacam HD* is a non-contact anterior segment imaging device that is based on the principles of rotating Scheimpflug photography. The instrument uses a monochromatic slit light source (i.e. a blue LED at 475 nm) and a Scheimpflug camera, which together rotate around the optical axis of the eye (Dubbelman et al. 2002). The Simulated K readings (based on anterior corneal curvature alone) can be obtained over a small central area (3 mm chord length) that allows comparison with other instruments.

2.2.3.4 OPD scanner (Nidek Co., Ltd, Gamagori, Japan)

The OPD scanner III assesses corneal curvature using computerised Placido disc topography, again utilising principles of reflection. A Placido disc is projected onto the cornea/tear film, and the computer then analyses thousands of points reflected from the whole cornea. It simulates keratometry readings (Ks) for a 3 mm chord length (Yao et al. 2006).

2.2.3.5 Medmont E300 (Medmont PTY Ltd., Camberwell, Victoria, Australia)

The Medmont is a computerised Placido disc cone videokeratometer. It has 32 Placido rings and measures 9,600 data points per scan. The simulated K-readings are the steep and flat radius of curvature found with a 3 mm chord length (Wang et al. 2012).

2.2.3.6 The TMS-5 (topographical modelling system, TOMEY Corp., Nagoya, Japan)

The TMS-5 incorporates both a 31-ring Placido disc topographer and Scheimpflug tomographer. The results from the Scheimpflug measurement and topographical measurement are combined to produce an adjusted measurement (Guilbert et al. 2012; Hoffmann et al. 2014).

2.2.3.7 Assessment Procedure

Each subject was assessed on two separate sessions by a single trained observer. A subgroup of 30 subjects was then assessed again with each instrument by a second trained observer within the second session to determine the inter-observer variability. The second observer was blind to the results from the first observer. A single randomly selected subject was assessed on 10 separate measurement sessions (separated by a minimum of 24 hours) by a single observer to determine the intra-observer variability for each instrument.

2.2.4 Statistical Analysis

2.2.4.1 Assumption of Normality

The one-sample Shapiro-Wilk test was used to determine if results from each measurement followed a normal distribution. Where the data followed a normal distribution, parametric analysis was used; non-parametric statistical analysis was used for non-normally distributed data. The data was analysed using SPSS software (Version 20, SPSSInc, IBM, Chicago, Illinois, USA.

2.2.5 Keratometry Reading Conversion for Analysis

All keratometry results were converted to rectangular Fourier form of mean spherical equivalent (MSE) and J_0/J_{45} Cartesian vectors representing the cylindrical power and axis as a combined vector for analysis. The MSE was calculated by adding half the cylindrical power to the spherical power: MSE = Sph + ½ Cyl. J_0 and J_{45} were converted into vectors using the following formulae:

$J_0 = J \cos(2\alpha(\text{alpha}))$ *Equation 2.1*

$J_{45} = J \sin(2\alpha(\text{alpha}))$. *Equation 2.2*

(Thibos et al. 2001)

2.2.6 Analysis

Inter-observer repeatability was assessed via the Intra-Class Correlation Coefficient (ICC) on a subgroup of 30 subjects who had been assessed by two separate examiners. Intra-observer repeatability was determined by examining the Coefficient of Variance (CoV) for the single subject who had been assessed 10 times on each device and by examining the Intra-Class Correlation (ICC) on 100 subjects where the measurements were performed twice by a single examiner. Bland-Altman plots were created with SigmaPlot (SYSTAT software Inc, San Jose, California, USA) and used to determine the agreement and therefore potential inter-changeability of the instruments. Pearson's correlations were used to determine the correlation of results between instruments. The difference between means was assessed using repeated measures ANOVA followed by a Bonferroni *post-hoc* test on the results shown to be significant.

2.3 Results

2.3.1 Normality of Data

The Shapiro-Wilk test found the data to be normally distributed ($p<0.05$).

2.3.2 Inter-observer Repeatability

The inter-observer repeatability for MSE (Table 2.1) was greater than 0.95 for all instruments. The inter-observer repeatability for J_0/J_{45} (Table 2.1) showed greater variability than that for MSE particularly in respect to the Medmont and Javal Schiøtz (Table 2.1). The Pentacam and IOLMaster demonstrated the greatest inter-observer repeatability.

The intra-observer and inter-observer ICC between visits for all 100 subjects shows similar pattern of results (Table 2.1). The Pentacam showed the highest correlation whilst the TMS-5 showed the lowest.

ICC		IOL Master	Pentacam	OPD	Medmont	Javal Schiøtz	TMS-5
Between 2 observers (n=30)	MSE	0.994	0.996	0.978	0.985	0.955	0.995
	J_0	0.901	0.933	0.517	0.289	0.454	0.522
	J_{45}	0.895	0.872	0.600	0.499	0.514	0.728
Between 2 visits (n=100)	MSE	0.991	0.981	0.966	0.976	0.977	0.892
	J_0	0.829	0.911	0.711	0.678	0.787	0.598
	J_{45}	0.903	0.870	0.733	0.603	0.715	0.288

Table 2.1: Inter-observer ICC between two observers for the second visit (n=30) and intra-observer ICC between visits for all 6 Instruments (n=100).

2.3.3 Intra-observer Repeatability

The intra-observer repeatability (CoV) for MSE (Table 2.2) was less than 0.4 for all instruments with the IOLMaster showing least variation between readings by the same observer. In contrast, the intra-observer repeatability of J_0/J_{45} (Table 2.2) showed much greater variability, particularly for the TMS- 5 and Javal Schiøtz. The Pentacam and IOLMaster performed the best for J_0/J_{45}.

CoV	IOLMaster	Pentacam	OPD	Medmont	Javal Schiøtz	TMS-5
MSE	0.1	0.3	0.3	0.2	0.3	0.2
J_0	11	8.8	17.6	18	23.8	31.2
J_{45}	6.9	8.7	24.1	32.6	57.6	49.3

Table 2.2: CoV (%) for all 6 Instruments (n=1)

2.3.4 Mean vs. Difference Plots

Bland-Altman comparison plots (Figures 2.1 and 2.2) indicated that the Pentacam and IOLMaster showed the greatest level of agreement for both MSE and J_0/J_{45}.

When assessing MSE the TMS-5 and Javal Schiøtz demonstrated the widest limits of agreement but when examining J_0/J_{45} the OPD scanner showed poorest agreement.

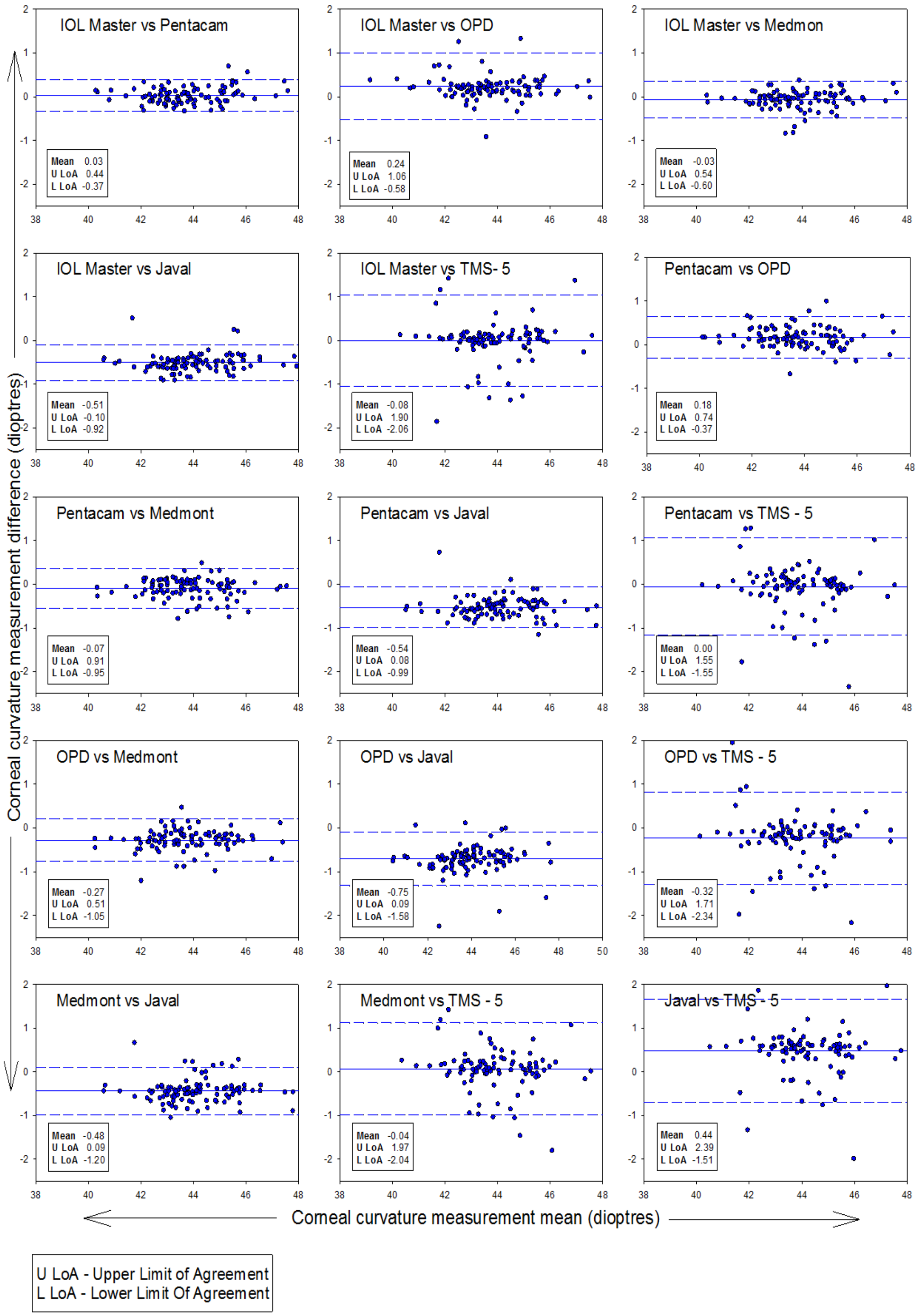

Figure 2.1: Bland-Altman comparison of MSE for all pairs

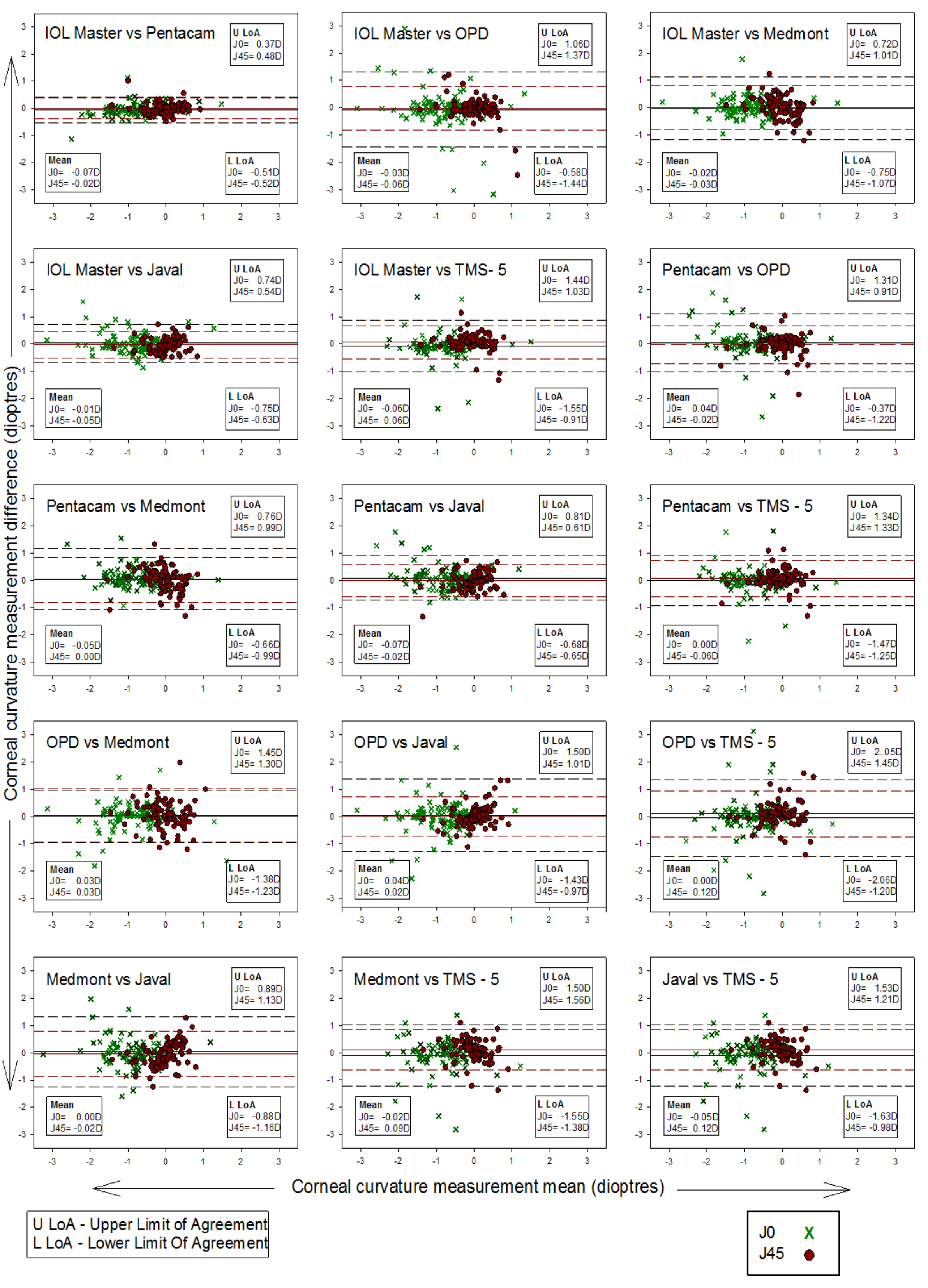

Figure 2.2: Bland-Altman comparison of J_0 and J_{45} for all pairs

2.3.5 Correlation

A strong positive correlation was found in the comparison of the MSE results for all combinations of pairs across the 6 instruments (r = 0.888-0.922, p<0.001). The correlation was strongest between Pentacam and IOLMaster (r = 0.992, p<0.001) and weakest between the TMS-5 and Javal Schiötz (r = 0.888, p < 0.001). Comparison of the results for the vertical and horizontal corneal astigmatism showed weaker correlation and more variability depending upon which pairings were assessed. The IOLMaster J_0 and J_{45} values show the strongest correlation when compared to the Pentacam (J_0: r = 0.934, p<0.001, J_{45}: r = 0.890, p<0.001). There was a much weaker correlation between the IOLMaster and the OPD (J_0: r = 0.720, p<0.001; J_{45}: r = 0.738, p<0.001), Medmont (J_0: r = 0.642, p<0.001; J_{45}: r = 0.835, p<0.001), Javal Schiotz (J_0: r = 0.0747, p<0.001; J_{45}: r = 0.531, p<0.001) and TMS-5 (J_0: r = 0. 648, p<0.001; J_{45}: r = 0. 5740, p<0.001).

2.3.6 Comparison of Means

Repeated measures ANOVA demonstrated a significant difference in MSE (F = 84.977, p<0.001). Post-hoc analysis showed that the OPD scanner results were significantly different from the other instruments, finding a lower MSE (flatter cornea) on average (p<0.01 in all cases). In comparison, the Javal Shiøtz also showed significantly different MSE (p<0.001) showing a higher average MSE (steeper cornea) in comparison with the other devices. In addition, the MSE measurement was significantly steeper with the Medmont when compared to the Pentacam ($p = 0.01$) (Table 2.3).

There were no significant differences between any of the average measures of the astigmatic vector components (J_0: $F = 1.047$ $p = 0.372$; J_{45}: $F = 1.210$, $p = 0.307$) (Table 2.3).

		IOL Master	Pentacam	OPD	Medmont	Javal Schiøtz	TMS-5
MSE	**Mean**	43.75	43.77	43.59	43.87	44.29	43.84
	SD	1.46	1.40	1.44	1.39	1.42	1.47
J_0	**Mean**	-0.83	-0.78	-0.81	-0.84	-0.84	-0.80
	SD	0.70	0.67	0.82	0.67	0.72	0.88
J_{45}	**Mean**	-0.02	0.00	0.04	0.01	0.02	-0.09
	SD	0.38	0.40	0.54	0.57	0.37	0.54

Table 2.3: Mean and Standard deviation of the MSE, J0 and J45 (n =100)

2.4 Discussion

Accurate assessment of corneal astigmatism is essential when choosing the power of an IOL to be implanted in cataract surgery. When using toric IOLs, a higher degree of accuracy is required to ensure that not only the power but also the orientation of the lens is positioned accurately to provide the optimum correction. The purpose of this study was to determine the repeatability and validity of 6 different instruments designed to measure corneal curvature in pre-surgical assessment.

In conventional cataract surgery, with non-toric IOLs, only the accuracy of MSE is the important measurement when assessing corneal curvature. It was unsurprising that all of the devices in the study demonstrated high MSE inter- and intra- repeatability.

Nevertheless, discrepancies were found between the MSE results when comparing the instruments. This variation may be due to differences in the optical and mathematical methods used to calculate corneal power. It was found that the manual keratometer provided a steeper MSE than the other instruments; the instruments that calculated sim-K results from Placido disc topography provided the flattest measurements; and the instruments that determined corneal curvature through automated keratometry or Scheimpflug imaging provided results flatter than manual keratometry but steeper than Placido disc topography.

Previous studies evaluating the results of the Javal Schiøtz with the IOL Master found that both provided similar results for MSE (Santodomingo-Rubido et al. 2002). Conversely, in the present study the manual keratometer was found to measure steeper than all other devices. The discrepancy found may be due to several factors. The manual keratometers results are formed from an estimation of corneal curvature based on the central 3.2mm zone as opposed to the central 2.3mm zone of the IOL Master. Unlike corneal topography and tomography, the manual keratometer assumes that the cornea is spherical in shape and cannot determine an aspheric profile. Furthermore, the manual keratometer has an inherent dependency on the examiner to accurately determine the end point.

In the present study, the IOLMaster provided a steeper corneal curvature than the Placido-disc topographers. These findings are in agreement with previous reports where the discrepancies in measurements have been attributed to the small area, which it uses to simulate the K readings (Elbaz et al. 2007; Shirayama et al. 2009).

Previous studies examining the validity of the Pentacam reported that it produced systematically flatter corneal curvature readings than other instruments (Elbaz et al. 2007; Whang et al. 2012). However, these studies used the net corneal power measurement rather than anterior corneal curvature of the Pentacam and hence the results are not comparable. Reuland and associates only used the anterior corneal curvature for assessment and found that the IOL Master and Pentacam showed comparable results (Reuland et al. 2007). In comparison, Savani and colleagues (2011) found that the Pentacam measured a flatter anterior corneal curvature. This difference may be due to the fact that, the authors used an older version of the Pentacam with a 25 scan setting.

The analysis of corneal astigmatism measurement separate to the MSE highlights the difficulty of accurately determining astigmatic power and orientation. The assessment of MSE is not dependent on the orientation of the power meridians and is more robust to erroneous readings affecting one meridian. In this study, the J_0 and J_{45} vectors described by Thibos et al (2001) are used for statistical analysis; this vector analysis allows the comparison of both orientation and power. Not all studies assessing keratometry assess this component separately to the MSE (Elbaz et al. 2007; Savini et al. 2009; Shirayama et al. 2009; Visser et al. 2012; Whang et al. 2012).

In comparison with the topographers and manual keratometer, the Pentacam and IOL Master demonstrated high repeatability between observers, visits and within observer repeatability for J_0/J_{45} (Tables 2.2 and 2.3). Additionally there was also a very good agreement shown with Bland-Altman plots (Figure 2.2). This is similar to previous studies whereby the Pentacam and IOLMaster demonstrate high intra-observer, inter-observer and between session repeatability for J_0/J_{45} (Santodomingo-Rubido et al. 2002; Chen et al. 2009; Read et al. 2009). The repeatability was weaker for those instruments based upon a topographic optical technique; this agrees with the findings of Wang and colleagues (Wang et al. 2012) who found that there was a much larger spread in results and poorer repeatability with such instruments.

Unlike Scheimpflug imaging, it is likely that the tear film has a significant influence on the repeatability of topographic keratometers. It can be proposed that the tear film has a larger influence on the assessment of astigmatism than it does on average corneal power due to the influence of localised changes to the tear film. As astigmatism is orientation specific, a localised disturbance to the tear film can influence readings along a specific meridian and hence distort the measurement of astigmatism. When assessing the concordance of devices, an interesting observation is that those instruments based around Placido disc corneal topography have produced a wider spread of data and more outliers in relation to the Scheimpflug and automated keratometry techniques. Nemeth et al (2001) reported changes in topographical results with tear film break up between blinks. This could provide further support to the influence of an unstable tear film creating disparate results and clear outliers in the data. The use of ocular lubricants prior to measurements may provide a more stable reading.

The limits of agreement shown in the Bland Altman plots demonstrate the disparity of agreement between some pairings of the instruments (Figures 2.1 and 2.2). If we consider a disagreement or error of 0.50D to be clinically significant, then the use of some instruments in combination could lead to a significant under or overestimation of corneal power analysis. The MSE comparison of the topographers, especially the TMS-5 and other instruments, showed limits of agreement over 0.50D as demonstrated in Figure 2.1: F, I, L, N and O. The comparison of the J_0 & J_{45} vector components in Figure 2.2 displays a similar increase in discrepancy for the TMS-5.

The IOLMaster 500 provided repeatable readings of J_0/J_{45}, which were similar to those of the Pentacam. The smaller measurement zone of 2.3 mm is likely to be an important factor as there is less chance of the measurements being influenced by more peripheral tear film changes; furthermore the integrated software of the IOLMaster 500 has numerous image quality checks that may further improve the reliability of the measurement.

Previous work has also shown the IOLMaster astigmatism assessment to be interchangeable with the Javal Schiøtz (Santodomingo-Rubido et al. 2002) and the Pentacam with the Medmont (Read et al. 2009). In contrast to this, the study reported here has shown much poorer agreement and repeatability when considering corneal astigmatism assessment with any of the other four devices. The intra-observer, inter-observer and inter-session repeatability are all much lower for the Medmont, OPD scanner, Javal Schiøtz and TMS-5 when assessing astigmatism.

This study had some limitations in design. The subjects who routinely wore soft contact lenses were advised to remove the lenses a minimum of 12 hours before the assessment. It has been suggested that the corneal shape can be affected by soft contact lens wear for 2 weeks or more, so a longer time period between wear and assessment would be suggested to increase the accuracy of the readings (Wang et al. 2002; Hashemi et al. 2008). In the current investigation, only 8 of the subjects were soft contact lens wearers (2 were infrequent wearers only), limiting the effect on the whole data group (n=100). Although the study was performed on healthy phakic subjects (18-60), the present results provided an indication of the repeatability validity and concordance of results predicted for an older subject group such those having cataract surgery.

2.5 Conclusion

This study has shown that when comparing the MSE measurements made by six different techniques, the variability among techniques is low. This is consistent with previous studies comparing these techniques. However, the observed variability between instruments is much greater when assessing corneal astigmatism (in vector form). As there is a need to obtain very accurate measurements, it is essential that there is a low variability in the results obtained by different observers and at different times. Based on the results in this study, the Pentacam and IOLMaster showed the best repeatability and agreement of the 6 instruments. Therefore, these instruments appear to be the best choice for use with toric cataract surgery assessments that require a higher accuracy in corneal astigmatism assessment. However, this requires further investigation in the post-operative environment. Specifically, future work needs to investigate the use of these two instruments in assessing the influence of corneal astigmatism on the ocular refraction in pseudophakic population. From this it would be hoped that improvements could be made that will reduce dependency on spectacles after cataract surgery.

Chapter 3 Surgically Induced Astigmatism

3.1 Introduction

3.1.1 Background

Technological advancements in ocular biometry have driven the development of more complex and accurate IOL power calculations. Patients and surgeons desire less spectacle dependency post-surgically (Agresta et al. 2012). Surgeons are seeking the optimum procedure for the correction of astigmatism as over 20% cataract patients have 1.25DC or more of corneal astigmatism (Ferrer-Blasco et al. 2009). An important consideration, in the astigmatic eye, is the shape change induced by the surgical incision. It has long been known that corneal incisions made during cataract surgery can alter the shape of the cornea (Shepherd 1989; Buzard et al. 1991; Steinert et al. 1991). This change in corneal shape is termed surgically induced astigmatism (SIA). It is generally accepted that an incision will cause a flattening effect to the meridian on which it sits (Tejedor et al. 2005). The size, location and type of incision have all been found to affect the post-surgical outcome (Kershner 1997; Linebarger et al. 1999; Reddy et al. 2007). The decrease in surgical incision size used (now generally ≤ 3mm) has reduced the amount of change that occurs to the cornea (Hayashi et al. 1995; Pfleger et al. 1996). Nevertheless, it has been widely established that there will still be a small change in corneal shape measured post-surgically (Hill 2008; Wei et al. 2012). Measuring SIA is achieved by assessing corneal power pre- and post-surgically and evaluating the resultant curvature changes.

3.1.2 Measurement of Corneal Curvature

The measurement of corneal curvature is vital in the calculation of surgically induced astigmatism. The previous chapter (2) demonstrated the poor repeatability and comparability of the corneal astigmatism readings obtained from different instruments. There are a number of potential sources of error that have been found to affect the accuracy of the readings. Firstly, instruments that utilise the reflection from the tear film (keratometers and Placido disc topographers) only measure the anterior corneal curvature. Curvature is an important measure for contact lens fitting but the power of the cornea is a more useful output for cataract and refractive surgery. To calculate power, reflection based instruments usually use a keratometric refractive index of 1.3375, based on a ratio of anterior to posterior surface shape of 1.13. However, studies examining this correct index to use are equivocal and it has been suggested that the ratio is closer to 1.20 (Fam et al. 2007; Ho et al. 2008). A second source of error is neglecting the posterior corneal surface shape. Studies have shown that by assuming the posterior surface profile, it leads to inaccurate corneal curvature assessment. The posterior cornea does not follow the anterior corneal shape consistently (Dunne et al. 1991; Ho et al. 2009; Wang et al. 2011; Koch et al. 2012; Miyake et al. 2015). Another consideration is the tear film stability. Break up of the tear film has been shown to decrease the accuracy of keratometry readings (Németh et al. 2001). Finally, it is difficult to summarise the shape of the cornea as it follows an aspheric profile. Few studies have examined how this aspheric corneal topography relates to overall refractive astigmatism. Alpins et al. (2012) found that corneal power related more to the ocular refraction if both paraxial and peripheral astigmatism was summarised and created a formula to describe the average shape across of the cornea (Alpins et al. 2012).

These sources of error are now well established but despite this, any difference in readings taken pre- and post-surgery have been wholly attributed to the corneal incisions and attributed as SIA. There has been no consideration for any error including instrument error. The precision of toric lens implant calculators is dependant in part upon the accuracy with which SIA can be predicted. This study aims to investigate how measurement error alone, when assessing corneal curvature, can cause a false determination of SIA.

3.1.3 Calculation of SIA

SIA is the change between the pre- and post-surgical corneal curvature induced by the corneal surgical incisions. There are multiple methods available to calculate the SIA. The most basic method is to determine the difference in absolute magnitude pre- and post-operatively. However, astigmatism is not accurately defined by magnitude alone and the orientation of the corneal meridians needs to be considered. The traditional method of describing corneal and refractive power is through the use of sphero-cylindrical expression. However, it is difficult to use this description of cylinder power when trying to describe the change in corneal shape as a whole.

The use of J_0 and J_{45} (vector analysis) provides Cartesian co-ordinates, which are useful descriptions of astigmatism and are more suitable for calculating astigmatic change. Stokes first described the use of vector analysis for determining the effect of obliquely crossed cylinders in 1849. This oblique cross cylinder methodology was then applied to the calculation of SIA and the *surgically induced refractive change* (SIRC) formula was proposed, along with a new definition of SIA. SIA is the magnitude vector change pre- and post- operatively (Holladay et al. 1992). Analysis of corneal change in the form of vector magnitude difference is still an oversimplification as it only assesses describes magnitude alone and disregards the axis. In 1975, Jaffe and Clayman developed this further by demonstrating three methods of calculating the change, using trigonometry(Jaffe et al. 1975). Later Holladay and colleagues built upon this to produce a demonstration of a series of equations that could calculate both the magnitude and the orientation of SIA (Holladay et al. 1992). There is a difficulty when using Cartesian vectors to assess groups of data. The orientation can be calculated on an individual basis but cannot be summarised as easily as the magnitude e.g. as mean or median change. The circular nature of the data prevents analysis by conventional methods.

Cravy et al (1979) and Naeser (2008) proposed an alternative method of analysis that could take into account orientation: the polar method (Cravy 1979; Naeser

2008). This method calculates the change in power along a specific reference orientation. If the incision site is taken as the reference orientation then polar analysis will generate data on the change of corneal shape relative to the incision site. The Cartesian method of determining SIA is more widely used and discussed among refractive surgeons, however, the disparity between the polar and Cartesian results is rarely discussed and requires detailed exploration.

Corneal curvature measurement error can result in the erroneous calculation of SIA. However, there is a shortage of studies examining the effect of this measurement error.

3.2 Aims

Two studies were conducted to evaluate the measurement of SIA: The first examined the consequences of corneal curvature measurement error alone on the calculation of SIA in a healthy phakic subject group who did not undergo any surgical procedure. The 'pseudo-SIA' was calculated with the keratometry readings taken at the two visits in lieu of cataract surgery (subjects from chapter 2). The second examined the SIA calculated in subjects who underwent small incision cataract surgery. This study was designed to determine the magnitude of Pseudo-SIA and investigate the significance the error has on the SIA calculated post-surgically.

3.3 Materials and Methods

3.3.1 Phakic Population (Pseudo-SIA group)

3.3.1.1 Subjects:

One-hundred healthy phakic subjects (32 Males, 68 Females) of mean age 36.0 ± 11.4yrs, were recruited from Plymouth University (UK). The principal investigator of the study (CH) recruited all participating subjects. The inclusion/exclusion criteria for the study were as follows:

3.3.1.1.1 Inclusion Criteria:

- Adult subjects aged 18 years old and above
- Able and willing to give informed consent to their inclusion into the study

3.3.1.1.2 Exclusion Criteria:

- Irregular astigmatism, as determined by a qualified optometrist.
- RGP contact lens wear, corneal dystrophies or other abnormal corneal pathology such as Fuchs' dystrophy and keratoconus
- Previous ocular surgery.
- Irregular or malformed eyelids e.g. ptosis, chalzion or severe blepharitis.

3.3.1.1.3 Sample size calculation

The size of the subject group was determined with an alpha level of 0.05 and a power of 80% confidence. Multiple sample size test calculations were carried out with the G*Power 3 (Heinrich Heine Universität, Düsseldorf, Germany) programme to determine the size with the assumption of a moderate effect size advised by Cohen's table comparison of paired means (effect size 0.50), correlation (effect size 0.30) and ANOVA analysis (effect size 0.25). A minimum sample size of 84 was required to satisfy power requirements across these analyses (Prajapati et al. 2010). Therefore, 100 volunteers were recruited to allow for dropouts or exclusion of some subjects throughout the study.

3.3.2 Pseudophakic Population (Surgical SIA Group)

Eighty-three subjects (36 Males, 47 females) of mean age 74.0 ± 10.1 years planning to undergo cataract surgery and recruited from the royal eye infirmary (Derriford Hospital, Plymouth UK). The principal investigator of the study (CH) recruited all participating subjects. The inclusion/exclusion criteria for the study were as follows:

3.3.2.1 Subjects:

3.3.2.1.1 Inclusion Criteria:

- Adult subjects aged 18 years old and above
- Previously consented to routine NHS cataract surgery
- Able and willing to give informed consent to their inclusion into the study

3.3.2.1.2 Exclusion Criteria:

- Irregular astigmatism, as determined by a qualified optometrist.
- Any pre-surgical corneal complications or pathology such as Fuchs' dystrophy and keratoconus
- Subjects who do not have routine cataract surgery and IOL implantation due to pre-existing or unexpected surgical complication.
- Irregular or malformed eyelids e.g. ptosis, chalzion or severe blepharitis.

3.3.2.1.3 Sample size calculation

Several sample size test calculations were carried out with the G*Power 3 (Heinrich-Heine Unversität, Düsseldorf) to determine the size that will allow reliable results for comparison of paired means (pre-surgical versus post-surgical change in shape) using a two-tailed paired t-test with medium effect size, 0.5 (Cohen's table), a two-tailed correlation of bivariate normal model (accuracy of predictive models) using a medium size effect, 0.3 (Cohen's table) and ANOVA analysis of repeated measures (across 3 visits), between factors using a medium size effect, 0.25 (Cohen's table) (Prajapati, 2010). These required 35, 84 and 70 subjects respectively; therefore a minimum sample size of 84 was required across these analyses. An alpha level of 0.05 and a beta of 0.8 were used in the calculations. Therefore, each group will require a minimum of 84 people.

3.3.2.2 Ethical Approval

All procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by the local REC committee (Ref: 13/SW/0229 on 16th October 2013), NHS R&D department (Ref: 13/P/106 on 20th October 2013) and University ethics committee (Ref: 13/14-188 on 23rd October 2013).

3.3.2.3 Surgical Procedure

All operations were performed by a single surgeon (NM), using a sub-tenon injected anaesthesia. A 2.8 mm clear corneal bi-planar incision was placed superior-temporally in all cases. Phacoemulsification, aspiration, and irrigation were performed through a 5.5 mm capsulorhexis using the Millennium phacoemulsification system (Bausch and Lomb, Rochester, N.Y., USA.). All IOLs were implanted into the capsular bag; the incision size of 2.8 mm was maintained throughout the procedure.

3.3.2.4 Intraocular Lens

The IOL implanted during the study was the *Tecnis ZA9003*; an aberration control Aspheric monofocal IOL made from acrylic, hydrophobic material. The IOL is a single piece open loop haptic 12 mm long and with a 6 mm optic.

3.3.3 Procedure

In the non-surgical population, subjects were examined at two visits, separated by at least 24 hours. There was no surgical intervention occurred between the two study visits.

In the surgical group subjects were seen on three separate visits:

- Visit 1 (V1) –Pre-operative visit
- Visit 2 (V2) – 3 to 6 weeks post-surgically
- Visit 3 (V3) – 3 to 6 months post-surgically

Corneal curvature was measured at each visit using three devices in a randomised order. The three devices were:

- Auto-keratometer *(IOLMaster 500: Carl Zeiss Meditec Inc., Jena, Germany)*
- Placido-disc topographer *(OPDscan III: Nidek Co., Ltd, Gamagori, Japan)*
- Scheimpflug tomographer *(Pentacam: Oculus Optikgeräte GmbH, Wetzlar, Germany).*

3.3.4 Analysis

3.3.4.1 Assumption of Normality

A one-sample Shapiro-Wilk test was used to determine if results from each measurement followed a normal distribution. Where the data followed a normal distribution, parametric analysis was used; non-parametric statistical analysis was used for abnormally distributed data.

3.3.4.2 Vector Calculation of SIA

All results were converted into rectangular Fourier form of mean spherical equivalent (MSE) and J_0/J_{45} vectors representing the cylindrical power and axis as a combined vector for analysis. The Analysis of the J_0/J_{45} vector components was used to determine the pseudo-SIA caused by the intersession reproducibility of corneal measurements in the absence of surgery.

$$\boldsymbol{J_0} = \boldsymbol{J}\ \boldsymbol{cos}(\boldsymbol{2\alpha}) \qquad \textit{Equation 3.1}$$

$$\boldsymbol{J_{45}} = \boldsymbol{J}\ \boldsymbol{sin}(\boldsymbol{2\alpha}) \qquad \textit{Equation 3.2}$$

$$\boldsymbol{SIA} = \sqrt{\left(\boldsymbol{J_{0\,Post\,op}} - \boldsymbol{J_{0\,Pre\,op}}\right)^2 + \left(\boldsymbol{J_{45\,Post\,op}} - \boldsymbol{J_{45\,Pre\,op}}\right)^2} \qquad \textit{Equation 3.3}$$

J_0 = vector representing the power along 180°

J_{45} = vector representing the power along 90°

SIA = Vector magnitude describing the surgically induced astigmatism change of corneal curvature (Thibos et al. 1997; Hill 2008)

3.3.4.3 Polar Calculation of SIA

$$\boldsymbol{KP(\phi)} = \left(S + Msin^2\left((\alpha + 90) - \phi\right)\right) - \left(S + Mcos^2\left((\alpha + 90) - \phi\right)\right)$$

$$= M\ (sin^2\left((\alpha + 90) - \phi\right) - cos^2((\alpha - 90) - \phi)$$

$$= -Mcos2((\alpha + 90) - \phi) \qquad \textit{Equation 3.4}$$

$$\boldsymbol{KP(\phi + 45)} = -Msin2\left((\alpha + 90) - \phi\right) \qquad \textit{Equation 3.5}$$

$$\boldsymbol{SEP} = 0.5\left(\left(S + Msin^2\left((\alpha + 90) - \phi\right)\right) + \left(S + Mcos^2\left((\alpha + 90) - \phi\right)\right)\right)$$

$$= S + 0.5(M) \qquad \textit{Equation 3.5}$$

$$(\boldsymbol{KP(\Phi)_{SIA}}, \boldsymbol{KP(\phi + 45)_{SIA}}) =$$

$$(KP(\phi)_{postop}\ , KP\left((\phi + 45)_{post\ op}\right) - (KP(\phi)_{preop}, KP\left((\phi + 45)_{preop}\right)$$

Equation 3.6

KP(Φ) = net refractive power (net curvature power) acting along the plane of Φ. A positive value indicates a steepening of the anterior cornea along the specified meridian, a negative value indicates flattening.

KP (Φ + 45) = power twisting the astigmatism direction towards the plane (net torsional power) through (Φ + 45). A positive value indicates counter-clockwise torque from the chosen meridian. A negative value indicates a clockwise torque from the chosen meridian.

SEP (spherical equivalent power) = average of the two orthogonal powers

$KP(\Phi)_{SIA}$ = Surgically induced astigmatism polar value 1

$KP(\Phi +45)_{SIA}$ = Surgically induced astigmatism polar value 2

M = magnitude of astigmatism

S = sphere

α = steepest meridian position

Φ = incision location

(Naeser 2008)

3.3.4.4 Statistical Analysis

The data was tested for normal distribution with the Shapiro-Wilk test. The data was not normally distributed so non-parametric analysis was carried out. Friedman ANOVA tests was used to detect significant differences between the instrument results produced by either the vector or polar method and if a significant difference was detected, then Wilcoxon paired rank tests were used to highlight which of the individual pairings of instrument data was significantly different. Lastly, the Surgical and Pseudo-SIA results were compared using the Mann-Whitney U test to find if there was a difference between the two subject group results.

3.4 Results

The data was not normally distributed in either of the groups.

3.4.1 Pseudo-SIA group

3.4.1.1 Vector Method

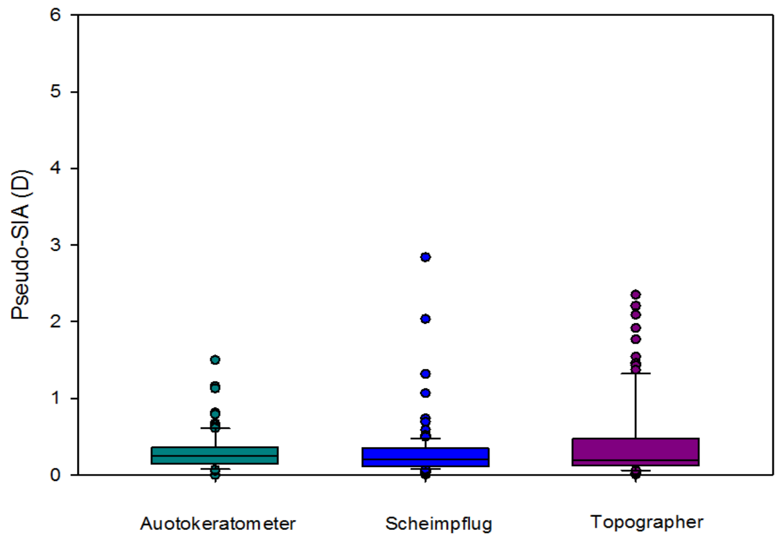

Figure 3.1: Box plot demonstrating the spread of Pseudo-surgically induced astigmatism calculated for each instrument for all subjects (n=100) with the Cartesian vector method

No significant difference was found between the results produced by the instruments (χ^2_3 = 3.554, p = 0.169).

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3.4.1.2 Polar Method

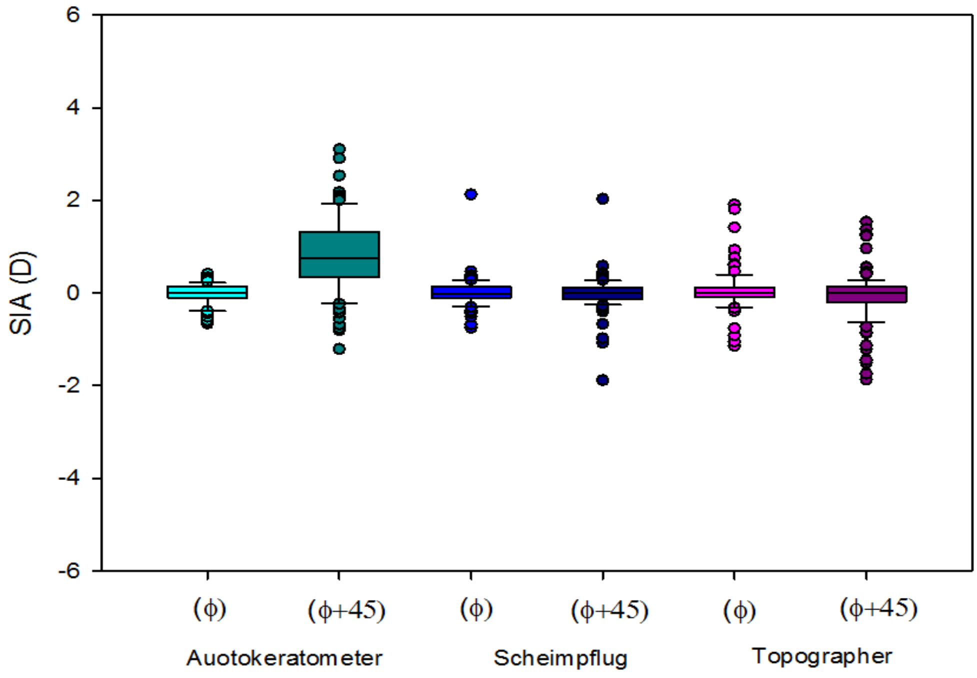

Figure 3.2: Box plot demonstrating the spread of Pseudo-surgically induced astigmatism calculated for each instrument for all subjects (n=100) with the Polar method.

There was no significant difference found between the **KP(ϕ)**$_{SIA}$ for all the instruments (χ^2_3 = 0.38, p= 0.827). There was a significant difference found between the **KP(ϕ+45)** $_{SIA}$ (χ^2_3 =87.32, p<0001). Post-hoc analysis revealed a significant difference between the results of autokeratometry and the other two instruments (Scheimpflug imaging, Z = -7.712, p <0.001 and Placido disc topography, Z = -6.945; p < 0.001). No significant difference was found between the Scheimpflug and Placido disc methods (Z = -.299, p = 0.765).

3.4.2 Surgical SIA group

3.4.2.1 SIA Calculated with Cartesian Vector Method

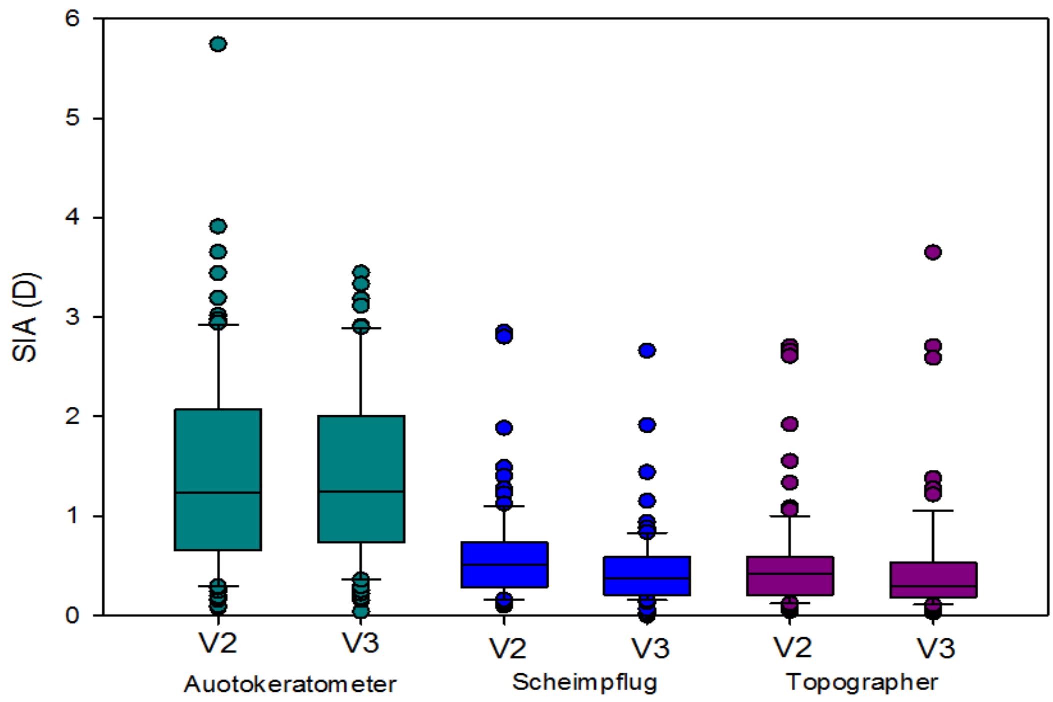

Figure 3.3: Box plot demonstrating the spread of the surgical group surgically induced astigmatism calculated for each instrument for all subjects (n=83) with the Cartesian vector method at Visit 2 (V2) and visit 3 (V3).

A significant difference was found between the results produced by the instruments at Visit 2 (V2: χ^2_3 = 48.607, p < 0.001). The Auto-keratometer SIA results were found to be significantly different from both the Scheimpflug (Z = -6.363, p < 0.001) and the Placido disc instrument results (Z = -6.386, p < 0.001). The scheimpflug and Placido disc instrument results were not found to be significantly different (Z = -1.926, p = 0.052). A significant difference was also found between the results produced by the instruments at Visit 3 (V3: $\chi^2_3 = 44.08$, $p < 0.001$). The Auto-keratometer SIA results were found to be significantly different from both the Scheimpflug ($Z = -6.218$, $p < 0.001$) and the Placido disc instrument ($Z = -5.653$, $p < 0.001$) results. The scheimpflug and Placido disc instrument results were not found to be significantly different ($Z = -0.583$, $p = 0.579$).

3.4.2.2 SIA Calculated with Polar Method

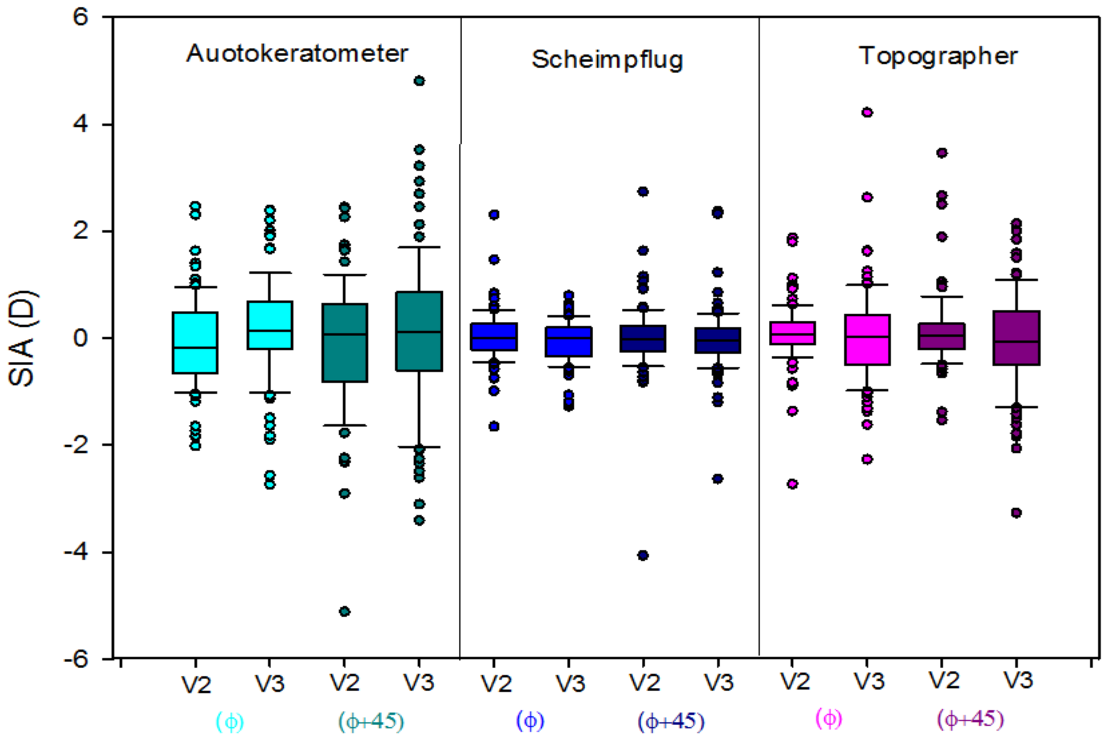

Figure 3.4: Box plot demonstrating the spread of the surgical group surgically induced astigmatism calculated for each instrument for all subjects (n=83) with the Polar method at Visit 2 (V2) and Visit 3(V3).

There was a significant difference found between the **KP(ϕ)**$_{SIA}$ for all the instruments at V2 (χ^2_3 = 6.432, p = 0.04). However, *post hoc* analysis found no significant pairwise difference (p > 0.05). The **KP(ϕ+45)** $_{SIA}$ was also similar when measured using the different instruments (χ^2_3 = 0.477, p = 0.788). There was a significant difference found between the **KP(ϕ)**$_{SIA}$ at V3 (χ^2_3 = 7.659, p = 0.022). Post hoc analysis revealed that these differences were between the autokeratometer and both the scheimpflug (Z = -2.426, p= 0.0015) and Placido-disc (Z = -2.022, p= 0.043) instruments. The Scheimpflug and Placido disc instruments provided similar results (Z = -0.820, p= 0.412). There was no significant difference found between the **KP(ϕ+45)** $_{SIA}$ (χ^2_3 = 1.091, p = 0.580).

3.4.3 Comparison of Groups

The SIA results produced by the two groups were compared using the Mann Whitney U test to determine if SIA readings produced by the same instruments were significantly different.

Mann-Whitney U test					
Value	Visit	Instrument	Autokeratometer	Scheimpflug	Topographer
Cartesian Vector	V2	***U***	4.603	-6.698	-3.603
		p	*<0.001*	*<0.001*	*<0.001*
	V3	***U***	-9.143	-4.444	-2.587
		p	*<0.001*	*<0.001*	*<0.001*
KP(ϕ)SIA	V2	***U***	-5.872	-1.596	-0.107
		p	*0.127*	*0.111*	*0.914*
	V3	***U***	-2.498	-0.568	-0.153
		p	*0.012*	*0.570*	*0.878*
KP(ϕ+45) SIA	V2	***U***	-1.526	-0.626	-0.064
		p	*<0.001*	*0.531*	*0.949*
	V3	***U***	*-4.851*	*-0.549*	*-0.384*
		p	*<0.001*	*0.583*	*0.701*

Table 3.1: Table displaying the U and p values for the Mann Whitney U test for the comparison of the Pseudo-SIA and Surgical SIA produced by each instrument. Significant results highlighted.

There were significant differences found between the groups when using Cartesian method to calculate SIA. Conversely, there was no difference found between the groups when using the polar method was used to calculate SIA apart from a torsional change with the autokeratometer.

3.5 Discussion

Understanding surgically induced astigmatism has been a key factor in surgical development and review. SIA was first described when incisions were large and the resultant change in astigmatism significantly affected the post-operative refractive error (Shepherd 1989; Buzard et al. 1991; Steinert et al. 1991). With the advent of micro-incisions, the SIA has decreased dramatically in recent years. Although there has been a steady reduction in SIA with decreasing incision size, there appears to have been a plateau around 0.50 DC. It is generally accepted that a small amount of SIA is to be expected with all surgeries. Hill determined that a 0.50 DC of SIA was generally found even in surgeries with incision of less than 2.4 mm (Hill 2008). The reduction in incision and therefore SIA associated with modern surgeries means that the error in measurement of the device used to determine the SIA must be very small to detect the change accurately.

The Pseudo-SIA results are a reflection of the significant contribution of the instrument error to SIA calculations. The auto-keratometer, Scheimpflug and Placido disc instrument all had similar median SIA results of ~0.20 D (Table 3.1) calculated by the Cartesian vector method. The upper and lower quartiles for the Placido disc indicate a large spread in results and this instrument produced the highest percentage of results over 0.50 DC, which is a commonly quoted minimum SIA expected in most modern surgeries (Hill 2008). The boxplots show a tight agreement of SIA for most of the results but the outliers demonstrate the common incidence of erroneous results that can be produced by the instruments (Figure

3.1). It has been suggested that an average of, or comparison of results from multiple machines should be used to reduce the incidence of this occurring (Magar et al. 2013). These results demonstrate the significant influence that instrument error can bear on the reported SIA results.

In the surgical group, the autokeratometer produced a significantly larger SIA than the Scheimpflug and Placido disc instruments. The Scheimpflug median SIA was 0.51 for at V2 and 0.41 at V3, this is similar to many studies previously reporting on average SIA for <3 mm incisions. Ofir and colleagues (2015) carried out a similar study comparing three difference instruments for the calculation of SIA for a 2.4 mm incision and found medians of 0.41 D for the autokeratometer, 0.45 D for a dual zone auto-keratometer and 0.47 D for a Placido-disc topographer. Wei and colleagues (2012) reported an average SIA of 0.82±0.49 D measured using a Placido–cone topographer after a 2.5 mm incision (Wei et al. 2012). Chang et al (2015) found ~0.60 D SIA one month after surgery with a 2.75 mm incision, measured with a different auto-keratometer, and ~0.50 D with a 2.2 mm incision group. In this study the Placido disc had a lower median (0.42 at V2 and 0.35 at V3) but greater interquartile range when compared to Scheimpflug imaging. Given the results from the phakic subjects it is conceivable that the large proportion of outlying results are attributable to instrument error and poor repeatability rather than surgical corneal shape change.

The non-surgical study population present in this study represents a "best case patient population" and highlights the contribution of machine error to the calculation of SIA. This population would be expected to be virtually absent of pseudo-SIA as they represent a healthy young population with a stable tear film. Despite this, the average pseudo SIA median ranged from 0.19-0.25 D; a significant proportion of the SIA found in many micro-incision surgery studies. The Scheimpflug readings provided the most consistent results with the tightest quartiles, the median error was 0.20D (Table 3.1) compared to a median surgical change of 0.40D found with the surgery (Table 3.3). The median Pseudo-SIA (error) for the autokeratometer was 0.25D and the surgical group median was 1.27D for V2 and 1.24D. Lastly, the Placido disc error was 0.19 and the median SIA measured was 0.42D at V2 and 0.35 at V3.

In comparison, the pseudo-SIA group median vector calculated through polar analysis along the incision axis ($KP(\phi)_{SIA}$) was similar for all instruments ($p>0.05$) and very close to 0, indicating little change in flattening along the incision meridian (Table 3.2). Similarly the Scheimpflug and Placido disc $KP(\phi+45)_{SIA}$ (along the meridian) results were not significantly different ($p= 0.765$) for the median polar co-ordinate orthogonal to the meridian. Interestingly the autokeratometer produced SIA results along the orthogonal ($KP(\phi+45)_{SIA}$) meridian that was larger with a greater number of outliers (Figure 3.3). The comparison with the vector results is quite significant. This will be partly due to the different descriptions these two methods offer. The polar method is describing the power along a specific meridian that takes into account the orientation but the vector results are a general description of change across the whole surface.

In the pseudophakic group, polar analysis of SIA along the incision meridian at the 3-6 month visit reveal that the autokeratometer produced a higher magnitude when compared with the Scheimpflug and Placido-disc. A study by Kim et al (2014) analysed SIA with the same polar method and reported a mean change of 0.31±0.54 and 0.56±0.42 along the scleral tunnel incision meridian for a 2.2mm and 2.75 mm incision respectively, measured with a Placido-disc topographer at 1-month post-operative. This was a little higher than the median change observed in this study along the incision meridian of 0.07 (QR -0.10, 0.30) found with the Placido disc topographer at a similar time point (V2). The scheimpflug polar SIA result at this stage was 0.01 (QR -0.23, 0.25) and the autokeratometer was -0.19(QR -0.60, 0.48). The difference could be attributed to the different incision types as Kim et al (2014) used scleral tunnel incisions, not clear corneal incision. It was also closer to the vertical meridian, incisions made along the vertical meridian tend to induce greater changes in astigmatism (Mendivil 1996; Wirbelauer et al. 1997; Altan-Yaycioglu et al. 2007; Ozyol et al. 2012) Another reason for the difference may be due to the methods of reporting the results, as this data was not normally distributed prompting reports of the medians not the means. The boxplots represent the data well, again with a clear demonstration of the number of outliers seen in the results (Figures 3.6-3.9). This is similar to the pseudo-SIA group (Figures 3.2 and 3.3), indicating that instrument error is the most likely cause - not surgical technique. This is seen with the SIA produced using both the vector and polar method calculations

When calculating the SIA, it is important to consider what the output actually means and how it describes the corneal shape change. The SIA calculated with the vector method produces a single result in dioptres, describing a combination of magnitude and orientation that is normally used in the description of astigmatism. This single result is required for toric IOL calculators that use the SIA to help predict the post-operative corneal shape. However, this outcome lacks any indication of how much of each component of magnitude and directional change affects this result. This study found a much greater change in astigmatism with the vector method compared to the polar method. The nature of the Cartesian vector calculations means that a change with significant axis rotation but minimal magnitude change can still result in a significant dioptric SIA e.g. a rotation of 30 degrees with no change in magnitude would results in a ~0.50D SIA. Yet, the alternative method of calculation, using polar co-ordinates, only describes the change relative to a specified meridian. Unfortunately, these results cannot be used in the predicted toric IOL calculators. The results appear to be much lower in this study, but it must be noted that the description is not of the whole cornea. As surgeons base their success on these calculations and plan future surgeries on these assumptions, it is important to understand correctly how to interpret the results and potential pitfalls of each calculation method. The comparison of vector and polar results appears significant and, depending upon which technique is used, the success of the surgery would vary greatly.

The surgical and pseudo-SIA group were compared to determine the difference between the SIA results produced by each machine. There was a significant difference found between all the SIA results produced by the Cartesian vector method for each of the instruments at V2 and V3. There was a difference found between the surgical and pseudo-SIA results calculated using the Polar method for the ($KP(\phi + 45)_{SIA}$) at V2 and both ($KP(\phi)_{SIA}$) and ($KP(\phi + 45)_{SIA}$) co-ordinates at V3 measured by the Auto-keratometer (table 3.1). However there was no difference along the ($KP(\phi)_{SIA}$) measured at V2 and any of the SIA co-ordinates calculated using the scheimpflug and topographical readings at V2 or V3. The conflicting SIA results infer that the difference between groups may not be due to the incision, or entirely attributed to instrument measurement error. Further investigations are required to investigate the extent that instrument error contributes to inaccurate SIA calculation, Future work should include a prospective study comparing repeated measurements of a group of patients undergoing routine surgery with an age matched control group.

A possible source of error between measurements could be attributed at least in part to eye rotation between measurements. Previous studies have tracked natural cyclotorsion between measurements. Seo and colleagues (2004) found an average rotation of 3.13±1.24° found with retinal photography. In a similar study Viestenz et al (2005) recorded an average movement of 2.3±1.7° with 6 months between measurements with 36% of subjects moving more than 3 degrees between measurements. Rotation of the eye would alter the axis measurement, altering the vector calculated for the corneal astigmatism.

It has been postulated that variation in corneal curvature measurement between readings could be due to diurnal variation in corneal curvature (Norrby et al. 2013). The time of day was not controlled in this study so this could be a contributing factor to the test-retest repeatability. However, previous work by Read et al (2009) found that the largest variation would be found in the first few hours upon waking . Change in curvature was due to changes in the swelling of the cornea. Most of the swelling was found in the peripheral cornea, this would not affect the keratometry readings as the machines were only looking at the central area, up to 3mm.

Other studies have advocated measurement of the posterior surface to increase accuracy of the surgically induced astigmatism calculation. Almost all of these machines measure only the anterior surface and use the standard keratometric refractive index to compensate for the effect of the posterior corneal shape (Gutmark et al. 2010). The introduction of Scheimpflug imaging has allowed the measurement of the back surface and the opportunity to incorporate the posterior shape into the calculations. The posterior corneal astigmatism has been found to contribute to overall corneal astigmatism and is no longer considered negligible (Koch et al. 2012). It has been postulated that not taking the posterior corneal surface into consideration can affect the accuracy of the SIA calculation. Cheng and colleagues (2011) carried out a study comparing the SIA calculated by only using a traditional keratometer with the standard keratometry index and a Pentacam that took into account both the anterior and posterior corneal surfaces. They found a statistically significant difference between the SIA calculated with only the anterior surface, compared to taking the posterior surface into account (Cheng et al. 2011). Nonetheless, this is reliant upon the high accuracy of the Pentacam. As this study has shown, the Pentacam, although highly accurate, will still have a small amount of measurement error that should be taken into account. Koch and colleagues (2013) also found a small degree of astigmatism measurement error with the Pentacam.

It has long been established that incision location is a key factor in the amount of surgical induced astigmatism induced during surgery. This study was unusual in looking at the effect of a superior-temporal incision. Studies concentrating on incisions placed superiorly, of similar size (2.7-2.8) have found SIA of 0.38±47D (Febbraro et al. 2015) to 0.65D (Chang et al. 2015). SIA induced by temporal incisions ranged from 0.65D (Luo et al. 2012) to 0.09D (Gobin et al. 2011) . Additionally 'on-axis' incisions had the largest range from 2.91 ±0.91D (Alio et al. 2011) to 0.49 ±0.29D (Ofir et al. 2015) (table 1.2). The majority have shown greater SIA than the superior temporal incision made in this study. This is in agreement with Ozyol & Ozyol (2014) who assessed four different locations (superior, temporal, superior temporal and superior nasal) and their results also found less SIA than other orientations, reporting 0.17D of SIA, which is similar to the ~0.20D reported in this study. There are a few potential reasons for the variation in SIA change with location. The first is due to the variation in distance from the apex as vertical distance from the apex to edge is shorter than in the horizontal meridian. Additionally, the lids and gravity may affect the healing of the incision. Lastly, x-ray diffraction has shown that the corneal fibrils change in density and direction in the peri-pupillary and limbal area (Meek et al. 1999; Boote et al. 2003). The distance from limbal edge to incision site can vary in clear corneal incisions and the incision may enter the cornea at different density and fibril orientations, altering the arrangement and inducing different corneal responses. The expected fibril arrangement is interrupted in astigmatism (Meek et al. 1999). This could also explain the large standard deviations and quartile ranges in the results reported.

It is clear that the instrument data error should not be ignored when calculating the SIA. It is necessary to quantify the margin of error in SIA readings due to instrument error. After this has been done, it should be taken account of when calculating the SIA. One method to help reduce the erroneous readings and errors is to average or compare multiple readings from different instruments. The impact of inaccurate keratometry can be quite significant, especially in the use of the vector method in looking at the surgical impact on the cornea. Depending upon which instrument is used to determine the pre and post-surgical corneal curvature, the size and location of the incision, the significance of the error can vary, as can the likelihood of an erroneous result.

The identification of the incision site was an obvious source of error in this study and difficult to assess. The method used in this study was subjective and open to error. The incision location and orientation was a manual assessment carried out with the slit lamp using the light beam orientation axis. In addition to this, the subjective nature of the measurement, it is open to error induced by head tilt and eye rotation which can occur between the slit lamp assessment and keratometry readings (Seo et al. 2004; Viestenz et al. 2005). This could significantly impact the accuracy of the calculation involving the incision site location.

3.6 Conclusion

The inherent error in corneal curvature measurement has been shown to cause a significant amount of pseudo-SIA. This pseudo-SIA may prevent the accurate assessment of the actual SIA induced by cataract surgery and result in overestimation of the change in corneal shape. Importantly, there is a significant disparity in the magnitude of SIA depending upon calculation method used. Lack of understanding of how shape change is described by each method leaves the analysis open to errors and misinterpretation. Therefore, magnitude of the reading cannot be wholly attributed to the surgical technique. Few studies have examined the effects of superior temporal incisions on corneal shape. The polar method of calculating SIA revealed that this location of incision resulted in a large torsional force. The Cartesian vector gives no indication of this directional force,

Further investigation into the causes of the errors and the possibility of reducing such errors is needed in the future. Additionally the impact of incorrect SIA readings and its use in pre-surgical planning should be highlighted. The accuracy of calculators used to predict post-operative shape change based on Cartesian vector SIA will also be affected by this error.

Chapter 4 Keratometric Measurement of Corneal Steepest Meridian Orientation after Cataract Surgery

4.1 Introduction

4.1.1 Developments in Cataract Surgery

Recent advancements in the techniques and technology used in cataract surgery have led to greater refractive expectations; the aim of the modern cataract operation is to reduce spectacle dependence post-operatively for the patient (Agresta et al. 2012). However, over 20% of the pre-cataract surgery population have significant (>1.25DC) pre-surgical corneal astigmatism (Hoffer 1980; Ferrer-Blasco et al. 2009; Khan et al. 2011) If uncorrected this corneal astigmatism reduces visual acuity (Wolffsohn et al. 2011) and can affect quality of life (Mencucci et al. 2013). There are a variety of options available to the surgeon to correct corneal astigmatism at the time of surgery, including toric IOLs and limbal relaxing incisions (Ouchi et al. 2009; Buckhurst et al. 2010; Mingo-Botín et al. 2010). The predictability of the corneal healing response is generally considered to be the main limitation of limbal relaxing incisions (Hirnschall et al. 2014). As a consequence, the use of toric IOLs has become more widespread (Pick et al. 2008). The effectiveness of a toric IOL is dependent on its accurate alignment with the post-surgical corneal steepest meridian; any misalignment of the astigmatic principle meridian reduces the effectiveness of the correction (Felipe et al. 2011).

Errors in the alignment of a toric IOL are influenced at several stages during the surgical procedure:

- Inaccurate identification of the pre-operative corneal steepest meridian during keratometry/topography/tomography
- Invalid prediction of corneal curvature as determined by a toric calculator
- Erroneous placement of corneal marking during or before the operation (Osher 2010)
- Incorrect placement of the toric IOL in reference to the corneal marking
- Rotation of the toric IOL post-operatively.

4.1.2 Relevant Background Information

The literature surrounding toric IOLs has largely been focused on the rotational stability of the IOLs (Koshy et al. 2010; Wolffsohn et al. 2010; Alberdi et al. 2012; Ferreira et al. 2012). It has been shown that the eye can rotate between repeated measurements taken with significant time intervals between readings e.g a day, week or month (Seo et al. 2004; Osher 2010). The changes in ocular position seen between supine and upright position can lead to inaccurate marking on the cornea used to guide lens alignment in surgery (Popp et al. 2012). However, there is a dearth of studies examining the accuracy of the toric calculators. This absence of scientific work may be due to the complex interaction between corneal biometry and the mathematical modelling of the corneal response to the incision.

It has been established that the smaller the incision, the smaller the amount of change in corneal shape will occur post-surgically (Hayashi et al. 1995; Pfleger et al. 1996). Hill concluded that a SIA of 0.50D is a typical value for an incision size of approximately 2.4mm (Hill 2008). This assertion is concurrent with many studies examining post-operative SIA (Hayashi et al. 1995; Hill 2008; Wei et al. 2012; Dewey et al. 2014) and is in keeping with the results of chapter 3 when using a Cartesian method of calculating SIA.

Hitherto, studies investigating the surgical influence on corneal astigmatism have determined the shape change by assuming that combination of the cornea and incision is similar to the combination of two thin lenses. It is assumed that the cornea and surgical incision act as two thin toric lenses in contact. If an incision is placed along the steepest meridian then the predicted post-operative astigmatic axis stays the same and the magnitude is calculated by subtracting the surgeons SIA from the pre-operative corneal astigmatism. However, if the incision is placed away from the steepest meridian then an oblique cross cylinder formulae is used to determine the resultant vector astigmatic force (Holladay et al. 2001; Thibos et al. 2001). Despite the widespread use of this vector model there is an absence of studies designed to determine if these calculations apply to a human cornea.

The assumed optical model predicts that the orientation of the steepest corneal meridian changes post-operatively in accordance with the location of the CCI. The assumption is that the steepest meridian moves away from the incision site post surgically. This prediction follows the oblique cross cylinder model for two thin toric lenses in contact and negates thickness. If the surgeon places the incision along the steepest corneal meridian then this discrepancy is irrelevant. However, less than 20% of surgeons place their incision along the steepest corneal meridian (Pick et al. 2008). A temporal incision site is the most popular location given its ease of access.

If an incision is placed away from the steepest corneal meridian, then the resultant predicted post-operative orientation lies away from the original pre-operative axis. The change in location is dependent on: the orientation of the incision relative to the corneal steepest meridian, the magnitude of corneal astigmatism, and the magnitude of surgically induced astigmatism. Figure 4.1 demonstrates the discrepancy

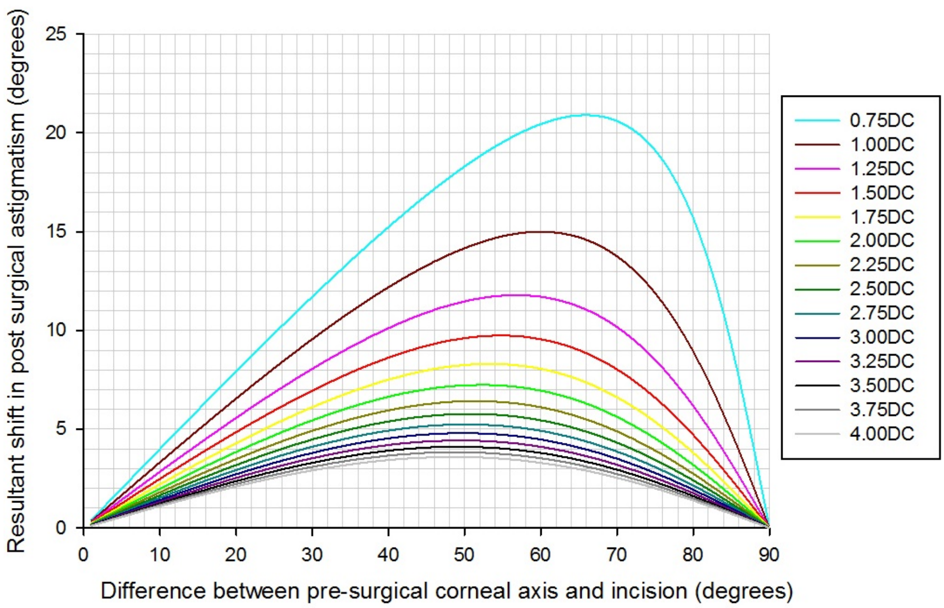

Figure 4.1: Graph representing the magnitude of the rotation (or misalignment) of the toric lens placement away from the pre-operative steepest meridian advised by the toric calculators if the surgeon used an oblique incision causing 0.50DC SIA. Each coloured line represents different magnitudes of pre-operative astigmatism.

Unless placed on axis, a CCI placed obliquely to the principal meridians of the cornea, will result in the predicted steepest corneal meridian lying away from the original position (Table 4.1). In the example of a cornea with 1.00 dioptres of with-the-rule astigmatism, according to the prediction of vector analysis, an incision placed superior-temporally will cause a 13° change in astigmatic axis. However, if this predicted change does not happen and the surgeon places the lens according to the results of the toric calculator then there will be a resultant misalignment of 13°: a loss of 40% in effectiveness (Figure 4.2). Table 1 demonstrates the effective power loss that would be seen across cylindrical (cyl) power of 1.00 - 3.50 DC if the IOLs were aligned 45 degrees away from the principal meridians.

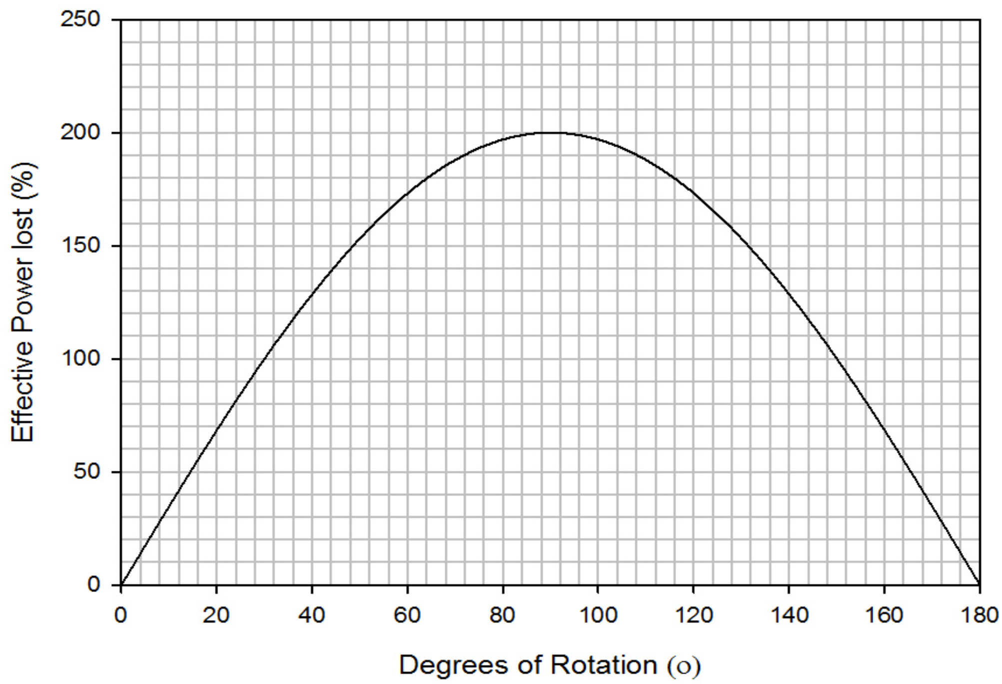

Figure 4.2: Loss of effective power due to rotation of a toric lens away from the required position.

IOL Cyl Power (DC)	Rotation (°)	Effective Power Loss (%)	Resultant Cylindrical Power (DC)
1.00	13	40	0.50
1.50	9	33	1.00
2.00	7	25	1.50
2.50	6.5	20	2.00
3.00	4.5	15	2.50
3.50	4	12	3.00

Table 4.1: Resultant effective power loss that can potentially occur if the toric IOL is rotated away from the principal meridian as advised by the toric calculator (combination of the two graphs in Figures 4.1 and 4.2).

The SIA value entered into a toric calculator is limited to a single value: magnitude of SIA as calculated using the Cartesian method. Therefore, the orientation of the SIA vector is not accounted for in the calculation. The description of SIA using the polar method comprises two components and is not compatible with the current commercially available toric calculators.

This study was designed to determine if toric calculators provide an accurate description of the changes to the corneal curvature that occur following cataract surgery when an incision is placed away from the steepest corneal meridian.

4.1.3 Aim of Study

In order to provide the most accurate and effective correction of corneal astigmatism using toric IOLs, the lens must be accurately aligned with the post-surgical corneal steepest meridian. Any misalignment from the required axis position reduces the effectiveness of the correction (Felipe, 2011). In order to place the lens in the correct position, the surgeon needs to predict the post-operative corneal astigmatism. It is widely assumed that the post-operative corneal power is the vector sum of the pre-operative corneal power and surgically induced astigmatism. There have been toric IOL calculators created to assist the surgeon in the pre-surgical planning that predict the post-operative corneal astigmatism and required IOL position. As a result, unless a clear corneal incision (CCI) is placed at the steepest meridian, a toric IOL is not placed along the original pre-operative steepest meridian and is instead placed along the assumed predicted post-operative astigmatism meridian.

The aim of this study is to investigate the validity of the current assumptions of corneal shape change induced by surgical incisions as predicted through vector analysis. This study will be comparing the predicted changes calculated by toric IOL calculators and the actual changes found after surgery.

4.2 Methods and Materials

4.2.1 Subjects:

This was a prospective study examining one hundred and forty five subjects (63 Males, 82 females) of mean age 74.6 ± 9.4 years. All of the group were planning to undergo cataract surgery and were recruited from the Royal Eye Infirmary (Derriford Hospital, Plymouth UK). The principal investigator of the study (CH) recruited all participating subjects. All data was collected between December 2013 and December 2014. The inclusion/exclusion criteria for the study were as follows:

4.2.1.1 Inclusion Criteria:

- Adult subjects aged 18 years old and above
- Previously consented to routine NHS cataract surgery
- Able and willing to give informed consent to their inclusion into the study

4.2.1.2 Exclusion criteria:

- Irregular astigmatism, as determined by a qualified optometrist.
- Any pre-surgical corneal complications or pathology such as Fuchs' dystrophy and keratoconus
- Subjects who do not have routine cataract surgery and IOL implantation due to pre-existing or unexpected surgical complication.
- Irregular or malformed eyelids e.g. ptosis, chalzion or severe blepharitis.

4.2.1.3 Sample size calculation

Several sample size test calculations were carried out with the G*Power 3 (Heinrich-Heine Unversität, Düsseldorf) to determine the size that will allow reliable results for comparison of paired means (pre-surgical versus post-surgical change in shape) using a two-tailed paired t-test with medium effect size, 0.5 (Cohen's table), a two-tailed correlation of bivariate normal model (accuracy of predictive models) using a medium size effect, 0.3 (Cohen's table) and ANOVA analysis of repeated measures (across 3 visits), between factors using a medium size effect, 0.25 (Cohen's table) (Prajapati, 2010). These required 35, 84 and 70 subjects respectively; therefore a minimum sample size of 84 was required across these analyses. An alpha level of 0.05 and a beta of 0.8 were used in the calculations. Therefore, each group will require a minimum of 84 people.

4.2.2 Ethical Approval

All procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by the local REC committee (Ref: 13/SW/0229 on 16th October 2013), NHS R&D department (Ref: 13/P/106 on 20th October 2013) and University ethics committee (Ref: 13/14-188 on 23rd October 2013).

4.2.3 Surgical Procedure

All operations were performed by one of two surgeons (NH/NM) using topical anaesthetic. A 2.8 mm clear corneal incision was placed superior-temporally in all cases. Phacoemulsification, aspiration, and irrigation were performed through a 5.5 mm capsulorhexis using the Millennium phacoemulsification system (Bausch and Lomb, Rochester, N.Y., USA.). All IOLs were implanted into the capsular bag; the incision size of 2.8 mm was maintained throughout the procedure.

4.2.4 Intraocular Lens

The IOL implanted during the study was the *Tecnis ZA9003.* It is an aberration control aspheric monofocal IOL made from acrylic, hydrophobic material. The IOL is a single piece open loop haptic 12 mm long with a 6 mm optic.

4.2.5 Methods

All Subjects attended a pre-operative study visit and two post-operative study visits:

- Visit 1 (V1)– Pre-operative visit
- Visit 2 (V2) – 3 to 6 weeks
- Visit 3 (V3) – 3 to 6 months

At each visit the following measures were taken:

- Corneal curvature
    - ⇒ Assessed using the Pentacam HR(Oculus).
- Incision Location
    - ⇒ The location of the incision was assessed postoperatively through slit lamp examination.

4.3 Statistical analysis

4.3.1 Assumption of Normality

The one-sample Shapiro-Wilk test was used to determine if results from each measurement followed a normal distribution. Where the data followed a normal distribution, parametric analysis was used; non-parametric statistical analysis was used for non-normally distributed data.

4.3.2 Prediction of post-operative corneal astigmatism

The 145 surgeries were performed by two surgeons NH (62 surgeries) and NM (83 surgeries). There was no significant difference found between the SIA for each surgeon and the average SIA calculated from the data using the Cartesian vector method was 0.50D (0.49D and 0.51D respectively).

The previously calculated SIA value of 0.50D (see above) was applied to the pre-surgical keratometry readings in various groups to determine the predicted axis change. One additional set of analysis was carried out with SIA of 0.25 D. The previous chapter investigated the contribution of instrument error to SIA, causing an overestimation of shape change, finding that the instrument error may be doubling the value in some cases. This nominal value of 0.25D was selected to investigate a smaller and potentially more realistic measure of the corneal shape change that can occur post-surgically. This may have an effect on the accuracy of the prediction calculations.

The Holladay Cravy Koch technique (1992) was used to determine the post-operative steepest corneal meridian position (Equations 4.1 to 4.4).

$$Tan\,2\theta = \frac{C_1 \sin 2\alpha}{C_1 + C_2 \cos 2\alpha}$$ *Equation 4.1*

$$A_T = A_1 + \theta$$ *Equation 4.2*

$$\alpha = A_2 + A_1$$ *Equation 4.3*

$$A_T = A_1 + \left(\frac{\tan^{-1}\left(\frac{C_2 \sin 2\alpha}{C_1 + C_2 \cos 2\alpha}\right)}{2}\right)$$ *Equation 4.4*

A_T = new axis position

A_1 = Incision or principal meridian axis (smallest numerical value)

A_2 = Incision or principal meridian axis (larger numerical value)

C_1 = Magnitude of astigmatism (D) for A_1

C_2 = Magnitude (D) for A_2

θ = Axis change between the lower orientation (Location of incision or flattest corneal meridian—lower value)

a = Difference in orientation between the flattest corneal meridian and incision location

4.3.3 Effective power correction

As it has been established that misalignment can reduce the effective correction of a toric IOL, the validity of the calculator should be assessed further. This was achieved by comparing the effective power loss that would result from using either the predicted post- operative axis position or the pre-operative steepest meridian. The actual post- operative axis position was used to determine the degree of misalignment that would occur or each position. The effective power loss was determine using the following equation:

$$Effective\ Power\ Loss\ (\%) = 200\ (sin\,\theta) \qquad \textit{Equation 4.5}$$

(Sanders et al. 1992; Felipe et al. 2011)

4.3.4 Toric IOL Models: Expected Residual Astigmatism

Using vector analysis, two models were created to calculate the correction that could be achieved with implantation of a range of Acrysof toric IOLs, one using and one ignoring the toric IOL calculator. The first model predicted the post-operative corneal shape using the toric IOL calculator methodology, and derived the most appropriate toric IOL lens that would be advised from manufacturers guidance (see Table 4.2) to best correct the predicted post-operative astigmatism. The post-operative shape measured was then used to calculate the residual astigmatism that would result from the use of the selected toric IOL and position advised by the calculator. The second model followed the same pattern but ignored the calculator and instead using the pre-operative corneal shape to guide the toric IOL lens choice and implantation alignment.

Acrysof Toric IOLs	SNAT range						
	3	4	5	6	7	8	9
Cylinder power (D)	1.50	2.25	3.00	3.75	4.50	5.25	6.00
Correction at the corneal plane (D)	1.03	1.55	2.06	2.57	3.08	3.60	4.11
Range of corneal astigmatism for lens choice |D)	0.75 - 1.29	1.29 - 1.81	1.81 - 2.32	2.32 - 2.83	2.83 - 3.34	8.34 - 3.86	≥ 3.86

Table 4.2: Cylindrical powers of a range of toric IOLs available in the SNAT range from Acrysof and the range of pre-surgical corneal astigmatism recommended for correction with each lens.

4.4 Results

Of the 145 subjects recruited at the beginning of the study, 14 were lost to follow up between visits 2 and 3, resulting in 131 subjects at V3.

For each individual subject's data set, the predicted post-operative corneal axis change was plotted against the actual corneal axis change. The correlation between these two changes in axis measurement was determined and means versus difference plots were used to examine the relationship between the two measures (Bland et al. 1986).

4.4.1 Comparison of actual and predicted corneal change

		0.50 SIA								0.25SIA	
		Whole group		Low Astigmatism		Medium Astigmatism		High Astigmatism		Whole group	
V2		*n=144*		*n=72*		*n=45*		*n=24*		*n=144*	
		Predicted	Actual	Predicted	Actual	Predicted	Actual	Predicted	Actual	Predicted	Actual
	Median	**11.2**	**1.2**	**18.1**	**2.0**	**10.8**	**-1.7**	**6.2**	**0.8**	**6.2**	**1.2**
	Lower Quartile	**6.4**	**-10.6**	**10.2**	**-14.6**	**5.3**	**-9.8**	**4.8**	**-8.5**	**3.4**	**-10.7**
	Upper Quartile	**19.8**	**14.6**	**30.9**	**22.5**	**13.1**	**12.5**	**8.4**	**6.0**	**10.8**	**14.6**
V3		*n=131*		*n=64*		*n=42*		*n=24*		*n=131*	
		Predicted	Actual	Predicted	Actual	Predicted	Actual	Predicted	Actual	Predicted	Actual
	Median	**11.2**	**2.9**	**20.5**	**7.0**	**9.2**	**2.6**	**6.2**	**2.2**	**6.0**	**2.9**
	Lower Quartile	**6.0**	**-6.5**	**10.5**	**-16.4**	**5.3**	**-5.1**	**3.8**	**-1.3**	**3.3**	**-6.5**
	Upper Quartile	**20.5**	**13.7**	**31.0**	**26.0**	**13.2**	**12.2**	**9.1**	**6.1**	**10.3**	**13.7**

Table 4.3: Medians, upper and lower quartiles for predicted versus actual change in steepest corneal meridian position at V2 and V3.

There was a significant difference found between the predicted and actual change in astigmatism for all groups using the surgeon specific SIA and a lower nominal value of SIA (0.25D) at V3 ($p<0.01$).

The median pre-operative corneal astigmatism was 0.74D (IQR 0.45, 1.10D) at V2 after surgery and 0.76D (IQR 0.47, 1.12D) at V3. The mean location of the superior-temporal corneal incision was 40.0 ± 26.9° from the steepest corneal meridian at V2 and 39.7 ± 22.9° in at V3. The actual change in the corneal steepest corneal meridian was lower than the predicted change at V2 ($p<0.001$). The actual median change in astigmatism measured after surgery (median = 0.0, IQR -0.16, 0.16D) was significantly lower than the predicted change in astigmatism magnitude (median = -0.27, IQR -0.40, -0.02D) after surgery ($p<0.001$).

4.4.2 Correlation of predicted versus actual axis change after surgery

There was no significant correlation found between the actual change in astigmatism position and the predicted change in astigmatism axis position for any of the data groups at V2 or V3 (Figures 4.3 and 4.4).

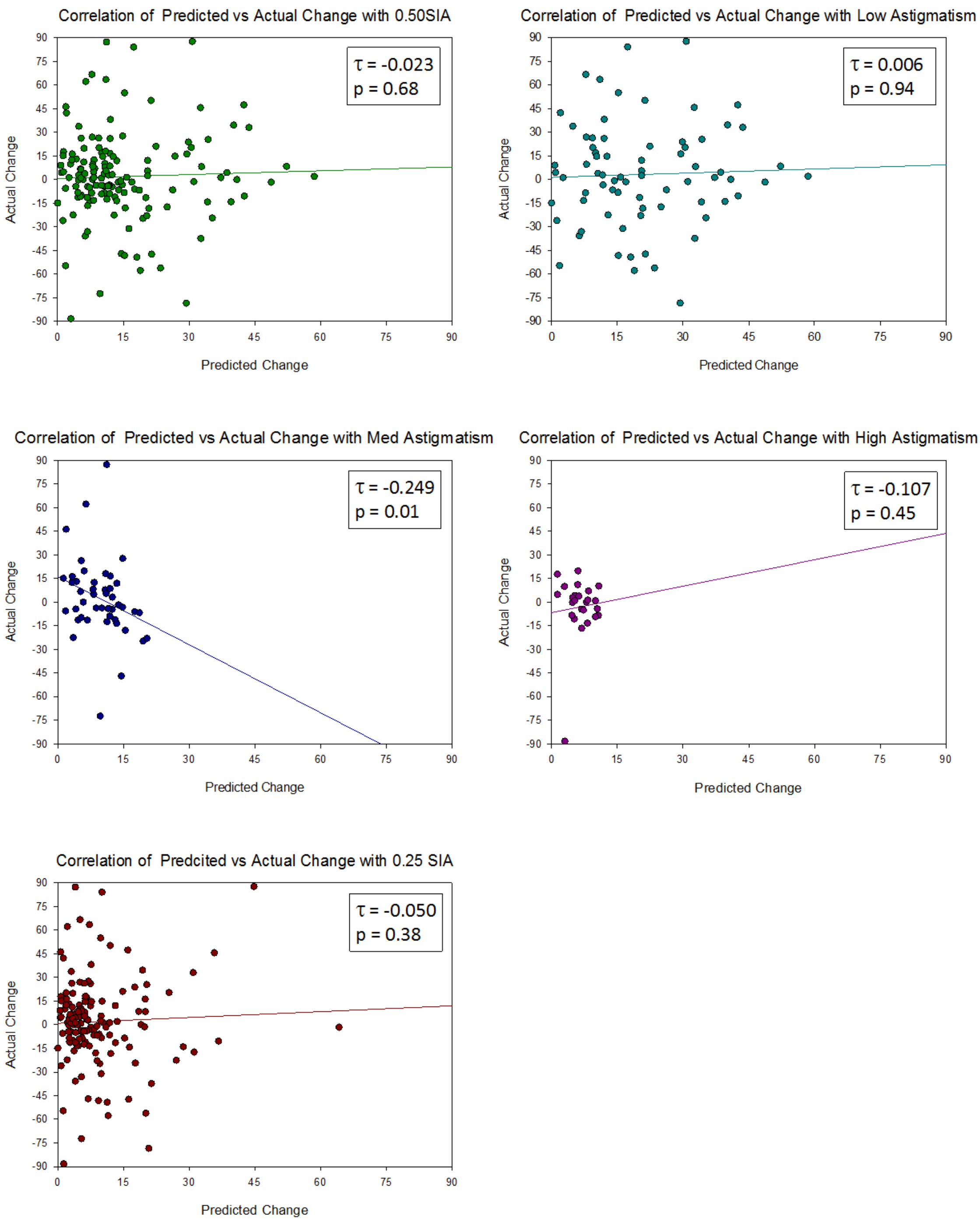

Figure 4.3: Correlation of actual versus predicted change in post- surgical axis at V2

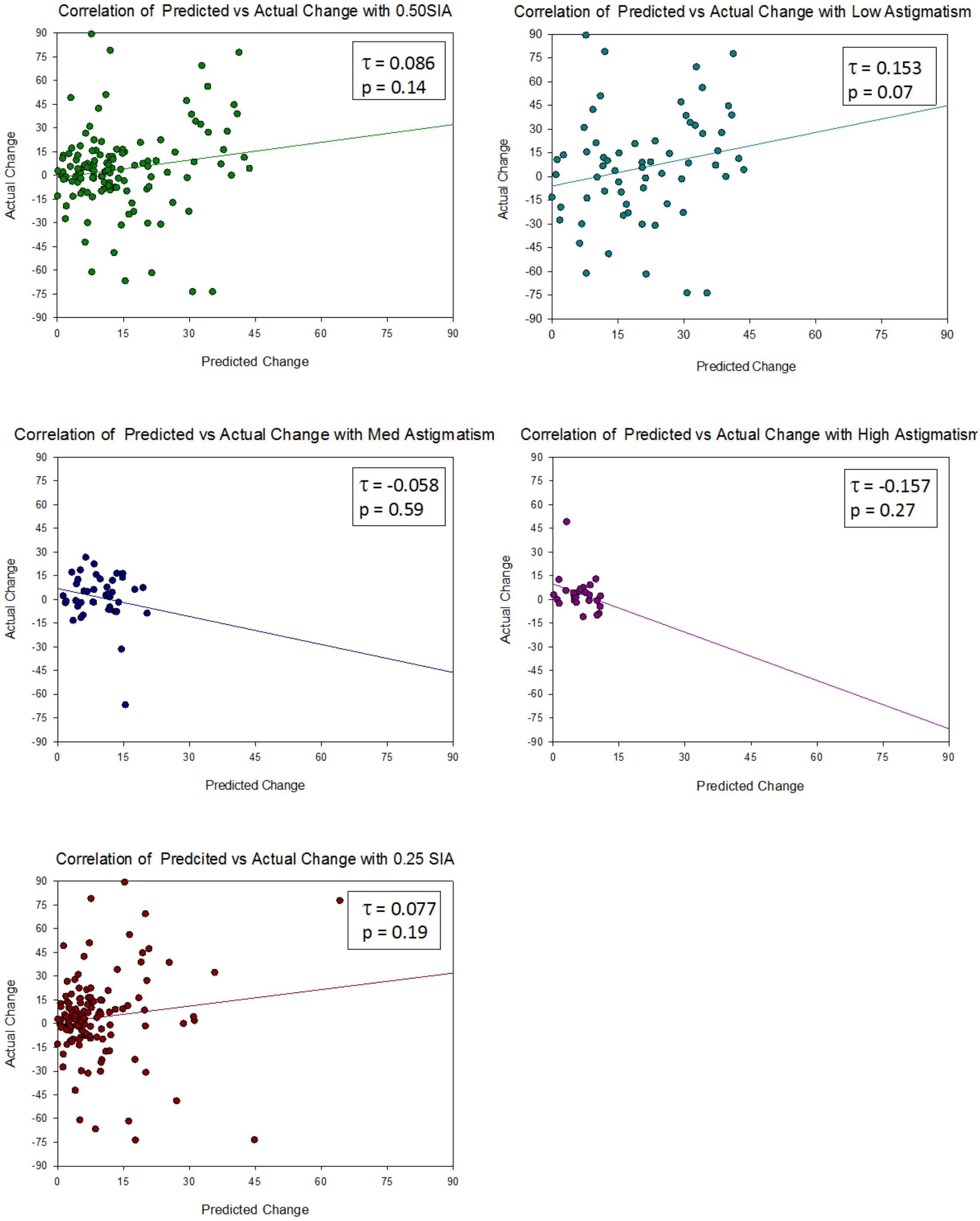

Figure 4.4: Correlation of actual versus predicted change in post- surgical axis at V3

4.4.3 Bland Altman Comparisons

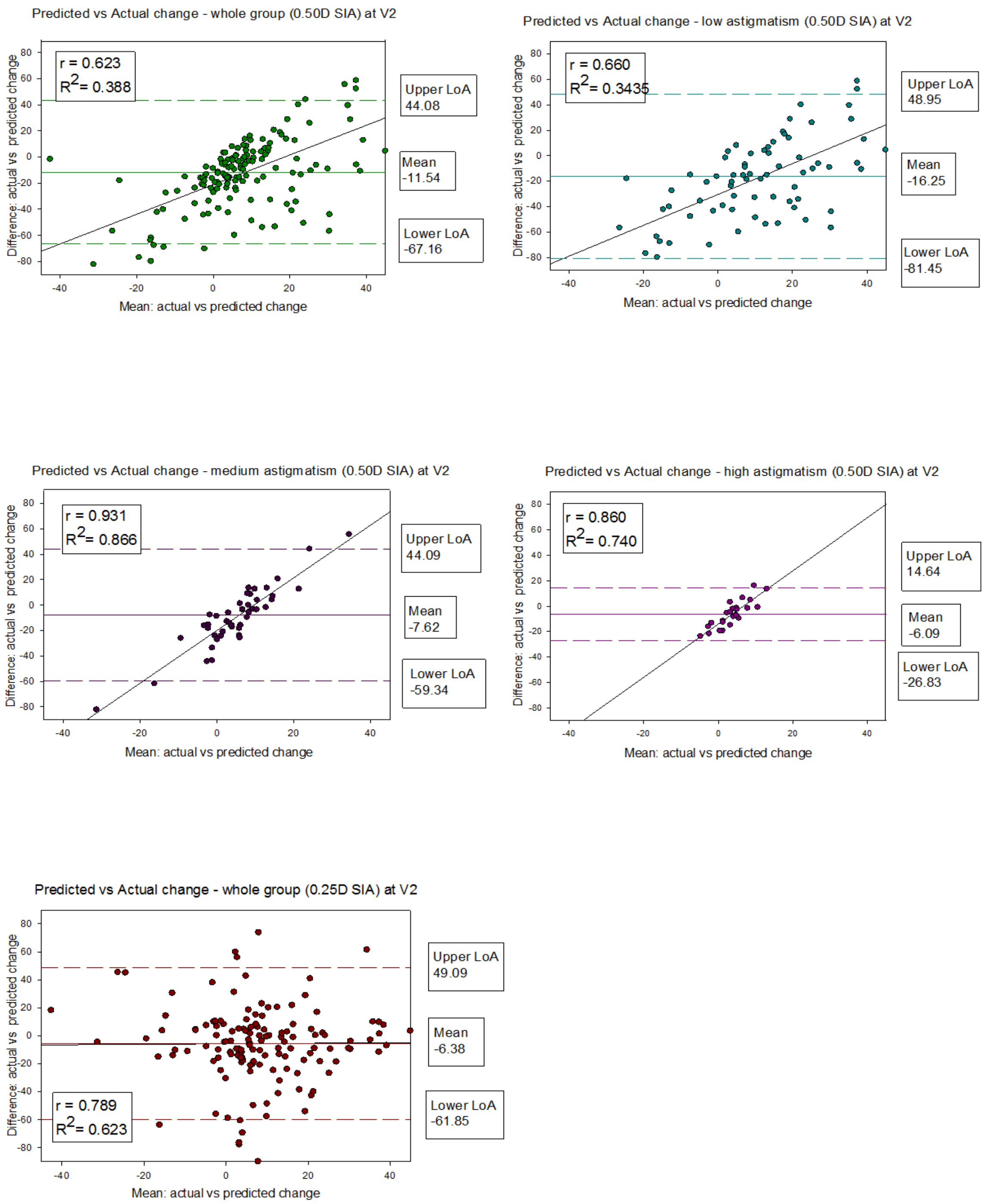

Figure 4.5: Bland Altman comparisons for predicted versus actual axis at V2.

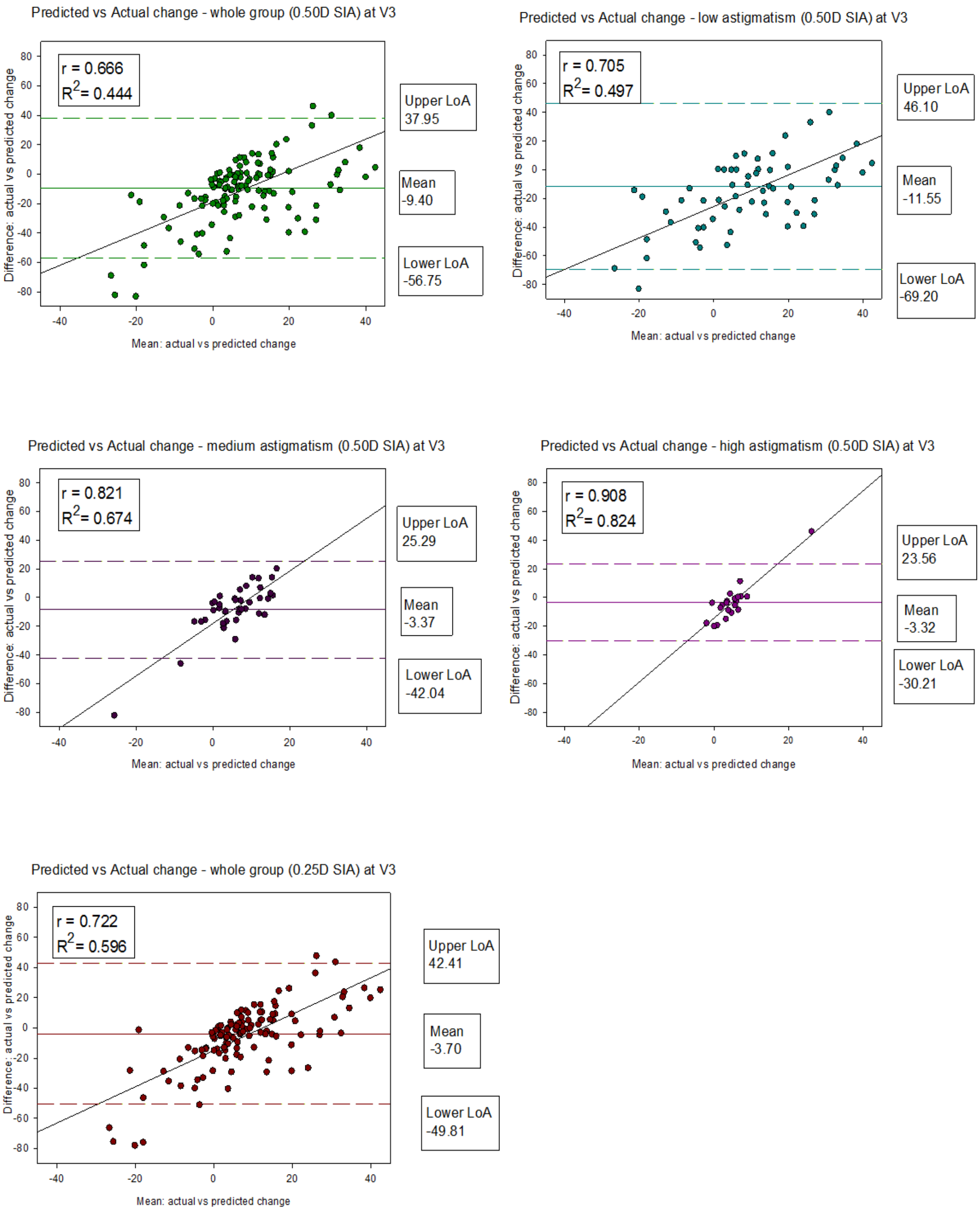

Figure 4.6: Bland Altman comparisons for predicted versus actual axis change at V3

All means versus difference plots for both V2 and V3 display significant proportional bias. The strength of the bias correlation and regression increases with increasing astigmatism as seen with the isolation of the medium and high astigmatism groups (Figures 4.5 and 4.6). V3 shows stronger bias in the groups than at V3. Additionally the used of the smaller SIA value also resulted in an increase in the bias compared to the surgeon–specified SIA level of 0.50D (Figures 4.5 and 4.6).

4.4.4 Correlation of Pre-Surgical and Post-Surgical Steepest Corneal Meridian

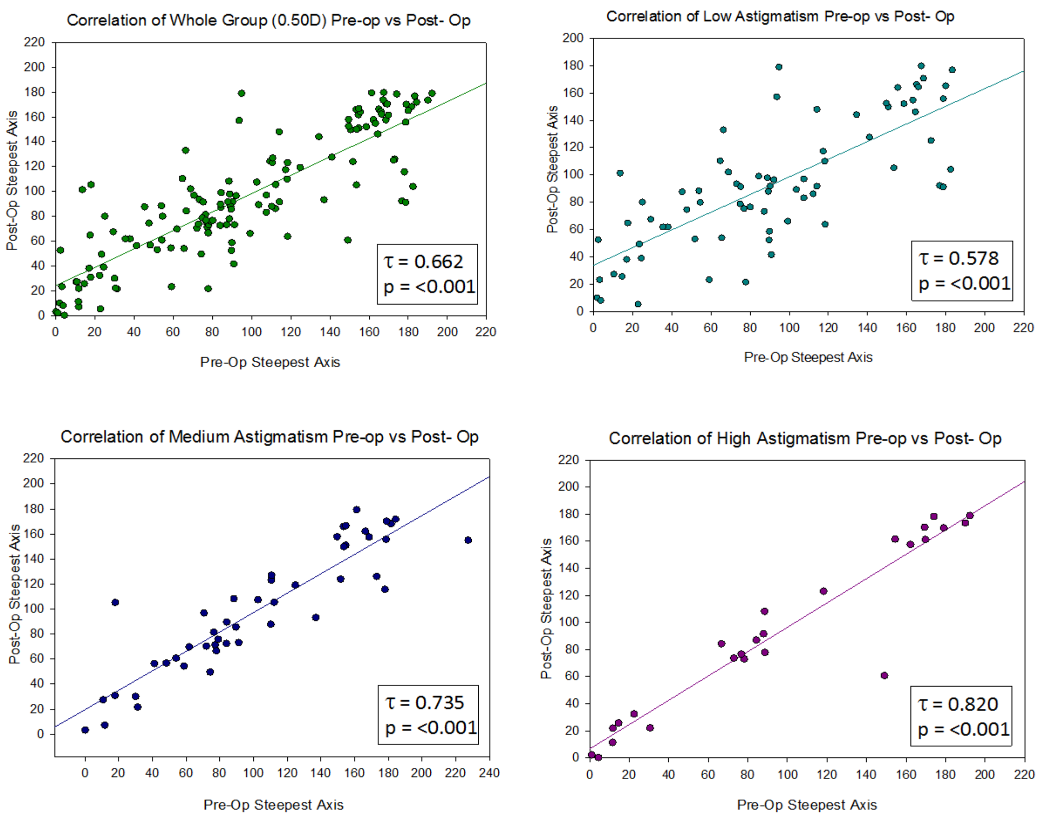

Figure 4.7: Graphs displaying the correlation of pre-surgical versus post-surgical (V2) steepest corneal meridian position.

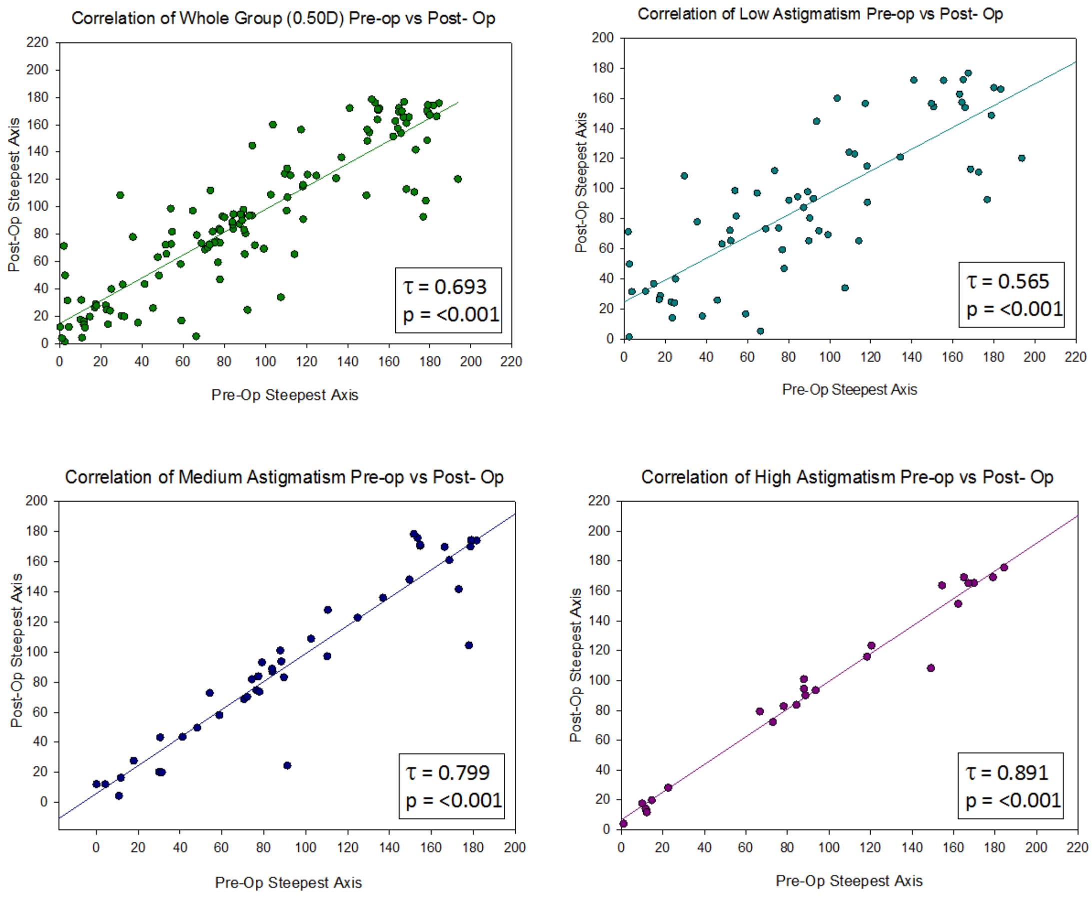

Figure 4.8: Graphs displaying the correlation of pre-surgical versus post-surgical (V3) steepest corneal meridian position.

There were moderate to high correlations between the pre- and post-operative axis data at both post-operative visits (V1 compared to V2 and V3). This indicates that the axis change is small, with higher levels of astigmatism showing the greatest correlation.

4.4.5 Comparison of Effective Power loss with IOL Alignment Position

The Pre-surgical and post-surgical axis measurements correlation was also assessed and the effective power loss that would result from placing an IOL aligned with the pre-surgical steepest axis versus the predicted steepest axis position was compared.

The effective power loss was calculated for the two potential positions for toric IOL implantation. The actual post-operative steepest corneal meridian position was compared to the pre-surgical position and the calculator predicted post-surgical position, to determine the difference in effective power loss that would occur if the lens was implanted in these positions.

Effective Power Loss of the Toric IOL Position (%)		0.50 SIA								0.25SIA	
		Whole group		Low Astigmatism		Medium Astigmatism		High Astigmatism		whole group	
V2		*n=145*		*n=73*		*n=47*		*n=25*		*n=145*	
		Pre-surgical	Predicted	Pre-surgical	Predicted	Pre-surgical	Predicted	Pre-surgical	Predicted	Pre-surgical	Predicted
	Median	**41.2**	**54.0**	**62.8**	**88.2**	**39.2**	**52.2**	**24.7**	**27.7**	**41.6**	**44.4**
	Lower Quartile	16.9	25.2	25.8	41.2	17.4	24.6	11.5	10.2	16.8	21.7
	Upper Quartile	86.7	111.3	119.2	142.9	61.8	81.9	37.8	52.7	87.2	98.5
V3		*n=131*		*n=64*		*n=42*		*n=24*		*n=131*	
		Pre-surgical	Predicted	Pre-surgical	Predicted	Pre-surgical	Predicted	Pre-surgical	Predicted	Pre-surgical	Predicted
	Median	**34.4**	**41.4**	**66.4**	**73.6**	**26.3**	**32.1**	**16.4**	**18.9**	**34.4**	**36.5**
	Lower Quartile	15.0	16.8	32.3	37.1	10.3	12.4	7.2	9.0	15.0	13.7
	Upper Quartile	77.8	78.5	125.6	119.6	47.5	56.7	31.3	45.5	77.2	70.6

Table 4.4: Medians, upper and lower quartiles for the percentage effective correction of astigmatism if the IOL was implanted according to the pre-operative corneal meridian or the predicted post-operative meridian

4.4.6 Wilcoxen's signed rank pairs

There was a significant difference found between the effective power loss seen with implantation of the lens in the pre-surgical position versus the calculator advised position for the group as a whole (Z = -3.038, p= 0.002), and the low (Z = -2.177, p = 0.029) or medium astigmatism group (Z= -2.296, p= 0.022) at V2. However, no difference is seen for the high astigmatism group or if the lower SIA value (0.25D) is used at V2 (Z= -1.547, p = 0.115 and Z= -1.735, p= 0.083 respectively). There was no significant difference found at V3 for any of the data groups (p>0.05 for all).

4.4.7 Model of the Toric IOL Correction

Two models were created for the correction that would have been achieved had a toric IOL been implanted for each of the subjects. The first model used the toric IOL calculator predicted corneal astigmatism (predicted) and the second ignored the calculator and used the pre-operative corneal astigmatism (actual). The two different models advised a different range power and number of toric IOLs for the subject population. The predicted model advised more toric IOLs were required and the two groups differed on the advised lens selection for the subjects who would require a correction (Table 4.7).

Model	Acrysof SNAT Toric IOL chosen by each model							
	3	**4**	**5**	**6**	**7**	**8**	**9**	**Total**
Predictor	61	25	9	6	0	0	1	102
Actual	51	16	4	4	0	1	0	76

Table 4.5: The number of each toric IOL recommended by the two different models and total of IOLs recommended for the same patient group.

The residual astigmatism that would be expected for each subject using the two models was calculated and compared. Paired comparisons were carried out, removing subjects that were recommended a lens by only one model.

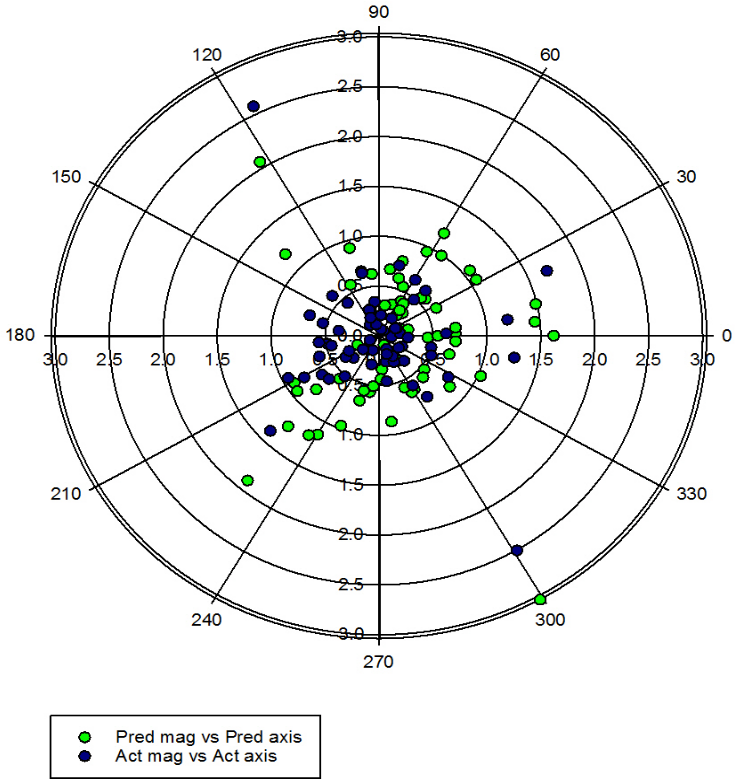

Figure 4.9: Residual astigmatism expected if the toric IOL calculator was used (predicted) or residual astigmatism expected without the toric IOL calculator (actual).

There was a significant difference between the data groups ($p<0.001$) with a higher median residual magnitude of astigmatism seen in the predicted group (median = 0.64D) versus the actual residual magnitude of astigmatism group (median = 0.40D). The correlation between the axis readings between the two groups was poor ($\tau = 0.382$, $p<0.001$). The median difference between the axis readings was 21.5° (IQR 8.55°, 71.37°). The percentage error of the predicted magnitude of residual astigmatism compared to the actual residual expected error was 105.5%.

4.5 Discussion

When an incision is placed oblique to the steepest corneal meridian, the toric calculator predicts that the orientation of this meridian changes and moves away from the incision site. This study found that the predicted corneal shape change (according to the toric calculator) was significantly different to the actual corneal shape changes that occurred. The median actual change found after 3-6 months (2.9°) was much lower than the median predicted (11.2°) change in astigmatism (Table 4.1). This discrepancy is affirmed through the means versus difference plots, which showed a mean overestimation of 11.5° at V2 and 9.4° at V3 (Figures 4.5 and 4.6). There was no significant correlation between the predicted change in the corneal steepest meridian and actual change for any of the groups (Table 4.2). Furthermore, in roughly 50% of subjects, the postoperative corneal principle meridian moved away from the incision site rather than towards as predicted. It can be inferred that the calculations are not just overestimating the change but that the cornea does not reshape in the uniform way that the calculations suggest.

The predictive formulae assume that both the cornea and CCI act as two thin toric lenses in contact and all corneas will act in a uniform way towards the incision of set size. However, this assumption does not appear to be valid for the human cornea. It is possible that other factors such as the corneal thickness, corneal rigidity or biomechanical properties may be factors that need to be incorporated into a prediction model. Denoyer and colleagues found that there was a negative correlation between pre-surgical hysteresis and surgically induced astigmatism, finding that high corneal hysteresis is related to lower SIA (Denoyer et al. 2013). The cornea response can change depending upon the biomechanical factors of the individual structure. Studies have shown that although corneal hysteresis initially decreases after surgery at 1 week, it returns to normal levels by 1 month post-surgically (Kucumen et al. 2008; Kandarakis et al. 2012). In addition to this, the calculations are heavily reliant upon the Cartesian vector value used for SIA. Yet, chapter 3 has shown that this provides a poor description of corneal change actually occurring. This will further contribute to the error in the prediction.

The Bland Altman comparisons provide another illustration of the poor agreement of the predicted and actual change in steepest corneal meridian position following cataract surgery. In addition to wide limits of agreement (LoA) between the two groups (both visits), all plots demonstrated a significant proportional bias at both V2 (Figure 4.5) and V3 (Figure 4.6). The LoA for the whole group was 44.08° to -67.16° at V2 and 37.95 to -56.75° at V3. As previously stated, when a lens is aligned 30 degrees away from the intended position, the intended correction provided by the toric IOL is reduced by 100%, beyond this, the resultant ocular astigmatism is increased rather than corrected by the toric IOL (Felipe et al. 2011). If the calculator had been used to plan a toric IOL implantation in the subjects, a large number would have had an IOL implanted placed at the incorrect location. This will decrease the effective correction of the lens or even increase the residual ocular astigmatism. At both visits, the bias within the comparison exhibited a strong correlation (V2: r = 0.623, V3: r = 0.666) and a moderate regression relationship (V2: R^2 = 38.8%, V3: R^2 = 44.4%) of the error. The LoA were narrowest for the high astigmatism (14.5° to -26.3° at V2 and 23.56 to -30.21 at V3) but this still demonstrates significant disparity in the agreement. Interestingly, the strength of the regression increased with increasing astigmatism at both visits, the regression for the high astigmatism plot was 74% at V2 and 82.4% at V3. Small misalignments will cause a more significant loss in effective power in high astigmatism; therefore smaller changes will be predicted with higher levels of astigmatism. This will have resulted in narrower limits of agreement and a more tightly packed spread of results around the regression line, not an increase in accuracy of the calculator. Overall, these plots indicate that there is a fundamental error in the calculations.

Chapter 3 found that the SIA was frequently overestimated and the true value is likely to be much smaller than that normally calculated. Therefore the analysis in this chapter was also carried out with a nominal SIA level of 0.25 DC in addition to the Surgeon specified SIA (0.50 DC). This was done to see if there would be an improvement in agreement of the results with a significantly smaller (and potentially more realistic) magnitude change that may be more representative of actual shape change. However, little to no improvement in agreement (Figures 4.3 and 4.4) or correlation (Figures 4.1 and 4.2) is seen with this. There is also still a significant difference between the predicted and actual change in axis position measured post-surgically at both V2 ($p = 0.002$) and V3 ($p < 0.001$). The use of a lower magnitude of SIA resulted in a lower median predicted change in axis position (6.2) but it was still higher than the actual change (1.2) both at V2 and V3 (6.0 and 2.9 respectively).

The equations used are dependent on the assumption that the resultant power of the cornea and corneal incision is similar to the combination of two optical thin lenses. If two optical lenses are placed in contact with principal meridians placed obliquely to one another, then the resultant principal meridian positions will be between the two original lens principal power positions. As a result, the calculations will always predict that the post-operative steepest meridian position will move away from the incision site. It was found that the steepest meridian position could actually move either towards or away from the incision location as seen in both the negative signs of the lower quartiles for each group comparison (Table 4.1). Additionally the equation predicts that no change greater than 45 degrees can occur. Again this was not always the case, actual change in astigmatism found could move either direction as much as 90 degrees although on average it was less than predicted (Figures 4.2 to 4.6.)

Higher levels of astigmatism are less likely to show large shifts in axis position and this is seen in Figures 4.2 to 4.6. The pre-surgical steepest axis position was compared to the post-surgical steepest axis position (Figures 4.7 to 4.8) and the correlation was found generally to be quite strong. The correlation was stronger in medium and high astigmatism groups isolated from the low astigmatism data that displayed poorer correlation, indicating more movement induced by surgery. This was to be expected and the calculators would also predict less movement in higher pre-surgical astigmatism.

The aim of this study was to determine the validity of the toric calculators, which are widely used in clinical practice. Currently, if surgeons are going to use an incision oblique to the steepest meridian, they have the choice of original steepest meridian or the position predicted by the calculator. The loss of effective power expected if a toric IOL was implanted in either position was calculated and compared to investigate which position would be the best choice. A lower median loss was seen if the IOL was aligned with the pre-surgical steepest axis position rather than the predicted model. For the high astigmatism and the 0.25 SIA group, effective power loss expected from the pre-surgical position was not significantly different from the predicted position ($p = 0.115$ and 0.083 respectively). When data was analysed from the later follow up (V3), which allowed more time for corneal stabilisation, there was no significant difference seen between the effective power losses expected using the pre-surgical steepest axis position compared to the predicted position produced by the calculators ($p>0.05$). This indicates that there will be little difference in effective correction when using either position. However, the median and quartiles were consistently lower with the pre-surgical position than the predicted position.

The median change reported is much lower than expected when compared to the median effective loss reported. The median change combines the changes going both towards (+) and against (-) the incision, however the effective loss is an absolute rotation away from the intended position irrespective of direction. This provides a clearer indication of the results that would occur after surgery for patients with toric IOLs implanted.

Two models were created to explore the potential correction that could be achieved with a commercially available (Acrysof) toric IOL. The first model used the toric IOL calculator (predicted data) to determine both the power and meridian of the post-operative corneal astigmatism. The second model used the pre-operative corneal astigmatism alone (actual data). A theoretical model of the amount of correction that would have occurred had a toric lens been implanted according to the predicted and actual data was calculated. There was a significant difference between the magnitudes in the two data groups, with a smaller median residual astigmatism in the actual change data group. Interestingly, there were a higher number of subjects recommended for a toric IOL (had a predicted post-operative astigmatism >0.75D) with the predicted model rather than the actual model. When an incision is placed more than 30 degrees away from the steepest meridian, the effective astigmatic error that the toric calculator predicts is higher than the original corneal astigmatism. There was also a poor correlation between the two data groups. As previously found with the initial effective power loss calculation, neither of the groups were significantly closer to the required actual post-operative axis position. Similarly, this is an indication that the calculator is predicting inaccurate changes post-surgically. These results contradict the previous effective correction analysis in the earlier paragraph. This model only used lens powers that are currently available, which limits the correction in some instances. However, the previous effective power loss assessment calculated the theoretical correction required by each individual cornea at the corneal plane but this is not currently available. Therefore, the results produced by the model are more realistic.

The verification of the toric calculator has partly been reliant upon the accurate measurement of the corneal incision location. However, as mentioned in chapter 3, the identification of the incision site was difficult to assess with a high degree of precision. There is a large margin of error not due only to the potential for eye and head rotation but the subjectivity of the measurement with the slit lamp. As demonstrated in figure 4.10, an oblique clear corneal incision, 2.8 mm in size, placed 1mm in from the limbal margin at 45° will subtend an angle of 29.9°. The investigator had to estimate the centre of the incision site to assess the incision location to within one degree.

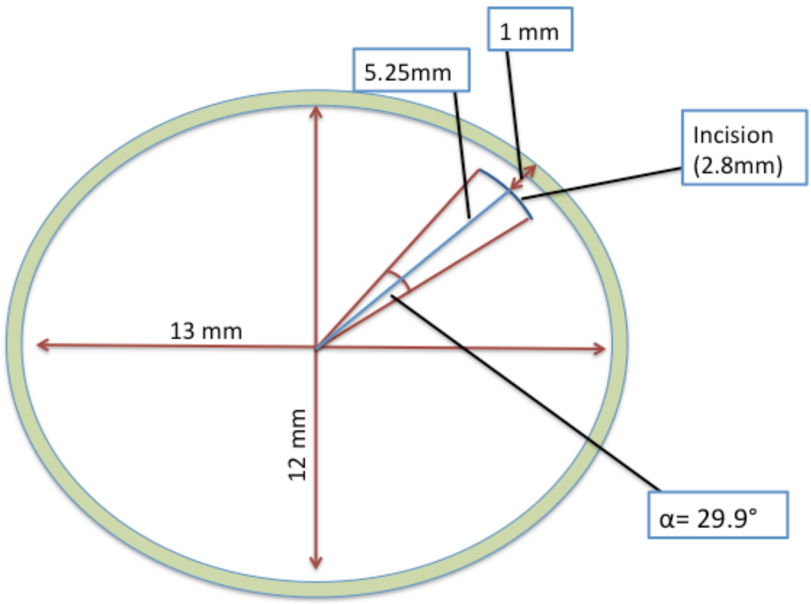

Figure 4.10: Depiction of the large angle (29.9°) subtending the 2.8mm clear corneal incision, using a Gullstrand eye.

Previous work has suggested that the corneal shape and astigmatism stabilises quickly after surgery, Masket et al (1996) has suggested that the cornea is stable just 2 weeks after surgery (Masket et al. 1996). Studies examining long term corneal astigmatism changes indicate that the SIA vector reduces over a 12-month period (Pfleger et al. 1996; Ermiş et al. 2004). Hayashi et al (2005), found that corneas change naturally with age (Hayashi et al. 1995). Hayashi et al conducted a follow up study (2011) that compared eyes after surgery against those that did not undergo surgery, and found that the shape of both sets of eyes will progress towards against the rule astigmatism and increase in astigmatism regardless of the surgery (Hayashi et al. 2011). It appears that it is not possible to predict corneal shape change. This continual change in corneal shape may further limit the effectiveness of the calculators

When the data was split into groups of astigmatism power in the V3 data set, there was a variation in the agreement between actual and predicted post-surgical shape. As we saw in the graph in Figure 4.1, the calculators predict less shape change in higher pre-surgical astigmatism, thus increasing the accuracy. The biggest error and deviation from actual change is seen in the lowest astigmatism group, which predicted large shifts that were not actually seen.

One significant limitation in this study and source of error is in the keratometry. Chapter 2 has shown the poor repeatability in steepest corneal meridian positions assessed by the variety of keratometers available. The toric calculators are reliant upon accurate measurement of astigmatism and the principal meridian positions for both the predictions of change and the pre-and post-surgical assessments. Any errors in the measurements will affect the accuracy of the pre and post-operative assessments and the prediction found by the calculations. Additionally the SIA is also reliant upon accurate keratometry and, as shown in chapter 3, this can also be affected by the error in keratometry. These multiple sources of error are present in the calculations used in this study.

4.6 Conclusions

Prior to this study, the use of toric calculators for predicting post-operative corneal shape, with oblique incisions, had not been validated. Despite this lack of evidence toric calculators are used to predict the post-operative steepest corneal meridian whenever a toric IOL is used. This study showed that the predication made by a toric calculator was not valid when using a clear corneal incision "off axis". Furthermore, the pre-operative steepest meridian was not any closer to the post-operative meridian than the predicted post-operative steepest meridian position. However, when based on the available range toric IOL powers, there was less residual astigmatism predicted when using the pre-operative steepest meridian axis measured compared to the calculator predicted post-operative steepest meridian axis. Overall, these results show that where possible a clear corneal incision should be placed along the steepest meridian ("on axis") so that the oblique calculation is not required. Where an 'off-axis' incision is used, the effective power of the toric IOL will be reduced if the IOL is placed on either the pre-operative steepest meridian or the steepest meridian predicted by the calculator. It is important to note that inaccuracy of keratometry plays a large role in the poor predictions of both the calculator and pre-operative measurements. Both the pre- and post-operative readings may not be accurate as seen in Chapter 2.

More research needs to be conducted to find a better predictive model for the post-operative corneal changes. This includes improvements to the keratometry instrument repeatability and reproducibility (as explored in chapter 2) when taking astigmatism measurements. Incorporating a more descriptive representation of SIA into the calculation, such as polar values (chapter 3), may improve the model. In order to provide the best post-operative correction with a toric IOL, it needs to fully correct the residual astigmatism that occurs post-surgery. Analysis of the relationship between residual refractive astigmatism and keratometry in a pseudophakic population will would explore this further. This will be examined in the next chapter.

Chapter 5 The Relationship between Subjective Refraction and Corneal Power in a Pseudophakic Population

5.1 Introduction

5.1.1 Background

Gullstrand's exact schematic eye defined the eye as having six refractive surfaces: this includes the anterior and posterior surfaces of each of the cornea, lens cortex and lens nucleus (Tunnacliffe 1997; Smith et al. 1998; Smith 2003). This schematic eye model provides a simplified account of the complex refractive nature of the crystalline lens but is still useful for understanding the distribution of power throughout the eye. The crystalline lens is responsible for roughly 1/3 of the refractive power of the eye, with the cornea responsible for the other 2/3. The presence of ocular astigmatism is attributed to at least one toric refractive surface present in the cornea (corneal astigmatism) or lens (lenticular astigmatism)(Shankar et al. 2004). It is well established that that there is a statistically significant linear relationship between ocular refraction and corneal astigmatism measured by keratometry. Javal first described this in 1890, postulating his rule that described the relationship between keratometric and refractive astigmatism (Javal, 1890; Equation 5.1).

Refractive astigmatism = 1.25 (keratometric astigmatism) -0.50 x 90 *Equation 5.1*

This infers that most of the ocular astigmatism is a consequence of corneal astigmatism. More recently, Grosvenor and colleagues found that the accuracy of Javal's rule improved with a small adjustment (Grosvenor and Ratnakaram, 1990; Equation 5.2).

Refractive astigmatism = 1.00 (keratometric astigmatism) -0.50 x 90 *Equation 5.2*

However, these rules were deemed to only apply to astigmatism orientated vertically (with the rule) or horizontally (against the rule). Oblique astigmatism is rarely referenced and was not incorporated into studies examining this relationship between ocular and corneal astigmatism.

5.1.2 The Relationship between Corneal and Refractive Astigmatism

Assessment of astigmatic magnitude alone is not a sufficient description. Modern day keratometry and astigmatism analysis is commonly assessed with the readings converted into the J_0 J_{45} vectors described by Thibos (1997). These describe the astigmatism magnitude along the vertical and horizontal planes, so take into account both magnitude and direction. They make use of Jackson cross cylinders where the J_0 vector (Equation 5.3) refers to the 90 and 180 orientations (with and against the rule) and the J_{45} vector (Equation 5.4) describes the reading in reference to the 45 and 135 oblique orientations (Thibos et al. 1997).

$$J_0 = \frac{J}{2}cos(2\alpha) \qquad \textit{Equation 5.3}$$

$$J_{45} = \frac{J}{2}sin(2\alpha) \qquad \textit{Equation 5.4}$$

Remon et al (2009) investigated the use of J_0 J_{45} vectors to explore the rule for all types of astigmatism. They found that two rules could be developed for each J_0 and J_{45}:

Refractive J_0 = 1.07 x corneal astigmatism – 0.28 *Equation 5*

Refraction J_{45} = 1.46 x corneal astigmatism + 0.03 *Equation 6*

All of these previous studies were based upon a phakic population and any discrepancy between corneal and ocular astigmatism was assumed to be attributable to the crystalline lens. Following pseudophakic exchange with a non-toric IOL any lenticular astigmatism should be removed. Given the linear relationship between corneal and refractive astigmatism (Javal 1890; Grosvenor et al. 1990), it can be inferred that the correlation between the corneal and ocular astigmatism should increase in a pseudophakic population, as the IOL optics are a known factor. However, corneal curvature has been shown to change with age. Corneal astigmatism can change from with the rule (WTR) to against the rule astigmatism (ATR) and there is an increase in the incidence of oblique astigmatism (Hayashi et al. 1995). As a result, the post-cataract population is likely to show a different relationship than that found in the younger population used to develop Javal's rule.

In 1992, Shimizu and colleagues (Shimizu et al. 1994) described the first toric IOL developed for the correction of corneal astigmatism. These lenses incorporate either a front or back surface toric surface and are aligned according to the astigmatism of the cornea. These lenses are becoming a more popular choice for the correction of astigmatism survey (Leaming 2004; Pick et al. 2008) and have been shown to be more effective when compared to the use of limbal relaxing incisions (Mendicute et al. 2009).

5.1.3 Measuring Corneal Astigmatism

In the clinical environment, there is a large range in instruments used to establish corneal astigmatism. These instruments often differ in the optical principles that they are based upon. Most of the instruments used to assess corneal curvature use reflections from the tear film to assess the anterior surface. These instruments use a keratometric index to try and take into account the refractive index of the cornea and the shape of the posterior surface. Many instruments use the index of 1.3375, first proposed by Javal, which calculates a 7.5mm radius as 45D (Gutmark et al. 2010).

Scheimpflug imaging has allowed the imaging of the posterior surface and may help better understand the corneal shape as a whole (Dubbelman et al. 2002). Incorporating the measurement of the posterior surface has been shown to improve the accuracy of the astigmatism assessment (Ho et al. 2009; Koch et al. 2012). This method has been proposed to assess the cornea free from the tear film (Dubbelman et al. 2002) as being free from the influence of the tear film. However, it could be speculated that the instrument is assessing the anterior surface, which is covered in the tear film when it is assessing the curvature. It is not entirely free from the influence of the tear film as it does not ignore the tear film on the anterior surface or eliminate it from the scam. Therefor it could be inferred that the influence in reduced but not eliminated.

There has also been recent re-evaluation of the keratometric index to improve the accuracy of the corneal astigmatism measurement. This index was originally based on the Gullstrand estimation of a ratio of curvature of 1.13 between anterior and posterior surfaces. Using Scheimpflug imaging, Fam and colleagues found the ratio to be 1.22 (Fam et al. 2007). Ho et al (2008) found that an index of 1.3281 was significantly more accurate. The keratometric index will only take into account a variation in magnitude, not axis orientation. Eom et al (2013) carried out a study looking at anterior corneal astigmatism and internal astigmatism (astigmatism attributed to the internal optics including the posterior corneal, anterior and posterior lenticular surfaces). They found that there was a disparity in the axis orientation of astigmatism between the anterior corneal and the internal optics (posterior cornea and lens) that meant that the total ocular astigmatism contributing to the manifest refraction could change significantly after surgery. In 10% of the cases, there was a 90° difference between the anterior corneal astigmatism and internal astigmatism measured (Eom et al. 2013). This study was carried out in a routine cataract clinic, and did not exclude any patients with less significant levels of astigmatism. The disparity may have been more common in the low astigmatism population.

The generalizability of Javal's rule can be questioned as it was developed on a sample population who predominantly exhibited with-the-rule astigmatism. Several studies have proposed that the posterior corneal surface does not follow a consistent ratio of curvature along all meridians (Koch et al. 2012; Eom et al. 2013; Bregnhøj et al. 2015). Koch and colleagues (2013) proposed that Keratometry has a tendency to overestimate the 'with the rule' astigmatism and underestimate the 'against the rule' astigmatism (Koch et al. 2013). Pinero and colleagues (2012) suggested using a sliding scale of keratometric indices depending upon the curvature measured (Piñero et al. 2012). Koch et al suggested that ophthalmological surgeons note the orientation of the astigmatism and use different nomogram in the calculation of the IOL powers used to best correct the vision (Koch et al. 2013).

The accuracy of this is highly dependent upon the accuracy of the instruments to determine corneal curvature. There are a variety of methodologies but most will only measure a small central corneal area (~3 mm). It has been previously suggested that the small central area measured is limiting the precision of the keratometry results. Alpins et al proposed that assessment over a larger are of the cornea provides a better indication of the corneal power (Alpins et al. 2012). This group, developed a formula to use greater areas of topographical maps to improve the accuracy of the reading (Alpins et al, 2012). The same research group added the posterior cornea measurement to this analysis, finding a better relationship between the refraction and keratometry(Alpins et al. 2015). However, Keller et al showed that refraction was unaffected by variations in pupil size, suggesting that paraxial rather than peripheral rays determine the refractive astigmatism (Keller et al, 1996). Contradictory to Alpins work, this suggests that in this instance the size of central area chosen is negligible.

5.1.4 Determining Corneal Power

Techniques based on reflection (keratometry and topography) measure the radius of curvature of the anterior corneal surface indirectly, as the reflections are from the tear film. Scheimpflug imaging and optical coherence tomography (OCT) allows an assessment of both the anterior and posterior corneal curvature. It is inferred to be free from the influence of the tear film The representation of corneal power requires knowledge of both curvature and refractive index. There are many ways in which this power can be determined which could lead to discrepancies between measurements:

5.1.4.1 <u>Sagittal Power</u>

Methods based on the reflection principle determine sagittal power. This is where the cornea is assumed to be a single refractive surface of known refractive index (Equation 5.7). This method assumes a specific relationship between the anterior and posterior corneal surface:

$$Kp = \left(\frac{n' - 1}{Kr}\right) 1000 \qquad \textit{Equation 5.7}$$

Kr = keratometry radius reading

Kp = keratometry power reading

n' = Refractive index of the cornea

5.1.4.2 <u>True Net Power</u>

Devices that measure the curvature of both the anterior and posterior corneal surface can provide a measure of true net power. This is the summated power of the anterior and posterior corneal surface (Equation 5.8). The limitation of this method is that it assumes that the two corneal surfaces act as two thin lenses in contact and does not account for the thickness of the cornea.

$$True\ Net\ Power(D) = \left(\frac{1.376-1}{r_{anterior\ surface}}\right)\times 1000 + \left(\frac{1.336-1.376}{r_{posterior\ surface}}\right)\times 1000$$

Equation 5.8

r_1 = radius of the anterior corneal surface

r_2 = radius of the posterior corneal surface

5.1.4.3 Total Corneal Refractive Power

This method provides a measure of corneal power through ray tracing (thick lens formula). Both the anterior and posterior surfaces are incorporated into the measurement as well as the thickness of the lens.

$$F_1 = \frac{1.376-1.000}{r_1}$$ *Equation 5.9*

$$F_2 = \frac{1.376-1.336}{r_2}$$ *Equation 5.10*

$$Total\ corneal\ refractive\ power = \frac{F_1+F_2-\frac{1.376}{t}F_1F_2}{1-\frac{1.376}{t}F_1} \qquad \textit{Equation 5.11}$$

F_1 = power of the anterior corneal surface

F_2 = power of the posterior corneal surface

T = thickness of the cornea

5.1.4.4 Holladay Equivalent K readings

The Holliday Equivalent K Reading also utilizes a thick lens equation approach. However, the result is then adjusted to be equivalent to a 1.3375 refractive index (sagittal power). This method of determining corneal power is proposed to be useful in cases where there is an atypical relationship between the anterior and posterior corneal surface. As such, it has been found to improve the accuracy of cataract surgery following laser refractive treatments.

Research examining the relationship between corneal astigmatism and ocular astigmatism has predominantly been conducted in a phakic population. The pseudophakic population is potentially very different. The topographical profile is likely to be different and the eye has undergone surgery, potentially altering the natural shape of the eye.

5.1.5 Aim

This study aimed to explore the relationship between ocular refractive astigmatism and corneal astigmatism in a pseudophakic population.

5.2 Methodology

5.2.1 Subjects

Ninety-six subjects of mean age 74.7±10.01 years (range 29-95 years) who had undergone cataract surgery with a *Tecnis ZA900* implant were recruited from the Royal Eye Infirmary (Plymouth, U.K.). The principal investigator of the study (CH) recruited all participating subjects. All data was collected between April 2013 and December 2013. The inclusion/exclusion criteria were as follows:

5.2.1.1 Inclusion Criteria

- Adult subjects aged 18 years old and above
- Able to give informed consent
- Traditional and uneventful phacoemulsification with implantation of the *Tecnis ZA900*

5.2.1.2 Exclusion Criteria

- Irregular astigmatism as determined by a qualified optometrist
- Previous corneal complications or ocular pathology including previous surgery, Fuch's dystrophy, keratoconus or glaucoma.
- Irregular or malformed eyelids caused by such conditions as ptosis, chalzion or severe blepharitis.

5.2.1.3 Sample size calculation

Several sample size test calculations were carried out with the G*Power 3 (Heinrich-Heine Unversität, Düsseldorf) to determine the size that will allow reliable results for comparison of paired means (manifest refraction versus keratometry corneal power) using a two-tailed paired t-test with medium effect size, 0.5 (Cohen's table), a two-tailed correlation of bivariate normal model (accuracy of predictive models) using a medium size effect, 0.3 (Cohen's table) and ANOVA analysis of repeated measures (across , 7 groups and 2 visits), between factors using a medium size effect, 0.25 (Cohen's table) (Prajapati, 2010). These required 35, 82 and 34 subjects respectively; therefore a minimum sample size of 82 was required across these analyses. An alpha level of 0.05 and a beta of 0.8 were used in the calculations. Therefore, each group will require a minimum of 82 people.

5.2.1.4 Procedure

Pre-operatively, an IOLMaster 500 (Carl Zeiss Meditec AG) and Pentacam HR were used to determine axial length and corneal power. To determine IOL power, the Hoffer Q IOL formula was used for short axial lengths and the SRK/T was used for all other axial lengths, in accordance with the College of Ophthalmologists' guidelines.

Invited study participants had been operated on by one of two surgeons using topical or local anaesthetic. In all cases, a Tecnis ZA900 monofocal IOL had been implanted in the capsular bag. This monofocal IOL is a single piece aspherical control hydrophobic acrylic IOL.

Fourteen subjects were lost to follow up between V1 and V2 hence 96 subjects (34 male, 52 female) attended V1 and 82 (34 males, 48 females) attended V2.

5.2.1.5 Ethical Approval

All procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by the local REC committee (Ref: 13/SW/0229 on 16th October 2013), NHS R&D department (Ref: 13/P/106 on 20th October 2013) and University ethics committee (Ref: 13/14-188 on 23rd October 2013)..

5.2.2 Measurements

All Subjects attended two post-operative study visits:

- Visit 1 (V1) – 3 to 6 weeks post-operative
- Visit 2 (V2) – 3 to 6 months post-operative

During the two study visits the following tests were performed on each subject:

5.2.2.1 Assessment of Corneal Curvature

Assessment of corneal curvature was carried out on each subject with three different instruments:

5.2.2.1.1 The IOLMaster 500 (Carl Zeiss Meditec Inc., Jena, Germany)

The IOLMaster uses automated keratometry to provide a measure of sagittal corneal power at a chord length of approximately 2.3 mm, using a refractive index of 1.3375.

5.2.2.1.2 The OPD Scanner (Nidek Co., Ltd, Gamagori, Japan)

The OPD Scanner is a Placido disc topographer. This study examined the measure of sagittal corneal power at a chord length of approximately 3.2 mm, using a refractive index of 1.3375.

5.2.2.1.3 The Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany)

The Pentacam HR is a Scheimpflug tomographer and builds a three-dimensional model of both the anterior and posterior surface of the cornea from multiple radial cross section images. The anterior surface assessment includes the tear film but does not reliant upon it to reflect the image as the topography and autokeratometry methods. This study used multiple outputs from this device:

- Pentacam Sagittal Measurement at a chord length of 3.2 mm using a refractive index of 1.3375
- Pentacam True Net Power at chord lengths of 3.2 mm.

- Pentacam Holladay Equivalent simulated K at a chord length of 4.5 mm.
- Total Corneal Refractive Power at chord lengths of 2 and 5 mm.

5.2.2.2 Refraction

A combination of both objective and subjective refraction was used to determine the ocular refractive error. Retinoscopy was carried out first with a Heine Retinoscope (Heine Optotechnik, Herrshing, Germany). Routine subjective refraction was carried out at 6m with a LogMAR chart on the Thomson Test Chart 2000 (Thomson Software Solutions, Hatfield, Herts, UK). The investigator carrying out the refraction was blind to the keratometry readings. The refraction endpoint with the cylinder determined by the Jackson cross cylinder technique and sphere endpoint was established at the best acuity with most positive correction.

5.2.3 Statistical analysis

5.2.3.1 Assumption of Normality

A Shapiro–Wilk test was used to determine if the results followed a normal distribution. Where the data followed a normal distribution, parametric analysis was used; for non-normally distributed data, non-parametric analysis approach was used.

5.2.3.2 Back Vertex Distance

The magnitude of ocular refractive error was converted to the corneal plane using the back vertex power equation (Equation 5.12).

$$Fcornea = \frac{Fsp}{1-dFsp} \qquad \textit{Equation 5.12}$$

Fcornea = the power at the cornea plane

Fsp = the power found in refraction at the spectacle plane

d = the BVD from the trial frame to the front of the cornea.

Both the ocular refraction and corneal astigmatism data was converted into the J_0 and J_{45} component vectors.

5.2.3.3 Comparison of Astigmatic Power

In order to compare the astigmatic power of the various readings, a number of statistical tests were utilised. A Friedman's ANOVA was used to determine if there was a significant difference between refraction and the keratometry power readings. If a difference was found then *post hoc* analysis was conducted using multiple Wilcoxon's signed rank tests with a Bonferoni correction. Differences versus means plots (Bland Altman, 1986) were created to examine the bias between measurements (the mean difference and upper/lower confidence intervals). Kendall's Tau correlation was used to examine the correlation between ocular refractive astigmatism and the corneal astigmatic power. A stepwise linear regression coefficient was calculated to determine the relationship of the ocular refractive astigmatism with the corneal astigmatic power. The data was split into groups of 'with the rule' astigmatism (WTR) where the steep axis is vertical, 'against the rule' astigmatism (ATR) where the axis is horizontal and oblique (neither vertical nor horizontal).

The exact groupings were:

1. WTR = 90±20°
2. ATR = 180±20°
3. Oblique = 21 to 69° and 111 to 159°

5.3 Results

5.3.1 Categorisation of Astigmatism According to Orientation

Visit	n	WTR	ATR	OBL
		180 ± 20°	90 ± 20°	21-69°, 101-159°
V1	96	12	58	26
V2	82	4	56	22

Table 5.1: Number of subjects categorised as WTR, ATR and oblique for each visit.

5.3.2 Comparison of Astigmatic Power

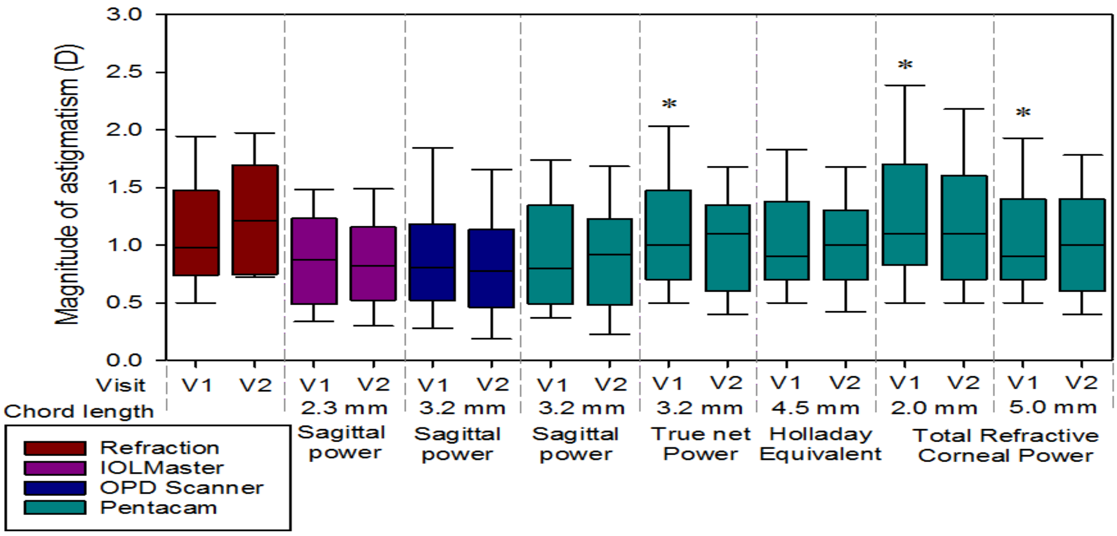

Figure 5.1: Absolute magnitude of astigmatic power at V1 (n=96) and V2 (n=82). No signficiant differences at V1 is marked as *

Comparison of the absolute magnitude of astigmatism for all subjects (Figure 5.1) revealed a significant difference between the astigmatic powers at both V1 ($\chi^2{}_7$ = 74.869, p < 0.001) and V2 ($\chi^2{}_7$ = 104.84, p < 0.001). Post Hoc analysis using multiple paired Wilcoxon signed rank tests revealed that the magnitude of astigmatism measured with refraction was greater than the corneal astigmatism sagittal power measurement with the IOLMaster (V1: Z = -3.475, p = 0.001; V2: Z = -5.874, p < 0.001), OPD scanner (V1: Z = -4.115, p < 0.001; V2: Z = -6.038, p < 0.001) and Pentacam (V1: Z = -2.832, p = 0.005; V2: Z = -4.701, p < 0.001). At V2, the total net corneal astigmatic power (Z = -2.973, p = 0.003) and total corneal refractive power with chord length 5.0 mm (Z = -3.195, p = 0.001) as well as the Holladay equivalent simulated corneal astigmatic power (Z = -3.472, p = 0.003) were less than the ocular refractive power. At V1, the total net corneal astigmatic power and total corneal refractive power with both chord lengths were similar to the ocular refractive astigmatic power (p > 0.007). However, at V2 this similarity was only found with total corneal refractive power of a 2mm chord length (Z = -0.403, p = 0.687).

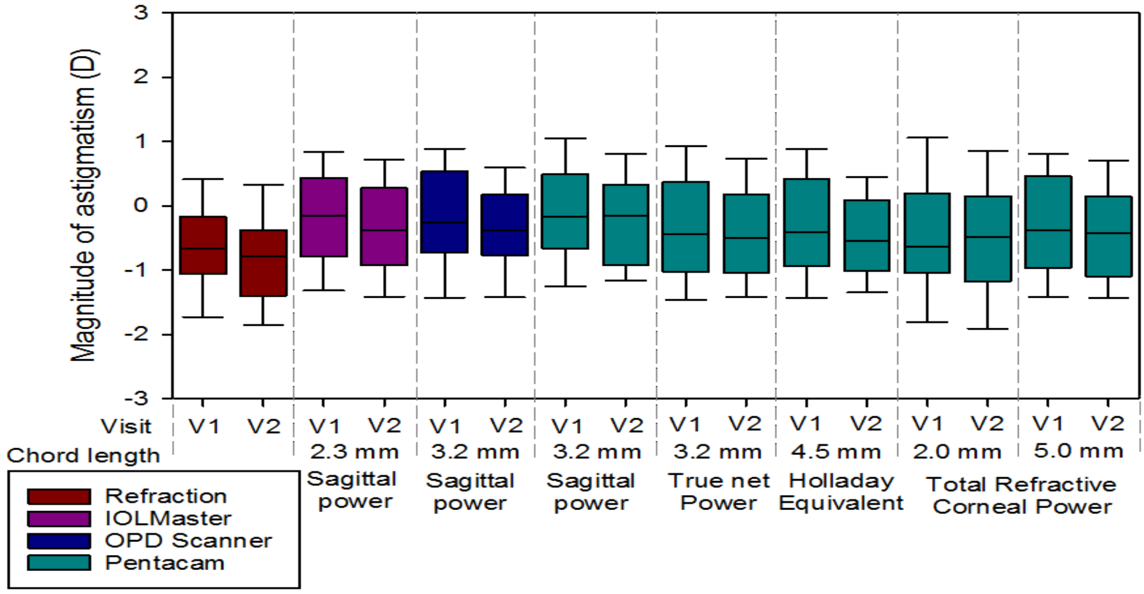

Figure 5.2: Magnitude of astigmatic power along J0 vector at V1 (n=96) and V2 (n=82). No significant differences at V1 are marked as *

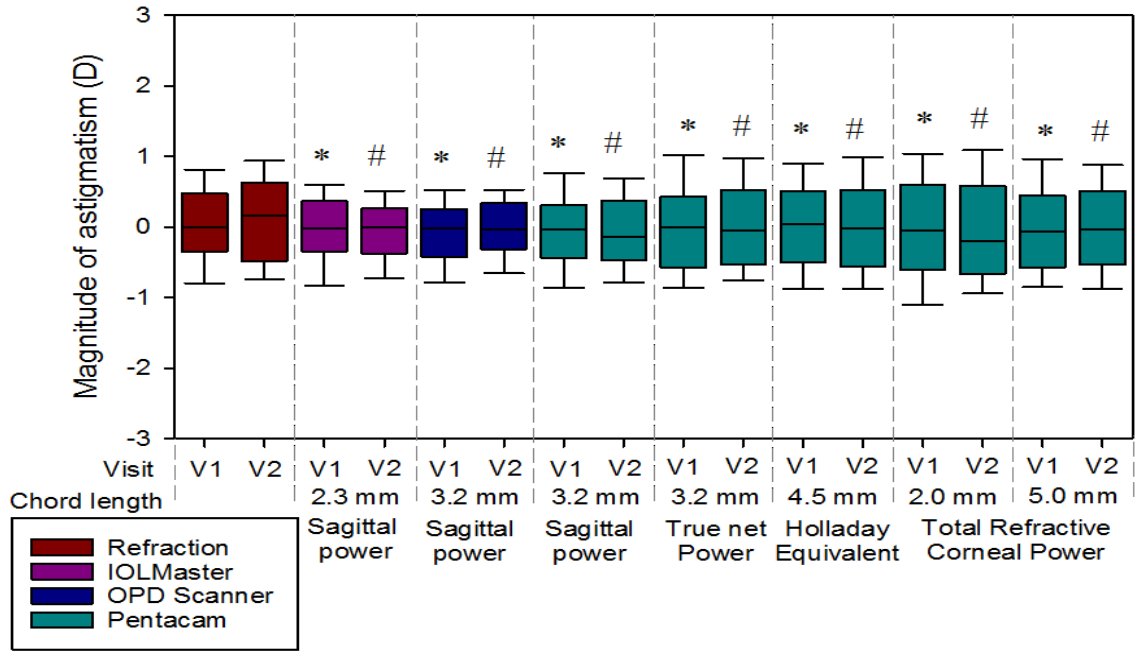

Figure 5.3: Magnitude of astigmatic power along J45 vector at V1 (n=96) and V2 (n=82). No significant differences at V1 is marked as * and no significant differences at V2 as ♯

There was a significant difference between the refractive astigmatism and corneal astigmatism along the J_0 vector (Figure 5.2) at V1 ($\chi^2{}_7 = 106.063$, $p < 0.001$) and V2 (($\chi^2{}_7 = 113.171$, $p < 0.001$). Multiple Wilcoxon paired tests revealed that the magnitude of ocular astigmatism along J_0 was more negative (with the rule) than all corneal astigmatic values ($p < 0.001$). The ocular refractive astigmatic power along J_{45} vector (Figure 5.3) was similar to the corneal astigmatic power at both V1 ($\chi^2{}_7 = 0.487$) and V2 ($\chi^2{}_7 = 0.780$).

5.3.3 Correlation of Corneal Astigmatism

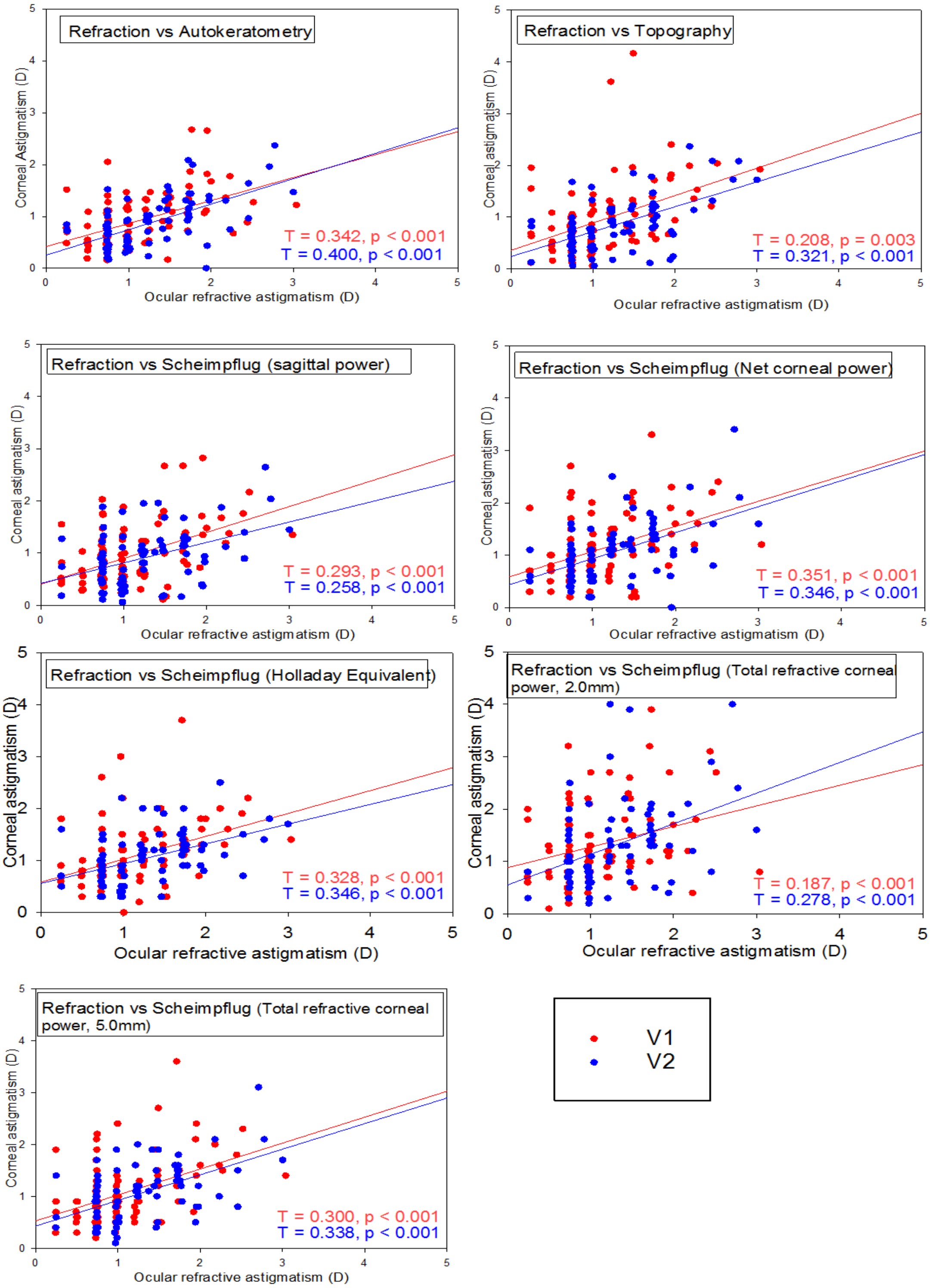

Figure 5.4: Correlation of the magnitude of astigmatism keratometry readings compared to the manifest refraction at V1 (n=96) and V2 (n=82).

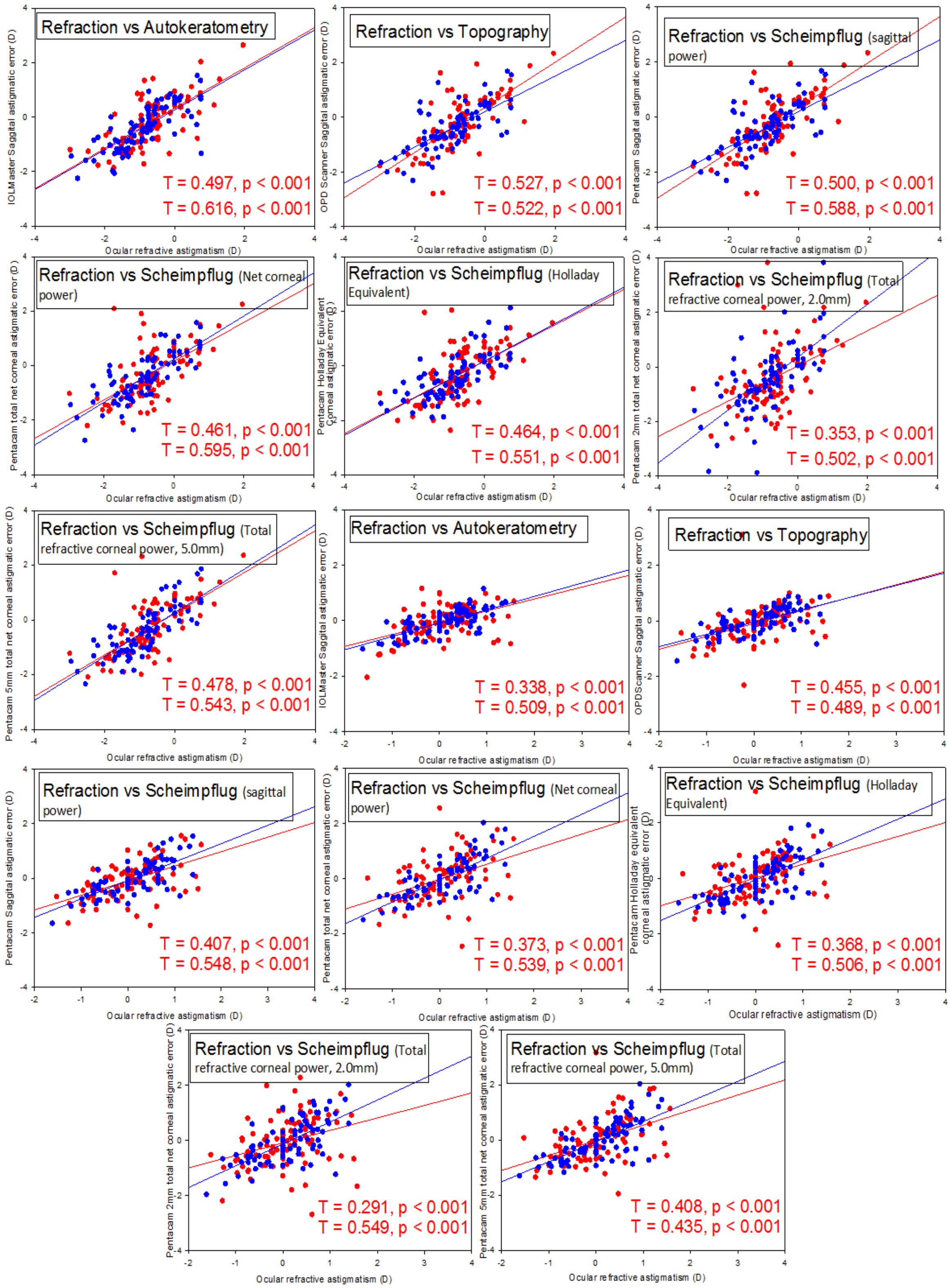

Figure 5.5: Correlation of the vector power along J0 and J45 for the keratometry readings and manifest refraction at V1 (n=96) and V2 (n=82).

Both the absolute and vector magnitude of corneal astigmatic power was significantly correlated with the ocular refractive astigmatism at both V1 and V2 ($p < 0.001$; Figure 5.4 & Figure 5.5). The J_0/J_{45} vector representation of corneal power at V2 demonstrated the highest correlation with ocular astigmatism (Figure 5.5).

5.3.4 Bland Altman Comparison

There was an apparent bias towards a higher magnitude of astigmatism found by the ocular refraction compared to that found when measuring sagittal corneal power (Figure 5.6). At V2, no apparent bias (-0.03 D) was present when using the total corneal refractive power at a chord length of 2 mm. However, at this chord length there was the greatest spread in the limits of agreements (3.04 D).

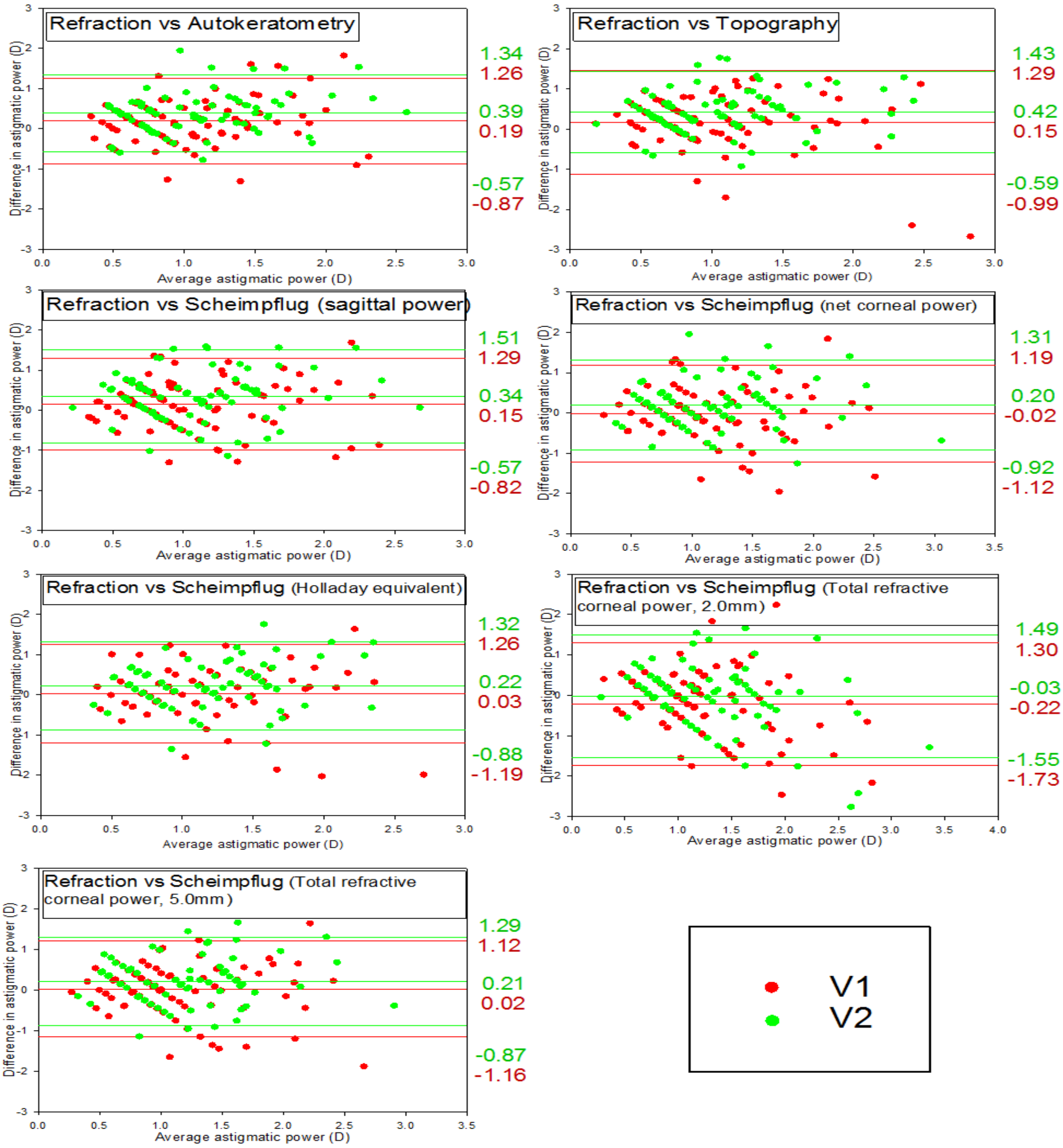

Figure 5.6: Difference versus means plot for the absolute magnitude of astigmatism at V1 (n=96) and V2 (n=82).

The vector representation of astigmatic power also showed a bias, with the refraction providing more 'against the rule' astigmatism (Figure 5.7). The total corneal refractive power at a chord length of 2 mm presented the lowest mean difference (0.39 D) but had the widest limits of agreement (3.45 D).

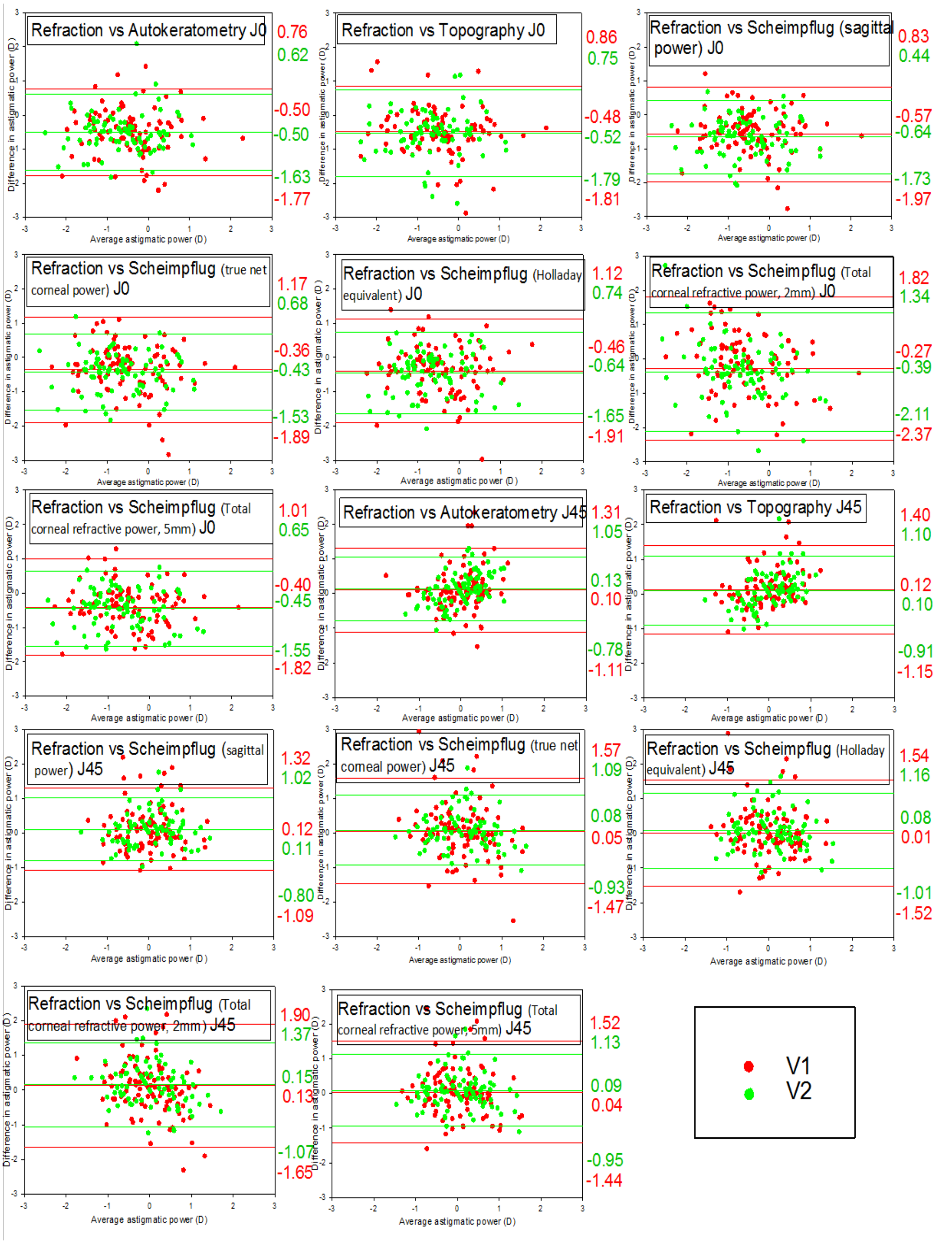

Figure 5.7: Difference versus means plot for the vector magnitude of astigmatism along J0/J45 at V1 (n=96) and V2 (n=82).

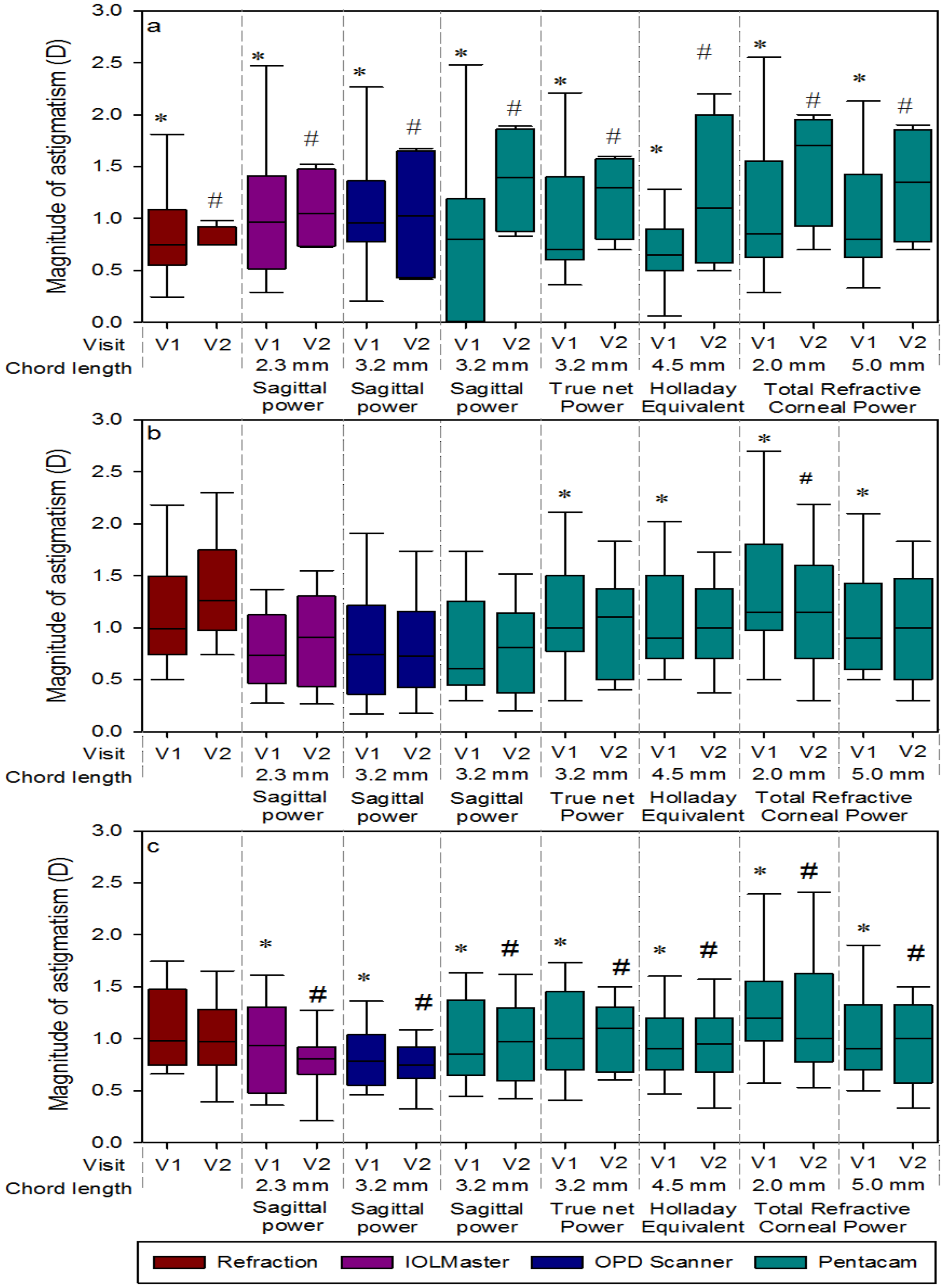

Figure 5.8: Absolute magnitude of astigmatic power categorised according to cylinder axis. a) With the rule; V1 (n=12), V2 (n=4). b) Against the rule; V1 (n=58), V2 (n=56). c) Oblique V1 (n=26), V2 (n=22). No significant differences at V1 is marked as * and no significant differences at V2 as #

The absolute magnitude of ocular refractive astigmatism was similar to the corneal astigmatic power in subjects categorised as having "with the rule astigmatism" at both V1 (χ^2_7 = 8.016, p = 0.331) and V2 (χ^2_7 = 9.424, p = 0.224). For subjects with astigmatism along the oblique meridians there was a significant difference with the Friedman's ANOVA at V1 (χ^2_7 = 18.069, p = 0.012) and V2 (χ^2_7 = 25.254, p = 0.001). However, *post hoc* analyses failed to find a significant pairwise difference (p > 0.007). A significant difference was found in subjects categorised as 'against the rule' (V1: χ^2_7 = 82.912, p <0.001; V2: χ^2_7 = 104.038, p < 0.001). *Post hoc* evaluation revealed that at V1 the magnitude of sagittal corneal power was smaller than the ocular refractive astigmatism with the IOLMaster (Z = -4.891, p < 0.001), OPD scanner (Z = -3.955, p < 0.001) and Pentacam (Z = -3.585, p < 0.001). At V2 the magnitude of refractive astigmatism was only similar to the total corneal refractive astigmatic power when measured at a chord length of 2 mm (Z = -1.999, p = 0.046).

5.3.4.1 Multiple Linear Regression

A multiple linear regression model showed that the IOLMaster measurement of corneal sagittal power accounted for 22.1% of the variance across the magnitude refraction astigmatism data at V1 (F= 27.98, p<0.001, Refraction astigmatism value = 0.519xIOLMaster astigmatism value + -0.629). A further 7.1% could be accounted for by including the Pentacam sagittal corneal power. At V2, the IOLMaster accounted for 34.8% of the variance across the refraction data and inclusion of the OPD increased this to 41.1%.

5.4 Discussion

The linear relationship between keratometry and refraction (Javal's rule) has been studied and refined frequently over the last 100 years. Although a linear relationship is frequently established statistically, its use clinically has often been questioned. Although the index will give a general description of the populations as a whole, use of these results clinically could result in significant errors in vision correction in individual patients (Remón et al. 2009; Piñero et al. 2012). Koch and colleagues proposed that keratometry has a tendency to overestimate the 'with the rule' astigmatism and underestimate the 'against the rule' astigmatism (Koch et al. 2012; Koch et al. 2013). Many have postulated the cause for the error, including whether the posterior cornea needs to be taken into account, or if a larger central area should be measured in keratometry. This study was designed to investigate the relationship between corneal curvature and refraction in a pseudophakic population. In the case of a pseudophakic population, the removal of the crystalline lens should simplify the optics. In theory, this should strengthen the relationship between refraction and keratometry in a phakic population. In particular, the study investigated how accurately keratometry readings can be transposed into corneal power in all types of astigmatism.

When analysing the magnitude of astigmatism of the group as a whole, only a weak linear relationship was found between the IOLMaster and refraction (22.1% at V1, increasing to 34.8% at V2). This shows that a most of the refraction data variance was not explained by the keratometry readings. Although this is a poor relationship, these findings are similar to Ho and colleagues who also found that their sagittal keratometry data was closer to the refraction data than the Scheimpflug readings (Ho et al. 2008). Grosvenor and Ratnakarem (1990) suggested that the relationship may not be a single straight linear line and will vary depending upon variations in corneal power. Elliot et al (1994) also found that keratometry did not fully agree with ocular refraction in this patient group.

The magnitude of astigmatism found by each keratometry technique was compared to the magnitude of astigmatism found by ocular refraction. The comparison of the data group showed that the sagittal power reading (IOLMaster, OPD and Pentacam) underestimated the refraction astigmatism at both visits. The Bland Altman plots illustrate the bias of the ocular refraction towards higher levels of astigmatism than the keratometry readings (Figure 5.6). The majority of the subject corneas were 'against the rule' so the trend of underestimation is similar to that seen by Koch et al (2012) when comparing sagittal keratometry readings to post-operative astigmatism. Previous work has shown that we underestimate the ratio of power between the anterior and posterior cornea and need to adjust the refractive index we use to convert keratometry radius to power. Ho et al and Fam et al both showed that a lower refractive index calculated by looking at both corneal surfaces increased the accuracy of the power measurement (Fam et al.

2007; Ho et al. 2008). A re-evaluation of the keratometric index could lead to an improvement in the sagittal power results.

It has been suggested that in order to correctly assess the cornea, the posterior surface must be taken into account as well as the front surface (Bae et al. 2004; Tejedor et al. 2005; Teus et al. 2010; Koch et al. 2012; Eom et al. 2013). It has been suggested that a consistent profile of posterior cornea may be expected, contributing around 0.50DC of ATR astigmatism (Bae et al. 2004). However, Ho et al (2009) found that the posterior curvature was more variable with 10.3% of posterior corneal surfaces displaying more than 0.50DC of astigmatism (Ho et al. 2009). The Pentacam readings looking at true net power, Holladay equivalent and total corneal refractive power readings all take the posterior surface into account in different ways. This has been suggested to increase the accuracy of the keratometry reading (Dunne et al. 1991; Ho et al. 2009; Mas et al. 2009; Koch et al. 2012). At V1 the Pentacam true net power, Holladay and total corneal refractive power readings (both chord lengths) were all similar to the refraction reading ($p>0.007$) but this relationship only reoccurred at V2 with the total refraction power 2mm chord reading.

There is a variation in the chord size used in instruments measuring corneal curvature and it is often assumed that to increase the area of corneal curvature measured will increase the accuracy of the corneal power assessment. The Bland Altman comparison in this study (Figure 5.6) showed that the 2mm chord of the total corneal refractive power reading was the closest to refractive astigmatism. This indicates that the smaller chord is a more accurate reflection of the refraction looking at paraxial rather than peripheral rays of light as Keller (1996) suggested. Yet, the same comparison also found a very large spread in the agreement, which could be due to the sensitivity of the smaller chord to decentration. If the apex of the cornea is not quite aligned with the centre of the chord, it can lead to a less accurate reading. In a large chord, there is a greater area measured so the apex is more likely to fall within this and the error of misalignment is less. A smaller chord measures a smaller area, so misalignment means that the apex can potentially be missed out or the misalignment becomes much more significant in the smaller area. Alpins et al (2015) developed a new algorithm, which merged multiple chord length measurements (including posterior corneal curvature) to determine corneal curvature. It was postulated that this would elicit a more accurate reading of corneal topographic astigmatism (CorT). This method decreases the influences of misalignment and corneal abnormalities and found a high comparability to ocular refraction (Alpins et al. 2015).

All the J_0 instrument data showed a significant difference to refraction, yet a stronger correlation than magnitude alone. This indicates a systematic underestimation by the instruments compared to the refraction (Figure 5.2). The J_{45} data means are more similar (Figure 5.3) and no significant difference was found, although the correlation in the data was weak. There is less oblique astigmatism in this group, which reduces the significance of the J_{45} data that describes oblique astigmatism. There was also highly significant correlation between the ocular refraction and J_0J_{45} data at both visits but it was highest at V2. Interestingly this indicates that the relationship is best explained with vectors than alone with the magnitude, as suggested originally by Remon et al (Remón et al. 2009). Similar to the magnitude data, the J_0 component when measured with a 2mm chord of the Pentacam total corneal refractive power reading had the least mean difference but widest limits of agreement (Figure 5.7).

Eom et al (2013) found that in 69.4% of eyes, the orientations of steepest astigmatic meridians of the anterior and posterior surface were oblique to one another. In 10% of cases, the steepest meridians were orthogonal, reducing the astigmatism overall (Eom et al. 2013). Bregenhoj et al (2015) also found that the magnitude of internal astigmatism varied with orientation of astigmatism. The average internal astigmatism was 0.86 @91 from the steepest corneal meridian in WTR corneas, 0.17 @97 in ATR corneas and 0.37 @95 in oblique corneas (Bregnhøj et al. 2015).

The results found when the data was split into WTR, ATR and oblique groups were similar to findings reported by Koch et al (2012). In the WTR group, there was no significant difference between the ocular refraction and all the keratometry readings at V1 and V2, but the median astigmatism found was higher with all instruments than the refraction at V2. This indicates an overestimation, as suggested by Koch (Koch et al. 2012; Koch et al. 2013). The low numbers at both V1 and V2 decrease power and significance of these results. Also in agreement with Koch et al's work (2012), there is a trend of underestimation of the ATR corneal power calculation in both groups of data between ocular refraction and sagittal corneal keratometry readings. The only reading found similar to the refraction was the 2mm chord total corneal refractive power reading ($p=0.046$) at V2. In the oblique group, there was a lot of variation in the medians of the instruments compared to the refraction but no significant difference was found between any sets of data and refraction at V1 or V2. As found with Koch's study, the oblique data showed no consistent pattern in of systematic error in the comparison of the astigmatic power.

There was poor agreement of the steepest meridian position between each instrument and the refraction, which will have affected the comparability of the data. Each subject was classified as WTR, ATR or oblique by the refraction data but often the axis recorded by the instrument would have resulted in a different classification for the same subject. The disparity between the posterior and anterior surface orientation could alter the summative axis orientation depending upon the instrument methodology.

The refraction data is not entirely reflected in the keratometry data. This could be attributed to a number of sources of error. The topographical readings reliant upon the tear film were less accurate e.g. the OPD scan. This could be due to dry eyes after the cataract surgery, destabilising the tear film. The results also stabilised and had much better concordance at V2 indicating that increased post-operative tear film stability after a longer period of recovery, improved the readings. Furthermore, it is possible that there is still an element of internal astigmatism that is not accounted for. The inclusion of posterior corneal data sometimes improved the linearity of the relationship between the refraction and keratometry. Nevertheless, there is still a further unknown factor within the eye's optics that contributes to refractive astigmatism. Teus (2010) suggests that there is another source of 'internal astigmatism'. This could be due to the IOL tilt or an influence from the retina. Elliot (1994) found that a Retinoscope or auto refractor result was always closer to refraction than keratometry, again indicating that internal astigmatism could be from an additional source. The instruments don't measure the influence of aberrations on the vision. Additionally astigmatic patients can re-interpret distorted vision and adapt, this occurs at a higher level in the brain than the eye (Guyton 1977). These could both influence the refractive result.

There are a few limitations in this study. The distribution of WTR, ATR and oblique astigmatism was not equal. In consequence, the results for the WTR and oblique groups are less significant due to smaller numbers of subjects.

5.5 Conclusion

The IOLMaster had the strongest linear relationship with the refraction data. However, the total corneal refractive power reading with the 2mm chord data was found to be most similar to the refraction. This suggests that a measure that incorporates a paraxial measurement area along with both anterior and posterior corneal data provides the most equivocal measurement of corneal astigmatism.

However, the results also indicate that the Scheimpflug imaging increases the variability of results when compared with autokeratometry. Corneal astigmatism may not be the only source of ocular astigmatism and this may limit the relationship that can be found between the reading of the keratometer and refraction.

One thing that is often neglected in the assessment of astigmatism is the axis. It can have a significant impact on the vision if it is not corrected property yet the accuracy of the axis is often overlooked when assessing keratometry. Eom (2013) has shown that the axis and orientation can be different on the two different surfaces (Eom et al. 2013). What is not known is how the summative axis is determined by each instrument methodology. This also requires investigation as a potential source of error.

Chapter 6 Accurate Determination of the Steepest Corneal Meridian Orientation

6.1 Introduction

6.1.1 Background

Pre-operative biometry, including the assessment of corneal curvature, has a major influence on the success of cataract surgery. Accurate keratometry is not only vital for pre-surgical calculations but can be used as a post-operative measurement of success. The increasing popularity of toric IOL implantation (Pick et al. 2008) has created an increased need for precise assessment of the principal meridians orientation (axis) to achieve the optimal correction of corneal astigmatism (Pick et al. 2008).

The previous chapter disparaged the use of the oblique cross cylinder formulae for predicting corneal power changes and proposed that both a clear corneal incision and toric IOL be placed along the steepest corneal meridian. Advocating this approach assumes that the orientation of the corneal principal meridian can be reliably identified and that corneal astigmatism translates to ocular refractive astigmatism.

Recent studies examining corneal power use horizontal and vertical vector components (J_0/J_{45}) (Thibos et al. 1997) to summate both power and orientation. However, vector analysis does not describe the orientation of the steepest corneal meridian. As such, there is a lack of studies that determine if the steepest meridian orientation can be reliably determined through keratometry and topography.

The cornea is responsible for ⅔ of the total refractive power of the eye and in a pseudophakic population; refractive astigmatism is generally wholly attributed to the corneal shape (Grosvenor et al. 1990; Elliott et al. 1994). A linear relationship between the manifest refraction and corneal shape has been found (Grosvenor et al. 1990; Remón et al. 2009). The shape of the cornea determines corneal astigmatism, the corneal curvature determines the refractive power and if the cornea is not spherical, it can vary in refractive power. It is defined as having two principal power meridians, which represent the lines of least, and most power. Therefore, the orientation of the corneal astigmatism should determine the orientation of the refractive astigmatism.

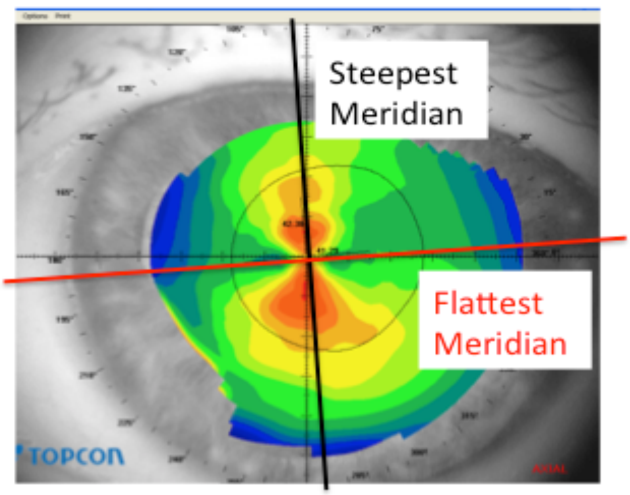

Figure 6.1: Topographical map with steepest and flattest meridian marked.

Thomas Young first described astigmatism in 1801, when attempting to neutralise the cornea power he discovered his own lenticular astigmatism (Atchison et al. 2010; Gutmark et al. 2010; Atchison et al. 2011). Gerson, Wilde and Jones later described corneal astigmatism. This was proven later by Sneff who was able to measure the astigmatism of the cornea quantitatively (Gutmark et al. 2010).

6.1.2 Keratometry

6.1.2.1 Measuring Corneal Astigmatism

Modern instruments measuring corneal curvature tend to be topographical devices. These instruments still make use of the reflection principals and measure the anterior surface via reflection from the tear film. In topography, the whole corneal surface is used as a convex mirror and the reflection of a known light source and diameter are analysed (Wolffsohn 2008; Gutmark et al. 2010). This method is highly reliant upon the tear film stability to produce accurate results. Previously it has been shown that the tear film break up can significantly affect the accuracy of the topography results (Németh et al. 2001). Similar to topography, autokeratometry measures only the anterior surface of the cornea. For example, the IOL master projects only 6 dots in a hexagonal pattern to determine the curvature (Santodomingo-Rubido et al. 2002). The gaps between the dots projected onto the cornea allow a potential source of error in axis measurement. Scheimpflug Imaging is an alternative way to measure corneal curvature. The methodology allows a choice in calculations used to determine the corneal power. This choice allows the option of whether to include the separate measurement of the posterior corneal surface, take account of corneal thickness or normalisation of the shape for a given refractive index. However, the measurement is taken with a number of scans at set intervals of rotation around a central point. Again, this will create gaps in the data (between the scans) that could potentially miss the steepest meridian, decreasing the accuracy.

A previous chapter (chapter 2) demonstrated the poor correlation between keratometry readings and manifest refraction. This was especially apparent in the assessment of corneal astigmatism for both orientation and magnitude. An additional objective in this study was to investigate whether the assessment of axis position displayed by a sagittal power topographical map can provide a more accurate assessment of axial position in comparison to that found in manifest refraction.

Removal of the cataract leaves the cornea as the sole optical refractive structure. The corneal shape can be assessed to determine the residual astigmatism and previous work has established a relationship between keratometry readings and manifest refraction in pseudophakic subjects (Grosvenor et al. 1990; Remón et al. 2009). Therefore, the orientation of the steepest corneal meridian should also align with the manifest refraction axis.

6.1.2.2 Challenges In Assessing Orientation

The instrumentation must be able to isolate the orientation of the steepest and flattest meridians, which generally can be at any orientation between 1-180 degrees. Obtaining accurate and repeatable readings can be a difficult task and thus far there has been little done to monitor the accuracy of the measurements. Many studies have shown the impact of incisions placed 'on-axis' (on the steepest meridian) to control post-surgical shape change or even as a method to reduce but little is mentioned of how the steepest meridian orientation is confirmed prior to surgery (Lever et al. 2000; Kaufmann et al. 2005; Freitas et al. 2014; Hayashi et al. 2014). The measurement of meridian orientation or axis is very susceptible to errors through eye rotation caused by cyclorotation of the eyes or head tilt changes between measurements. It has been shown that the eye naturally rotates between assessments, finding. It has been observed that on average the eye can rotate 2.3 to 3.18° between measurements on average, this will potentially change the axis reading of an eye over repeated measurements. It will also reduce the accuracy of determining the steepest meridian. The rotation between readings will lower the repeatability and induce an error in the assessment of the any change in axis position after corneal procedures (Chernyak 2004; Seo et al. 2004; Viestenz et al. 2005). Osher (2010) proposed an idea to use iris fingerprint technology to determine the axis accurately (Osher 2010). Miyata (2011) also proposed a new technique to mark the cornea before the topography measurements. This increased the accuracy of the alignment by taking into account the rotation between measurements that result from different head positions and posture in surgery into account (Miyata et al. 2011). As stated previously, misalignment of the lens or flattening incision with the principal meridians will result in a poorer vision correction of astigmatism.

6.1.2.3 The Effect of the Orientation of Astigmatism

Astigmatism is classed as steep and a flat principal meridian, which are orthogonal to one another. In the manufacture of optical lenses to correct astigmatism, the orientation of the principal meridians (rotation of the orthogonal principal powers) makes no difference to the optical quality of the lens (e.g. a lens orientated at 5 degrees is similar to that orientated at 15 degrees). However, in vision it has been found that the orientation of the principle meridians can alter the uncorrected vision and blurring of an image more significantly. Wolffsohn et al (2011) found that distance vision was worse with astigmatism orientated at 180 (against the rule) or 45 degrees (oblique) than 90 degrees (with the rule). Additionally reading was worse with uncorrected astigmatism at 180 degrees than 45 and 90 degrees.

6.1.2.4 Analysing Steepest Meridian Orientation (Axis)

Orientation data (circular data) is difficult to analyse, an extra complication with axis data is that the steepest meridian position runs from 1-180° not 0-360°. This often causes additional issues when changes cross the 180 line. If 10° and 170° are averaged numerically, the average will be calculated as 90° and not the real answer of 180°. A common method of avoiding this issue is to double the angle during analysis (Holladay et al. 1992).

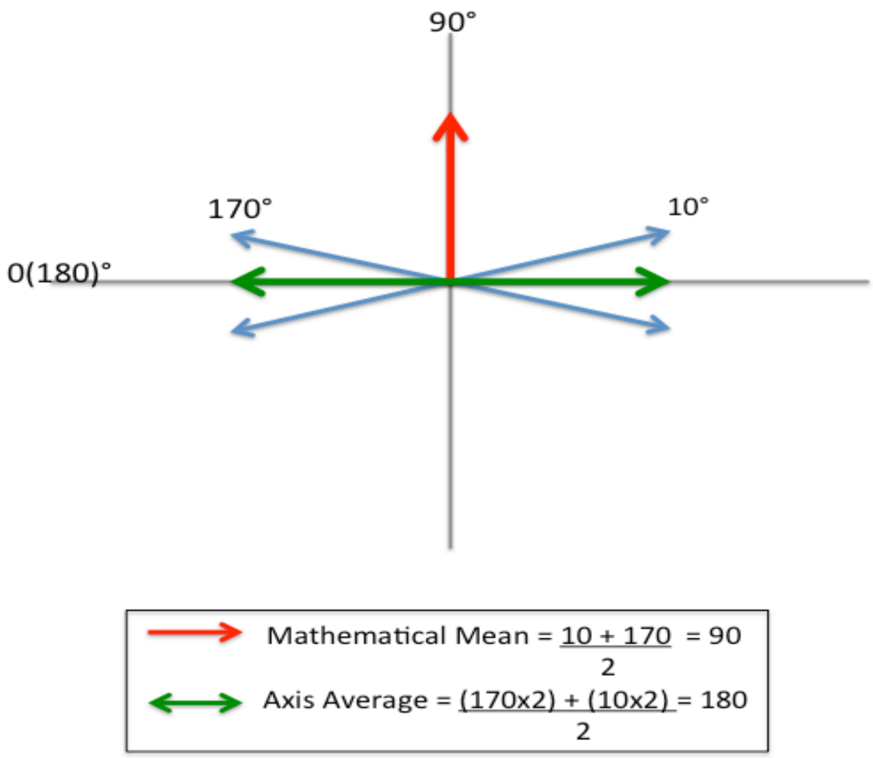

Figure 6.2: Diagram demonstrating the difference between calculating the mean in straight and circular data. The green arrow represents the actual mean axis and the red arrow depicts the incorrect mathematical average axis for 10 and 170°.

6.1.3 Aim

The aim of this study was to investigate the agreement between the steepest corneal meridian orientation (axis) measured by three instruments and the subjective manifest refraction result found in a pseudophakic population. This study compared the axis readings produced by the instruments to determine which of the various methodologies utilised by the IOLMaster, Pentacam and OPD scan is most similar to the manifest refraction. This includes the simK results and readings taking the posterior surface into account. Lastly, a subjective assessment of the topographical maps produced will also be included in the comparison.

6.2 Materials and Methods

6.2.1 Subjects

This study assessed fifty-eight healthy pseudophakic eyes (27 right, 31 left) of subjects aged 75.11 ± 9.71 years old. All subjects had undergone cataract extraction and IOL replacement, 3-6 months previous to the assessment at the Royal Eye Infirmary (Derriford Hospital, Plymouth, UK). All data was collected between April 2014 and December 2014. All subjects were recruited by the principal investigator (CH) using the following inclusion and exclusion criteria:

6.2.1.1 Inclusion Criteria:

- Adult subjects aged 18 years old and above
- Had routine NHS cataract surgery
- Able and willing to give informed consent to their inclusion into the study
- Astigmatism of 0.75DC or more, determined by refraction and converted to the corneal plane.

6.2.1.2 Exclusion Criteria:

- Irregular astigmatism.
- Any pre-surgical corneal complications or pathology such as Fuchs' dystrophy and keratoconus
- Subjects with unexpected surgical complications.
- Irregular or malformed eyelids e.g. ptosis, chalzion or severe blepharitis.
- Unreliable keratometry or topography reading produced by any of the instruments used in the study

6.2.1.3 Procedure

Pre-operatively, an IOLMaster 500 (Carl Zeiss Meditec AG) and Pentacam HR were used to determine axial length and corneal power for all participants. To determine IOL power, the Hoffer Q IOL formula was used for short axial lengths and the SRK/T was used for all other axial lengths, in accordance with the College of Ophthalmologists' guidelines.

Invited study participants had been operated on by one of two surgeons using topical or local anaesthetic. In all cases, a *Tecnis ZA900* monofocal IOL had been implanted in the capsular bag. This monofocal IOL is a single piece aspherical control hydrophobic acrylic IOL.

6.2.2 Ethical Approval

All procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by the local REC committee (Ref: 13/SW/0229 on 16th October 2013), NHS R&D department (Ref: 13/P/106 on 20th October 2013) and University ethics committee (Ref: 13/14-188 on 23rd October 2013).

6.2.3 Measurements

All Subjects attended a follow up (FU) post-operative study visit 3- 6 months after the surgery. The following methods of obtaining a measurement of corneal astigmatism axis were carried out:

6.2.3.1 Refraction

A combination of both objective and subjective refraction was used to determine the ocular refractive error (manifest refraction). Retinoscopy was carried out first with a Heine Retinoscope (Heine Optotechnik, Herrshing, Germany). Routine subjective refraction was carried out at 6m with a LogMAR chart on the Thomson Test Chart 2000 (Thomson Software Solutions, Hatfield, Herts, UK). The investigator carrying out the refraction was blind to the keratometry readings.

6.2.3.1.1 Back Vertex Distance

In order to compare the results of the manifest refraction to the instruments assessments of the corneal curvature, the refraction result had to be converted to the corneal plane. This was calculated with the back vertex power equation (Equation 6.1).

$$Fcornea = \frac{Fsp}{1-dFsp} \qquad \textit{Equation 6.1}$$

Fcornea = the power at the cornea plane

Fsp = the power found in refraction at the spectacle plane

d = the BVD from the trial frame to the front of the cornea.

6.2.3.1.2 Conversion of the Refraction Axis to Keratometry Axis

The axis reading in refraction is perpendicular to the axis orientation of the steepest meridian. In order to compare the data sets, the manifest refraction reading was adjusted by 90°.

6.2.3.2 Assessment of Corneal Curvature

Assessment of corneal curvature was carried out on each subject with three different instruments:

6.2.3.2.1 The IOLMaster 500 (Carl Zeiss Meditec Inc., Jena, Germany)

The IOLMaster was used to provide a measure of sagittal corneal power and axis reading of the principal meridians at a chord length of approximately 2.3 mm.

6.2.3.2.2 The OPD Scanner (Nidek Co., Ltd, Gamagori, Japan)

The sim-K results from the OPD Scanner were used to determined the axis of the steepest meridians at a chord length of approximately 3.2 mm.

6.2.3.2.3 The Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany)

This study used multiple outputs from the Pentacam HR:

- Pentacam Sagittal Measurement at a chord length of 3.2 mm 1.3375
- Pentacam True Net Power at chord lengths of 3.2 mm.
- Pentacam Holladay Equivalent simulated K at a chord length of 4.5 mm.
- Total Corneal Refractive Power at chord lengths of 2 and 5 mm.

6.2.4 Topographical Image Analysis

The topographical maps produced by the Pentacam and OPD scan were exported from the instruments after the reading was taken, into an image analysis programme (Image J software, National Institute of Health, USA). The map was assessed subjectively, looking at the colour code for cornea power, to determine the steepest area of the cornea. Then a line was fitted, running from limbus to limbus, crossing the centre of the cornea, along the steepest area. This method was not repeated, simulating the procedure used in a standard hospital setting.

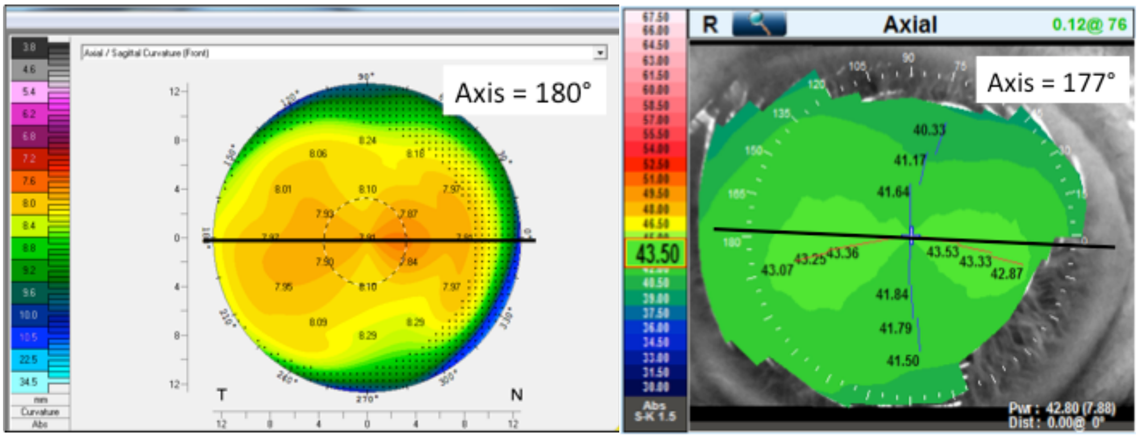

Figure 6.3: Topographical maps from Pentacam and OPD scan with subjective steepest meridian orientation measurement marked on the same subject.

6.2.5 Statistical analysis

6.2.5.1 <u>Assumption of Normality</u>

A Shapiro–Wilk test was used to determine if the results followed a normal distribution. Where the data followed a normal distribution, parametric analysis was used; for non-normally distributed data, non-parametric analysis approach was used.

6.2.5.2 Sample size calculation

Several sample size test calculations were carried out with the G*Power 3 (Heinrich-Heine Unversität, Düsseldorf) to determine the size that will allow reliable results for comparison of paired medians (the difference between manifest refraction axis and each instrument keratometry axis reading) using a two-tailed paired Wilcoxen rank test with medium effect size, 0.5 (Cohen's table), a two-tailed correlation of bivariate normal model (accuracy of predictive models) predicting a moderate correlation (effect size) 0.5 (Cohen's table) and ANOVA analysis of repeated measures (across 9 groups and 2 measures), between factors using a large size effect, 0.30 (Cohen's table) (Prajapati, 2010). These required 35, 29 and 36 subjects respectively; therefore a minimum sample size of 40 was required across these analyses. An alpha level of 0.05 and a beta of 0.8 were used in the calculations.

6.2.5.3 Comparison of Axis orientation

In order to compare the axis orientation determined by the different instruments and methodologies, a number of statistical tests were utilised. Due to the circular nature of axis data, there are limitations in the statistical analysis of the axis readings alone. In this study, the analysis was carried out on the difference between the manifest refraction and each methodology, assessing the accuracy in comparison to refraction. A Friedman's ANOVA was used to determine if there was a significant difference between each methodology. If a difference was found then post hoc analysis was conducted using multiple Wilcoxen's signed rank tests with a Bonferoni correction (0.05/ 9 = 0.006) Kendall's Tau correlation was used to examine the correlation each methodology to manifest refraction. Additionally the data was split into groups of low astigmatism and high astigmatism.

The exact groupings were:

Low Astigmatism	=	0.75 to 1.24D
High Astigmatism	=	>1.25D

6.3 Results

The absolute difference between the manifest refraction axis reading and the axis reading produced by the keratometers and subjective analysis of the topography maps was calculated. This data was assessed for normal distribution using a Shapiro-Wilk test. The data was not normally distributed; therefore, non-parametric testing was carried out ($p<0.05$).

6.3.1 Categorisation of Astigmatism Magnitude

Visit	**Whole group**	**Low Astigmatism**	**High Astigmatism**
		0.75 – 1.24D	**>1.25D**
n	58	32	26
Median Astigmatism (D)	-1.22	-0.98	-1.72

Table 6.1: Demographic data including the n for each group and the median of astigmatism.

6.3.2 Comparison of Axis difference

Difference in Axis Position	**IOL Master**	**OPD Scan**	**Pentacam**					**OPD**	**Pentacam**
	Sagittal power			**True net power**	**Holliday equivalent K readings**	**Total corneal refractive power**		**Topographical Axis Reading**	
Chord length	*2.3*	*3.2*	*3.2*	*3.2*	*4.5*	*2*	*5*	*N/A*	*N/A*
Median	**11.00**	**14.80**	**11.60**	**12.00**	**8.25**	**7.80**	**10.05**	**10.51**	**9.50**
Lower Quartile	5.00	6.35	5.35	4.00	3.80	3.75	4.70	4.26	5.00
Upper Quartile	25.50	29.58	28.45	23.00	17.40	17.38	22.23	21.41	25.00

Table 6.2: Difference in axis position compared to manifest refraction in a pseudophakic population (n=58)

The agreement between each instrument and manifest refraction were compared (Figure 6.3). There was no statistically significant difference found among the different comparisons despite a large number of outliers ($X^2 = 14.872$, $p = 0.063$).

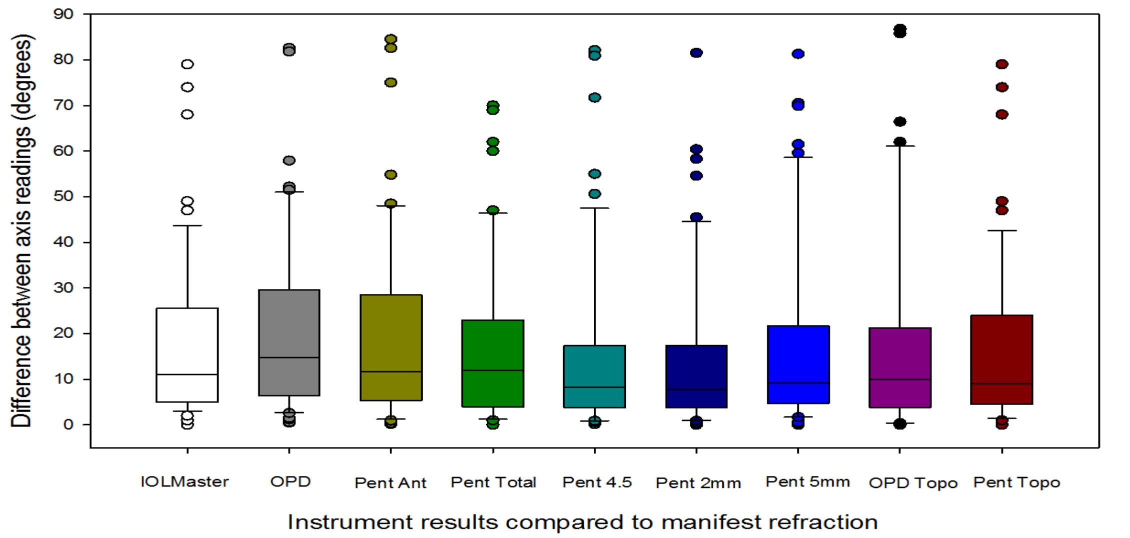

Figure 6.4: Boxplots demonstrating the difference between manifest refraction and each of the instrument results produced, for the whole group of data.

6.3.3 Comparison of Axis for High and Low Astigmatism

6.3.3.1 <u>Low Astigmatism</u>

Difference in Axis Position	**IOL Master**	**OPD Scan**	**Pentacam**					**OPD**	**Pent.**
	Sagittal power			**True net power**	**Holliday equivalent K readings**	**Total corneal refractive power**		**Topographical Axis Reading**	
Chord length	*2.3*	*3.2*	*3.2*	*3.2*	*4.5*	*2*	*5*	*N/A*	*N/A*
Median	**17.50**	**23.65**	**16.60**	**16.00**	**6.60**	**6.90**	**10.05**	**10.58**	**17.50**
Lower Quartile	4.00	5.98	2.30	4.25	3.10	0.93	2.00	2.91	4.00
Upper Quartile	30.00	42.05	38.78	26.00	24.40	26.13	23.90	21.41	30.00

Table 6.3: Difference in axis position compared to manifest refraction in a pseudophakic population (low astigmatism group, n=32)

The agreement between each instrument and manifest refraction were compared for the low astigmatism group (Figure 6.4). There was a statistically significant difference found among the different comparisons (X^2 = 21.934, p=0.0.05). Post hoc testing found that the difference between the Pentacam total refractive power (2mm chord) readings and manifest refraction were significantly lower than both the Pentacam sagittal and true net power readings compared with refraction (Z = -3.842, p<0.001 and Z= -2.926, p= 0.003 respectively).

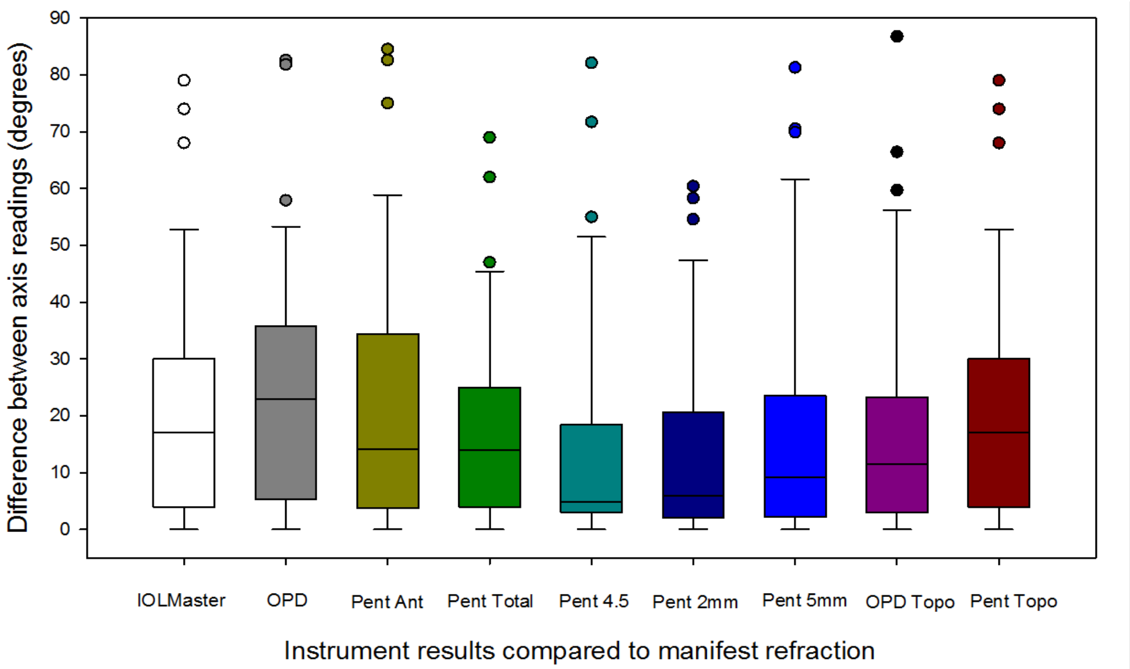

Figure 6.5: Boxplots demonstrating the difference between manifest refraction and each of the instrument results produced, for the low astigmatism group of data.

6.3.3.2 High Astigmatism

Difference in Axis Position	IOL Master	OPD Scan	Pentacam					OPD	Pent.
	Sagittal power			True net power	Holliday equivalent K readings	Total corneal refractive power		Topographical Axis Reading	
Chord length	*2.3*	*3.2*	*3.2*	*3.2*	*4.5*	*2*	*5*	*N/A*	*N/A*
Median	**7.00**	**10.70**	**8.40**	**8.00**	**8.70**	**7.90**	**5.80**	**7.43**	**7.00**
Lower Quartile	4.00	5.20	4.40	3.00	3.00	3.20	3.60	3.51	4.00
Upper Quartile	14.00	18.00	12.50	14.00	13.50	12.00	15.30	19.66	12.00

Table 6.5: Difference in axis position compared to manifest refraction in a pseudophakic population (high astigmatism group, n=27)

The agreement between each instrument and manifest refraction were compared for the low astigmatism group (Figure 6.5). There was no statistically significant difference found among the different comparisons (X^2 = 7.254, p=0.509).

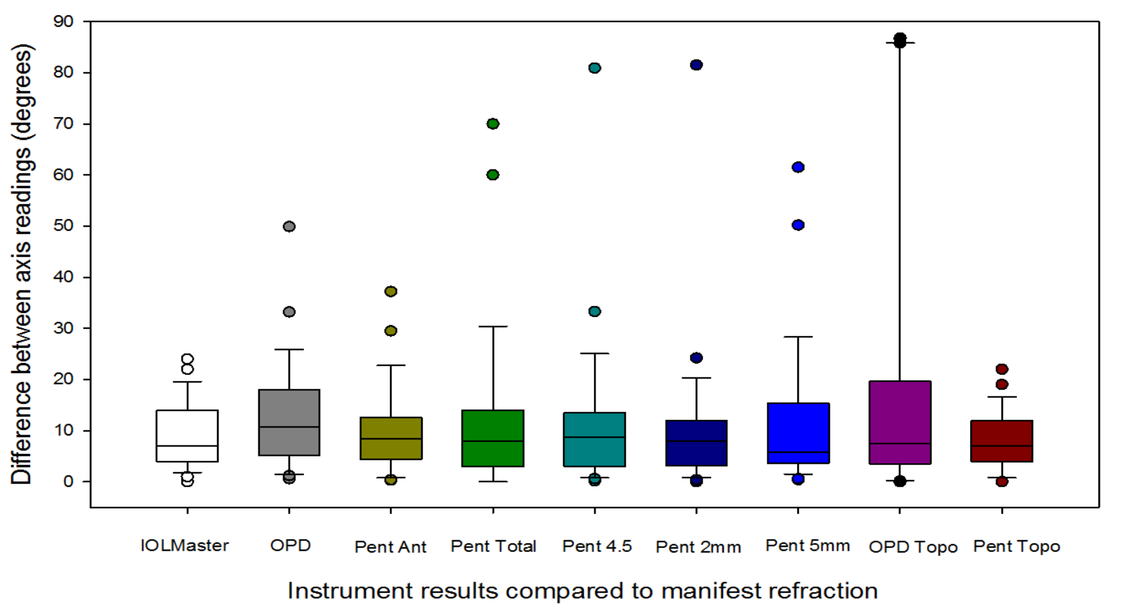

Figure 6.6: Boxplots demonstrating the difference between manifest refraction and each of the instrument results produced, for the high astigmatism group of data.

6.3.4 Correlation Between Manifest Refraction and Instrumentation Axis Readings.

6.3.4.1 <u>Whole Group</u>

Correlations (Kendall's Tau)		τ	*P value*
IOLMaster		0.643	*<0.001*
OPD scan		0.593	*<0.001*
Pentacam	Sagittal	0.654	*<0.001*
	True Net Power	0.620	*<0.001*
	4.5 SimK	0.615	*<0.001*
	Refractive Power 2mm	0.639	*<0.001*
	Refractive Power 5mm	0.629	*<0.001*
OPD	Topographical Map	0.640	*<0.001*
Pentacam		0.730	*<0.001*

Table 6.5: Correlation of the manifest refraction axis readings to the instrument and topography readings (whole group).

Generally, there was a significant moderate to strong correlation between the manifest refraction and each instrument reading for the whole group. The OPD scan showed the weakest correlation (τ =0.593, p<0.001) and the Pentacam topographical map displayed the strongest correlation (τ =0.730, p<0.001) across the whole data set.

6.3.4.2 Low Astigmatism

Correlations (Kendall's Tau)		τ	*P value*
IOLMaster		0.582	*<0.001*
OPD scan		0.629	*<0.001*
Pentacam	Sagittal	0.675	*<0.001*
	True Net Power	0.675	*<0.001*
	4.5 SimK	0.675	*<0.001*
	Refractive Power 2mm	0.675	*<0.001*
	Refractive Power 5mm	0.675	*<0.001*
OPD	Topographical Map	0.768	*<0.001*
Pentacam		0.582	*<0.001*

Table 6.6: Correlation of the manifest refraction axis readings to the instrument and topography readings (low astigmatism).

In the low astigmatism group there was a significant moderate to strong correlation between the manifest refraction and each instrument readings. The Pentacam topographical map and IOLMaster showed the weakest correlation ($\tau = 0.582$, $p<0.001$) and the OPD topographical map displayed the strongest correlation ($\tau = 0.768$, $p<0.001$) across the data set.

6.3.4.3 High Astigmatism

Correlations (Kendall's Tau)		τ	*P value*
IOLMaster		0.774	*<0.001*
OPD scan		0.520	*<0.001*
Pentacam	Sagittal	0.673	*<0.001*
	True Net Power	0.568	*<0.001*
	4.5 SimK	0.605	*<0.001*
	Refractive Power 2mm	0.605	*<0.001*
	Refractive Power 5mm	0.520	*<0.001*
OPD	Topographical Map	0.774	*<0.001*
Pentacam		0.738	*<0.001*

Table 6.7: Correlation of the manifest refraction axis readings to the instrument and topography readings (high astigmatism).

Similar to previous comparisons, there was a significant moderate to strong correlation between the manifest refraction and each instrument readings in the high astigmatism group. The OPD scan and Pentacam total refractive power across a 5mm chord showed the weakest correlation (τ =0.520, $p<0.001$) and both the OPD topographical map and IOLMaster displayed the strongest correlation (τ = 0.774, $p<0.001$) across the data set.

6.4 Discussion

The precision of the corneal steepest meridian or axis measurement is essential to the alignment and implantation of toric IOLs to correct corneal astigmatism. In the pseudophakic patient the post-surgical residual astigmatism is normally attributed entirely to the cornea shape. With the increased use of toric IOLs, it is imperative that we can accurately predict and decide upon the best alignment position for the IOL. There are a variety of instruments and methods used to determine the corneal astigmatism. Many studies have reported good repeatability of the instruments (Read et al. 2009; Visser et al. 2012; Wang et al. 2012). However, as stated previously in chapter 2, these studies concentrate on the mean spherical equivalent and vector analysis (Santodomingo-Rubido et al. 2002; Srivannaboon et al. 2012; Whang et al. 2012; Magar et al. 2013; Hoffmann et al. 2014; Srivannaboon et al. 2015). The repeatability and agreement of the axis element alone is often neglected. Misalignment of a toric lens can significantly reduce the vision (Felipe et al. 2011) so the accuracy of the axis reading remains important. This study was designed to assess the accuracy of axis measurement using keratometry and topography maps in comparison with the manifest refraction.

It has previously been inferred that the corneal shape is responsible for the ocular astigmatism post-cataract surgery (as the crystalline lens has been removed) and linear relationships between the manifest refraction and corneal shape have been found (Grosvenor et al. 1990; Remón et al. 2009). The emphasis of these findings has been on the magnitude of the astigmatism, not the orientation of the axis.

There was some investigation including axis but only as part of vector analysis (Remón et al. 2009). Chapter 5 has highlighted the discrepancies in the measurement of astigmatism magnitude when comparing keratometry to manifest refraction. In this study the axis data has been analysed independently and the analysis indicates that the keratometry and topography readings do not appear to agree with the axis found in the manifest refraction results. There is little work looking at the axis element of the astigmatism reading either as agreement between instruments or in comparison to the manifest refraction. There was one other study which also reported a large variation across different instrument axis readings and found significant improvement in agreement for axis measurements when two or more methods were combined and averaged (Browne et al. 2014).

Due to the circular nature of the data, it was the difference between manifest refraction and each instrument that was calculated and compared. The median differences found by the instruments were not significantly different for the whole group and the high astigmatism group data. Only the Pentacam total refractive power (2mm chord length) comparison was found to have a significantly lower difference than the Pentacam sagittal and true net power readings (<0.004). However, these median difference results produced would all be considered clinically significant as a clinically acceptable level of error, misalignment or rotation of toric IOLs is normally around 5° (Montés-Micó et al. 2009; Koshy et al. 2010; Wolffsohn et al. 2010; Browne et al. 2014). The lowest median value was the Pentacam total corneal power (2mm cord), of 7.8° compared to the OPD scan median of 14.8° (whole group, Table 6.2). This would be a loss of effective power of

24.4% and 51% respectively. The quartiles demonstrated that 50% of the difference between axis data lies between 3.8 to 6.4° (lower quartiles) and 17.4 to 29.6° (upper quartile). This means that half the measurements taken could lead to an effective power loss of around 13.3 -22.3% up to 80 – 98,8%. The boxplots represent the large spread in the data clearly, with long tails and outliers reaching near to 90° for each instrument and methodology. This study has found that the various methods of keratometry used could lead to unacceptable levels of misalignment of toric IOLs. The high astigmatism group should have a more easily defined meridian position but over 50% of the results found by the instruments differed by more than the clinically acceptable level of misalignment (5°). This could introduce a source of error and misalignment of toric IOLs.

As previously stated, a misalignment of 30 degrees reduces the effective correction of the toric IOL by 100%. Beyond this, where a lens is misaligned by more than 30 degrees, the introduction of the lens could be inducing astigmatism rather than correcting it (Felipe et al. 2011). Ho et al. (2009) carried out a study comparing two different readings produced by the Pentacam: anterior and total corneal power. The study found an absolute mean difference of 3.2°±4.4° (range 0 to 57.8°) (Ho et al. 2009). This was lower than difference between the median anterior and total refractive power Pentacam readings found in this study (3.8°, Table 6.2). When the data was split into the low astigmatism group, the difference increased and decreased significantly in the high astigmatism group. In the low astigmatism group there is a difference of 9.7° (Table 6.3) and 0.5° (Table 6.4) in the high astigmatism group, with the Pentacam total refractive power producing an axis reading much closer to the manifest refraction each time. The anterior cornea measurement appears much less accurate than the readings taking into account the whole cornea. It has been shown that there is a difference in axis orientation between the anterior and posterior surfaces (Eom et al. 2013). It can be inferred that taking both into account should improve the agreement between keratometry and refraction.

There was moderate to high correlation across all instruments compared to manifest refraction for the whole group data (Table 6.5). The highest correlation for the whole group was found for the Pentacam topography ($\tau = 0.730$, $p<0.001$) and the lowest was the OPD scan ($\tau = 0.593$, $p<0.001$). In the low astigmatism group (Table 6.6) the highest correlation was with the OPD topography ($\tau = 0.768$, $p<0001$) and the lowest correlation was with the IOLMaster ($\tau= 0.582$, $p<0.001$). In the high astigmatism group (Table 6.7) the highest correlation was with the IOLMaster and OPD topography ($\tau = 0.774$, $p<0.001$) and the lowest was with the Pentacam total refractive power (5 mm) and OPD scan ($\tau = 0.520$, $p<0.001$). Although these are strong correlations, considering the degree of accuracy expected from these instruments, there should be a much stronger relationship in order to ensure an accurate reading from each methodology.

There are some known sources of error with the instruments used in this study. The IOLMaster measures the curvature with 6 fixed points. Meridians that fall outside or among these points are likely to be measured with less accuracy. The Pentacam also measured the corneal curvature at set intervals with the rotating camera, allowing data gaps. However, the OPD scan, which analyses the whole cornea, still has its limitations. It is very dependent upon a stable tear film, which an older post- surgical population does not often display. Nemeth et al found that the break-up of the tear film after blinking could alter the keratometry reading, thus indicating that a dry eye, with a poor tear film will have unreliable results (Németh et al. 2001).

Overall the comparison of manifest refraction and the two topographical map axis assessments showed a poorer agreement than the other instrument readings. This may be due to the subjective nature of the assessment, allowing a high degree of human error. In addition to this, the majority of the corneal maps produced did not display a clear and obvious meridian and demonstration of the steepest and flattest meridian s across the entire cornea. These maps are a reflection of the whole corneal surface, not just the central zone used in keratometry. A higher correlation was found between the OPD maps and refraction axis readings but the difference between the subjective topographical readings and the manifest refraction was high in all data groups. This would potentially lead to a significant level of error in assessment.

The error in keratometry readings and topography readings can be attributed to many different sources. The first as mentioned previously is a poor tear film, which would be present in the study population of elderly eyes (Nemeth et al. 2014). In addition to this, the posterior cornea surface has been shown to influence the overall corneal power and astigmatism orientation (Cheng et al. 2011; Koch et al.

2012). It has been shown that the axis and orientation can be different on the two different surfaces. What is not known is how these are combined to result in the summative axis measured in manifest refraction and how can this be measured by keratometry (Eom et al. 2013). Teus et al (2010) also suggests that there may be another source of internal astigmatism that may contribute to the manifest refraction. Elliot (1994) also reported a greater accuracy of Retinoscopy over keratometry in determining the refraction in pseudophakic eyes, supporting this argument. Additionally recent studies have found that the keratometry readings from the cornea may not wholly explain the refractive astigmatism measured in a pseudophakic population and there is some suggestion of an internal astigmatism not caused by the cornea (Bregnhøj et al. 2015).

Lastly, Norrby et al (2013) suggested that some diurnal variations could occur, altering the shape of the corneal and reducing repeatability of the readings. If each one or any of these factors influenced the results, it could go to explain why the results seemed so inaccurate and agreement so poor.

6.5 Conclusions

Both simulated keratometry readings and topography map analysis had poor agreement with the manifest refraction axis and the majority of readings showed a disagreement far outside a clinically acceptable level. This indicated a large potential error in the toric IOL placement, and could result in misalignment and ineffective correction of the astigmatism. Repeated measures and comparison of instruments axis readings may be needed to achieve a more accurate assessment of corneal axis. Further work needs to be done to determine and improve the accuracy and repeatability of the readings. Additionally the source of post-operative astigmatism needs to be explored in more detail.

Chapter 7 The Effect of Loss of Contrast and Form Deprivation on Vision and Mobility tasks

7.1 Introduction

7.1.1 Background

One third of people over the age of 65 fall each year in the UK (approx. 3 million). Each year hip fractures (mostly caused by falls) cost around £2 billion. Many people never fully recover their mobility and it is estimated that one in five patients die within 3 months of the fall despite treatment (Treml et al. 2011; AgeUK 2012). Impaired vision (a reduction in vision that cannot be improved with a refractive correction) has been shown to be an important risk factor in falls in the elderly (Lord et al. 2001). Reduced contrast sensitivity, visual fields loss, poor depth perception and low contrast visual acuity have all been isolated as independent factors that can lead to increased incidence of falls (Lord et al. 2001; Black et al. 2005; Dhital et al. 2010). More specifically, reductions in vision due to cataracts or uncorrected refractive error are both considered risk factors of falling in the elderly (Woolf 2003). Lastly, differences in visual acuity (best corrected vision) with one eye with high and the other with low acuity can be as high a risk factor as bilateral moderate reduction in vision (Lord et al. 2001).

7.1.2 Uncorrected Astigmatism and Cataract Surgery

Uncorrected astigmatism is known to reduce visual acuity (Peters 1961; Kobashi et al. 2012) and can impede various tasks including reading, using the computer and viewing a mobile phone (Wolffsohn et al. 2011). Astigmatism is the term used to describe an eye that is not optically spherical, where there are two principal meridians of differing refractive power. Oblique astigmatism (where the principal meridians are at not orientated vertical or horizontally) in particular can alter foot placement on steps affecting balance and mobility, which in turn could increase the risk of falling (Johnson et al. 2013).

Cataracts are known to reduce visual acuity for both distance and near and contrast sensitivity as well as cause symptoms such as glare, halos and changes in colour saturation (Allen et al. 2006). The symptoms vary with the patient and type of opacity but common to all types is a loss of contrast sensitivity (Allen et al. 2006). Improvements are seen in contrast sensitivity, stereo acuity, colour saturation and visual acuity for both distance and near tasks after surgery (McGwin Jr et al. 2006).

When cataract surgery is carried out in the NHS, almost all patients are given monocular intraocular lenses (IOLs) and toric IOLs are not offered despite the routine measurement of corneal astigmatism. It has been found that around 20% of the population has significant astigmatism (≥1.25DC), which is left uncorrected without the use of specialist toric IOLs (Ferrer-Blasco et al. 2009). So, while current standards aim to achieve within 0.50- 1.00D of emmetropia (Gale et al.

2007), a significant portion of population will fall below this with a much poorer visual correction post-surgically.

7.1.3 Vision and Body Sway

Postural stability and balance are reliant on a complex mixture of sensory inputs received from the vestibular (head movement), proprioceptors (mechanical changes to the body) and visual cortex (vision) that is not quite fully understood (Guerraz et al. 2008). Vision provides us with both self-motion (egocentric) feedback (from the previously mention sensory input) and knowledge of the presence and motion of objects in the environment (exocentric feedback). These feedback systems ensure that we can maintain upright stance. However, vision has been shown to have a significant part to play in maintaining stability (Fitzpatrick et al. 1994; Butler et al. 2008; Sarabon et al. 2013). Studies have shown that elimination of vision in young healthy subjects alters postural stability (Fitzpatrick et al. 1994). This effect increases with less stable stances such as narrow or single leg or on less solid surfaces (e.g. foam) (Sarabon et al. 2013; Tomomitsu et al. 2013). However, it has been found that other sensory input could compensate for the loss of vision in these stances (Sarabon et al. 2013). Sarabon et al (2013) found that although there was a linear increase in anterior posterior sway with decrease in stance stability, this was not seen in the medial lateral sway. It has been suggested that there was a sensory reweighting that increases the proprioceptive and vestibular systems input to compensate for the loss of vision. Rinaldi et al

(2009) also observed this change, finding that healthy adults and older children have been shown to be able to '*downweigh*' the visual information used to balance if it is eliminated or visual information is deemed unreliable, in their case with moving walls (Rinaldi et al. 2009).

Butler et al (2008) explored this further comparing the effect of vision elimination on postural stability in subjects with leg muscle weakness due to childhood polio and aging changes. The study found that although there was little difference in postural stability with eyes open, vision elimination had a more significant effect on postural stability in those with muscle weakness than healthy normal subjects (Butler et al. 2008). Due to the mixture of sensory inputs used in stability, a healthy adult can choose to ignore or reduce the significance of one factor (source of information) if eliminated or deemed less reliable e.g. the vision. However, in a subject with muscle weakness, such as much of the elderly population, the demand for other sensory input including vision for balance increases. As cataracts cause a reduction and change in vision, the effect on standing balance has been investigated on multiple occasions. Large review studies found investigating the rate of falls before and after cataract surgery have speculated that cataracts can lead to an increase in falls (Brannan et al. 2003; Tseng et al. 2012) and surgery will reduce this risk. Conversely to this, despite finding some improvements in contrast sensitivity and near acuity, McGwin and colleagues (2006) did not find a decrease in falls after surgery (McGwin Jr et al. 2006). Schwartz et al (2005) investigated this in more detail and measured standing balance in the patients' pre and post cataract surgery. The group used 4 force plates to detect the changes in pressure from the toe and heel of each foot, using the fluctuations and differences between the vertical pressure on each plate to determine the stability of the individual. There was a significant difference in the sway intensity between the pre and post-operative data, indicating an increase in stability or balance. Combination of the posturographic data also found that the risk of falling decreased for the post-surgical group overall. They could therefore infer that an individual's stability improves after cataract surgery indicating that the reduced vision caused by cataracts reduces the standing balance (Schwartz et al. 2005). This again underlines the significant input vision plays in the balance and stability of an individual.

7.1.4 Vision, Gait and Balance

Our vision is an important part of our balance and gait, and is used to continually adapt to our surroundings (Patla 1997). The exocentric and egocentric information is used to move towards goals or avoid objects in the environment, respectively. If the vision is uncorrected or impaired then it could affect stability and mobility, increasing risk of falling. Nevitt et al (1991) reviewed the risk factors for falling and found that 47% of falls were caused by hazards e.g. stairs, curbs or steps/ slippery surfaces. 39% of subjects were walking at the time of the accident, 20% were going up or downstairs. According to a more recent observation of the cause of falls by Robinovitch and colleagues (2013), the most common cause of falls is attributed to an incorrect shift in balance (47%) and the next most common is tripping over a bump or lump (41%). Other factors, such as the integration of vision with other sensory and motor systems and the impact of cognition, aging and other disease pathologies could contribute to these statistics. However, vision also seems to be a vital element within these described falling mechanisms.

It has been found that earlier cataract surgery and increase in vision post-surgically may reduce the occurrence of falls (Brannan et al. 2003; Tseng et al. 2012). Reduced vision caused by cataracts has been shown to change standing balance (Schwartz et al. 2005; Johnson et al. 2009). Conversely, studies carried out by McGwin et al (McGwin Jr et al. 2006) and Supuk et al (Supuk et al. 2013) both carried questionnaires to investigate rate of falls before and after cataract surgery and found that there was no significant association between cataract surgery and falling. The conflicting results warrant further investigation into the association between vision and balance during mobility tasks.

7.1.5 Vision and Balance in Functional Activities

Vision plays a key role in processing and planning for mobility tasks such as avoiding obstacles, planning routes and when to stop and start locomotion (Patla 1997; Patla 1998). Humans need to be able to determine the direction and speed of barriers and obstacles in the set pathway. They also must be able to distinguish between a moving environment and the movement of themselves and interpret it thus. Much of locomotion and balance is reliant upon optical flow, which allows animals to determine motion and direction based on the orientation and changes in the visual environment around them (Lee et al. 1977; Gibson 2009). When conflicting information of between vision and non-visual information is presented, the vision input can dominate the response (Lee et al. 1977). Therefore, it can be inferred that the reduction in vision could alter the processes in mobility and obstacle negotiation. Older patients are at higher risk of falling than their younger counterparts (AgeUK 2012) and a reduction in vision can increase the risk of falling (Black et al. 2005; Dhital et al. 2010). Subjects with central vision loss have shown increased head flexion when stepping up to a raised surface, compensating for vision loss. This leads to increased sway and a potential reduction in balance (Timmis et al. 2014). This demonstrates the reliance upon vision to successfully carry out many mobility tasks. It has been shown that shifting weight incorrectly i.e. stepping up or down is the most common cause of falls, followed by tripping over an object (Robinovitch et al. 2013). This may be due to changes in vision, as foot placement is altered when stepping on or off a single step or kerb when the vision is interrupted or blurred (Elliott et al. 2010; Buckley et al. 2011). In particular, induced oblique astigmatism was shown to alter foot placement on a step (Johnson et al. 2013).

Negotiating stairs accounted for 20% of falls in the study carried out by Nevitt et al (1991) and a significant portion of accidental deaths in older adults (Startzell et al. 2000). Most accidents occur on either the first or last step (Templer 1992). This is likely due to the fact the majority of stairs climbed rely on previous motor experience (ie the previous step(s)) to guide the accuracy of the step (Shinya et al.

2012). Only the first and last steps require significant visual input for stepping accuracy.

Elderly people have also been shown to reduce their foot clearance on steps and Foster et al (2015) indicated that stairs should be marked with a horizontal vertical illusion to encourage greater foot clearance and reduce incidence of falls. Uncorrected astigmatism has been shown to alter foot placement and cataracts reduce contrast and edge detection (Dhital et al. 2010; Johnson et al. 2013) However, dynamic balance has not been measured in these studies, which have been limited to standing measurements, or single steps due to the limitations of camera based systems. Measurement of an individual over multiple steps will allow more information of visual input and the effect of astigmatism and cataracts on this task in a more realistic setting.

Humans plan obstacle negotiation or changes in routes around 2 steps ahead (Patla 2003). If vision is reduced or impaired, e.g. by cataracts or uncorrected astigmatism this could prevent an accurate assessment of the obstacle from two steps or more away. This is turn may alter how well the negotiation or steeping over the obstacle is carried out. Cataracts often cause reduced contrast sensitivity (Dhital et al. 2010) and may affect edge detection, this can cause a patient to miss objects with low contrast on a footpath. Uncorrected astigmatism can also affect foot placement (Johnson et al. 2013) and may also affect how well the obstacle is avoided despite detection. It could affect dynamic balance during functional activities e.g. obstacles and stairs negotiation. Despite the most falls occuring during incorrect shift in balance (47%) or tripping over a bump or lump (41%) (Robinovitch et al. 2013), no previous studies have examined the effect of astigmatism and form deprivation on balance during these high-risk daily activities.

Accelerometers and smart devices have been used in recent work to measure movement and position of subjects (Mancini et al. 2011; Steins et al. 2014). The use of the recently developed x-IMU (the versatile Inertial Measurement Unit) allows us to track the movement of the body (or centre of mass) during many different functional activities without the restraints of the external factors such as position of a camera and location of the activities. This will be the first study to examine the effect of artificially induced uncorrected astigmatism and cataracts on dynamic balance in healthy participants during functional activities such as walking on stairs or avoiding an obstacle when walking along a path. If the mobility and balance are compromised by the changes in vision, it could lead to unnecessary falls and injuries that will be both costly to the NHS and traumatic for the individual and their loved ones. It is proposed that implantation of the more expensive toric IOLs could save the NHS money by reducing falls and hip fractures.

7.1.6 Aims

The objectives of this study are to determine if astigmatic distortion and form deprivation caused by cataracts cause changes to standing balance and balance during mobility tasks such as walking over an obstacle or up and downstairs.

7.2 Methods and Materials

7.2.1 Subjects

15 healthy presbyopic subjects aged 47.8 ± 4.9 years old (6 females, 9 males) were recruited from the School of Health Professions staff population by the chief investigator (CH). All data was collected between January and April 2015. All subjects participated with fully informed written consent and the approval of the University Ethics committee.

7.2.2 Design

7.2.2.1 Inclusion Criteria

- Presbyopic adults (40-60 years old)
- No current balance, mobility problems including compromised gait or current injury.
- Good ocular health and full visual fields (self-reported by subject).
- Able and willing to give informed consent.

7.2.2.2 Exclusion criteria

- Reduced vision, amblyopia or visual field loss
- Cataracts or other ocular pathology or disease
- Reduced visual acuity (lower than 6/9), amblyopic or visual field defect

7.2.2.3 <u>Patient group justification</u>

This study was not carried out on a cataract population to avoid confounding factors induced by the other common aging co-morbidites that affect balance. A presbyopic subject population was chosen to create a more similar level of balance with early lens opacity and physical aging changes. This population is more similar to a pre-cataract population than young healthy normal subjects (<40 yeas old).

7.2.2.4 <u>Sample Size Calculation</u>

Based on values of the dynamic balance measurement, JERK scores in asymptomatic participants during a standing balance task (mean ± SD: 0.065 ± 0.024) (Mancini et al. 2012), we have powered the study to be able to detect a 15% between normal and altered vision in asymptomatic participants during the postural task. This results in an effect size of 0.74. To detect such a difference with a power of 0.80 and a significance level of 0.05, a sample size of at least 13 participants has been determined by the G*Power 3 programme (Faul et al. 2007) in this repeated measures design study. Therefore, 15 participants were recruited for this study.

7.2.3 Ethical Approval

All procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by University ethics committee (Ref: 13/14-254 on 25th June 2014).

7.2.4 Methods

Following recruitment, all subjects submitted their refractive error from a sight test carried out in the last 12 months. The subjects were required to carry out the trials with three specific refractive error states with and without simulated cataracts.

7.2.4.1 Simulation of Cataracts (Form Deprivation)

Bangerter foils have been shown to cause form deprivation resulting in loss of contrast sensitivity (Perez et al. 2010). This is similar to cataract symptoms of visual impairment (Steinert 2010). Bangerter foils of grade 0.4 were chosen to simulate the cataract symptoms; these were the most readily available and most suitable choice. Perez et al (2010) showed that this grade lead to the greatest degradation of the vision and loss of contrast sensitivity although similar results were shown with 0.6 and 0.3. The 0.8 foil has been shown to produced the most consistent results, but the reduction of vision was not as significant. During the trials the subject was to wear one of two pairs of wrap around frames. One had bangerter foils (0.4) stuck on and the other had no foil. These two frames were used to simulate vision with and without cataracts.

7.2.4.2 Calculation of Contact Lens Refraction

The first refractive state was fully corrected (Plano), the second was moderate oblique astigmatism (-1.50DC) and the third was with high oblique astigmatism (3.00DC). Oblique astigmatism has been shown to reduce the vision more significantly (Freitas et al. 2014) and cause a more significant change in foot placement than other forms of astigmatism, fully corrected vision and with clear crystalline lens (Johnson et al. 2013). This study was verifying a novel technique for measuring instability due to vision loss. Therefore, oblique astigmatism was chosen to provoke a measurable response with this new method. Through vector analysis contact lenses prescriptions were calculated to result in the following refractive errors:

Refraction 1:

OD: Plano

OS: Plano

Refraction 2:

OD: +0.75/-1.50x45

OS: +0.75/-1.50x135

Refraction 3:

OD: +1.50/-3.00 x45

OS: +1.50/-3.00x135

The Holladay-Cravy-Koch method of analysis was used (Holladay et al. 1992) in Excel (*Microsoft Office, Microsoft, Redmond, Washington*) to determine the required prescription.

S_1 = Subject's spherical power (D) for A_1 (smallest numerical axis value)

S_2 = Required spherical power (D) for A_2 (larger numerical axis value)

S_T = target spherical value (D)

A_1 = steepest axis (smallest numerical value)

A_2 = steepest axis (larger numerical value)

A_T = Required steepest axis position

C_1 = Subject's magnitude of astigmatism (D) for A_1

C_2 = Required magnitude (D) for A_2

C_T = Target magnitude of astigmatism (D)

θ = Axis change between the lower orientation (Location of incision or flattest corneal meridian) — lower value

a = Difference in orientation between the flattest corneal meridian and incision location

The established equations are:

1. $A_T = A_1 + \theta$ *(Equation 7.1)*

2. $a = A_2 - A_1$ *(Equation7.2)*

3. $tan2\theta = \frac{C_2 sin2a}{C_1 + C_2 cos2a}$ *(Equation 7.3)*

4. $S = C_1 sin^2(\theta) + C_2 sin^2(a - \theta)$ *(Equation 7.4)*

5. $C_T = C_1 + C_2 - 2s$ *(Equation 7.5)*

6. $S_T = S + S_1 + S_2$ *(Equation 7.6)*

Therefore:

7. $S = \frac{C_1 + C_2 - C_T}{2}$ *(Equation 7.7)*

8. $S_2 = S_T - S_1 - S$ *(Equation 7.8)*

9. $A_2 = a + A_1$ *(Equation 7.9)*

10. $tan2\theta = \frac{C_2 sin2a}{C_1 + C_2 cos2a}$ *(Equation 7.10)*

11. To find alpha, graphs were used to plot the crossover between the equations using a range in values for alpha. The equations were as follows:

    a. $y = (tan2(\theta))(C_2 cos2a)$ *(Equation 7.11)*

    b. $y = C_2 sin2a$ *(Equation 7.12)*

    c. The crossover point was the determined value for alpha.

7.2.4.3 Visit Routine

Each subject was required to attend one single assessment session. Centre of mass position was measured throughout each activity. One accelerometer (*Pro-Move system, Inertia Technology B.V, Netherlands*) was placed over the L3 spinous vertebrae. This assessed trunk stability at the centre of mass (COM). This position has been shown to reliably reflect centre of mass as the rotation of the pelvis and thorax neutralize each other at this point (Henriksen et al. 2004; Steins et al. 2014). It gives a true assessment of the subject's stability.

The same battery of mobility tests were carried out with the three different visual corrections, with and without the Bangerter foil glasses used to induce cataract symptoms of visual impairment. Each test was conducted 3 times and the average reading for each used in the analysis to maintain high repeatability of the assessments. Calculating the ICC for each assessed the repeatability of the three tasks.

Contact lenses were worn to induce the various vision states. A set of CLs was inserted at the beginning of each round of tasks and the subjects were given 2-3 minutes to adapt to the new prescription and lens as most contact lenses have stabalised after this period (Momeni-Moghaddam et al. 2014).

Figure 7.1: A subject carrying out the obstacle negotiation and stairs tasks.

7.2.4.4 Standing Balance

Standing balance with corrected vision is used to a baseline for comparison with other visual conditions. The subject stood 50 cm in front of a large screen and the standing balance measured while an optokinetic stimulus (sideways moving) vertical spatial frequency target of 0.1068 cycle/degrees was projected onto the screen as used in previous work assessing the relationship between body sway and vision(Bunn et al. 2015). This method is similar to previous assessments in a pre and post-operative cataract population (Anand et al. 2002; Schwartz et al. 2005).

The standing balance was measured by determining the Jerk in standing for each condition. Jerk is a mathematical function of the time derivative of the acceleration and is a measure of dynamic stability. It looks at how an individual controls balance or decelerates movements towards imbalance. This stability score has previously been shown to be sensitive enough to detect small changes in balance between early stage untreated Parkinson's patients and healthy controls (Mancini et al. 2011). The resultant JERK was measured using the following (Equation 7.13):

$$JERK = \frac{1}{2}\int_0^t \left(\frac{dAccAP}{dt}\right)^2 + \left(\frac{dAccML}{dt}\right)^2 \qquad \textit{(Equation 7.13)}$$

(Flash et al. 1985; Mancini et al. 2011)

AccML and AccAP are the acceleration components measured in the medial lateral (forwards/ backwards plane) and anterior posterior (side tilt plane) directions. This is a function of the time derivative of the acceleration and is a measure of dynamic stability. It assess an individual control of balance or the deceleration movement that occur during the correction of imbalance.

7.2.4.5 Navigating Stairs

In this task, the subject's movement was monitored while climbing up and down a small flight of stairs (11 steps). Previously the assessment of step velocity while stepping off a single block allowed a clear indication of stability and perception of the step while wearing multifocal spectacle lenses (Timmis et al. 2014).

7.2.4.6 Obstacle Navigation

One small obstacle (a lump) was placed under the matt (randomly changing position along the walkway for each individual measurement) and the subject was recorded while navigating along the matt. The subject was aware that here would be a lump, which they were instructed to step over, but were blind to the location until the commencement of the task (they had their back to the walkway until the start of the measurement).. This assessment was designed to determine if the cataract and or astigmatism affected the subject's stability in negotiating obstacles

(Timmis 2014). Matts were placed along the side of the pathway and an investigator was alongside the subject to intervene if they lost their balance.

During both the stairs and obstacle negotiation task, this study measured the mean peak angle, velocity and acceleration of COM (centre of mass) in three planes of movements: rotational (yaw, along the transverse plane), forwards/ backwards (pitch, along the sagittal plane) and side tilt (roll, along the frontal plane) when negotiating the obstacle. COM is the gold standard of balance assessment as it represents the centre and base of stability and is the biomechanical centre of support.

7.2.4.7 Outcome Measurements for Mobility Tasks

For the movement tasks: walking up and downs stairs and stepping over an obstacle (obstacle negotiation), the sensors tracked the mean peak angle, velocity and acceleration of the subject's centre of mass. Each was calculated along three planes of movement: forwards/ backwards, rotational and side tilt. The centre of mass was assessed as the true direct measurement of the subject's stability and balance.

Normalised angular velocity and acceleration were calculated as:

Normalised angular velocity $\hat{\omega} = \frac{\omega}{\sqrt{g/l_0}}$

(Equation 7.14)

Normalised angular acceleration $\hat{\alpha} = \frac{\alpha}{g/l_0}$ *(Equation 7.15)*

(Hof 1996)

7.2.4.8 Statistical Analysis

Excel (*Microsoft Office, Microsoft, Redmond, Washington, USA*) and SPSS (*Statistical Package for Social Sciences, Version 21, IBM, Armonk, New York, USA*) software were used to analyse the data. The data was tested for normal distribution with Shapiro-Wilks test. The data was not normally distributed so a non-parametric analysis was carried out ($p<0.05$).

7.2.4.8.1 Standing Balance Task Data Analysis

The average reading of the three trials during the standing balance tasks was determined in the analysis. Statistical analysis was performed using SPSS. The data was tested for normal distribution with Shapiro-Wilks test. Due to the small numbers and the abnormal distribution of the data, non-parametric analysis was carried out.

An intraclass correlation coefficient ($ICC_{3,3}$) was used to determine the repeatability of the tasks (Portney et al. 2009). Friedman ANOVA tests were used to find any significant differences between the different visual conditions and the Plano condition. Post-hoc analysis (Wilcoxon rank paired testing) was run to determine which visual corrections showed a difference. The level of significance was set at 0.05.

7.2.4.8.2 Mobility Activities Data Analysis

The average reading for each task was in the analysis. All data was also normalised for variations in gait by adjusting for leg length.

An intraclass correlation coefficient ($ICC_{3,3}$) was used to determine the repeatability of the tasks (Portney et al. 2009). Friedman ANOVA tests were used to find any significant differences between the different visual conditions overall. When required, post-hoc analysis (Wilcoxon rank paired testing) was run to determine pair wise comparisons. To avoid an increased chance of a type I error from repeated testing of the data, the alpha level was divided by the number of conditions (6), alpha= 0.05/6=0.008 ~0.01.

7.3 Results

7.3.1 ICC (Repeatability and Reliability)

Each tasks was repeated three times with each visual condition. The ICC was calculated for each task (mean of the three repetitions) to determine the repeatability and reliability of the results found in this study.

7.3.1.1 ICC: Standing Balance Task (Mean JERK Score)

ICC	Plano	Plano + induced cataract	1.50DC	1.50 DC + induced cataract	3.00 DC	3.00 DC + induced cataract
	0.972	0.976	0.992	0.995	0.967	0.971

Table 7.1: ICC for mean JERK score from three measurement trials of standing balance

7.3.1.2 ICC: Upstairs, Downstairs and Obstacle Negotiation

Task		Upstairs			Downstairs			Obstacle Negotiation		
ICC		Rot	F/B	Side	Rot	F/B	Side	Rot	F/B	Side
Mean Peak Angle	Plano	0.668	0.685	0.845	0.793	0.928	0.814	0.958	0.797	0.910
	Plano +induced cataract	0.376	0.666	0.694	0.750	0.641	0.654	0.838	0.809	0.791
	1.50DC	0.859	0.598	0.566	0.852	0.935	0.121	0.875	0.978	0.959
	1.50DC +induced cataract	0.293	0.447	0.631	0.794	0.569	0.648	0.937	0.866	0.908
	3.00 DC	0.293	0.162	0.560	0.672	0.933	0.855	0.901	0.767	0.844
	3.00 DC +induced cataract	0.500	0.656	0.740	0.840	0.865	0.691	0.950	0.976	0.623
Mean Peak Velocity	Plano	0.738	0.747	0.414	0.835	0.640	0.865	0.973	0.962	0.980
	Plano + induced cataract	0.929	0.838	0.891	0.950	0.853	0.967	0.968	0.973	0.815
	1.50DC	0.947	0.803	0.858	0.848	0.868	0.600	0.908	0.730	0.888
	1.50DC +induced cataract	0.884	0.883	0.897	0.869	0.910	0.925	0.966	0.966	0.767
	3.00 DC	0.842	0.818	0.848	0.646	0.824	0.826	0.949	0.935	0.743
	3.00 DC + induced cataract	0.926	0.762	0.575	0.884	0.886	0.970	0.949	0.940	0.937
Mean Peak Accel.	Plano	0.753	0.813	0.581	0.663	0.658	0.673	0.927	0.657	0.795
	Plano + induced cataract	0.930	0.798	0.938	0.902	0.904	0.878	0.716	0.880	0.842
	1.50DC	0.905	0.885	0.797	0.648	0.908	0.897	0.951	0.883	0.888
	1.50 DC + induced cataract	0.888	0.855	0.778	0.925	0.921	0.923	0.961	0.845	0.898
	3.00 DC	0.833	0.935	0.930	0.702	0.778	0.592	0.898	0.850	0.713
	3.00 DC + induced cataract	0.961	0.780	0.692	0.936	0.886	0.837	0.985	0.971	0.980

Table 7.2: ICC for the mean peak angle, velocity and acceleration along all planes of movement during obstacle negotiation.

7.3.2 Outcome Measures Results

1.1.1.1 Standing Balance Task: JERK

The mean JERK was calculated for each trial and used for the comparison of each visual condition. A significant difference was found between the mean JERK scores with different vision states during the standing balance tests ($X_2{}^6$ = 29.091, p <0.001). Further testing with Wilcoxen signed rank test found that there was a significant difference between the Plano condition and all other conditions with the exception of the 3.00 DC + induced cataract group. The jerk was significantly greater for Plano + induced cataract, 1.50DC and 1.50 DC + induced cataract than Plano ($p < 0.05$). However, the jerk was significantly less in 3.00 DC and 3.00 DC + induced cataract in comparison to Plano ($p < 0.05$).

There was no difference between the median JERK scores of the Plano and 3.00 DC + induced cataract trials. The median was significantly lower in the 3.00 DC than the Plano trial, and a significantly higher median was found in all other trials.

Refractive Condition	Plano	Plano +induced cataract	1.50DC	1.50 DC +induced cataract	3.00 DC	3.00 DC +induced cataract
Median	1347	2853.00*	2230.00*	2331.33*	579.67*	1066.67
LQ	868.33	2188.67	1959	717	161.67	765
UQ	1769.33	3643.67	3138.33	3343.67	1261.67	1119

Table 7.3: Medians, upper (UQ) and lower (LQ) quartiles for standing balance under different refractive conditions.

*$p < 0.05$, significant difference between altered vision and Plano condition.

7.3.2.1 Upstairs

7.3.2.1.1 Upstairs: Medians, Upper and Lower Quartiles

Upstairs										
Refractive condition		Forwards/ backwards			Rotation			Side Tilt		
		M	**LQ**	**UQ**	**M**	**LQ**	**UQ**	**M**	**LQ**	**UQ**
Mean Peak Angle	**Plano**	**17.67**	15.17	19.42	**11.00**	9.50	15.75	**8.33**	7.00	10.59
	Plano +induced cataract	**16.33**	14.84	19.83	**12.00**	8.84	21.42	**7.33**	6.50	10.00
	1.50 DC	**17.00**	15.84	22.50	**12.00**	9.67	15.46	**8.00**	7.00	9.59
	1.50 DC + induced cataract	**19.00**	15.67	20.33	**12.00**	10.67	13.50	**8.67**	6.50	9.67
	3.00 DC	**16.33**	15.00	18.83	**13.67**	12.17	15.33	**9.33**	7.50	12.17
	3.00 DC +induced cataract	**17.00**	14.17	21.17	**12.00**	10.00	16.83	**9.00**	7.33	10.88
Normalised Mean Peak Velocity	**Plano**	**10.38**	9.19	13.81	**13.43**	12.04	14.99	**13.10**	10.31	15.37
	Plano +induced cataract	**12.54**	9.50	13.88	**13.15**	11.01	13.98	**10.80**	9.45	12.99
	1.50 DC	**11.97**	9.70	14.18	**13.54**	11.60	14.75	**11.12**	9.62	14.76
	1.50 DC + induced cataract	**10.58**	9.23	14.96	**12.00**	10.21	13.80	**10.90**	9.16	14.09
	3.00 DC	**11.89**	10.24	14.68	**13.34**	10.86	15.29	**12.32**	9.35	13.85
	3.00 DC +induced cataract	**10.91**	9.86	15.01	**12.28**	10.28	13.93	**12.54**	9.99	14.34
Normalised Mean Peak Accel	**Plano**	**26.65**	22.50	31.27	**30.69**	27.79	38.26	**28.33**	23.69	34.07
	Plano +induced cataract	**24.22**	23.27	27.36	**30.68**	27.83	37.62	**26.57**	23.67	27.92
	1.50 DC	**27.54**	24.02	34.69	**33.25**	27.92	37.29	**27.41**	24.29	34.90
	1.50 DC + induced cataract	**28.29**	22.55	31.14	**29.95**	27.01	35.11	**27.45**	23.36	30.26
	3.00 DC	**30.31**	25.03	35.94	**32.47**	23.77	41.48	**26.48**	23.10	32.73
	3.00 DC +induced cataract	**27.86**	23.02	32.79	**31.01**	24.60	37.85	**28.05**	22.81	34.26

Table 7.4: Median (M), upper (UQ) and lower (LQ) quartiles for the COM mean peak angle, velocity and acceleration during the upstairs task for all visual conditions.

7.3.2.1.2 Upstairs: Boxplots

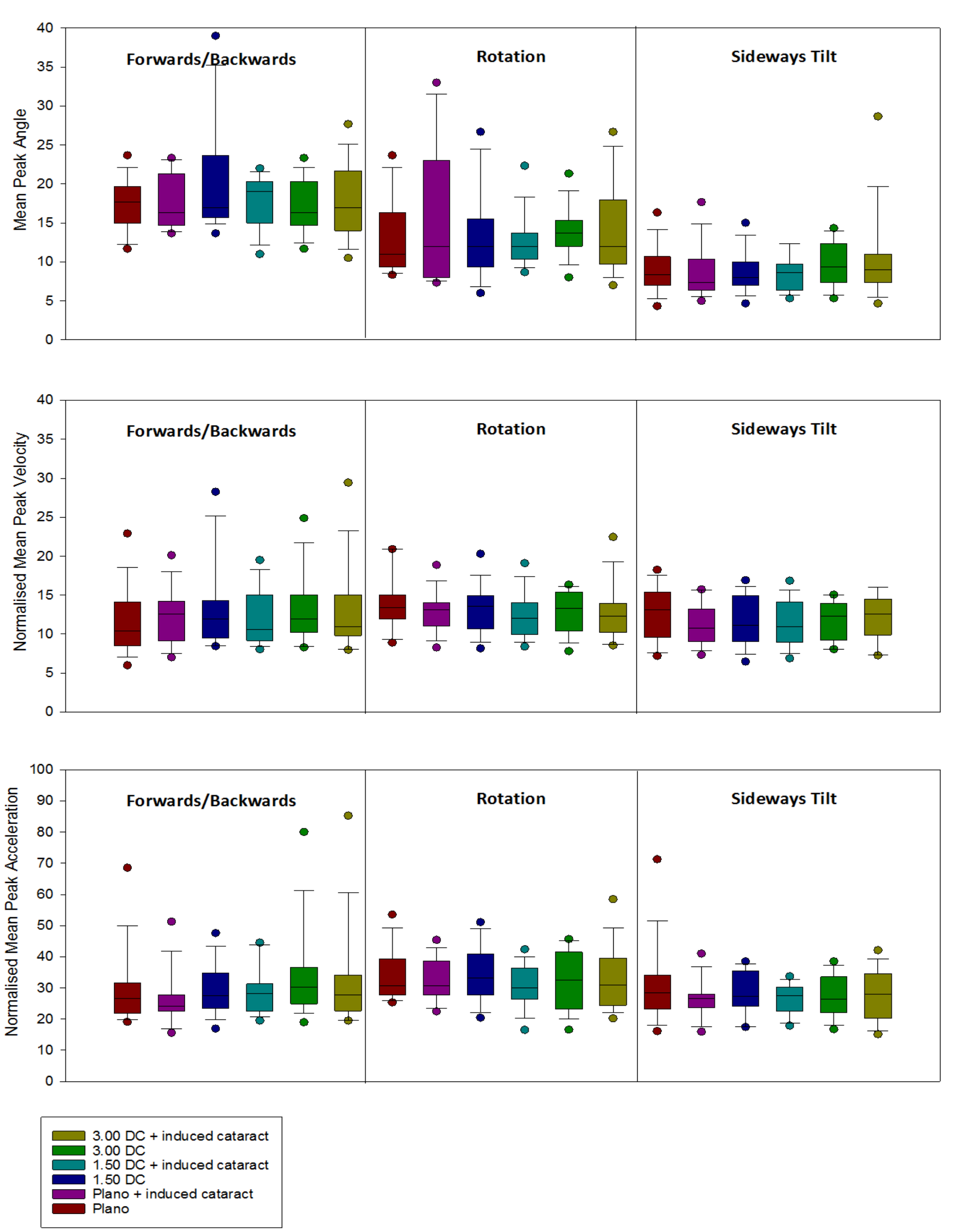

Figure 7.3: Boxplots for the COM mean peak angle, normalised mean peak velocity and acceleration when walking upstairs for all subjects.

7.3.2.1.3 Upstairs: Friedman's ANOVA

Upstairs				
Friedman ANOVA		Forward/ Backwards	Rotation	Side Tilt
Mean Peak Angle	X^2_6	4.603	2.249	37.03
	p	0.446	0.814	<0.001
Normalised Mean Peak Velocity	X^2_6	2.282	9.109	6.1
	p	0.809	0.105	0.297
Normalised Mean Peak Acceleration	X^2_6	8.212	8.981	5.019
	p	0.145	0.11	0.414

Table 7.5: Table displaying the X^2 and p values for the Friedman ANOVA tests for the upstairs task. Significant results highlighted.

7.3.2.1.4 Wilcoxon Paired Rank Testing

7.3.2.1.4.1 P values of the comparison of mean peak angle deviation: side tilt

Refractive Condition	Plano	Plano +induced cataract	1.50 DC	1.50 DC +induced cataract	3.00 DC	3.00 DC +induced cataract
Plano		0.277	0.551	0.344	0.315	0.470
Plano +induced cataract	0.277		0.820	0.694	0.172	0.093
1.50 DC	0.551	0.820		0.615	0.044	0.124
1.50 DC + induced cataract	0.344	0.694	0.615		0.108	0.463
3.00 DC	0.315	0.172	0.044	0.108		0.410
3.00 DC +induced cataract	0.470	0.093	0.124	0.463	0.410	

Table 7.6: p values for the comparison of the COM mean peak angle deviation - side tilt: paired comparisons, significant differences highlighted.

There were no significant differences found when the individual pairs were compared.

7.3.2.2 Downstairs

7.3.2.2.1 Downstairs: Medians, Upper and Lower Quartiles

Downstairs										
Refractive condition		**Forwards/ backwards**			**Rotation**			**Side Tilt**		
		M	LQ	UQ	**M**	LQ	UQ	**M**	LQ	UQ
Mean Peak Angle	**Plano**	**9.00**	6.67	11.83	**10.00**	8.50	12.67	**4.67**	3.67	6.67
	Plano +induced cataract	**9.00**	6.84	10.00	**11.17**	9.50	14.33	**5.00**	3.33	6.92
	1.50 DC	**8.00**	6.67	11.67	**8.84**	7.84	13.33	**4.33**	3.84	8.25
	1.50 DC + induced cataract	**8.33**	7.00	11.25	**10.00**	8.34	14.17	**4.67**	4.17	6.75
	3.00 DC	**6.67**	5.67	9.75	**9.67**	8.75	11.33	**11.00**	8.33	11.83
	3.00 DC +induced cataract	**8.67**	7.17	10.59	**11.67**	9.42	14.67	**6.00**	4.50	6.83
Normalised Mean Peak Velocity	**Plano**	**13.74**	11.02	16.90	**15.27**	12.05	16.99	**7.16**	6.48	9.19
	Plano +induced cataract	**13.74**	11.02	16.90	**15.27**	12.05	16.99	**7.16**	6.48	9.19
	1.50 DC	**15.17**	11.70	17.73	**15.20**	11.56	17.79	**9.01**	6.11	11.27
	1.50 DC + induced cataract	**14.21**	11.88	16.12	**14.14**	11.72	16.35	**7.09**	6.21	11.52
	3.00 DC	**14.72**	11.47	17.79	**14.45**	11.61	15.82	**8.15**	6.02	10.51
	3.00 DC +induced cataract	**13.45**	10.59	17.05	**13.41**	11.72	17.94	**7.84**	6.64	9.91
Normalised Mean Peak Accel	**Plano**	**40.87**	32.09	52.17	**34.11**	28.66	49.87	**20.25**	14.43	25.24
	Plano +induced cataract	**36.70**	31.94	40.92	**32.66**	26.52	43.44	**20.72**	15.70	21.54
	1.50 DC	**42.39**	33.18	45.63	**32.81**	29.27	41.63	**21.82**	15.93	24.64
	1.50 DC + induced cataract	**40.07**	34.05	44.82	**35.66**	25.96	39.76	**20.72**	15.79	25.87
	3.00 DC	**38.01**	31.85	44.51	**32.66**	29.44	39.85	**20.47**	16.05	25.87
	3.00 DC +induced cataract	**37.34**	29.54	44.55	**31.79**	29.69	34.95	**20.45**	18.51	22.33

Table 7.7: Median (M), upper (UQ) and lower (LQ) quartiles for the COM mean peak angle, velocity and acceleration during the downstairs task for all visual conditions.

7.3.2.2.2 Downstairs: Boxplots

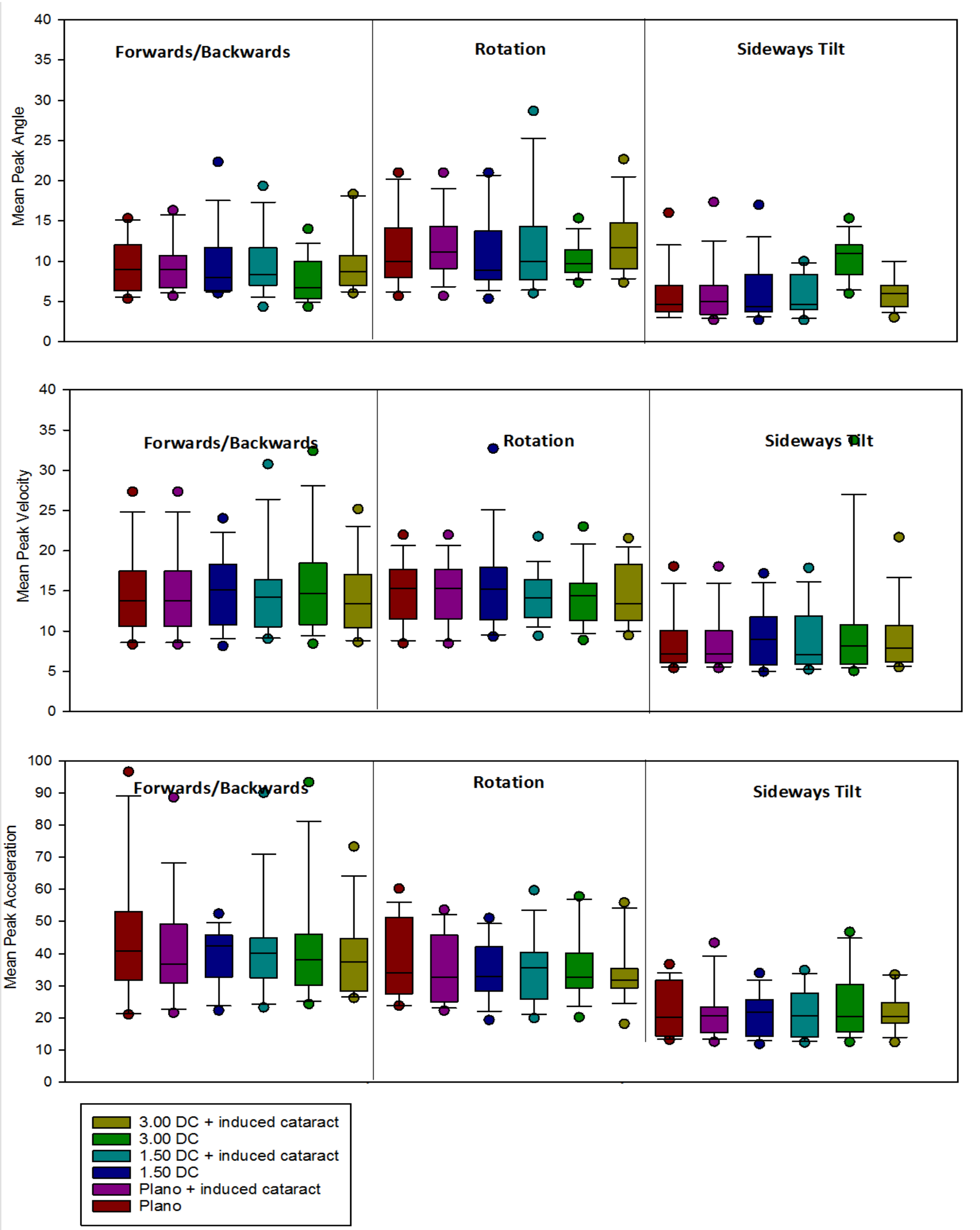

Figure 7.4: Boxplots for the COM mean peak angle, normalised velocity and acceleration when walking downstairs.

7.3.2.2.3 Friedman's ANOVA:

Downstairs				
Friedman ANOVA		Forward/ Backwards	Rotation	Side Tilt
Mean Peak Angle	X^2_6	15.069	4.153	24.15
	p	0.01	0.528	<0.001
Normalised Mean Peak Velocity	X^2_6	3.079	1.031	4.684
	p	0.688	0.96	0.456
Normalised Mean Peak Acceleration	X^2_6	2.048	2.309	2.619
	p	2.048	2.309	2.619

Table 7.8: Table displaying the X^2 and p values for the Friedman ANOVA tests for the downstairs task. Significant results highlighted.

7.3.2.2.4 Wilcoxon Paired Rank Testing

7.3.2.2.4.1 <u>P Values of the Comparison of Mean Peak Angle Deviation: Forwards/ Backwards</u>

Refractive Condition	**Plano**	**Plano +induced cataract**	**1.50 DC**	**1.50 DC +induced cataract**	**3.00 DC**	**3.00 DC +induced cataract**
Plano		0.53	0.158	0.421	0.649	0.484
Plano +induced cataract	0.53		0.08	0.73	0.235	0.666
1.50 DC	0.158	0.08		0.552	0.41	0.147
1.50 DC + induced cataract	0.421	0.73	0.552		0.177	0.826
3.00 DC	0.649	0.235	0.41	0.177		0.133
3.00 DC +induced cataract	0.484	0.666	0.147	0.826	0.133	

Table 7.9: P values for the comparison of the COM mean peak angle deviation - forwards/ backwards paired comparisons.

Although the Friedman's ANOVA test indicated that there were some significant differences (Table 7.11), there were no significant differences found in the paired comparisons. There is a difference in the median values of the *3.00 DC* group and the other visual conditions that may have caused the false positive result.

7.3.2.2.4.2 <u>P Values of the comparison of Mean Angle Deviation: Side Tilt</u>

Refractive Condition	Plano	Plano +induced cataract	1.50 DC	1.50 DC +induced cataract	3.00 DC	3.00 DC +induced cataract
Plano		0.649	0.600	0.916	0.002	0.413
Plano +induced cataract	0.649		0.470	0.477	0.002	0.278
1.50 DC	0.600	0.470		0.551	0.009	0.326
1.50 DC + induced cataract	0.916	0.477	0.551		0.001	0.637
3.00 DC	0.002	0.002	0.009	0.001		0.001
3.00 DC +induced cataract	0.413	0.278	0.326	0.637	0.001	

Table 7.10: P values for the comparison of the COM mean peak angle deviation - side tilt: paired comparisons, significant differences highlighted.

There were significant differences found between the *3.00 DC* and *all* visual conditions ($p<0.01$).

7.3.2.3 Obstacle Negotiation Task

7.3.2.3.1 Medians, Upper and Lower Quartiles

Obstacle Negotiation										
Refractive condition		**Forwards/ backwards**			**Rotation**			**Side Tilt**		
		M	**LQ**	**UQ**	**M**	**LQ**	**UQ**	**M**	**LQ**	**UQ**
Mean Peak Angle	**Plano**	**9.00**	6.67	11.83	**10.00**	8.50	12.67	**4.67**	3.67	6.67
	Plano +induced cataract	**9.00**	6.84	10.00	**11.17**	9.50	14.33	**5.00**	3.33	6.92
	1.50 DC	**8.00**	6.67	11.67	**8.84**	7.84	13.33	**4.33**	3.84	8.25
	1.50 DC + induced cataract	**8.33**	7.00	11.25	**10.00**	8.34	14.17	**4.67**	4.17	6.75
	3.00 DC	**6.67**	5.67	9.75	**9.67**	8.75	11.33	**11.00**	8.33	11.83
	3.00 DC +induced cataract	**8.67**	7.17	10.59	**11.67**	9.42	14.67	**6.00**	4.50	6.83
Normalised Mean Peak Velocity	**Plano**	**13.74**	11.02	16.90	**15.27**	12.05	16.99	**7.16**	6.48	9.19
	Plano +induced cataract	**13.74**	11.02	16.90	**15.27**	12.05	16.99	**7.16**	6.48	9.19
	1.50 DC	**15.17**	11.70	17.73	**15.20**	11.56	17.79	**9.01**	6.11	11.27
	1.50 DC + induced cataract	**14.21**	11.88	16.12	**14.14**	11.72	16.35	**7.09**	6.21	11.52
	3.00 DC	**14.72**	11.47	17.79	**14.45**	11.61	15.82	**8.15**	6.02	10.51
	3.00 DC +induced cataract	**13.45**	10.59	17.05	**13.41**	11.72	17.94	**7.84**	6.64	9.91
Normalised Mean Peak Accel	**Plano**	**40.87**	32.09	52.17	**34.11**	28.66	49.87	**20.25**	14.43	25.24
	Plano +induced cataract	**36.70**	31.94	40.92	**32.66**	26.52	43.44	**20.72**	15.70	21.54
	1.50 DC	**42.39**	33.18	45.63	**32.81**	29.27	41.63	**21.82**	15.93	24.64
	1.50 DC + induced cataract	**40.07**	34.05	44.82	**35.66**	25.96	39.76	**20.72**	15.79	25.87
	3.00 DC	**38.01**	31.85	44.51	**32.66**	29.44	39.85	**20.47**	16.05	25.87
	3.00 DC +induced cataract	**37.34**	29.54	44.55	**31.79**	29.69	34.95	**20.45**	18.51	22.33

Table 7.11: Median (M), upper (UQ) and lower (LQ) quartiles for the COM mean peak angle, velocity and acceleration during the downstairs task for all visual conditions.

7.3.2.3.2 Obstacle Negotiation: Boxplots

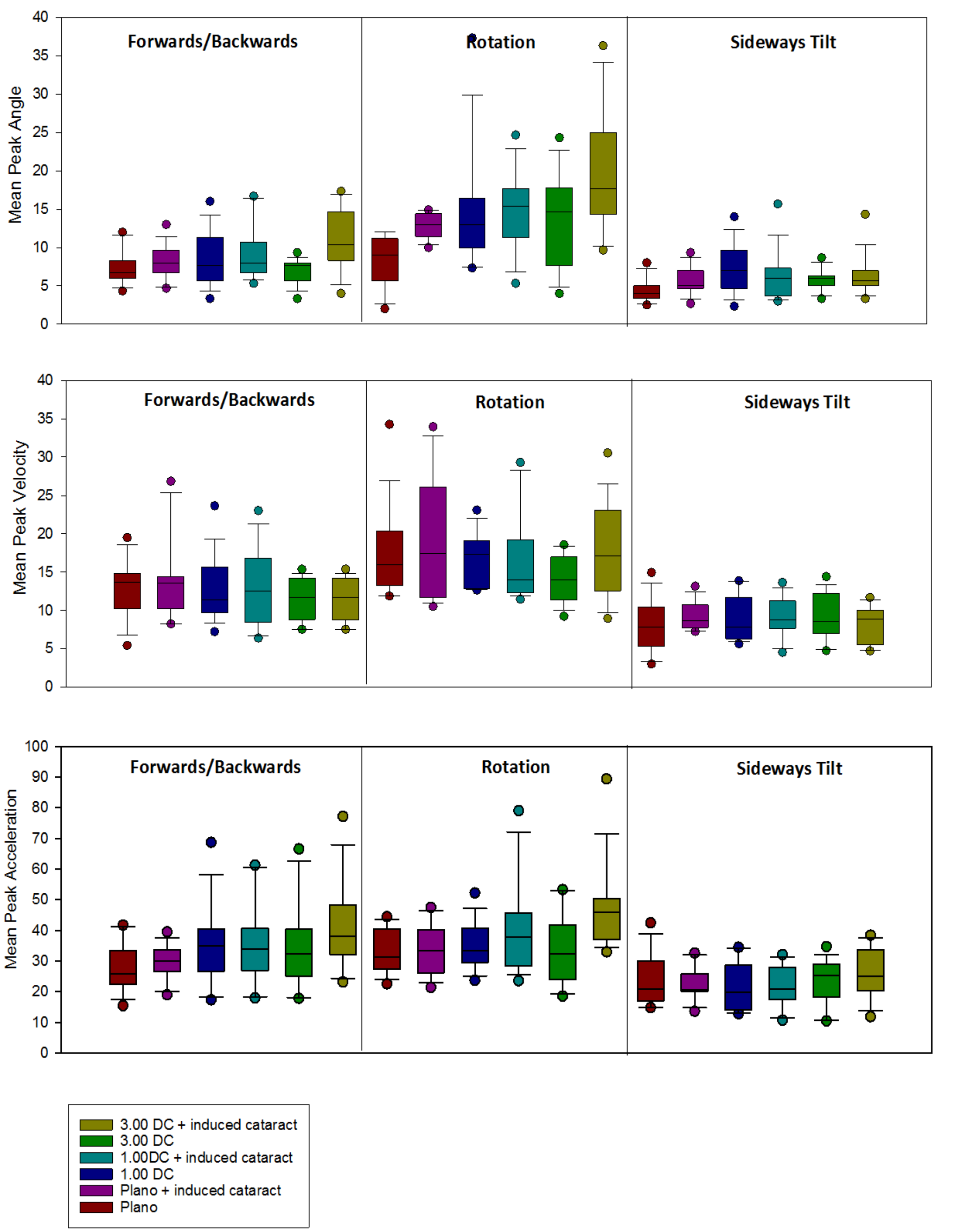

Figure 7.5: Boxplots for the COM mean peak angle, normalised velocity and acceleration during obstacle negotiation.

7.3.2.4 Friedman's ANOVA: Obstacle Negotiation

Obstacles				
Friedman ANOVA		Forwards/ Backwards	Rotation	Side Tilt
Mean Peak Angle	X^2_6	16.456	9.694	12.574
	p	0.006	0.084	0.028
Normalised Mean Peak Velocity	X^2_6	8.539	6.24	3.873
	p	0.138	0.284	0.568
Normalised Mean Peak Acceleration	X^2_6	17.745	33.697	5.897
	p	0.003	<0.001	0.316

Table 7.12: Table displaying the X^2 and p values for the Friedman ANOVA tests for the upstairs task.

7.3.2.4.1 Wilcoxon Paired Rank Tests

7.3.2.4.1.1 P Values of the Comparison of Mean Peak Angle Deviation: Forwards/ Backwards (Obstacle Negotiation)

Refractive Condition	**Plano**	**Plano +induced cataract**	**1.50 DC**	**1.50 DC +induced cataract**	**3.00 DC**	**3.00 DC +induced cataract**
Plano		0.401	0.280	0.012	0.490	0.004
Plano +induced cataract	0.401		0.972	0.460	0.209	0.043
1.50 DC	0.280	0.972		0.320	0.142	0.023
1.50 DC + induced cataract	0.012	0.460	0.320		0.015	0.077
3.00 DC	0.490	0.209	0.142	0.015		0.002
3.00 DC +induced cataract	0.004	0.043	0.023	0.077	0.002	-

Table 7.13: P values for the comparison of the COM mean peak angle deviation (forwards/ backwards) paired comparisons, significant differences highlighted.

There was a significant difference found between the *Plano* and *3.00 DC + induced cataract* conditions (p= 0.004). There was also a difference between the two *3CD* conditions, *with* and *without the cataract* (p= 0.002).

7.3.2.4.1.2 P Values of the Comparison of Mean Peak Angle Deviation: Side Tilt (Obstacle Negotiation)

Refractive Condition	Plano	Plano +induced cataract	1.50 DC	1.50 DC +induced cataract	3.00 DC	3.00 DC +induced cataract
Plano		0.025	0.006	0.039	0.007	0.041
Plano +induced cataract	0.025		0.105	0.972	0.629	0.382
1.50 DC	0.006	0.105		0.197	0.140	0.088
1.50 DC + induced cataract	0.039	0.972	0.197		0.753	0.842
3.00 DC	0.007	0.629	0.140	0.753		0.826
3.00 DC +induced cataract	0.041	0.382	0.088	0.842	0.826	

Table 7.14: P values for the comparison of the COM mean peak angle deviation (side tilt) paired comparisons, significant differences highlighted.

There was a difference found between the *Plano* condition and both the *1.50 DC* and *3.00 DC* conditions (p= 0.006 and 0.007 respectively).

7.3.2.4.1.3 P Values of the Comparison of Mean Peak Acceleration Deviation: Forwards/Backwards (Obstacle Negotiation)

Refractive Condition	Plano	Plano +induced cataract	1.50 DC	1.50 DC +induced cataract	3.00 DC	3.00 DC +induced cataract
Plano		0.112	0.031	0.047	0.069	0.001
Plano +induced cataract	0.112		0.078	0.1400	0.211	0.003
1.50 DC	0.031	0.078		1.000	0.91	0.036
1.50 DC + induced cataract	0.047	0.140	1.000		0.955	0.099
3.00 DC	0.069	0.211	0.910	0.955		0.027
3.00 DC +induced cataract	0.001	0.003	0.036	0.099	0.027	

Table 7.15: P values for the comparison of the COM mean peak acceleration deviation (forwards/ backwards) paired comparisons, significant differences highlighted.

There was a significant difference found between the *3.00 DC + induced cataract* and *both Plano* conditions (Plano: p=0.001, Plano with cataracts p= 0.003).

7.3.2.4.1.4 P Values of the Comparison of Mean Peak Acceleration Deviation: Rotational (Obstacle Negotiation)

Refractive Condition	Plano	Plano +induced cataract	1.50 DC	1.50 DC +induced cataract	3.00 DC	3.00 DC +induced cataract
Plano		0.609	0.532	0.069	0.865	0.001
Plano +induced cataract	0.609		0.551	0.036	0.91	0.001
1.50 DC	0.532	0.551		0.069	0.691	0.001
1.50 DC + induced cataract	0.069	0.036	0.069		0.047	0.011
3.00 DC	0.865	0.91	0.691	0.047		0.001
3.00 DC +induced cataract	0.001	0.001	0.001	0.011	0.001	

Table 7.16: P values for the comparison of the COM mean peak acceleration deviation (rotational) paired comparisons, significant differences highlighted.

There was a difference between the *3.00 DC + induced cataract* and *all* other visual conditions (p<0.01) apart from *1.50 DC + induced cataract* (p=0.011).

7.4 Discussion

This study was designed to investigate the effect that uncorrected astigmatism with and without cataracts had on three balance and mobility tasks: standing balance, walking up or downstairs and negotiating an obstacle while walking along a path. Vision plays a key role in our ability to navigate and traverse the world around us but is not the only source of information processed to allow stable gait and mobility with other sources of information coming from the somatosensory and vestibular systems and motor efference copy (Nashner et al. 1982; Patla 1997; Patla 1998). Cataracts reduce both vision and contrast sensitivity and have been postulated to decrease stability and increase risk of falling (Brannan et al. 2003; Schwartz et al. 2005; Tseng et al. 2012). However, other research studies using questionnaires to document the incidence of falling before and after surgery havw not found any significant relationship between the two (McGwin Jr et al. 2006; Supuk et al. 2013). NHS cataract surgeries use only spherical IOLs leaving uncorrected astigmatism after the surgery. Therefore, patients with pre-existing corneal astigmatism before surgery are left with poorer uncorrected vision after the procedure. Uncorrected astigmatism has been shown to reduce visual acuity (Wolffsohn et al. 2011; Kobashi et al. 2012).

7.4.1 Repeatability

As this technique was a novel method for testing these visual changes, the ICC was used to assess the reliability of the results. The $ICC_{3\,3}$ (Table 7.1) for median JERK measured during the postural standing task was high, ranging from 0.967-0.995 with the six visual conditions. The method of testing was shown to be repeatable and results reliable. This is in agreement with the work of Mancini et al (2012) who used this method to determine changes in standing balance for people with early Parkinson's disease (Mancini et al. 2011; Mancini et al. 2012).

The mean peak angle, velocity and acceleration displacement of COM measured during the stairs tasks showed a larger variation in repeatability (Table 7.2). The ICC for angle displacement for all three directions was higher for the least blurred vision (0.685-0.845 for up and 0.793-0.928 for downstairs). The ICC was much lower when using the highest level of astigmatism (0.162-0.560 for up and 0.672 – 0.933 for downstairs). The blurring of the vision may have decreased the repeatability of the tasks due to change in the visual information. Although there was some indication that the adaptation time may increase with blurring of the vision, there was no ordered effect seen in the results. The ICC for velocity displacement was generally much higher, ranging 0.414 – 0.947 for upstairs and 0.600 – 0.950 for downstairs. The range for acceleration deviation was 0.581 – 0.961 for up and 0.663 – 0.936 for downstairs. The low numbers in the study may have contributed to the variations in the ICC for the task. This is a novel technique, as other work has not been done over the same range of steps with this system.

The obstacle negotiation task also had good repeatability. The ICC for angle deviation ranged from 0.791- 0.980. The range for mean velocity deviation was 0.767 – 0.980 and the acceleration deviation were 0.657- 0.971.

The high repeatability in this task suggests that the results produced are reliable and repeatable

7.4.2 Standing

This study was designed to investigate the effect that uncorrected astigmatism with and without cataracts had on standing balance (Nashner et al. 1982; 1997; Patla 1998; Brannan et al. 2003; Schwartz et al. 2005; McGwin Jr et al. 2006; Wolffsohn et al. 2011; Kobashi et al. 2012; Tseng et al. 2012; Supuk et al. 2013). As this technique was a novel method for testing these visual changes, the ICC was used to assess the reliability of the results. The $ICC_{(3,3)}$ (Table 7.1) for mean JERK measured during the postural standing task was high, ranging from 0.967-0.995 with the six visual conditions. The method of testing was shown to be repeatable and the results reliable. This is in agreement with the work of Mancini et al (2011, 2012) who used this method to determine changes in standing balance for people with early Parkinson's disease (Mancini et al. 2011; Mancini et al. 2012).

The median JERK score was found to be highest in the trials where the subjects were fully corrected with induced cataracts (*Plano + induced cataract*) (Table 7.3). Therefore, the subjects appeared to be least stable with loss of contrast caused by the simulated cataracts. This is in agreement with Schwartz et al (2005) who found that cataracts reduced standing balance in patients despite wearing their best refractive correction (Schwartz et al. 2005). Brannan et al and Tseng et al both found that earlier cataract removal reduced the incidence of falling, agreeing that impaired vision caused by the cataracts can contribute to falling (Brannan et al. 2003; Tseng et al. 2012).

Conversely, to this, the higher astigmatism trials found different results. The lowest median JERK scores were in the 'high astigmatism (*3.00 DC*) trial' which was found to be significantly different ($p < 0.05$, Table 7.2) and the 'high astigmatism mixed with cataracts (3.00 DC + induced cataracts) trial', which was not significantly different from the *fully corrected* (Plano) trial ($p=0.056$). This indicates that the subjects were more stable with most astigmatic blur and loss of contrast. As previous work has highlighted the importance of vision in standing balance (Fitzpatrick et al. 1994; Bunn et al. 2015) and indicated that reduced or impaired vision is likely to decrease standing balance (Anand et al. 2002; Schwartz et al. 2005; Tomomitsu et al. 2013), the results of this study contradicted this.

In this study, the subjects were found to be more stable in the visual state with most astigmatic blur and loss of contrast. It has been shown that there is a linear relationship between body sway and a moving stimulus e.g. wall of the room. Subjects tend to move in the direction of the movement (Bronstein 1986; Day 2002; Guerraz et al. 2008). The influence of the sideways moving target (used in this study) may have reduced due to the increase of the blurred vision as it downweighs the information provided by the vision. Therefore, it could be inferred that the blurring of the spatial frequency target, reduced its effect on standing balance. In addition to this, the input of vision in balance, in combination with the vestibular system and proprioceptor signals is a phenomenon that is not entirely understood (Guerraz et al. 2008). If a threshold is reached in the healthy population where vision is deemed unreliable then perhaps sensory weighting takes place to either down-weight vision or up-weight the remaining intact and 'reliable' sensory systems (Nashner et al. 1982; McCollum et al. 1996). This means that the brain may have responded to the increased blurred vision caused by high astigmatism (both groups: 3.00DC and 3.00DC + induced cataracts) by decreasing the importance of the information provided by the eyes. If the vision input is less important then the influence will be less, reducing the sway induced by the target. Lastly, the spatial frequency targets will have been seen less clearly with increased form deprivation and distortion.

The results of this study raised another possibility that there may be some conditions in which balance is less impaired in people with poor vision (Baker et al. 2007; Kotecha et al. 2013). Visual perturbations in daily activities such as standing in front of moving traffic (rather than tasks that require visual information for accurate completion such as stair climbing and obstacle avoidance) may induce less disruption of balance in people with poor visual acuity simply because they are unable to see the visual stimulus as accurately and therefore it has less effect on balance. The lines of the screen being less distinct may have simply reduced the influence of the visual stimulus.

The most common cause of falls is incorrect weight shift and tripping over an obstacle (Robinovitch et al. 2013). Standing balance assessment may not be a challenging enough task as it does not detect the effect of astigmatic distortion on dynamic balance where there a significant weight shifting during activities of daily living.

7.4.3 Up and downstairs

There was a significant difference found in mean peak side tilting angle when walking downstairs (Table 7.9). The mean peak angle was different with *high astigmatism* (3.00 DC) compared to all visual conditions. The median and quartile angle range (11.00°, IQR 8.33, 12.00°) is almost double that of the other median and quartile peak angles measured under the other visual conditions (4.67-6.00°, IQR 3.33-4.33, 7.00-8.33°). During the study, subjects did note that taking the first step down was difficult to judge in this state. Anticipation may have caused some of the hesitation or perceived difficulty with this part of the task. Reynolds et al (2003) demonstrated this with a broken escalator experiment that showed that learned behaviours and expected changes can alter out foot placement and balance with simple tasks (such as stepping on a broken escalator) (Reynolds et al. 2003). Changes in astigmatism have also previously been shown to all have contributed to changes in foot placement when stepping up or down (Johnson et al. 2013).

Additionally the initial Friedman ANOVA test indicated a difference in the forwards bending (positive change) for downstairs but, further analysis with paired testing found no significant differences (Table 7.9). There were also no significant differences found between the mean peak angle (Tables 7.5-7.7), velocity (Tables 7.9 – 7.11) and acceleration (Tables 7.13 – 7.15) deviations in different visual conditions for any direction of movement when the subject walked up a short flight of stairs. The medians and quartiles were also similar for all visual conditions. There was also no significant difference found in the mean peak velocity (Tables 7.23 – 7.25) or acceleration (Tables 7.27 – 7.29) when walking downstairs in any direction of movement. Likewise, there was no difference found for rotational peak angle when moving downstairs. In this case the median peak angle is much lower for the high astigmatism (3.00 DC) condition but the quartiles are similar to the other visual states so has little consequence.

With only one change indicated among the whole data set, it suggests that the blurring from both the cataract and astigmatism (or a combination of the two) had little affect on the ability to walk up the stairs, they did not sway or lose their balance in any of the three directions overall. The *high astigmatism* (3.00 DC) did alter side tilt angle movement going downstairs indicated by a slightly larger peak in sideways movement by the participants on this task.

Walking up and downstairs is a routine task that most people carry out without incident on a daily basis. When looking at an older population, Nevitt found that 20% of falls reported occurred when walking up or downstairs (Nevitt et al. 1991).

Falls on stairs are a significant proportion of accidental deaths in older adults (Startzell et al. 2000). However, the contribution of vision to walking up and downstairs is complex. It has been found that once a person has walked up one or two steps, muscle memory will ensure that the leg will create the appropriate foot clearance required (Shinya et al. 2012). This may be the reason why most accidents occur either at the first or last step or when step heights are variable (Templer 1992). It can be inferred that the first and last steps require more visual input. The first step is the one requires the visual information to help establish foot clearance (Shinya et al. 2012) and vision input is required to determine stopping to changing the locomotion (Patla 1997). Given the importance of vision at the beginning and end of stair descent it may be instructive in future to analyse these components separately from "steady sate" stair descent as previously shown with the broken escalator phenomenon (Reynolds et al. 2003).

Previous work looking at vision and stairs has concentrated on the foot placement and clearance of an individual as a measure of how the vision is influencing the ability to traverse the stairs. Changes in astigmatism and spectacle magnification have all contributed to changes in foot placement when stepping up or down (Elliott et al. 2010; Johnson et al. 2013). A key part of climbing or descending stairs is edge detection; the stairs used in this project are the stair design commonly encountered in daily life in public buildings, which had a contrast strip adjacent to the edge. The placement of the high contrast strip could alter the foot placement of subjects with reduced contrast sensitivity caused by cataracts when walking downstairs, and that the safest place to put the strip was at the edge of the step

(Foster et al. 2014). The set of stairs used in this study had clear edges that were clearly marked and easy to detect. Most homes do not have high contrast strips and this can increase the difficulty in edge detection and change the foot placement. Foster et al (2014) also found that when the subjects were walking down plain steps without any contrast strip, they were more likely to scuff their heels or reduce foot clearance to less than 5 mm. Stairs in homes that do not have high contrast strips may present a more challenging task and increased risk of falling or loss of balance. However the presence of the handrail as an additional safety feature also reduce the incidence of falling especially in a geriatric population (Maki et al. 2008) Future work could assess this task in the home environment with carpeted stairs that affect somatosensory feedback and different patterned carpets that affect visual information.

7.4.4 Obstacle Negotiation

The results from the obstacle task were different to the stairs and standing balance tasks. Some significant differences of mean peak angle were found between the parings of visual conditions in the forwards movement (seen in the positive number) and side tilt angle deviation (Table 7.13). Additionally there was also a difference seen in the mean peak acceleration in the forwards and rotational directions (Table 7.12) The *high astigmatism with cataracts* (3.00 DC + induced cataracts) group saw an increase in forwards bending acceleration compared to both the *fully corrected (*Plano*)* and the *high astigmatism (3.00 DC)* group (Table

7.14). This increased forward bending acceleration of the centre of mass may due to the task requirement of stepping over the obstacle, which is a forwards motion, not sideways (as would be seen in moving around an object), which would be more likely to alter the rotation or side tilt.

The mean peak side tilt angle of the COM for both *moderate* and *high* levels of astigmatism (1.50 DC and 3.00 DC) were significantly different ($p < 0.01$) from the *fully corrected* (Plano) condition (Table 7.15), again this is an indication that the astigmatism is altering stability when avoiding the obstacle. There was no difference was found for the rotation peak angle (Table 7.13). This result is a less obvious change, as there is no change in rotation. It is likely that changes to side tilt would be accompanied by changes in rotation. As it is known that tripping over an object was one of the most common causes of falls in the elderly (Robinovitch et al. 2013), it could be inferred that the vision may play a significant role in this. When stepping over or avoiding an object, humans typically fixate on a required landing target and plan the steps over obstacle two-steps ahead (Patla 2003; Buckley et al. 2011). If from the distance of two steps away, the astigmatism is distorting the position of the object, then the difficulty in stepping over will increase and an error in the choice of stable movements can occur.

In the analysis of the acceleration peak deviations, there were also some significant differences found. In the forward/backwards direction, there was a significant peak difference between the both *fully corrected conditions, with and without cataracts* (Plano and Plano + induced cataracts) and the both the *high astigmatism* *with cataracts* and *without cataracts* (3.00 DC and 3.00 DC + induced cataracts) groups (Table 7.16). The median and quartiles for the *high astigmatism* conditions (32.47-38.18) are up to 25% higher than the fully corrected (Plano) conditions (28.88-29.88). This indicates that the change in astigmatism is causing the patient to greatly increase their forward body sway (indicating poorer balance) or to suddenly alter their speed to adjust their balance in the task. This result is similar to that seen in the mean peak angle. Forwards movement and motion will rely on optical looming that shows objects getting bigger on the retina relative the to decreasing distance we are from it, as a way of avoiding oncoming obstacles (Schiff et al. 1962). A significant difference was also found for rotational direction (Table 7.17), with a difference between the *high astigmatism with cataracts* (3.00 DC + induced cataracts) and all conditions apart from *moderate astigmatism with cataracts* (1.50 DC + induced astigmatism). Again, this result is less conclusive with the absence of changes in side tilt. We would expect to see changes to both directions as the same source of information is used. Rotation and side tilting of the COM will be influenced by visual flow, which is the processing of the moving and changing positions of objects around us, this is used to alter speeds and directions (Mohler et al. 2007). The mixture of the cataracts and astigmatism is again shown to cause significant problems in properly detecting the object and stepping over it without any changes to balance or body sway easily in this task. The changes in vision were obviously problematic enough to alter the planning of the step. None of our subjects fell or tripped but while wearing the highest astigmatism and cataracts, the obstacle task may have required more careful planning, hence the changes in angle position and acceleration.

This was the first study to examine the COM during obstacle negotiation. The largely high reported ICC (state level here e.g. >0.8) indicated good reliability; allowing us to draw conclusions from the results gained in the study.

The main limitation of this study was in the use of relatively young healthy participants and the small sample size for the pilot work. These results were gained using healthy individuals who were younger than the target elderly, pre- and post-cataract population. It is likely that the changes we saw would be amplified in older individuals with less balance and stability due to other co-morbidities and age. A larger and older subject group would provide much more powerful and meaningful results. Assessing the peak of each variable does risk measuring an artefact or freak change, the high ICC scores indicate a good repeatability of this measure. However, this is a measure commonly used in the analysis of balance with Lord et al often reporting on peak sway using this method (Lord et al. 2007). People without balance impairments rarely have large freak changes, so this assessment may be deemed unrealistic.. Further, the task conditions were laboratory based. Despite providing a standardised method for this initial exploration, more marked differences may be seen in the home environment with natural obstacles outside where there are more distracting visual cues (Brodie et al. 2015; Brodie et al. 2015). In addition to this, dual-taking studies have shown that additional vision and auditory stimulus that require a response during both postural balance and locomotion tasks can cause of the required actions (the response or balance/locomotion) to be slowed (due to down-weighting) or impaired e.g. a slower reaction time to a stimulus or poorer balance (Baker et al. 2007; Siu et al. 2008).

There was a significant limitation in the design of the study, as it did not allow for the subjects to adapt to the induced astigmatism. In a post-cataract population, those with uncorrected astigmatism will have adapted to their new refractive error and the blur to some degree. However, in adults can take a significant amount time (Guyton 1977) e.g. over days or weeks, which could not be replicated in the lab. In addition to this, the distortion and magnification issues associated with induced astigmatism are due to spectacle lenses. This was avoided by using contact lenses, placing the correction on the cornea (Guyton 1977). Previous work investigating the adaptation and reduction in visual acuity due to astigmatism found that the effect varied greatly depending upon the pre-existing astigmatism, the orientation of the existing astigmatism in relation to the induced direction and most importantly on the higher order aberrations (HOAs). If the HOAs were not corrected, then the disparity between pre-existing astigmatics and non-astigmatics disappeared (Vinas et al. 2013). Again this could not be controlled in this experiment and the population seen at the hospital would have a range in refractive errors.

7.5 Conclusions

The obstacle negotiation task showed excellent sensitivity to changes in vision with a resulting impact on balance during the task e.g. as vision is increasingly impaired with the addition of astigmatic distortion and form deprivation, balance measures indicate increasing levels of impairment. It is a more challenging (and realistic) test for the subject and indicated more significant and useful results. There was a clear change in forward leaning when attempting to step over the obstacle

Subjects with simulated induced cataract and/or low levels of uncorrected astigmatism demonstrated poorer balance during standing balance with a moving visual stimulus. This is in agreement with previous studies. However, when the refractive blur was increased to high levels of astigmatism, the subjects were less affected when compared to the trial with fully corrected vision. It can be postulated that increased refractive blurring, reduced the influence of the visual stimulus, showing 'down-weighting' of visual information.

The standing balance with the moving stimulus may overestimate the balance in people with poorer vision due to refractive error such as high astigmatism. Future studies should look at the effect of refractive error and cataracts on the dynamic balance of activities with significant weight shifting when a fall is more likely to occur (Robinovitch et al. 2013).

The method of assessing the subjects walking up and down stairs and their standing balance were not found to be as successful for detecting changes due to form deprivation and loss of contrast. Falls from a standing position are unusual.. The use of the JERK score has been shown to be successful for neurological conditions but was not so for these visual changes. The stairs task used is also not challenging enough. A patient with blurred vision due to cataract or uncorrected astigmatism (or both) may not notice balance problems when walking up or downstairs. However, differences were seen in stair descent and these may be more marked if analysis concentrated on the first and last steps.

The loss of contrast sensitivity and form deprivation does have an effect on stability during obstacle negotiation. The removal of cataracts could increase the stability and balance for a patient post-surgically. Additionally the choice of correction given during the surgery is also important. If the astigmatism is left uncorrected, the form deprivation also affects the stability. A study following astigmatism cataract patients should be carried out to determine the effect further. Lastly, these novel techniques for assessing the effect of vision on mobility warrants further investigation and could also be applied to other causes of reduced vision.

Chapter 8 Summary and Conclusion

8.1 Summary

Modern day cataract surgery techniques have evolved over a continuous process of development and refinement over the last century, not least by the efforts of Sir Harold Ridley, the pioneer of IOL implantation (as discussed in Chapter 1). Cataract surgery is now considered a routine operation and an expected treatment required for much of the elderly population. The surgery no longer concentrates simply in the removal of the cateractous lens. It has now improved to such an extent that it has evolved into an opportunity to correct the refractive vision. In order to provide a full correction of refractive error, the surgery must also address corneal astigmatism present in ~20% of the population. Uncorrected astigmatism after cataract surgery can potentially lead to poorer balance and mobility. Toric IOLs provide this opportunity but in order to provide the best correction, these require a much more precise measurement of the corneal power and understanding of surgical induced shape change that can occur as a result of surgery. Hitherto, the surgeon has used a combination of a modern day keratometer reading, a vector calculation of the surgeon specific incision based surgically induced astigmatism (SIA) in a toric IOL calculators (also utilising vector methods) to predict the post-operative shape and guide the surgery. However, this process has many sources of error that could reduce the effectivity of the correction provided by the surgery.

8.2 Comparison of Reliability and Repeatability of Corneal Curvature Assessment with Six Keratometers

Accurate assessment of corneal astigmatism is imperative for implantation of toric IOLs and any errors in the results could impact on the effectiveness of the correction provide by the lens. The study aimed to investigate the repeatability and agreement in the measurement of corneal astigmatism by different commercially available devices. The results in chapter 2 showed that the keratometers measure the mean spherical equivalent (MSE) accurately, with a high repeatability and have reasonably good agreement. This is appropriate for the implantation of spherical IOLs. Yet, when the corneal astigmatism measurement was assessed with vector analysis, the repeatability and comparability of the results was much poorer. The IOLMaster and Pentacam performed best out of the 6 instruments and had the best agreement of results but again the repeatability was much lower when assessing corneal astigmatism than the MSE readings. It can be postulated that this level of error could potentially lead to errors in the implantation of toric IOLs.

8.3 Calculation of Surgically Induced Astigmatism

Keratometry instruments have been shown to have a significant margin of error but the readings are used to determine SIA without any consideration of this error. The aim of chapter 3 was to investigate the impact that instrument error would have on the calculated SIA result. The instrument error was referred to as a *'Pseudo-SIA'*. The SIA can be calculated using various methods developed over the years but the most commonly used are the Cartesian vector method and the polar method. Overall, it was found that instrument error between readings could contribute significantly to the SIA, causing pseudo-SIA. This results in an overestimation of the shape change actually occurring. Use of the Cartesian vector method found much higher levels of pseudo-SIA than the Polar method. The instrument error leads to overestimation of the change in shape occurring due to the incision. The results of chapters 2, 5 and 6, lead to the inference that most of this will be caused by poor repeatability of the readings. Changes in axis have a much bigger influence on the Cartesian vector results and cause a much larger resultant SIA. In the case of the Pentacam, the instrument error led to ~50% increase in the reported SIA. The instrument error was much smaller when measured with the Polar method. This is mainly due to the fact the calculation takes into account the axis position. If surgeons intend to continue using this method to assess the surgery, the instrument error must be calculated and taken into account. This will allow a more realistic value of change to be produced in the calculations.

8.4 Keratometric Measurement of Corneal Steepest Meridian Orientation after Cataract Surgery

If an incision is placed 'off-axis' when implanting toric IOLs, this can potentially lead to a change in post-operative corneal astigmatism orientation. Toric calculators were established to predict the post-operative corneal shape and advise on the best choice of lens power and axis orientation with which the lens should be aligned. Hitherto, the validity of these calculations has not been established. The study in chapter 4 was designed to investigate the validity of the toric IOL calculator predictions of corneal shape change induced by surgical incisions and determine the effectiveness of the IOL power and position that would be advised. It was found that the corneas did not re-act to the incision in a uniform and predictable manner. The post-operative change in steepest meridian position varied greatly and was significantly different from the predicted results. The results also showed that the steepest meridian position could move both towards and away from the incision.

The findings in this study suggest that the oblique cross cylinder formula is not valid for predicting the corneal response to an incision. When an incision is placed away from the steepest corneal meridian, use of the toric calculator was not shown to increase the effectivity of the correction in comparison to ignoring the calculator. Alternatively, if the surgeon carried out the incision 'on-axis' then there is no reason for an oblique change in the position to occur. These results are not are in agreement with chapter 3 that demonstrated that the Cartesian descriptor of SIA as magnitude alone is a poor representation of corneal change.

8.5 The Relationship between Subjective Refraction and Corneal Power Measurements in a Pseudophakic Population.

Keratometry has been shown to have errors (chapter 2) and the vector assessment masks whether the magnitude, axis or both elements of the reading are erroneous. The study in chapter 5 aimed to assess the accuracy of keratometry instruments when measuring the magnitude of corneal astigmatism utilising the various methodologies available: autokeratometry (IOLMaster), topography (OPD scan), tomography (Pentacam) and subject analysis of topographical maps. It found poor agreement between all methods of keratometry and the manifest refraction results for magnitude of astigmatism. The instruments often underestimated the magnitude of astigmatism but not with a systematic error. Previously, refractive astigmatism has been wholly attributed to the cornea and inaccuracies have been postulated to be due to an inappropriate keratometry index, neglecting the posterior cornea or measuring only a small central area. Conversely to this, these results found that the IOLMaster (with the small chord size) had the strongest linear relationship with refraction. However, the Pentacam total corneal refractive power reading with the 2mm chord data was most similar to the refraction. This indicates that paraxial not peripheral rays are responsible for the refraction so the instruments using a small central area will have a closer relationship with the refraction result. It also emphasises the importance of taking both surfaces of the cornea and the thickness into account when calculating the corneal power. Nonetheless, there was high degree of variability and a lot of outliers in the comparison of the total refractive power data and the refraction. This indicated that the small chord length was very sensitive to misalignment, leading to significant inaccuracies. Each incidence of poor agreement is a potential error in the choice of toric IOL power and reduction of the effective correction provided by the lens.

8.6 Measurement of the Steepest Meridian Axis of Corneal Astigmatism

Determining the orientation of the steepest meridian position (axis) is a vital element of the pre-surgical assessment. In chapter 6, the study aimed to assess the accuracy of axis readings produced by the same keratometry methodologies assessed in chapter 5. There was a large disagreement between the axis readings produced by all keratometry methods versus the manifest refraction. The agreement was very poor across the data groups, even when the high astigmatism was isolated. This study found that the majority (~75%, demonstrated by the quartiles) of readings taken showed a disagreement compared to manifest refraction that was outside a clinically acceptable level of 5°. Additionally a large percentage of the differences (~25% in some instances) were actually above 30°, which would lead to an increase of existing uncorrected astigmatism. The axis rotation has a much more significant impact on the effective correction than an error in the magnitude of astigmatism magnitude. Furthermore, the measurement of axis has now also been shown to have a greater margin of error than the magnitude of astigmatism. Therefore, the likelihood of an inaccurate pre-surgical assessment and resultant misalignment appears to be very high.

8.7 The Effect of Loss of Contrast and Form Deprivation on Vision and Mobility tasks

The thesis has stated many limitations in accuracy of toric IOL implantation but not correcting the astigmatism during cataract surgery, leaves the patient with reduced vision. The aim of this study was to investigate the effect form deprivation caused by uncorrected astigmatism and loss of contrast (due to cataracts) has on standing balance and balance during routine mobility tasks. This was carried out with a novel measurement technique. Simulated uncorrected astigmatism and cataracts were both found to alter the balance of the patient during obstacle negotiation when walking on a low contrast surface. In an older population when balance has been reduced by a combination of age and other co-morbidities, these results may be magnified. The study has helped determine which tasks this type of vision loss affected. Standing balance is an indication of balance of an individual but the importance of vision used for this task compared to obstacle avoidance or climbing stairs varies. It has often been used as the indicator of falls with other changes including cataract or neurological conditions. However, in the case of standing balance, although there was some reduction in balance due to cataracts and low astigmatism but this effect was not seen with high astigmatism. Despite this the changes seen with obstacle negotiation indicate that implantation of a toric IOL to correct the residual corneal astigmatism post-surgically could potentially reduce the chance of falling for the patient.

8.8 Limitation of Current Work and Proposed Future Investigations

8.8.1 Keratometry Repeatability

There were a few known sources of error that were not minimised when taking the readings. These include: lack of repeated readings, no control of time after blink for measurement, medications were not accounted for, some particiapnts were soft contact lens wearers, dry eyes was not assessed and the refraction was not assessed.

8.8.1.1 Lack of Multiple Readings

Only one reading was taken at each session, multiple readings would have improved the accuracy of the results. This was to simulate results gained in a real hospital environment where there is not time to take multiple readings.

8.8.1.2 Control of time after blink

It has been suggested that tear film break up can affect the leratometry readings for many of the instruments. This could have been assessed and controlled if the measurements were all taken at a set time after blink. However, most of the instruments took the readings automatically, so this variable could not be controlled.

8.8.1.3 Medications and Side Effects

Some medications can affect corneal thickness, swelling and the tear film. In this study, the participant medications were not assessed and controlled. The results may have been affected by drug side-effects.

8.8.1.4 Contact Lens Wear

In chapter 2, some of the participants were contact lens wearers and had only removed their lenses 12 hours prior to the measurements. Contact lens wear has been shown to alter the corneal shape for weeks after wear (see chapter 2). However, only 8 (out of the 100) subjects were soft contact lens wearers (2 were infrequent wearers only), limiting the effect on the whole data group.

8.8.1.5 Dry Eyes

Lastly, in the pseudophakic population, many of the participants had dry eyes, either previous to the surgery or induced by the medications and procedure and the tear film instability will reduce the accuracy of the readings. The use of artificial tears in all participants may have improved the readings taken. Although the instruments used in the study provide guidance on acceptable readings and notably poorer reading were repeated.

8.8.1.6 Use of Poor Keratometry Readings in Calculations

n chapters 3 and 4, the validity of the SIA and toric IOL prediction calculators were shown to be poor due to the comparison of keratometry readings taken at later visits (with or without surgery). However, these readings taken at the second and third visits were carried out with the same instruments shown to have inherent errors and poor accuracy so comparison and results derived from these have less significance.

8.8.2 Reduction in Power of Results due to Small Sample Sizes

A limitation in the studies carried out in chapter 6 was the numbers of subjects analysed. This was lower than anticipated. Post-hoc power analysis determined that the average effect size of the whole group was 0.42 resulting in a power of 92% for this data set (n=58). In the high astigmatism group the effect size was 0.4 resulting in a power of 54% for this data set (n=26). The low astigmatism group had an effect size of 0.60, which resulted in a power of 96% for this data set (n=32). This reduces the significance of the results for this chapter. A much larger sample size for high astigmatism would provide a more powerful set of reliable results.

8.8.3 Comparison of Manifest Refraction to Keratometry

With no gold standard or definitive assessment of the actual corneal astigmatism, the manifest refraction was used to assess the accuracy of the instrument measurements. This was done because the residual astigmatism after surgery is normally attributed to the cornea wholly, although this has been disputed of late (Teus et al. 2010). However, the process of refraction is subjective and this can lead to errors in results just as easily as the problems affecting the instruments. The first of which is human error, both from patient and practitioner when seeking the best outcome from the subjective answers given by the patient. Correction of astigmatism incurs many problems with adaptation and re-interpretation that the brain is required to do to tolerate the correction that has been found. Most qualified optometrist will routinely adjust or compromise on the prescription dispensed to provide the most comfortable correction for the patient (Howell-Duffy 2013) Most of the problems occurring with spectacles are a result of magnification and distortion induced by the optical lenses. Yet, the patient will have undergone a significant change in vision and optical power of the eye through the surgery, It can be assumed that they will also have to adapt to these and the brain will need to re-interpret the image to 'normalise' what they are seeing. We have no 'gold standard' with which to compare the keratometry too thus improving the results gained by the instrument is a difficult task. Although it must not be forgotten that a much higher level of repeatability and reproducibility should still be sought at this stage.

8.8.4 No Corneal Biomechanical Measurements

No corneal biomechanical readings were analysed in this thesis. Chapter 4 showed that the cornea was not acting in a uniform way and the exact reasons for this are unclear and difficult to investigate without more information. The introduction of the Ocular Response Analyser (*Reichert Technologies, Depew, NY, USA*) and the Corvis (*Oculus Inc, Wetzlar, Germany*) have increased our understanding of corneal biomechanics. The results from these instruments would have allowed more insight into how the cornea reacted to the incision and if there was a relationship that could be identified.

8.8.5 Simulated Form Deprivation and Loss of Contrast.

The study carried out in chapter 7 was a pilot study that recruited only 15 healthy presbyopic (but not pre-cataract) subjects. The form deprivation caused by the uncorrected astigmatism and losses of contrast from the cataracts were both simulated for the subject group. Due to adaptation and re-interpretation of the vision processed by the brain, this will never fully emulate the vision experienced by 'real patients'. To confirm and build upon the findings of this study it would need to be carried out within a cataract population with uncorrected astigmatism to determine the effect. Inducing astigmatism and cataracts will not precisely emulate the symptoms experienced by the actual patients due to the adaption to astigmatic changes in the image.

8.8.6 Mismatched Group Sizes

In chapters 3, 4, 5 and 6 the group sizes were not even in the comparisons. This will have affected the reliability of the comparison of the data. This is hard to control due to drop outs in the study and the population distribution of astigmatism e.g. with the rule, against the rule and oblique or levels of astigmatism which are not evenly distributed.

8.8.7 Poor Control of Times between Visits

The time between visits in chapters 3,4,5 and 6 was not equal for all participants. The data was collected in a busty hospital clinic and the availability of the clinics and patients as well as difficulty with the administration meant that this variable could not be kept consistent. Each individual was seen between 3-6 weeks and 3-6 months but the variability may have affected the changes seen between the 1st and 2nd follow-ups.

8.9 Clinical Implications

Further investigation is needed to improve the current keratometers to the standard required to achieve highly accurate pre-surgical assessment and fully understand the corneal shape changes that occur with surgery. Presently if a toric IOL is implanted, the best procedure is to repeat the measurements multiple times with multiple instruments to achieve more reliable results. The linear regression assessment in chapter 5 did show an increase in the relationship between refraction and keratometry with the use of multiple instruments. In the use of topographers, dry eye drops may be recommended to increase the tear film stability. The use of toric calculators was less accurate than the use of the pre-surgical measurement and would result in a higher residual astigmatism. However, if the incision is place 'on-axis' then the changes in corneal astigmatism should be more predictable.

8.10 Future Work

This thesis has brought to light a number of areas that require further investigation in the future.

8.10.1 Improving the Accuracy of Keratometry

There are some known sources of the errors in keratometry that should be assessed and methods sought to eliminate these. The first is poor tear film stability; continued use of artificial tear, particularly preceding the measurement may improve the repeatability and accuracy of the readings.

Corneal stability and healing is not fully understood. Firstly, the point of stabilisation after surgery needs to be determined, previous literature on this topic is conflicting. It has been reported to heal in as little as two weeks (Masket et al. 1996) whereas other research has advised a much longer period of change over 12 months (Pfleger et al. 1996) This confusion may be explained by Hayashi et al (2011) who found that corneas (both with and without cataract surgery) continue to change shape with age, the steepest corneal meridian will move towards an oblique or against-the-rule position (Hayashi et al. 2011). Corneal biomechanics measurements may shed some light on the response. The surgeon needs a target to aim for that will be best correction long term, if it is a moving target, the best compromise must be decided upon..

8.10.1.1 Use of Polar Method to predict post-operative corneal shape change

Although keratometry is still a limiting factor, the polar method of analysis was shown to be more accurate than the Cartesian method of calculating the corneal shape change (SIA). The current algorithms and calculators use the vector, as it is a single value that can easily be incorporated into the equation. If the prediction calculators were revised to allow incorporation of the polar value, the results would be a lot more accurate.

8.10.2 Further investigation into internal astigmatism

If the cornea does not fully explain the total ocular refraction and astigmatism then the improvements of keratometry for pre-surgical assessment will have limited use. The contribution and existence of 'internal astigmatism' needs to be explored in more detail to determine if this can be assessed and taken into account. This will improve the pre-surgical prediction of required correction with a toric IOL for the optimum refractive correction

8.10.3 The effect of reduced vision on mobility and balance

The standing balance and stair climbing did not show change with high levels of form deprivation and low contrast. Nevertheless the methods of assessment proved highly repeatable and could be used to assess the impact of other changes in vision to standing balance in subjects with other co-morbidities affecting balance such as Parkinson's disease. In the assessment of vision, it could be inferred that the stairs and standing tasks were too insensitive.

The obstacle negotiation task was also repeatable and did indicate changes in balance from both cataracts and higher levels of uncorrected astigmatism (simulated) from the healthy subjects. It can be inferred that the ability to detect and step over the object was affected by the changes in vision. This study should be repeated on an elderly cataract population with pre-existing uncorrected astigmatism. Two groups of patients should be monitored and compared, the first undergoing spherical IOL implantation (NHS) leaving the astigmatism uncorrected. The second group would have toric IOL implanted (Private). The difference in postural stability during obstacle negotiation could indicate the success of the toric IOLs in reducing the chances of falling post-surgically.

8.11 Conclusion

The implantation of toric IOLs could potentially improve not just the uncorrected visual acuity in reading tasks but may reduce the risk of falling for the individual. This could be of great benefit to a patient, especially if they have any other co-morbidity that already affects mobility and balance. In order to provide the most accurate and beneficial correction there are many areas of current pre-surgical planning that need to be validated and improved upon. The accuracy of keratometry when measuring corneal astigmatism has been shown to have large errors, especially the axis reading which pays such an essential role in the alignment of the toric IOL. Toric calculators are not valid and do not improve the effectively of the correction. In order to predict the corneal response, further work into the biomechanics of the cornea needs to be done to determine how the corneal will react and what causes it to do so.

Appendices

A.1 IOL Power Determination (Chapter 4)

Pre-operatively an IOLMaster 500 (Carl Zeiss Meditec AG) and Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) were used to determine axial length and corneal power. To determine IOL power, the Hoffer Q IOL formula was used for short axial lengths, (<22 mm; College of Ophthalmologists' Guidelines) and the SRK/T was used for all other axial lengths; emmetropia was the target in all cases.

A.2 Study 1 Documents

Consent Form

EYE RESEARCH WITH PLYMOUTH UNIVERSITY

Title of Project:
Repeatability and Reliability of 6 different Keratometers

Name of Researcher taking consent:…………………………………………………

1. I confirm that I have read and understood the patient information sheet for the above study and have had the opportunity to ask questions
2. I understand that the information collected during this study will remain strictly confidential and accessible only to appropriate members of the research team.
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without affecting my medical or care or legal rights.
4. I agree that auditors, monitors, regulatory authorities and ethics committees may have restricted access to my medical records.

Signature:……………………………………………………………………………….Date…………..

Full Name:……………………………………………………………………………………………..……..

Address: ..…………………………………………………………………………………... ……………

…….

As the chief investigator responsible for this research or a designated deputy, I confirm that the nature and purpose of this research have been explained to the participant named above.

Investigators Name:………………………………………………………………………….

Investigators Signature: …………………………………… Date………………

If you have any queries, do not hesitate to contact us.

Contact Details for Principal Investigator:
Catriona Hamer
Post Graduate Researcher in Optometry
School of Health Professions
Peninsula Allied Health Centre
Plymouth University
Derriford Road
PL6 8BH
Tel: +44(0) 1752 588 828
Email: catriona.hamer@plymouth.ac.uk

Patient Information Sheet

EYE RESEARCH WITH PLYMOUTH UNIVERSITY

Project title: *Repeatability and Reliability of six different Keratometers*

Chief Investigator: *Mrs Catriona Hamer*
Co - Investigators: *Dr Phillip Buckhurst*

We would like to invite you to participate in a new research study. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. This information sheet explains the background and aims of the study. Please take time to read it carefully and discuss it with others if you wish. If there is anything that is unclear, or if you would like more information, please ask us. Your participation in this study is entirely voluntary.

Why have I been invited?
We are looking for adult volunteers (18 years or older) with no history of prior ocular surgery, previous or current ocular diseases or RGP contact lens wear. Those who wear soft contact lenses will be required to remove them 24 hours before any assessments.

What is the aim of the project?
This experiment has been designed to look at the accuracy of 6 different instruments that can measure the corneal curvature (keratometry). Keratometry is the name given to the measurement of the curvature of the cornea. It is used in contact lens fittings, corneal abnormality diagnosis and for some pre-surgical assessments e.g. for cataract surgery.
You will be assessed with all the machines on two separate occasions. These measurements are non- contact tests that will not touch or cause any changes to the eye itself.
We wish to find the most accurate and repeatable method of measuring keratometry out of the machines available at Plymouth University. This information will be used for future investigations that require keratometry to be done.

What would I have to do?
The investigators will arrange to carry out the assessments in two separate occasions. One single participant will be required to present on 10 occasions. Participation is voluntary and you are free to withdraw from this investigation at any point in time.
What will happen to me if I take part?
If you consent to participate in this study, the cornea of your right eye will be assessed by 6 different non-contact instruments on either two, three or ten separate occasions, depending upon which group you are randomly assigned to. These visits will occur at least 24 hours apart. Some subjects will be randomly assigned into a group that will be assessed by a second investigator during the second visit, others will have additional test carried out with an induced head tilt. The head tilt assessment will be carried out by the initial examiner. One single group will be required to be seen 10 times for repeated assessment by the initial examiner.

Do I have to take part?
No. It is entirely up to you whether or not to take part. If you decide to take part you may choose to withdraw at any time without giving any reason. If you decide not to take part, your rights and care will not be affected in any way. If you decide to take part you will be asked to sign a consent form. You will be given a signed copy of the consent form and an information sheet for your own records

Will my records be confidential?
All information collected about you during the course of this research will be kept strictly confidential. Your records may be looked at by the research team involved in this study and the monitoring or audit team approved by the university. All information will be stored electronically on a computer which is password protected, in a document file that is also password protected. All information will be handled in compliance with the Data Protection Act (1998).

Your name and address (which we need in order to contact you) will be stored separately from the other information you supply during the project so that you cannot be identified from your study records.)
What are the potential risks or benefits of taking part?

Risks
As the assessments are non- contact, there should be minimal risks to ocular health. There will be no intervention in routine eye health care and all assessments will be carried out by trained professionals.

Benefits
This study will not intervene into the subjects normal eye care procedures. The assessments are non-contact and will not affect the ocular surface.

Participating in this study should not have any effect on any of your insurance policies (for example critical illness, mortgage repayment, health and private medical insurance). However, please consider that if we do identify a health concern during the course of this study this may affect your future health / medical insurance policies, please seek advice if you wish.

What if something goes wrong?
The assessments taken are non- contact and will not affect the health of the anterior ocular structures.

Who is organising the study?
This study is being organised within the Optometry research team at Plymouth university. It will be carried out on University campus with University owned equipment.
Who has reviewed this study?

All university research is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Plymouth University Research Ethics Committee.

What will happen to the results of the research study?
The results of this study will help us to highlight the best instrument to use in future studies based at Plymouth University that rely heavily on keratometry results.

This work is likely to be published in optometry and ophthalmology journals and may be presented at conferences for these audiences.

The subjects will be informed of any publications and informed of how to access them.

Your rights
Your participation in this study is entirely voluntary. You may withdraw at any time without giving a reason for withdrawal or without it affecting your current or future treatment in any way.
What if I have any further questions or require further information?

If you have any questions about our project, either now or in the future, please feel free to contact either of the

Chief investigator: Catriona Hamer	Co-Investigator: Dr Phillip J Buckurst BSc(Hons) MCOptom PhD
Post graduate Researcher	Lecturer in Optometry
FF01	Room SF30
School of Health Professions	School of Health Professions
Peninsula Allied Health Centre	Peninsula Allied Health Centre
Plymouth University	Plymouth University
Derriford Road	Derriford Road
Plymouth	Plymouth
PL6 8BH	PL6 8BH
Tel: 01752 588828	Tel: +44(0) 1752 588 884
catriona.hamer@plymouth.ac.uk	Email: phillip.buckhurst@plymouth.ac.uk

What if I have a complaint?

Should you have reason to complain about the way you have been treated at any stage during the study you can contact Dr Phillip Buckhurst Lead PhD supervisor (contact details above)

Alternatively, you can make your complaint directly to Catriona Hamer, the Chief Investigator involved in this study (contact details above)

Thank you for taking the time to read this information sheet.

Signed.. Date.............................
Name..

****Signed and dated by the Lead Researcher, with contact details*

RESEARCH WITH PLYMOUTH UNIVERSITY

3 April 2013

CONFIDENTIAL
Catriona Hamer
School of Health Professions
Faculty of Health, Education & Society
Plymouth University
Room FF01
Peninsula Allied Health Centre
Derriford Road
Plymouth, PL6 8BH

Dear Catriona

Application for Approval by Faculty Research Ethics Committee

Reference Number: 12/13-111
Application Title: Assessment of corneal curvature

I am pleased to inform you that the Committee has granted approval to you to conduct this research.

Please note that this approval is for three years, after which you will be required to seek extension of existing approval.

Please note that should any MAJOR changes to your research design occur which effect the ethics of procedures involved you must inform the Committee. Please contact Claire Butcher on (01752) 585337 or by email claire.butcher@plymouth.ac.uk

Yours sincerely

Professor Michael Sheppard, PhD, AcSS,
Chair, Research Ethics Committee -
Faculty of Health, Education & Society and
Peninsula Schools of Medicine & Dentistry

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Committee

A.3 Study 2 Documents

Plymouth Hospitals NHS
NHS Trust

EYE RESEARCH WITH PLYMOUTH UNIVERSITY

Consent Form

(Version 2 –17/09/2013)

Department of Optometry, School of Health Professions, Faculty of Health, Education and Society, Plymouth University

TITLE: *Anterior Eye Shape following Cataract Surgery*

Name of Researchers: Professor Nabil Habib, Dr David Adams, Dr Phillip Buckhurst, Mrs Catriona Hamer, Professor Christine Purslow and Dr Hetal Buckhurst.

Please initial the boxes:

1. I confirm that I have read and understand the information sheet (Version 1) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without my medical care or legal rights being affected. ☐

3. I am willing to allow access to my medical records by authorized people but understand that strict confidentiality will be maintained. The purpose of this is to ensure that the study is being carried out correctly. ☐

4. I agree to take part in the above study ☐

Name of patient	*Date*	*Signature*
Name of person taking Consent (if different from researcher)	*Date*	*Signature*
Researcher	*Date*	*Signature*

Plymouth Hospitals NHS
NHS Trust

EYE RESEARCH WITH PLYMOUTH UNIVERSITY

(Version 2 – 17/09/2013)

PATIENT INFORMATION SHEET

Project title: *Anterior Eye Shape after Cataract Surgery*

Chief Investigator: *Professor Nabil Habib*
Co - Investigators: *Dr David Adams, Dr Phillip Buckhurst, Mrs Catriona Hamer, Professor Christine Purslow, Dr Hetal Buckhurst.*

We would like to invite you to participate in a new research study. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. This information sheet explains the background and aims of the study. Please take time to read it carefully and discuss it with others if you wish. If there is anything that is unclear, or if you would like more information, please ask us. Your participation in this study is entirely voluntary.

<u>Why have I been invited?</u>

We are looking for routine cataract surgery candidates aged 18 years old and over.

<u>What is the aim of the project?</u>

The overall aim of the study is to investigate and observe what changes in shape occur to the front surface of eye (the cornea) following incisions during cataract surgery. There are currently many theories that predict what shape change will occur but they have never been proven. In order for us to investigate these theories, non-invasive, non-contact tests will be carried out before and after surgery to compare the predicted shape and the actual shape changes found after surgery. In addition to this, the study will investigate how much other characteristics of the eye (e.g. corneal thickness) or the intraocular lens (IOL) implanted to replace the cataract affect the vision after surgery.

<u>What do I do now?</u>

Take time to read the information sheet and discuss it with your family and friends if you wish.

<u>What will happen to me if I take part?</u>

If you consent to participate in this study, a routine examination will be carried out with two additional measurements performed; this will take 30 minutes in total, 20 minutes for the routine assessments, 5 minutes for the additional measurements and 5 minutes to complete a questionnaire. All of the machines used in the assessment are non-contact and will not touch or interfere with the eye or surgical process. This is a purely observational study that looks to assess the outcomes of a routine procedure.

The routine examination consists of a health check, vision assessment, intraocular pressure measurement and ocular structure pre-surgical measurements. The additional assessments include measurement of the front curvature of the eye and an assessment of the movement of the tissues at the front of the eye (cornea) during the intraocular pressure measurement.

The health check of the eye will be carried out with a bright light and microscope. After this your vision will be assessed by reading a chart with and without any glasses you own. The intraocular pressures will be measured with a tonometer. This is a device that is routinely used to measure the pressure of the eyes by blowing a puff of air on to the front of your eyes. The characteristics of the front surface of the eye (cornea) will be assessed with two different instruments; one will flash blue rings of light and the other will require you to focus on a small flashing light while it scans the eye. Lastly a machine will take essential pre-surgical measurement of the eye (such as the length of the eye) while you look at a small central light. Each measurement will only take a few minutes to perform.

One additional follow up visit will be required 3-4 months after the surgery, repeating the above assessments. In addition to this, a short questionnaire will be given at the first and final visits to gather information about your vision and glasses worn.

Will any expenses be paid?

The first and second assessments will be part of your routine appointments for the cataract surgery procedure. A third, extra appointment will be required at 3-4 months after the surgery, and a nominal fee of £10 will be given to cover travel expenses, including the car parking fee for this additional visit.

Do I have to take part?

No. It is entirely up to you whether or not to take part. If you decide to take part you may choose to withdraw at any time without giving any reason. If you decide not to take part your usual healthcare will not be affected in any way.

If you decide to take part you will be asked to sign a consent form. You will be given a signed copy of the consent form and an information sheet for your own records.

If you consent to the study and at any point during the study are thought to have lost mental capacity and ability to consent to participate, you will be removed from the study and will no longer be assessed. The data gathered up to this point will be retained for use in the study.

Will my records be confidential?

All information collected about you during the course of this research will be kept strictly confidential. It is a requirement that your involvement in this study is noted in your medical records. Your medical records may be looked at by the research team involved in this study and the monitoring or audit team approved by the hospital. All information will be stored electronically on a computer which is password protected, in a document file that is also password protected. All information will be handled in compliance with the Data Protection Act (1998).

Your name and address (which we need in order to contact you) will be stored separately from the other information you supply during the project so that you cannot be identified from your study records.

<u>What are the potential risks or benefits of taking part?</u>

Risks
There are no additional risks associated with the procedure if you participate in this study. All assessments are non-contact and will not alter the treatment or surgical procedure.

Benefits
Though participating in this will not alter your procedure or treatment as part of your routine cataract surgery. It is hoped that the results of this study will help to improve the outcomes of cataract surgery for patients in the future.

Participating in this study should not have any effect on any of your insurance policies (for example critical illness, mortgage repayment, health and private medical insurance). However, please consider that if we do identify a health concern during the course of this study this may affect your future health / medical insurance policies, please seek advice if you wish.

<u>What if something goes wrong?</u>

As this study does not intervene into the surgical procedure, the risks relate to the surgery itself. These are the same as if you wish not to take part. However, in the unlikely event, negligent harm will be covered by the NHS. No special arrangements have been made for non-negligent harm to patients.

<u>Who is organising the study?</u>

The organisers of the study are Professor Nabil Habib from Derriford Hospital and Dr Phillip Buckhurst, Mrs Catriona Hamer, Dr Hetal Buckhurst and Prof Christine Purslow from the School of Health Professions, Plymouth University.

<u>Who has reviewed this study?</u>

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Research and Development team at Derriford Hospital and the South West Research Ethics Committee.

What will happen to the results of the research study?

The results will show if the previous assumptions predicting corneal shape changes due to surgery were accurate or not. It will also highlight the characteristics that influence the change in shape or vision changes after surgery most. The results will be used to show if the post-surgical outcome can be predicted accurately and how best to do it.

We will aim to talk about the work at meetings in this country and abroad, for example the annual Association in Research in Vision and Ophthalmology conference and we will aim to publish the findings widely in medical journals, for example the 'Journal of Cataract and Refractive Surgery', which is available on line. Your data will always remain anonymous and your name will not appear on any of the results.

You are most welcome to request a copy of the results of the project should you wish.

Your rights

Your participation in this study is entirely voluntary. You may withdraw at any time without giving a reason for withdrawal or without it affecting your current or future health care treatment in any way.

What if I have any further questions or require further information?

If you have any questions about our project, either now or in the future, please feel free to contact either:

Professor Nabil Habib
Consultant Opthalmologist FRCS FRCOpthal
Royal Eye Infirmary
Plymouth
PL4 6PL
nabil.habib@nhs.net
+44 (0)1752 439357

Mrs Catriona Hamer
BSc(Hons)
Post graduate Researcher in Optometry
Room FF01
School of Health Professions
Peninsula Allied Health Centre
Plymouth University
Derriford Road
Plymouth
PL6 8BH

What if I have a complaint?

Should you have reason to complain about the way you have been treated at any stage during the study you can access the NHS patient advisory liaison service (PALS) who will be able to advise and help you (pals@phnt.swest.nhs.uk or 01752 439884).

Alternatively, you can make your complaint directly to Prof Nabil Habib, the Chief Investigator involved in this study (contact details as above).

Thank you for taking the time to read this information sheet.

Lead Researcher:

****Signed and dated by the Lead Researcher, with contact details****

Name:____

Signature: ____

Date:________________________________

Health Research Authority
NRES Committee South West - Frenchay
Bristol Research Ethics Committee Centre
Level 3, Block B
Whitefriars
Lewins Mead,
Bristol
BS1 2NT

16 October 2013

Mr Nabil Habib
Consultant ophthalmologist
Royal Eye Infirmary
Royal Eye Infirmary
Plymouth
PL6 8DH

Dear Mr Habib

Study title:	**Anterior eye shape following Cataract Surgery**
REC reference:	**13/SW/0229**
Protocol number:	**N/A**
IRAS project ID:	**110270**

Thank you for your letter of 19 September 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Mrs Naaz Nathoo, nrescommittee.southwest-frenchay@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		n/a
Covering Letter		n/a
Evidence of insurance or indemnity		02 August 2013
Investigator CV		23 July 2013
Other: CV Dr Phillip Buckhurst		22 July 2013
Other: CV Mrs Catriona Hamer		22 July 2013
Other: CV Hetal Buckhurst		22 July 2013
Other: CV Christine Purslow		10 July 2013
Other: Project approval form		21 January 2013
Participant Consent Form: Anterior Eye Following Cataract Surgery	2.0	17 September 2013
PIS: Anterior Eye Shape following Cataract Surgery	2.0	17 September 2013
Protocol	1	24 July 2013
Questionnaire: QoV questionnaire		
REC application		22 July 2013
Response to Request for Further Information		19 September 2013

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/SW/0229	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely

Dr Robert Beetham
Chair

Email:nrescommittee.southwest-frenchay@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Dr Phillip Buckhurst*
Dr Lisa Vickers, Plymouth Hospitals NHS Trust

RESEARCH WITH PLYMOUTH UNIVERSITY

23rd October 2013

CONFIDENTIAL
Catriona Hamer
Room FF01
School of Health Professions
Peninsula Allied Health Centre
Plymouth University
Derriford Road
Plymouth
PL6 8BH

Dear Catriona

Application for Approval by Faculty Research Ethics Committee

Reference Number: 13/14-188
Application Title: **Anterior eye shape following cataract surgery**

I am pleased to inform you that the Committee has granted approval to you to conduct this research.

Please note that this approval is for three years, after which you will be required to seek extension of existing approval.

Please note that should any MAJOR changes to your research design occur which effect the ethics of procedures involved you must inform the Committee. Please contact Sarah Jones (email sarah.c.jones@plymouth.ac.uk).

Yours sincerely

Professor Michael Sheppard, PhD, AcSS,
Chair, Research Ethics Committee -
Faculty of Health & Human Sciences and
Peninsula Schools of Medicine & Dentistry

Faculty of Health & Human Sciences
Plymouth University
Drake Circus
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Professor Michael Sheppard
CQSW BSc MA PhD AcSS
Chair, Faculty Research Ethics
Committee

A.4 Study 3 Documents

EYE AND VISION RESEARCH WITH PLYMOUTH UNIVERSITY

Consent Form

Title of Project: The Effect of Astigmatic distortion and form deprivation on Mobility

Name of Researcher taking consent:………………………………………………

1. I confirm that I have read and understood the patient information sheet for the above study and have had the opportunity to ask questions ☐
2. I understand that the information collected during this study will remain strictly confidential and accessible only to appropriate members of the research team. ☐
3. I agree that auditors, monitors, regulatory authorities and ethics committees may have restricted access to my medical records. ☐
4. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without affecting my medical or care or legal rights. ☐

Signature:……………………………………………………………………Date………………………………..

Full Name:……………………………………………………………………………………..

Address:……
……

As the chief investigator responsible for this research or a designated deputy, I confirm that the nature and purpose of this research have been explained to the participant named above.

Investigators Name:………………………………………………………………………………

Investigators Signature:…………………… ………………………………… Date………………

If you have any queries, do not hesitate to contact us.

Catriona Hamer
Post-graduate Researcher MCOptom BSc (Hons)
FF01 , PAHC
Derriford Road
PL6 8BH
01752 588828
catriona.hamer@plymouth.ac.uk

(Two copies to be signed, one copy is to be kept by the participant and one copy is kept by the research team.)

Patient Information Sheet

EYE AND VISION RESEARCH WITH PLYMOUTH UNIVERSITY

Project title: ***The Effect of Astigmatic distortion and form deprivation on Mobility***

Chief Investigator: ***Catriona Hamer***

Co - Investigators: Dr Hetal Buckhurst, Dr Gary Shum, Prof Christine Purslow, Prof Jon Marsden, Dr Phillip Buckhurst.

We would like to invite you to participate in a new research study. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. This information sheet explains the background and aims of the study. Please take time to read it carefully and discuss it with others if you wish. If there is anything that is unclear, or if you would like more information, please ask us. Your participation in this study is entirely voluntary.

Why have I been invited?

We are looking for adult volunteers (40 to 65 years old) with no current balance, mobility problems including compromised gait or current injury. Each participant must also have good ocular health, full visual fields and normal binocular visual acuity. In addition to this they must not have any current balance, mobility problems including compromised gait or current injury.

What is the aim of the project?

This experiment has been designed to find out if a person's stability and mobility is affected after cataract surgery if their vision is not fully corrected and they are left with uncorrected astigmatism. Astigmatism is the where the surfaces in the eye are not spherical, there are two principal meridians of curvature, the flattest and steepest curvatures, forming two separate focal points in the eye, blurry the vision. This study aims to measure the stability and movement during routine mobility tasks while each participant is wearing contact lenses simulating astigmatism and the correction of astigmatism and spectacles that simulate cataracts. This will allow a comparison of before and after cataract surgery, with and without astigmatism.

What would I have to do?

You will participate in one assessment sessions monitoring stability during basic mobility tasks, the session will last up to 2 hours maximum. Participation is voluntary and you are free to withdraw from this investigation at any point in time.

What will happen to me if I take part?

If you consent to participate in this study, you will perform a series of basic mobility tasks while wearing a sensor to track your movements and stability. You will also be wearing contact lenses and spectacles provided of different optical corrections to simulate uncorrected astigmatism and cataract. Use of the contact lenses including insertion and removal will under the supervision of a fully trained optometrist. The same basic mobility tasks will be performed at each session.

Do I have to take part?
No. It is entirely up to you whether or not to take part. If you decide to take part you may choose to withdraw at any time without giving any reason. If you decide not to take part will not be affected in any way. If you decide to take part you will be asked to sign a consent form. You will be given a signed copy of the consent form and an information sheet for your own records.

Will my records be confidential?
All information collected about you during the course of this research will be kept strictly confidential. Your records may be viewed by the research team involved in this study and if the study is audited this will include a monitoring or audit team approved by the university. All information will be stored electronically on a computer which is password protected, in a document file that is also password protected. All information will be handled in compliance with the Data Protection Act (1998).

Your name and address (which we need in order to contact you) will be stored separately from the other information you supply during the project so that you cannot be identified from your study records.

What are the potential risks or benefits of taking part?

Risks
There is a small risk that the participant will lose their balance when carrying out the mobility tasks with the induced astigmatism. All tasks will be performed with a banister or researcher along side to help if the participant feels they are losing their balance. The use of contact lenses for the study will be under the supervision of an optometrist. In the very unlikely event that the participant falls while carrying out the task and is injured, appropriate medical assistance will be provided.

Benefits
This study looks to improve information is the choice of lenses implanted in future cataract surgeries. The study will not intervene with a participants ocular correction or eye care procedures.

Participating in this study should not have any effect on any of your insurance policies (for example critical illness, mortgage repayment, health and private medical insurance). However, please consider that if we do identify a health concern during the course of this study this may affect your future health / medical insurance policies, please seek advice if you wish.

What if something goes wrong?
An optometrist will supervise the use of contact lenses and monitor the health of the eyes with their use. In the unlikely event there a problem arises with the ocular health, the Optometrist will manage and monitor the occurrence. If the participant loses their balance in the tasks a

Who is organising the study?
This study is being organised by the Optometry and Physiotherapy research teams in the School of Health Professions, Plymouth University. It will be carried out on University campus with University owned equipment.

Who has reviewed this study?
All university research is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Plymouth University Research Ethics Committee.

What will happen to the results of the research study?

These results will help in the investigation of the benefits of implanting toric Intraocular lenses (IOLs) instead of standard spherical IOLs in cataract surgery. It will show the effect of leaving a patient with uncorrected astigmatism after cataract surgery compared with the correction of astigmatism with toric IOLs. The results will be published as part of a PhD thesis and in ophthalmic and ophthalmological journals. The participants will be informed of any publications and information on how to access them.

Your rights
Your participation in this study is entirely voluntary. You may withdraw at any time without giving a reason for withdrawal or without it affecting your current or future treatment in any way.

What if I have any further questions or require further information?
If you have any questions about our project, either now or in the future, please feel free to contact either Catriona Hamer or Dr Phillip Buckhurst (see details below):

Chief investigator: Catriona Hamer

Post graduate Researcher
FF01
School of Health Professions
Peninsula Allied Health Centre
Plymouth University
Derriford Road
Plymouth
PL6 8BH
Tel: 01752 588828
catriona.hamer@plymouth.ac.uk

Co-Investigator: Dr Phillip J Buckhurst
BSc(Hons) MCOptom PhD
Lecturer in Optometry
Room SF30
School of Health Professions
Peninsula Allied Health Centre
Plymouth University
Derriford Road
Plymouth
PL6 8BH
Tel: +44(0) 1752 588 884
Email: phillip.buckhurst@plymouth.ac.uk

What if I have a complaint?

Should you have reason to complain about the way you have been treated at any stage during the study you can contact Dr Phillip Buckhurst.

Alternatively, you can make your complaint directly to Catriona Hamer the Chief Investigator involved in this study (contact details below).

Thank you for taking the time to read this information sheet.

Thank you for taking the time to read this information sheet.

Signed.. Date..............................

Name..

****Signed and dated by the Lead Researcher.*

RESEARCH
WITH
PLYMOUTH
UNIVERSITY

25th June 2014

CONFIDENTIAL

Catriona Hamer
Room FF01
School of Health Professions
Peninsula Allied Health Centre
Plymouth University
Derriford Road
Plymouth PL6 8BH

Dear Catriona

Application for Approval by Faculty Research Ethics Committee

Reference Number: 13/14-254
***Application Title:* The Effect of Astigmatic distortion and form deprivation on Mobility**

I am pleased to inform you that the Committee has granted approval to you to conduct this research.

Please note that this approval is for three years, after which you will be required to seek extension of existing approval.

Please note that should any MAJOR changes to your research design occur which effect the ethics of procedures involved you must inform the Committee. Please contact Sarah Jones (email sarah.c.jones@plymouth.ac.uk).

Yours sincerely

Professor Michael Sheppard, PhD, AcSS,
Chair, Research Ethics Committee -
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Peninsula Schools of Medicine & Dentistry

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W www.plymouth.ac.uk

Professor Michael Sheppard
CQSW BSc MA PhD AcSS
Chair, Faculty Research Ethics
Committee

References

Abdelhafiz, A. H. and Austin, C. A. (2003). "Visual factors should be assessed in older people presenting with falls or hip fracture." *Age and Ageing* **32**(1): 26-30.

AgeUK (2012). Later life in the United Kingdom.

Agresta, B., Knorz, M. C., Donatti, C. and Jackson, D. (2012). "Visual acuity improvements after implantation of toric intraocular lenses in cataract patients with astigmatism: a systematic review." *BMC Ophthalmology* **12**(1): 41.

Alberdi, T., Macias-Murelaga, B., Bascaran, L., Goni, N., de Arregui, S. S. and Mendicute, J. (2012). "Rotational stability and visual quality in eyes with Rayner toric intraocular lens implantation." *Journal of Refractive Surgery* **28**(10): 696-701.

Alio, J., Rodriguez-Prats, J. L., Galal, A. and Ramzy, M. (2005). "Outcomes of microincision cataract surgery versus coaxial phacoemulsification." *Ophthalmology* **112**(11): 1997-2003.

Alio, J. L., Grzybowski, A., El Aswad, A. and Romaniuk, D. (2014). "Refractive lens exchange." *Survey of Ophthalmology* **59**(6): 579-598.

Alio, J. L., Pinero, D. P., Plaza-Puche, A. B. and Chan, M. J. (2011). "Visual outcomes and optical performance of a monofocal intraocular lens and a new-generation multifocal intraocular lens." *Journal of Cataract and Refractive Surgery* **37**(2): 241-250.

Alio, J. L., Pinero, D. P., Tomas, J. and Aleson, A. (2011). "Vector analysis of astigmatic changes after cataract surgery with toric intraocular lens implantation." *Journal of Cataract and Refractive Surgery* **37**(6): 1038-1049.

Alio, J. L., Pinero, D. P., Tomas, J. and Plaza, A. B. (2011). "Vector analysis of astigmatic changes after cataract surgery with implantation of a new toric multifocal intraocular lens." *Journal of Cataract and Refractive Surgery* **37**(7): 1217-1229.

Allen, D. and Vasavada, A. (2006). "Cataract and surgery for cataract." *British Medical Journal* **333**(7559): 128-132.

Alpar, J. J. (1985). "Modification of the Kratz incision with a scleral marking and a temporary silk suture for astigmatic control." *Journal - American Intra-Ocular Implant Society* **11**(5): 491-493.

Alpins, N. (2001). "Astigmatism analysis by the Alpins method." *Journal of Cataract and Refractive Surgery* **27**(1): 31-49.

Alpins, N., Ong, J. K. and Stamatelatos, G. (2015). "Corneal topographic astigmatism (CorT) to quantify total corneal astigmatism." *Journal of Refractive Surgery* **31**(3): 182-186.

Alpins, N., Ong, J. K. Y. and Stamatelatos, G. (2012). "New method of quantifying corneal topographic astigmatism that corresponds with manifest refractive cylinder." *Journal of Cataract and Refractive Surgery* **38**(11): 1978-1988.

Alpins, N. A. and Goggin, M. (2004). "Practical astigmatism analysis for refractive outcomes in cataract and refractive surgery." *Survey of Ophthalmology* **49**(1): 109-122.

Altan-Yaycioglu, R., Akova, Y. A., Akca, S., Gur, S. and Oktem, C. (2007). "Effect on astigmatism of the location of clear corneal incision in phacoemulsification of cataract." *Journal of Refractive Surgery* **23**(5): 515-518.

Anand, V., Buckley, J., Scally, A. and Elliott, D. B. (2002). "The effect of refractive blur on postural stability." *Ophthalmic and Physiological Optics* **22**(6): 528-534.

Apple, D. (2000). "Evolution of Cataract Surgery and Intraocular Lenses (IOLs)." *Survey of Ophthalmology* **45**(1): S53-S69.

Atchison, D. A. and Charman, W. N. (2010). "Thomas Young's contribution to visual optics: the Bakerian Lecture "on the mechanism of the eye"." *J Vis* **10**(12): 16.

Atchison, D. A. and Charman, W. N. (2011). "Thomas Young's contributions to geometrical optics." *Clinical & Experimental Optometry* **94**(4): 333-340.

Bae, J. G., Kim, S. J. and Choi, Y. I. (2004). "Pseudophakic residual astigmatism." *Korean journal of ophthalmology : KJO* **18**(2): 116-120.

Baker, K., Rochester, L. and Nieuwboer, A. (2007). "The immediate effect of attentional, auditory, and a combined cue strategy on gait during single and dual tasks in Parkinson's disease." *Archives of Physical Medicine and Rehabilitation* **88**(12): 1593-1600.

Bamashmus, M. A. (2010). "Traditional Arabic technique of couching for cataract treatment in Yemen." *European Journal of Ophthalmology* **20**(2): 340-344.

Bellan, L. (2008). "The evolution of cataract surgery: The most common eye procedure in older adults." 1-5.

Benjamin, W. J. and Borish, I. M. (2007). Borish's Clinical Refraction, Butterworth-Heinemann.

Bennett, A. G. and Rabbetts, R. B. (1991). "What radius does the conventional keratometer measure?" *Ophthalmic and Physiological Optics* **11**(3): 239-247.

Bennett, A. G., Rabbetts, R. B. and (1998). Clinical Visual Optics.

Black, A. and Wood, J. (2005). "Vision and falls." *Clinical and Experimental Optometry* **88**(4): 212-222.

Bland, J. M. and Altman, D. G. (1986). "Statistical methods for assessing agreement between two methods of clinical measurement." *Lancet* **1**(8476): 307-310.

Blomstedt, P. (2014). "Cataract surgery in ancient Egypt." *Journal of Cataract and Refractive Surgery* **40**(3): 485-489.

Boote, C., Dennis, S., Newton, R. H., Puri, H., Meek, K. M., Boote, C. and (2003). "Collagen Fibrils Appear More Closely Packed in the Prepupillary Cornea: Optical and Biomechanical Implications." **44**(7): 2941-2948.

Bourne, W. M. (2003). "Biology of the corneal endothelium in health and disease." *Eye (Lond)* **17**(8): 912-918.

Braga-Mele, R., Chang, D., Dewey, S., Foster, G., Henderson, B. A., Hill, W., Hoffman, R., Little, B., Mamalis, N., Oetting, T., Serafano, D., Talley-Rostov, A., Vasavada, A. and Yoo, S. (2014). "Multifocal intraocular lenses: relative indications and contraindications for implantation." *Journal of Cataract and Refractive Surgery* **40**(2): 313-322.

Brannan, S., Dewar, C., Sen, J., Clarke, D., Marshall, T. and Murray, P. I. (2003). "A prospective study of the rate of falls before and after cataract surgery." *British Journal of Ophthalmology* **87**(5): 560-562.

Bregnhøj, J. F., Mataji, P. and Naeser, K. (2015). "Refractive, anterior corneal and internal astigmatism in the pseudophakic eye." *Acta Ophthalmologica* **93**(1): 33-40.

Brodie, M., Lord, S., Coppens, M., Annegarn, J. and Delbaere, K. (2015). "Eight weeks remote monitoring using a freely worn device reveals unstable gait patterns in older fallers." *IEEE Transactions on Biomedical Engineering*.

Brodie, M., Wang, K., Delbaere, K., Persiani, M., Lovell, N., Redmond, S., Del Rosario, M. and Lord, S. (2015). "New methods to monitor stair ascents using a wearable pendant device reveal how behavior, fear, and frailty influence falls in octogenarians." *IEEE Transactions on Biomedical Engineering*.

Bronstein, A. M. (1986). "Suppression of visually evoked postural responses." *Experimental Brain Research* **63**(3): 655-658.

Browne, A. W. and Osher, R. H. (2014). "Optimizing Precision in Toric Lens Selection by Combining Keratometry Techniques." *Journal of Refractive Surgery* **30**(1): 67-72.

Buckhurst, P. J., Wolffsohn, J. S., Davies, L. N. and Naroo, S. A. (2010). "Surgical correction of astigmatism during cataract surgery." *Clinical and Experimental Optometry* **93**(6): 409-418.

Buckley, J. G., Timmis, M. A., Scally, A. J. and Elliott, D. B. (2011). "When Is Visual Information Used to Control Locomotion When Descending a Kerb?" *PloS One* **6**(4): e19079.

Bunn, L. M., Marsden, J. F., Voyce, D. C., Giunti, P. and Day, B. L. (2015). "Sensorimotor processing for balance in spinocerebellar ataxia type 6." *Movement Disorders*.

Butler, A. A., Lord, S. R., Rogers, M. W. and Fitzpatrick, R. C. (2008). "Muscle weakness impairs the proprioceptive control of human standing." *Brain Research* **1242**: 244-251.

Buzard, K. A. and Shearing, S. P. (1991). "Comparison of postoperative astigmatism with incisions of varying length closed with horizontal sutures and with no sutures." *Journal of Cataract and Refractive Surgery* **17**: 734-739.

Calladine, D., Evans, J. R., Shah, S. and Leyland, M. (2012). "Multifocal versus monofocal intraocular lenses after cataract extraction." **9**: CD003169.

Chan, T. C., Cheng, G. P., Wang, Z., Tham, C. C., Woo, V. C. and Jhanji, V. (2015). "Vector Analysis of Corneal Astigmatism After Combined Femtosecond-Assisted Phacoemulsification and Arcuate Keratotomy." *American Journal of Ophthalmology*.

Chang, M., Kang, S. and Kim, H. M. (2012). "Which keratometer is most reliable for correcting astigmatism with toric intraocular lenses?" **26**(1): 1-5.

Chang, S. W., Su, T. Y. and Chen, Y. L. (2015). "Influence of ocular features and incision width on surgically induced astigmatism after cataract surgery." *Journal of Refractive Surgery* **31**(2): 82-88.

Chen, D. and Lam, A. K. (2009). "Reliability and repeatability of the Pentacam on corneal curvatures." *Clinical and Experimental Optometry* **92**(2): 110-118.

Cheng, H. (1989). "Causes of cataract." **298**(6686): 1470.

Cheng, L.-S., Tsai, C.-Y., Tsai, R. J.-F., Liou, S.-W. and Ho, J.-D. (2011). "Estimation accuracy of surgically induced astigmatism on the cornea when neglecting the posterior corneal surface measurement." *Acta Ophthalmologica* **89**(5): 417-422.

Chernyak, D. A. (2004). "Cyclotorsional eye motion occurring between wavefront measurement and refractive surgery." *Journal of Cataract and Refractive Surgery*.

Chylack, L. T., Jr., Wolfe, J. K., Singer, D. M., Leske, M. C., Bullimore, M. A., Bailey, I. L., Friend, J., McCarthy, D. and Wu, S. Y. (1993). "The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group." *Archives of Ophthalmology* **111**(6): 831-836.

Cillino, S., Casuccio, A., Di Pace, F., Morreale, R., Pillitteri, F., Cillino, G. and Lodato, G. (2008). "One-year outcomes with new-generation multifocal intraocular lenses." *Ophthalmology* **115**(9): 1508-1516.

Cravy, T. V. (1979). "Calculation of the change in corneal astigmatism following cataract extraction." *Ophthalmic Surgery* **10**(1): 38-49.

Cumming, R. G., Mitchell, P. and Smith, W. (2000). "Diet and cataract." **107**(3): 1-7.

Dam-Johansen, M. and Olsen, T. (1997). "Induced astigmatism after 4 and 6 mm scleral tunnel incision - A randomized study." *Acta Ophthalmologica Scandinavica* **75**(6): 669-674.

Day, L. (2002). "Randomised factorial trial of falls prevention among older people living in their own homes." *BMJ* **325**(7356): 128-128.

de Vries, N. E. and Nuijts, R. M. (2013). "Multifocal intraocular lenses in cataract surgery: literature review of benefits and side effects." *Journal of Cataract and Refractive Surgery* **39**(2): 268-278.

Denoyer, A., Denoyer, L., Halfon, J., Majzoub, S. and Pisella, P. J. (2009). "Comparative study of aspheric intraocular lenses with negative spherical aberration or no aberration." *Journal of Cataract and Refractive Surgery* **35**(3): 496-503.

Denoyer, A., Ricaud, X., Van Went, C., Labbé, A. and Baudouin, C. (2013). "Influence of corneal biomechanical properties on surgically induced astigmatism in cataract surgery." *Journal of Cataract and Refractive Surgery* **39**(8): 1204-1210.

Dewey, S., Beiko, G., Braga-Mele, R., Nixon, D. R., Raviv, T., Rosenthal, K. and ASCRS Cataract Clinical Committee, I. a. I. S. (2014). "Microincisions in cataract surgery." *Journal of Cataract and Refractive Surgery* **40**(9): 1549-1557.

Dhital, A., Pey, T. and Stanford, M. R. (2010). "Visual loss and falls: a review." *Eye* **24**(9): 1437-1446.

Dua, H. S., Faraj, L. A., Said, D. G., Gray, T. and Lowe, J. (2013). "Human Corneal Anatomy Redefined A Novel Pre-Descemet's Layer (Dua's Layer)." *Ophthalmology* **120**(9): 1778-1785.

Dubbelman, M., Weeber, H. A., van der Heijde, R. and Volker-Dieben, H. J. (2002). "Radius and asphericity of the posterior corneal surface determined by corrected Scheimpflug photography." *Acta Ophthalmologica Scandinavica* **80**(4): 379-383.

Dunne, M. C., Royston, J. M. and Barnes, D. A. (1991). "Posterior corneal surface toricity and total corneal astigmatism." *Optometry and Vision Science* **68**(9): 708-710.

Efron, N. (2010). Contact Lens Practice, Elsevier.

Elbaz, U., Barkana, Y., Gerber, Y., Avni, I. and Zadok, D. (2007). "Comparison of Different Techniques of Anterior Chamber Depth and Keratometric Measurements." *American Journal of Ophthalmology* **143**(1): 48-53.

Elliott, D. B. and Chapman, G. J. (2010). "Adaptive gait changes due to spectacle magnification and dioptric blur in older people." *Investigative Ophthalmology and Visual Science* **51**(2): 718-722.

Elliott, D. B., Patla, A. and Bullimore, M. A. (1997). "Improvements in clinical and functional vision and perceived visual disability after first and second eye cataract surgery." *British Journal of Ophthalmology* **81**(10): 889-895.

Elliott, M., Callender, M. G. and Elliott, D. B. (1994). "Accuracy of Javal's rule in the determination of spectacle astigmatism." *Optometry and Vision Science* **71**(1): 23-26.

Eom, Y., Nam, K. T., Kang, S. Y., Kim, H. M. and Song, J. S. (2013). "Axis difference between corneal and internal astigmatism to consider for toric intraocular lenses." *American Journal of Ophthalmology* **156**(6): 1112-1119 e1112.

Eom, Y., Yoo, E., Kang, S. Y., Kim, H. M. and Song, J. S. (2013). "Change in efficiency of aspheric intraocular lenses based on pupil diameter." *American Journal of Ophthalmology* **155**(3): 492-498 e492.

Eppig, T., Scholz, K., Loffler, A., Messner, A. and Langenbucher, A. (2009). "Effect of decentration and tilt on the image quality of aspheric intraocular lens designs in a model eye." *Journal of Cataract and Refractive Surgery* **35**(6): 1091-1100.

Ermiş, S. S., Inan, U. U. and Oztürk, F. (2004). "Surgically induced astigmatism after superotemporal and superonasal clear corneal incisions in phacoemulsification." *Journal of Cataract and Refractive Surgery* **30**(6): 1316-1319.

Fam, H.-B. and Lim, K.-L. (2007). "Validity of the keratometric index: Large population-based study." *Journal of Cataract and Refractive Surgery* **33**(4): 686-691.

Faul, F., Erdfelder, E., Lang, A.-G. and Buchner, A. (2007). "G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences." *Behavior Research Methods* **39**(2): 175-191.

Febbraro, J. L., Wang, L., Borasio, E., Richiardi, L., Khan, H. N., Saad, A., Gatinel, D. and Koch, D. D. (2015). "Astigmatic equivalence of 2.2-mm and 1.8-mm superior clear corneal cataract incision." *Graefes Archive for Clinical and Experimental Ophthalmology* **253**(2): 261-265.

Felipe, A., Artigas, J. M., Díez-Ajenjo, A., García-Domene, C. and Alcocer, P. (2011). "Residual astigmatism produced by toric intraocular lens rotation." *Journal of Cataract and Refractive Surgery* **37**(10): 1895-1901.

Ferreira, T. B. and Almeida, A. (2012). "Comparison of the visual outcomes and OPD-scan results of AMO Tecnis toric and Alcon Acrysof IQ toric intraocular lenses." *Journal of Refractive Surgery* **28**(8): 551-555.

Ferrer-Blasco, T., Montes-Mico, R., Peixoto-de-Matos, S. C., Gonzalez-Meijome, J. M. and Cervino, A. (2009). "Prevalence of corneal astigmatism before cataract surgery." *Journal of Cataract and Refractive Surgery* **35**(1): 70-75.

Fitzpatrick, R. and McCloskey, D. I. (1994). "Proprioceptive, visual and vestibular thresholds for the perception of sway during standing in humans." *Journal of Physiology* **478**(Pt 1): 173-186.

Flash, T. and Hogan, N. (1985). "The coordination of arm movements: an experimentally confirmed mathematical model." *Journal of Neuroscience* **5**(7): 1688-1703.

Foster, R. J., Hotchkiss, J., Buckley, J. G. and Elliott, D. B. (2014). "Safety on stairs: influence of a tread edge highlighter and its position." *Experimental Gerontology* **55**: 152-158.

Foster, R. J., Whitaker, D., Scally, A. J., Buckley, J. G. and Elliott, D. B. (2015). "What you see is what you step: the horizontal-vertical illusion increases toe clearance in older adults during stair ascent." *Investigative Ophthalmology and Visual Science* **56**(5): 2950-2957.

Freitas, G. O., Boteon, J. E., Carvalho, M. J. and Pinto, R. M. C. (2014). "Treatment of astigmatism during phacoemulsification." *Arquivos Brasileiros de Oftalmologia* **77**(1): 40-46.

Gale, R. P., Saldana, M., Johnston, R. L., Zuberbuhler, B. and McKibbin, M. (2007). "Benchmark standards for refractive outcomes after NHS cataract surgery." *Eye* **23**(1): 149-152.

Garzon, N., Poyales, F., de Zarate, B. O., Ruiz-Garcia, J. L. and Quiroga, J. A. (2015). "Evaluation of rotation and visual outcomes after implantation of monofocal and multifocal toric intraocular lenses." *Journal of Refractive Surgery* **31**(2): 90-97.

Gibson, J. J. (2009). "Reprinted from The British Journal of Psychology (1958), 49, 182-194: Visually controlled locomotion and visual orientation in animals." *British Journal of Psychology* **100**(Pt 1A): 259-271.

Gil, M. A., Varon, C., Rosello, N., Cardona, G. and Buil, J. A. (2012). "Visual acuity, contrast sensitivity, subjective quality of vision, and quality of life with 4 different multifocal IOLs." *European Journal of Ophthalmology* **22**(2): 175-187.

Glasser, A. and Campbell, M. (1998). "Presbyopia and the optical changes in the human crystalline lens with age." **38**(2): 209.

Glasser, A. and Campbell, M. C. (1999). "Biometric, optical and physical changes in the isolated human crystalline lens with age in relation to presbyopia." **39**(11): 1-25.

Gobin, L., Tassignon, M. J., Wouters, K. and De Groot, V. (2011). "Surgically induced astigmatism after intraocular lens implantation using the bag-in-the-lens technique." *Journal of Cataract and Refractive Surgery* **37**(6): 1015-1019.

Goerig, M., Bacon, D. and van Zundert, A. (2012). "Carl Koller, cocaine, and local anesthesia: some less known and forgotten facts." *Regional Anesthesia and Pain Medicine* **37**(3): 318-324.

Gray, M., DaSilva, P. and (2010). NHS Atlas of Variations. NHS.

Grosvenor, T. and Ratnakaram, R. (1990). "Is the relation between keratometric astigmatism and refractive astigmatism linear?" *Optometry and Vision Science* **67**(8): 606-609.

Grzybowski, A. and Ascaso, F. J. (2014). "Sushruta in 600 B.C. introduced extraocular expulsion of lens material." *Acta Ophthalmol* **92**(2): 194-197.

Gudmundsdottir, E., Arnarsson, A. and Jonasson, F. (2005). "Five-year refractive changes in an adult population: Reykjavik Eye Study." *Ophthalmology* **112**(4): 672-677.

Guerraz, M. and Bronstein, A. M. (2008). "Ocular versus extraocular control of posture and equilibrium." *Neurophysiologie Clinique* **38**(6): 391-398.

Guilbert, E., Saad, A., Grise-Dulac, A. and Gatinel, D. (2012). "Corneal thickness, curvature, and elevation readings in normal corneas: Combined Placido–Scheimpflug system versus combined Placido–scanning-slit system." *Journal of Cataract and Refractive Surgery* **38**(7): 1198-1206.

Gutmark, R. and Guyton, D. L. (2010). "Origins of the Keratometer and its Evolving Role in Ophthalmology." *Survey of Ophthalmology* **55**(5): 481-497.

Guyton, D. L. (1977). "Prescribing cylinders: The problem of distortion." *Survey of Ophthalmology* **22**(3): 177-188.

Guzowski, M., Fraser-Bell, S., Rochtchina, E., Wang, J. J. and Mitchell, P. (2003). "Asymmetric refraction in an older population: the Blue Mountains Eye Study." *American Journal of Ophthalmology* **136**(3): 551-553.

Hashemi, H., Firoozabadi, M. R., Mehravaran, S. and Gorouhi, F. (2008). "Corneal stability after discontinued soft contact lens wear." *Contact lens & anterior eye : the journal of the British Contact Lens Association* **31**(3): 122-125.

Hayashi, K., Hayashi, H. and Hayashi, F. (1995). "Topographic analysis of the changes in corneal shape due to aging." *Cornea* **14**(5): 527-532.

Hayashi, K., Hayashi, H., Nakao, F. and Hayashi, F. (1995). "The Correlation between Incision Size and Corneal Shape Changes in Sutureless Cataract Surgery." *Ophthalmology* **102**(4): 550-556.

Hayashi, K., Hirata, A., Manabe, S.-I. and Hayashi, H. (2011). "Long-Term Change in Corneal Astigmatism After Sutureless Cataract Surgery." *American Journal of Ophthalmology* **151**(5): 858-865.

Hayashi, K., Masumoto, M. and Takimoto, M. (2015). "Comparison of visual and refractive outcomes after bilateral implantation of toric intraocular lenses with or without a multifocal component." *Journal of Cataract and Refractive Surgery* **41**(1): 73-83.

Hayashi, K., Yoshida, M. and Yoshimura, K. (2014). "Effect of steepest-meridian clear corneal incision for reducing preexisting corneal astigmatism using a meridian-marking method or surgeon's intuition." *Journal of Cataract and Refractive Surgery* **40**(12): 2050-2056.

He, M., Huang, W., Li, Y., Zheng, Y., Yin, Q. and Foster, P. J. (2009). "Refractive error and biometry in older Chinese adults: the Liwan eye study." *Investigative Ophthalmology and Visual Science* **50**(11): 5130-5136.

Henriksen, M., Lund, H., Moe-Nilssen, R., Bliddal, H. and Danneskiod-Samsoe, B. (2004). "Test-retest reliability of trunk accelerometric gait analysis." *Gait and Posture* **19**(3): 288-297.

Hildreth, H. R. (1952). "Daviel, modern surgeon." *Transactions of the American Ophthalmological Society* **50**: 23-29.

Hill, W. (2008). "Expected effects of surgically induced astigmatism on AcrySof toric intraocular lens results." *Journal of Cataract and Refractive Surgery* **34**(3): 364-367.

Hirnschall, N., Gangwani, V., Crnej, A., Koshy, J., Maurino, V. and Findl, O. (2014). "Correction of moderate corneal astigmatism during cataract surgery: toric intraocular lens versus peripheral corneal relaxing incisions." *Journal of Cataract and Refractive Surgery* **40**(3): 354-361.

Ho, J.-D., Tsai, C.-Y. and Liou, S.-W. (2009). "Accuracy of corneal astigmatism estimation by neglecting the posterior corneal surface measurement." *American Journal of Ophthalmology* **147**(5): 788-795- 795.e781-782.

Ho, J.-D., Tsai, C.-Y., Tsai, R. J.-F., Kuo, L.-L., Tsai, I.-L. and Liou, S.-W. (2008). "Validity of the keratometric index: evaluation by the Pentacam rotating Scheimpflug camera." *Journal of Cataract and Refractive Surgery* **34**(1): 137-145.

Hof, A. L. (1996). "Scaling gait data to body size." *Gait and Posture* **4**(3): 222-223.

Hoffer, K. (2010). The evolution of the Intraocular Lens. Cataract Surgery. Steinert, R. F. California, UAS, Saunders, Elsevier**:** 419-438.

Hoffer, K. J. (1980). "Biometry of 7,5000 cataractous eyes." **90**(3): 360-368.

Hoffmann, P. C., Abraham, M., Hirnschall, N. and Findl, O. (2014). "Prediction of Residual Astigmatism After Cataract Surgery Using Swept Source Fourier Domain Optical Coherence Tomography." *Current Eye Research* **39**(12): 1178-1186.

Hoffmann, P. C. and Hütz, W. W. (2010). "Analysis of biometry and prevalence data for corneal astigmatism in 23,239 eyes." **36**(9): 1-7.

Holladay, J. T., Cravy, T. V. and Koch, D. D. (1992). "Calculating the Surgically Induced Refractive Change Following Ocular Surgery." *Journal of Cataract and Refractive Surgery* **18**(5): 429-443.

Holladay, J. T., Moran, J. R. and Kezirian, G. M. (2001). "Analysis of aggregate surgically induced refractive change, prediction error, and intraocular astigmatism." *Journal of Cataract and Refractive Surgery* **27**(1): 61-79.

Howell-Duffy, C. (2013). Scientific evidence to support the art of prescribing spectacles. PhD, Bradford University.

Jaffe, N. S. and Clayman, H. M. (1975). "The Pathophisiology of Corneal Astigmatism after Cataract Extraction." *Transactions - American Academy of Ophthalmology and Otolaryngology* **79**: 615-630.

Jalie, M. (1984). The Principles of Ophthalmic Lenses.

Jampel, R. S. (1999). "The effect of technology on the indications for cataract surgery." *Documenta Ophthalmologica* **98**(1): 95-103.

Javal, E. (1890). Mémoires d'ophtalmométrie. France, G. Masson, Éditeu.

Jester, J. V., Murphy, C. J., Winkler, M., Bergmanson, J. P. G., Brown, D., Steinert, R. F. and Mannis, M. J. (2013). "Lessons in corneal structure and mechanics to guide the corneal surgeon." *Ophthalmology* **120**(9): 1715-1717.

Johnson, L., Elliott, D. B. and Buckley, J. G. (2009). "Effects of gaze strategy on standing postural stability in older multifocal wearers." *Clinical and Experimental Optometry* **92**(1): 19-26.

Johnson, L., Supuk, E., Buckley, J. G. and Elliott, D. B. (2013). "Effects of induced astigmatism on foot placement strategies when stepping onto a raised surface." *PloS One* **8**(5): e63351.

Kandarakis, A., Soumplis, V., Karampelas, M., Koutroumanos, I., Panos, C., Kandarakis, S. and Karagiannis, D. (2012). "Response of corneal hysteresis and central corneal thickness following clear corneal cataract surgery." *Acta Ophthalmologica* **90**(6): 526-529.

Kanski, J. J. (2003). Clinical Ophthalmology, Butterworth Heinemann.

Kaufmann, C., Peter, J., Ooi, K., Phipps, S., Cooper, P., Goggin, M. and Queen Elizabeth Astigmatism Study, G. (2005). "Limbal relaxing incisions versus on-axis incisions to reduce corneal astigmatism at the time of cataract surgery." *Journal of Cataract and Refractive Surgery* **31**(12): 2261-2265.

Kershner, R. M. (1997). "Clear Corneal Cataract Surgery and the Correction of Myopia, Hyperopia, and Astigmatism." *Ophthalmology* **104**(3): 381-389.

Khan, M. I. and Muhtaseb, M. (2011). "Prevalence of corneal astigmatism in patients having routine cataract surgery at a teaching hospital in the United Kingdom." **37**(10): 1751-1755.

Khokhar, S., Lohiya, P., Murugiesan, V. and Panda, A. (2006). "Corneal astigmatism correction with opposite clear corneal incisions or single clear corneal incision: comparative analysis." **32**(9): 1432-1437.

Knox Cartwright, N. E., Johnston, R. L., Jaycock, P. D., Tole, D. M. and Sparrow, J. M. (2010). "The Cataract National Dataset electronic multicentre audit of 55,567 operations: when should IOLMaster biometric measurements be rechecked?" *Eye (Lond)* **24**(5): 894-900.

Kobashi, H., Kamiya, K., Shimizu, K., Kawamorita, T. and Uozato, H. (2012). "Effect of axis orientation on visual performance in astigmatic eyes." *Journal of Cataract and Refractive Surgery* **38**(8): 1352-1359.

Koch, D. D., Ali, S. F., Weikert, M. P., Shirayama, M., Jenkins, R. and Wang, L. (2012). "Contribution of posterior corneal astigmatism to total corneal astigmatism." *Journal of Cataract and Refractive Surgery* **38**(12): 2080-2087.

Koch, D. D., Jenkins, R. B., Weikert, M. P., Yeu, E. and Wang, L. (2013). "Correcting astigmatism with toric intraocular lenses: Effect of posterior corneal astigmatism." *Journal of Cataract and Refractive Surgery* **39**(12): 1803-1809.

Kohnen, T. (2014). "Corneal incisions with femtosecond lasers." *Journal of Cataract and Refractive Surgery* **40**(4): 513.

Koretz, J. F., Cook, C. A., Kaufman, P. L., Koretz, J. F., Cook, C. A. and Kaufman, P. L. (1997). "Accommodation and presbyopia in the human eye. Changes in the anterior segment and crystalline lens with focus." **38**(3): 569-578.

Koshy, J. J., Nishi, Y., Hirnschall, N., Crnej, A., Gangwani, V., Maurino, V. and Findl, O. (2010). "Rotational stability of a single-piece toric acrylic intraocular lens." *Journal of Cataract and Refractive Surgery* **36**(10): 1665-1670.

Kotecha, A., Chopra, R., Fahy, R. T. and Rubin, G. S. (2013). "Dual tasking and balance in those with central and peripheral vision loss." *Investigative Ophthalmology and Visual Science* **54**(8): 5408-5415.

Kucumen, R. B., Yenerel, N. M., Gorgun, E., Kulacoglu, D. N., Oncel, B., Kohen, M. C. and Alimgil, M. L. (2008). "Corneal biomechanical properties and intraocular pressure changes after phacoemulsification and intraocular lens implantation." *Journal of Cataract and Refractive Surgery* **34**(12): 2096-2098.

Lass, J. H., Benetz, B. A., Gal, R. L., Kollman, C., Raghinaru, D., Dontchev, M., Mannis, M. J., Holland, E. J., Chow, C., McCoy, K., Price, F. W., Jr., Sugar, A., Verdier, D. D. and Beck, R. W. (2013). "Donor age and factors related to endothelial cell loss 10 years after penetrating keratoplasty: Specular Microscopy Ancillary Study." *Ophthalmology* **120**(12): 2428-2435.

Leaming, D. V. (2004). "Practice styles and preferences of ASCRS members - 2003 survey." *Journal of Cataract and Refractive Surgery* **30**(4): 892-900.

Lee, D. N. and Lishman, R. (1977). "Visual control of locomotion." *Scandinavian Journal of Psychology* **18**(3): 224-230.

Lens, A., Nemeth, S. C. and Ledford, J. K. (1999). Ocular Anatomy and Physiology. New Jersey, USA, Slack Incorporated.

Lever, J. and Dahan, E. (2000). "Opposite clear corneal incisions to correct pre-existing astigmatism in cataract surgery." *Journal of Cataract and Refractive Surgery* **26**(6): 803-805.

Leyland, M. (2004). "Validation of Orbscan II posterior corneal curvature measurement for intraocular lens power calculation." *Eye (Lond)* **18**(4): 357-360.

Lindstrom, R. (2010). Polymethylmethacrylate Intraocular lenses. Cataract Surgery. Steinert, R. F. California, USA, Suaders, Elsivier**:** 439-4448.

Linebarger, E. J., Hardten, D. R., Shah, G. K. and Lindstrom, R. L. (1999). "Phacoemulsification and modern cataract surgery." *Survey of Ophthalmology* **44**(2): 123-147.

Lord, S., Sherrignton, C., Menz, H. and Close, J. (2007). Falls in Older People: Risk Factors and Strategies for Prevention, Cambridge Universit Press 26 - 49.

Lord, S. R. and Dayhew, J. (2001). "Visual risk factors for falls in older people." *Journal of the American Geriatrics Society* **49**(5): 508-515.

Luo, L., Lin, H., He, M., Congdon, N., Yang, Y. and Liu, Y. (2012). "Clinical evaluation of three incision size-dependent phacoemulsification systems." *American Journal of Ophthalmology* **153**(5): 831-839 e832.

Magar, J. B. A., Cunningham, F. and Brian, G. (2013). "Comparison of Automated and Partial Coherence Keratometry and Resulting Choice of Toric IOL." *Optometry and Vision Science* **90**(4): 385-391.

Maki, B. E., Perry, S. D., Scovil, C. Y., Peters, A. L., McKay, S. M., Lee, T. A., Corbeil, P., Fernie, G. R. and McIlroy, W. E. (2008). "Interventions to promote more effective balance-recovery reactions in industrial settings: new perspectives on footwear and handrails." *Industrial Health* **46**(1): 40-50.

Mamalis, N., Brubaker, J., Davis, D., Espandar, L. and Werner, L. (2008). "Complications of foldable intraocular lenses requiring explantation or secondary intervention - 2007 survey update." *Journal of Cataract and Refractive Surgery* **34**(9): 1584-1591.

Mancini, M., Horak, F. B., Zampieri, C., Carlson-Kuhta, P., Nutt, J. G. and Chiari, L. (2011). "Trunk accelerometry reveals postural instability in untreated Parkinson's disease." *Parkinsonism & Related Disorders* **17**(7): 557-562.

Mancini, M., Salarian, A., Carlson-Kuhta, P., Zampieri, C., King, L., Chiari, L. and Horak, F. B. (2012). "ISway: a sensitive, valid and reliable measure of postural control." *Journal of Neuroengineering and Rehabilitation* **9**(1): 59.

Mas, D., Espinosa, J., Domenech, B., Perez, J., Kasprzak, H. and Illueca, C. (2009). "Correlation between the dioptric power, astigmatism and surface shape of the anterior and posterior corneal surfaces." *Ophthalmic and Physiological Optics* **29**(3): 219-226.

Masket, S. and Tennen, D. G. (1996). "Astigmatic stabilization of 3.0 mm temporal clear corneal cataract incisions." *Journal of Cataract and Refractive Surgery* **22**(10): 1451-1455.

Masket, S., Wang, L. and Belani, S. (2009). "Induced Astigmatism With 2.2-and 3.0-mm Coaxial Phacoemulsification Incisions." *Journal of Refractive Surgery* **25**(1): 21-24.

McCollum, G., Shupert, C. L. and Nashner, L. M. (1996). "Organizing sensory information for postural control in altered sensory environments." *Journal of Theoretical Biology* **180**(3): 257-270.

McGwin Jr, G., Gewant, H. D., Modjarrad, K., Hall, T. A. and Owsley, C. (2006). "Effect of Cataract Surgery on Falls and Mobility in Independently Living Older Adults." *Journal of the American Geriatrics Society* **54**(7): 1089-1094.

McKee, H. D., Irion, L. C. D., Carley, F. M., Brahma, A. K., Jafarinasab, M. R., Rahmati-Kamel, M., Kanavi, M. R. and Feizi, S. (2014). "Re: Dua et al.: Human corneal anatomy redefined: a novel pre-Descemet layer (Dua's layer) (Ophthalmology 2013;120:1778–85)." *Ophthalmology* **121**(5): e24-e25.

Meek, K. M. and Newton, R. H. (1999). "Organization of collagen fibrils in the corneal stroma in relation to mechanical properties and surgical practice." **15**(6): 695-699.

Mencucci, R., Giordano, C., Favuzza, E., Gicquel, J.-J., Spadea, L. and Menchini, U. (2013). "Astigmatism correction with toric intraocular lenses: wavefront aberrometry and quality of life." *British Journal of Ophthalmology* **97**(5): 578-582.

Mendicute, J., Irigoyen, C., Ruiz, M., Illarramendi, I., Ferrer-Blasco, T. and Montes-Mico, R. (2009). "Toric intraocular lens versus opposite clear corneal incisions to correct astigmatism in eyes having cataract surgery." *Journal of Cataract and Refractive Surgery* **35**(3): 451-458.

Mendivil, A. (1996). "Comparative study of astigmatism through superior and lateral small incisions." **6**(4): 389-392.

Mingo-Botín, D., Muñoz-Negrete, F. J., Won Kim, H. R., Morcillo-Laiz, R., Rebolleda, G. and Oblanca, N. (2010). "Comparison of toric intraocular lenses and peripheral corneal relaxing incisions to treat astigmatism during cataract surgery." *Journal of Cataract and Refractive Surgery* **36**(10): 1700-1708.

Miyake, T., Shimizu, K. and Kamiya, K. (2015). "Distribution of Posterior Corneal Astigmatism According to Axis Orientation of Anterior Corneal Astigmatism." *PloS One* **10**(1).

Miyata, K., Miyai, T., Minami, K., Bissen-Miyajima, H., Maeda, N. and Amano, S. (2011). "Limbal relaxing incisions using a reference point and corneal topography for intraoperative identification of the steepest meridian." *Journal of Refractive Surgery* **27**(5): 339-344.

Mohler, B. J., Thompson, W. B., Creem-Regehr, S. H., Pick, H. L., Jr. and Warren, W. H., Jr. (2007). "Visual flow influences gait transition speed and preferred walking speed." *Experimental Brain Research* **181**(2): 221-228.

Momeni-Moghaddam, H., Naroo, S. A., Askarizadeh, F. and Tahmasebi, F. (2014). "Comparison of fitting stability of the different soft toric contact lenses." *Cont Lens Anterior Eye* **37**(5): 346-350.

Montés-Micó, R., Cerviño, A. and Ferrer-Blasco, T. (2009). "Intraocular lens centration and stability: efficacy of current technique and technology." **20**(1): 33-36.

Montés-Micó, R., Ferrer-Blasco, T. and Cerviño, A. (2009). "Analysis of the possible benefits of aspheric intraocular lenses: Review of the literature." *Journal of Cataract and Refractive Surgery* **35**(1): 172-181.

Moon, S. C., Mohamed, T. and Fine, I. H. (2007). "Comparison of Surgically Induced Astigmatisms after Clear Corneal Incisions of Different Sizes." *Korean journal of ophthalmology : KJO* **21**(1): 1.

Muller-Jensen, K., Fischer, P. and Siepe, U. (1999). "Limbal relaxing incisions (LRI) for correcting astigmatism in clear corneal cataract surgery." *Der Ophthalmologe* **96**(7): 432-436.

Naeser, K. (2008). "Assessment and statistics of surgically induced astigmatism." *Acta Ophthalmologica* **86 Suppl 1**(thesis1): 5-28.

Nangia, V., Jonas, J. B., Sinha, A., Matin, A., Kulkarni, M. and (2010). "Refractive error in central India: the Central India Eye and Medical Study." **117**(4): 693-699.

Nashner, L. M., Black, F. O. and Wall, C., 3rd (1982). "Adaptation to altered support and visual conditions during stance: patients with vestibular deficits." *Journal of Neuroscience* **2**(5): 536-544.

Nemeth, G., Berta, A., Szalai, E., Hassan, Z. and Modis, L. (2014). "Analysis of surgically induced astigmatism on the posterior surface of the cornea." *Journal of Refractive Surgery* **30**(9): 604-608.

Németh, J., Erdélyi, B. and Csákány, B. (2001). "Corneal topography changes after a 15 second pause in blinking." *Journal of Cataract and Refractive Surgery* **27**(4): 589-592.

Nevitt, M. C., Cummings, S. R. and Hudes, E. S. (1991). "Risk Factors for Injurious Falls: a Prospective Study." *Journal of Gerontology* **46**(5): M164-M170.

Ninn-Pederson, K. (1992). "Cataract patients in a defined Swedish population 1986-1990." 10-15.

Norrby, S., Hirnschall, N., Nishi, Y. and Findl, O. (2013). "Fluctuations in corneal curvature limit predictability of intraocular lens power calculations." *Journal of Cataract and Refractive Surgery* **39**(2): 174-179.

Ofir, S., Abulafia, A., Kleinmann, G., Reitblat, O. and Assia, E. I. (2015). "Surgically induced astigmatism assessment: comparison between three corneal measuring devices." *Journal of Refractive Surgery* **31**(4): 244-247.

Ophthalmologists, R. C. o. (2010). Cataract Surgery Guidelines. London, The Royal College of Ophthalmologists.

Osher, R. H. (2010). "Iris fingerprinting: New method for improving accuracy in toric lens orientation." *Journal of Cataract and Refractive Surgery* **36**(2): 351-352.

Ouchi, M. and Kinoshita, S. (2009). "Prospective Randomized Trial of Limbal Relaxing Incisions Combined with Microincision Cataract Surgery." *Journal of Refractive Surgery* **26**(8): 594-599.

Oyster, C. W. (1999). The Human Eye, Sinauer Associates.

Ozyol, E. and Ozyol, P. (2012). "The relation between superior phacoemulsification incision and steep axis on astigmatic outcomes." **32**(6): 565-570.

Packer, M., Chu, Y. R., Waltz, K. L., Donnenfeld, E. D., Wallace, R. B., 3rd, Featherstone, K., Smith, P., Bentow, S. S. and Tarantino, N. (2010). "Evaluation of the aspheric tecnis multifocal intraocular lens: one-year results from the first cohort of the food and drug administration clinical trial." *American Journal of Ophthalmology* **149**(4): 577-584.e571.

Pandey, S. K., Milverton, E. J. and Maloof, A. J. (2004). "A tribute to Charles David Kelman MD: ophthalmologist, inventor and pioneer of phacoemulsification surgery." *Clinical & Experimental Ophthalmology* **32**(5): 529-533.

Patla, A. E. (1997). "Understanding the roles of vision in the control of human locomotion." *Gait and Posture* **5**(1): 54-69.

Patla, A. E. (1998). "How is human gait controlled by vision." *Ecological Psychology*.

Patla, A. V., J. (2003). "How far ahead do we look when required to step on specific locations in the travel path during locomotion?" *Experimental Brain Research* **148**(1): 133-138.

Perez, G. M., Archer, S. M. and Artal, P. (2010). "Optical characterization of Bangerter foils." *Investigative Ophthalmology and Visual Science* **51**(1): 609-613.

Pesudovs, K., Elliott, D. B. and (2001). "The Evolution of Cataract Surgery."

Peters, H. B. (1961). "The relationship between refractive error and visual acuity at three age levels " *Optometry and Vision Science* **38**(4): 194-198.

Pfleger, T., Skorpik, C., Menapace, R., Scholz, U., Weghaupt, H. and Zehetmayer, M. (1996). "Long-term course of induced astigmatism after clear corneal incision cataract surgery." *Journal of Cataract and Refractive Surgery* **22**(1): 72-77.

Pick, Z. S., Leaming, D. V. and Elder, M. J. (2008). "The fourth New Zealand cataract and refractive surgery survey: 2007." *Clinical & Experimental Ophthalmology* **36**(7): 604-619.

Piñero, D. P., Camps, V. J., Mateo, V. and Ruiz-Fortes, P. (2012). "Clinical validation of an algorithm to correct the error in the keratometric estimation of corneal power in normal eyes." *Journal of Cataract and Refractive Surgery* **38**(8): 1333-1338.

Popp, N., Hirnschall, N., Maedel, S. and Findl, O. (2012). "Evaluation of 4 corneal astigmatic marking methods." *Journal of Cataract and Refractive Surgery* **38**(12): 2094-2099.

Portney, L. and Watkins, M. (2009). Foundations of clinical research : applications to practice. New Jersey, USA, Pearson.

Prajapati, B., Dunne, M. and Armstrong, R. (2010). "Sample size estmation and statistical power analysis." *Optometry Today*.

Read, S. A., Collins, M. J., Iskander, D. R. and Davis, B. A. (2009). "Corneal topography with Scheimpflug imaging and videokeratography: Comparative study of normal eyes." *Journal of Cataract and Refractive Surgery* **35**(6): 1072-1081.

Reddy, B., Raj, A. and Singh, V. P. (2007). "Site of Incision and Corneal Astigmatism in Conventional SICS versus Phacoemulsification." *Annals of Ophthalmology* **39**(3): 209-216.

Remón, L., Benlloch, J. and Furlan, W. D. (2009). "Corneal and refractive astigmatism in adults: a power vectors analysis." *Optometry and vision science : official publication of the American Academy of Optometry* **86**(10): 1182-1186.

Reuland, M. S., Reuland, A. J., Nishi, Y. and Auffarth, G. U. (2007). "Corneal radii and anterior chamber depth measurements using the IOLMaster versus the Pentacam." *Journal of Refractive Surgery* **23**(4): 368-373.

Reynolds, R. F. and Bronstein, A. M. (2003). "The broken escalator phenomenon." *Experimental Brain Research* **151**(3): 301-308.

Riley, A. F., Grupcheva, C. N., Malik, T. Y., Craig, J. P. and McGhee, C. N. (2001). "The Auckland Cataract Study: demographic, corneal topographic and ocular biometric parameters." *Clinical & Experimental Ophthalmology* **29**(6): 381-386.

Rinaldi, N. M., Polastri, P. F. and Barela, J. A. (2009). "Age-related changes in postural control sensory reweighting." *Neuroscience Letters* **467**(3): 225-229.

Rink, H. (1987). "Cataractogenic risk factors." **15**: 66-76.

Robinovitch, S. N., Feldman, F., Yang, Y., Schonnop, R., Leung, P. M., Sarraf, T., Sims-Gould, J. and Loughin, M. (2013). "Video capture of the circumstances of falls in elderly people residing in long-term care: an observational study." *Lancet* **381**(9860): 47-54.

Roh, H. C., Chuck, R. S., Lee, J. K. and Park, C. Y. (2015). "The effect of corneal irregularity on astigmatism measurement by automated versus ray tracing keratometry." *Medicine (Baltimore)* **94**(13): e677.

Rosen, E., Barry, P. and (2013). European Society of Cataract & Refractive Surgeons: A History, European Society of Cataract and Refractive Surgery.

Roy, P. N., Mehra, K. S. and Deshpande, P. J. (1975). "Cataract surgery performed before 800 B.C." **59**(3): 171-171.

Samuelson, S. W., Koch, D. D. and Kuglen, C. C. (1991). "Determination of maximal incision length for true small-incision surgery." **22**(4): 204-207.

Sanders, D., Granbow, H. and Shepherd, J. (1992). The Toric IOL.

Santodomingo-Rubido, J., Mallen, E., Gilmartin, B. and Wolffsohn, J. S. (2002). "A new non-contact optical device for ocular biometry." *British Journal of Ophthalmology* **86**(4): 458-462.

Sarabon, N., Rosker, J., Loefler, S. and Kern, H. (2013). "The effect of vision elimination during quiet stance tasks with different feet positions." *Gait and Posture* **38**(4): 708-711.

Savini, G., Barboni, P., Carbonelli, M. and Hoffer, K. J. (2009). "Accuracy of Scheimpflug corneal power measurements for intraocular lens power calculation." *Journal of Cataract and Refractive Surgery* **35**(7): 1193-1197.

Schiff, W., Caviness, J. A. and Gibson, J. J. (1962). "Persistent fear responses in rhesus monkeys to the optical stimulus of "looming"." *Science* **136**(3520): 982-983.

Schwartz, S., Segal, O., Barkana, Y., Schwesig, R., Avni, I. and Morad, Y. (2005). "The effect of cataract surgery on postural control." *Investigative Ophthalmology and Visual Science* **46**(3): 920-924.

Scialdone, A., Gaetano, F. and Monaco, G. (2013). "Visual performance of 2 aspheric toric intraocular lenses: comparative study." **39**(6): 1-9.

Seddon, J., Fong, D., West, S. K. and Valmadrid, C. T. (1995). "Epidemiology of risk factors for age-related cataract." **39**(4): 323-334.

Seo, J. M., Kim, K. K., Kim, J. H., Park, K. S. and Chung, H. (2004). Measurement of ocular torsion using digital fundus image. 26th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, IEEE. **3:** 1711-1713.

Shankar, S. and Bobier, W. R. (2004). "Corneal and lenticular components of total astigmatism in a preschool sample." *Optometry and Vision Science* **81**(7): 536-542.

Shepherd, J. R. (1989). "Induced astigmatism in small incision cataract surgery." *Journal of Cataract and Refractive Surgery* **15**(1): 85-88.

Sherwin, J. C., Kelly, J., Hewitt, A. W., Kearns, L. S., Griffiths, L. R. and Mackey, D. A. (2011). "Prevalence and predictors of refractive error in a genetically isolated population: the Norfolk Island Eye Study." *Clinical & Experimental Ophthalmology* **39**(8): 734-742.

Shimizu, K., Misawa, A. and Suzuki, Y. (1994). "Toric intraocular lenses: Correcting astigmatism while controlling axis shift." *Journal of Cataract and Refractive Surgery* **20**(5): 523-526.

Shimoda, T., Shimoda, G., Hida, W. T., Nakano, C. T., Motta, A. F., Guimaraes, A. S. and Tzelikis, P. F. (2014). "Visual outcomes after implantation of a novel refractive toric multifocal intraocular lens." *Arquivos Brasileiros de Oftalmologia* **77**(2): 71-75.

Shinya, M., Popescu, A., Marchak, C., Maraj, B. and Pearson, K. (2012). "Enhancing memory of stair height by the motor experience of stepping." *Experimental Brain Research* **223**(3): 405-414.

Shirayama, M., Wang, L., Weikert, M. P. and Koch, D. D. (2009). "Comparison of Corneal Powers Obtained from 4 Different Devices." *American Journal of Ophthalmology* **148**(4): 528-535.e521.

Siu, K.-C., Lugade, V., Chou, L.-S., van Donkelaar, P. and Woollacott, M. (2008). "Dual-task interference during obstacle clearance in healthy and balance-impaired older adults." *Aging Clinical and Experimental Research* **20**(4): 349-354.

Smith, G. (2003). "The optical properties of the crystalline lens and their significance." **86**(1): 3.

Smith, G. and Pierscionek, B. K. (1998). "The optical structure of the lens and its contribution to the refractive status of the eye." *Ophthalmic and Physiological Optics* **18**(1): 21-29.

Sparrow, J. M., Bron, A. J., Brown, N. A., Ayliffe, W. and Hill, A. R. (1986). "The Oxford Clinical Cataract Classification and Grading System." **9**(4): 207-225.

Srivannaboon, S., Chirapapaisan, C., Chonpimai, P. and Koodkaew, S. (2015). "Comparison of corneal astigmatism measurements of 2 optical biometer models for toric intraocular lens selection." *Journal of Cataract and Refractive Surgery* **41**(2): 364-371.

Srivannaboon, S., Ling, L. K., Cheng, A. C., Bor, F. H. and (2007). A Clinician's Guide to Slit Scanning Corneal Topography

Srivannaboon, S., Soeharnila, Chirapapaisan, C. and Chonpimai, P. (2012). "Comparison of corneal astigmatism and axis location in cataract patients measured by total corneal power, automated keratometry, and simulated keratometry." *Journal of Cataract and Refractive Surgery* **38**(12): 2088-2093.

Startzell, J. K., Owens, D. A., Mulfinger, L. M. and Cavanagh, P. R. (2000). "Stair negotiation in older people: A review." *Journal of the American Geriatrics Society* **48**(5): 567-580.

Steinert, R. F. (2010). Cataract Surgery, Elsevier Health Sciences.

Steinert, R. F., Brint, S. F., White, S. M. and Fine, I. H. (1991). "Astigmatism after small incision cataract surgery: a prospective, randomized, multicenter comparison of 4-and 6.5-mm incisions." *Ophthalmology* **98**(4): 417-424.

Steins, D., Sheret, I., Dawes, H., Esser, P. and Collett, J. (2014). "A smart device inertial-sensing method for gait analysis." *Journal of Biomechanics* **47**(15): 3780-3785.

Supuk, E., Alderson, A., Davey, C. J., Scally, A., Green, C., Litvin, N. and Elliott, D. B. (2013). Why Does Cataract Surgery Not Reduce Falls Rate as Much as You Would Expect? British Congress of Optometry and Vision Science.

Tan, J. S., Wang, J. J., Younan, C., Cumming, R. G., Rochtchina, E. and Mitchell, P. (2008). "Smoking and the long-term incidence of cataract: the Blue Mountains Eye Study." **15**(3): 155-161.

Tejedor, J. and Murube, J. (2005). "Choosing the Location of Corneal Incision Based on Preexisting Astigmatism in Phacoemulsification." *American Journal of Ophthalmology* **139**(5): 767-776.

Templer, J. A. (1992). The Staircase - studies of hazards, falls, and safer design. CAmbridgge, MIT Press.

Teus, M. A., Arruabarrena, C., Hernández-Verdejo, J. L., Sales-Sanz, A. and Sales-Sanz, M. (2010). "Correlation between keratometric and refractive astigmatism in pseudophakic eyes." *Journal of Cataract and Refractive Surgery* **36**(10): 1671-1675.

Thibos, L. N. and Horner, D. (2001). "Power vector analysis of the optical outcome of refractive surgery." *Journal of Cataract and Refractive Surgery* **27**(1): 80-85.

Thibos, L. N., Wheeler, W. and Horner, D. (1997). "Power vectors: An application of Fourier analysis to the description and statistical analysis of refractive error." *Optometry and Vision Science* **74**(6): 367-375.

Timmis, M. A., Scarfe, A. C., Tabrett, D. R. and Pardhan, S. (2014). "Kinematic analysis of step ascent among patients with central visual field loss." *Gait and Posture* **39**(1): 252-257.

Tomomitsu, M. S., Alonso, A. C., Morimoto, E., Bobbio, T. G. and Greve, J. M. (2013). "Static and dynamic postural control in low-vision and normal-vision adults." *Clinics (Sao Paulo)* **68**(4): 517-521.

Treml, J., Husk, J., Lowe, D. and Vasilakis, N. (2011). "Falling standards, broken promises. Report of the national audit of falls and bone health in older people 2010." *Royal Collge Of Physicians*.

Trikha, S., Turnbull, A. M. J., Morris, R. J., Anderson, D. F. and Hossain, P. (2013). "The journey to femtosecond laser-assisted cataract surgery: new beginnings or a false dawn?" *Eye (Lond)* **27**(4): 461-473.

Tseng, V. L., Yu, F., Lum, F. and Coleman, A. L. (2012). "Risk of Fractures Following Cataract Surgery in Medicare Beneficiaries." *JAMA* **308**(5): 493-501.

Tunnacliffe, A. H. (1993). Visual Optics.

Tunnacliffe, A. H. (1997). Introduction to Visual Optics.

Verhulst, E. and Vrijghem, J. C. (2001). "Accuracy of intraocular lens power calculations using the Zeiss IOL master. A prospective study." *Bulletin de la Société Belge d'Ophtalmologie*(281): 61-65.

Viestenz, A., Seitz, B. and Langenbucher, A. (2005). "Evaluating the eye's rotational stability during standard photography: effect on determining the axial orientation of toric intraocular lenses." *Journal of Cataract and Refractive Surgery* **31**(3): 557-561.

Vinas, M., de Gracia, P., Dorronsoro, C., Sawides, L., Marin, G., Hernandez, M. and Marcos, S. (2013). "Astigmatism impact on visual performance: meridional and adaptational effects." *Optometry and Vision Science* **90**(12): 1430-1442.

Visser, N., Berendschot, T. T. J. M., Verbakel, F., de Brabander, J. and Nuijts, R. M. M. A. (2012). "Comparability and repeatability of corneal astigmatism measurements using different measurement technologies." *Journal of Cataract and Refractive Surgery* **38**(10): 1764-1770.

Vitale, S., Ellwein, L., Cotch, M. F., Ferris, F. L., 3rd and Sperduto, R. (2008). "Prevalence of refractive error in the United States, 1999-2004." *Archives of Ophthalmology* **126**(8): 1111-1119.

Wang, L., Mahmoud, A. M., Anderson, B. L., Koch, D. D. and Roberts, C. J. (2011). "Total Corneal Power Estimation: Ray Tracing Method versus Gaussian Optics Formula." *Investigative Ophthalmology & Visual Science* **52**(3): 1716-1722.

Wang, Q., Savini, G., Hoffer, K. J., Xu, Z., Feng, Y., Wen, D., Hua, Y., Yang, F., Pan, C. and Huang, J. (2012). "A Comprehensive Assessment of the Precision and Agreement of Anterior Corneal Power Measurements Obtained Using 8 Different Devices." *PloS One* **7**(9): e45607.

Wang, X., McCulley, J. P., Bowman, R. W. and Cavanagh, H. D. (2002). "Time to resolution of contact lens-induced corneal warpage prior to refractive surgery." *CLAO Journal* **28**(4): 169-171.

Wei, Y.-H., Chen, W.-L., Su, P.-Y., Shen, E. P. and Hu, F.-R. (2012). "The influence of corneal wound size on surgically induced corneal astigmatism after phacoemulsification." *Journal of the Formosan Medical Association* **111**(5): 284-289.

Whang, W.-J., Byun, Y.-S. and Joo, C.-K. (2012). "Comparison of refractive outcomes using five devices for the assessment of preoperative corneal power." *Clinical & Experimental Ophthalmology* **40**(5): 425-432.

Wilson, R. S. and Roper-Hall, M. J. (1982). "Effect of age on the endothelial cell count in the normal eye." *British Journal of Ophthalmology* **66**(8): 513-515.

Wilson, S. E., Lin, D. T., Klyce, S. D., Reidy, J. J. and Insler, M. S. (1990). "Topographic changes in contact lens-induced corneal warpage." *Ophthalmology* **97**(6): 734-744.

Wirbelauer, C., Anders, N., Pham, D. T. and Wollensak, J. (1997). "Effect of incision location on preoperative oblique astigmatism after scleral tunnel incision." *Journal of Cataract and Refractive Surgery* **23**(3): 365-371.

Wolffsohn, J. S. (2008). Ophthalmic Imaging, Elsevier Health Sciences.

Wolffsohn, J. S., Bhogal, G. and Shah, S. (2011). "Effect of uncorrected astigmatism on vision." *Journal of Cataract and Refractive Surgery* **37**(3): 454-460.

Wolffsohn, J. S. and Buckhurst, P. J. (2010). "Objective analysis of toric intraocular lens rotation and centration." *Journal of Cataract and Refractive Surgery* **36**(5): 778-782.

Wong, H. C., Davis, G. and Della, N. (1994). "Corneal astigmatism induced by superior versus temporal corneal incisions for extracapsular cataract extraction." *Australian and New Zealand Journal of Ophthalmology* **22**(4): 237-241.

Woolf, A. D. (2003). "Preventing fractures in elderly people." *British Medical Journal* **327**(7406): 89-95.

Yao, K., Tang, X. and Ye, P. (2006). "Corneal astigmatism, high order aberrations, and optical quality after cataract surgery: microincision versus small incision." *Cornea*.

Zaki, A. A., Elalfy, M. S., Said, D. G. and Dua, H. S. (2015). "Deep anterior lamellar keratoplasty--triple procedure: a useful clinical application of the pre-Descemet's layer (Dua's layer)." *Eye (Lond)* **29**(3): 323-326.

Zigman, S., Datiles, M., Torczynski, E., Zigman, S., Datiles, M., Torczynski, E. and (1979). "Sunlight and human cataracts." **18**(5): 1-6.

Bibliography

Benjamin, W. J. and I. M. Borish (2007). Borish's Clinical Refraction, Butterworth-Heinemann.

Bennett, A. G., R. B. Rabbetts and (1998). Clinical Visual Optics.

Lens, A., S. C. Nemeth and J. K. Ledford (1999). Ocular Anatomy and Physiology. New Jersey, USA, Slack Incorporated.

Oyster, C. W. (1999). The Human Eye, Sinauer Associates.

Rosen, E., P. Barry and (2013). European Society of Cataract & Refractive Surgeons: A History, European Society of Cataract and Refractive Surgery.

Steinert, R. F. (2010). Cataract Surgery, Elsevier Health Sciences.

Tunnacliffe, A. H. (1997). Introduction to Visual Optics.