OBJECTIVE AND SUBJECTIVE EVALUATION OF DYSPHOTOPSIA IN NORMAL AND POST-OPERATIVE EYES

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Doctor of Philosophy

ASTON UNIVERSITY

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Abstract

The principle theme of this thesis is the measurement of dysphotopsia, a common complaint in both the ageing population and after cataract or refractive surgery. Despite the availability of multiple objective and subjective methods to measure dysphotopsia, no single method is in common use, nor are photic effects commonly measured prior to cataract or refractive surgery. In this thesis, objective measures are taken using the Aston halometer and *C-Quant*, whilst subjective complaints are graded using simulated images.

Whilst many previously published studies have reported monocular halometry results, an early study in the thesis found monocular halo areas to be approximately 30 % larger ($P < 0.001$) than the binocular area, indicating the effect of binocular summation on objective measures of halo area. The thesis investigates the link between objective measures and subjective complaints of dysphotopsia. Subjective complaints were not linked to binocular halo area ($P = 0.478$), monocular halo area ($P = 0.896$) or *C-Quant* straylight values ($P = 0.128$). Halometry and *C-Quant* also showed no relationship ($P = 0.229$). The results highlight the difficulties in being able to predict the potential subjective complaints a patient may experience from objective measures alone. However, a weak correlation was found between binocular halo area and subjective night halo complaints ($r_s = 0.330$, $r_s^2 = 0.109$, $P < 0.001$), which may be due to the fact that halo area assessed would relate directly to the night halo image on the photographic images of photic phenomena (PIPP) plates.

Binocular and monocular halo areas both increased with age ($r_s = 0.449$, $r_s^2 = 0.202$, $P < 0.001$ and $r_s = 0.403$, $r_s^2 = 0.162$, $P < 0.001$, respectively) in healthy eyes (n = 141, age range 18 – 82 years). Retinal straylight values also increased significantly with age ($r_s = 0.457$, $r_s^2 = 0.209$, $P < 0.001$), as did subjective grading ($r_s = 0.314$, $r_s^2 = 0.099$, $P < 0.001$). The results indicate a significant age-related increase in dysphotopsia, even in healthy eyes, which is attributed to media changes over time.

Due to the effects of a bright light source on the pupil size, and the issue of senile miosis, this programme of research considered, for the first time, whether pupil size had an effect on the size of the halo area measured with halometry. No significant difference in halo area with various simulated pupil sizes (4.5, 6.0 and 7.5 mm) was detected ($\chi^2_{(3)} = 7.56$, $P = 0.056$)**.** The Aston halometer is therefore a robust way to evaluate dysphotopsia without measuring or controlling pupil size.

A longitudinal study tracked photic effects in individuals for a year after laser-assisted in situ keratomileusis, and another measured dysphotopsia pre- and up to a year post-cataract surgery. Subjective complaints resolved by 3 months post-refractive surgery, objective halo area took 6 months to resolve post-cataract surgery and up to 12 months post-corneal refractive surgery. A glare effect ratio was calculated for binocular halometry (median = 1.28; IQR 0.75 – 2.15) and retinal straylight (median = 5.63; IQR 2.72 – 7.97). The glare effect ratio is independent of age, and it is suggested that the glare effect ratio could be used to identify individuals most at risk of significant subjective complaints of dysphotopsia following procedures such as corneal refractive surgery.

Key words: Dysphotopsia, glare, halos, photic phenomena, refractive surgery.

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$$Lower\ Outliers < First\ Quartile - (1.5\ x\ IQR)$$

LIST OF ABBREVIATIONS

2AFC – 2-Alternative Forced Choice

ARCHA – Aston Research Centre for Healthy Ageing

BAC – Base and Age Corrected

BAT – Brightness Acuity Tester

CDVA – Corrected Distance Visual Acuity

CIE – Commission Internationale de l'Eclairage

CTT – Classic Test Theory

DGI – Disability Glare Index

EDTRS – Early Treatment Diabetic Retinopathy Study

ESD – Estimated Standard Deviation

FDT – Functional Disability Test

IOLs – Intraocular Lenses

IQR – Interquartile Range

LASEK – Laser-assisted sub epithelial keratectomy

LASIK – Laser-assisted in situ keratomileusis

LED – Light Emitting Diode

LOCS – Lens Opacities Classification System

LogMAR – Logarithm of the Minimum Angle of Resolution

MTF – Modular Transfer Function

Nd:YAG – Neodymium-doped yttrium aluminium garnet

NHS – National Health Service

PCO – Posterior Capsule Opacification

PERK – Prospective Evaluation of Radial Keratotomy

PIPP – Photographic Images of Photic Phenomena

PMMA – Polymethyl Methacrylate

PRK – Photorefractive Keratotomy

PVD – Perceived Visual Disability

RK – Radial Keratotomy

Sqd – Square degrees

UCVA – Uncorrected Visual Acuity

UHB – University Hospitals Birmingham

VA – Visual Acuity

CHAPTER 1

DYSPHOTOPSIA AND ITS EVALUATION

1.1. General introduction

Dysphotopsia including glare and halos is common after cataract surgery with implantation of intraocular lenses (IOLs), or after laser refractive surgery (Tester *et al.*, 2000, Gutierrez *et al.*, 2003, Jabbur *et al.*, 2004, Souza *et al.*, 2006, Cervino *et al.*, 2011, de Vries and Nuijts, 2013). It is usually more profound in patients fitted with multifocal IOLs (Akutsu *et al.*, 1993). Despite good distance and near visual acuity, quality of life may be affected if activities such as night driving are compromised (Tester *et al.*, 2000, Souza *et al.*, 2006). Previously published work report dysphotopsia such as glare and halos as being the most common cause of dissatisfaction (Tester *et al.*, 2000, Souza *et al.*, 2006, de Vries and Nuijts, 2013). As many as 50 % of those implanted with IOLs complain of glare symptoms (Woodward *et al.*, 2009, de Vries *et al.*, 2011, Chang *et al.*, 2012). Multifocal IOLs are more likely to cause photic phenomena than monofocal IOLs (Leyland and Pringle, 2006). Some patients only experience mild subjective complaints; however, there are a few who find it that detrimental to their quality of life that they request the precarious procedure of IOL explantation (Davison, 2000, Mamalis, 2000, Tester *et al.*, 2000, Pepose, 2008, Mainster and Turner, 2012). No evidence based approach is in use pre-operatively to attempt to identify individuals who might be most severely affected subjectively; with surgeons basing the decision of whether to operate on the patients' personality rather than using a clinical method (Pepose, 2008, Braga-Mele *et al.*, 2014).

Almost a century of research into dysphotopsia has resulted in vast literary coverage of the subject. As such, rather than offering an exhaustive review of previous literature, this report considers key matters most relevant to the author's research. Different definitions of dysphotopsia are detailed, along with the theories and causes. Methods used to measure amounts of dysphotopsia are discussed, with particular attention paid to halometry and the retinal straylight.

1.2. What is dysphotopsia?

Dysphotopsia describes any undesirable light-related visual phenomenon and may be experienced by both phakic and pseudophakic patients (Tester *et al.*, 2000). Dysphotopsia is classified into two main types; positive and negative. Negative dysphotopsia denotes the perception of a dark crescent in the temporal visual field (Schwiegerling, 2006, Osher, 2008). Positive dysphotopsia encompasses effects such as flashes of light, arcs,

increased light sensitivity, glare, halos (Tester *et al.*, 2000), and is perhaps the most common type experienced by patients (Souza *et al.*, 2006, de Vries and Nuijts, 2013).

There are many different ways in which to describe the term glare. Glare is the result of light entering the eye that does not aid vision, usually too intense or a variable environmental luminance across the visual field (Wordenweber, 2010). Inevitably, most adults will have experienced glare at some point. For example, when driving towards the sun while it is low in the sky, driving at night with on-coming cars with undipped headlights, or walking down dark streets at night with poorly shielded street lamps. These sources of glare involve small bright lights in a relatively darker field, making it difficult to see objects near to the source of glare (Smith, 2002). This is known as disability glare, also known as physiological glare (Vos, 2003b, Schreuder, 2008). Glare is not only caused by small bright light sources, but can also occur when the extended field of view is brighter than we can normally adapt to (Smith, 2002). Sunlight reflecting off snow at high altitudes often has this effect. Extended light sources with luminance of greater than about 10,000 cd/m^2 usually lead to some feeling of discomfort (Smith, 2002). Fresh snow in bright sunlight can have a luminance of up to 30,000 cd/m^2, which is usually beyond the comfort zone (Smith, 2002). Glare of this type is called discomfort glare, also known as psychological glare (Vos, 2003b, Schreuder, 2008).

Thus there are two main types of glare; discomfort glare and disability glare. In simple terms, discomfort glare is glare that causes discomfort, without leading to a decrease in vision. In contrast, disability glare may not cause any discomfort, but leads to some loss of vision (Smith, 2002).

The term disability glare is used when the visibility of an object is reduced due to a bright light source in the visual field (Koch, 1989, Aslam *et al.*, 2007b, Allen *et al.*, 2009). The resultant increase in intraocular light scatter or straylight from the bright light source causes a veiling glare and a loss of contrast across the retinal image (Vos, 1984, van den Berg, 1995, Aslam *et al.*, 2007b, Allen *et al.*, 2009). A loss in contrast typically reduces the observer's ability to distinguish detail within a visual scene. Contrast is decreased by a factor equal to background luminance divided by the sum of veiling and background luminances (Smith, 2002, Narisada and Schreuder, 2004). Veiling luminance from straylight depends on (1) the illuminances that glare sources produce at the observer's eye and the angular distance between those sources and the observer's visual axis (Holladay, 1926, Vos, 1984, Smith, 2002) and (2) the observer's age and pigmentation (Wolf, 1960, Vos, 1984, Elliott and Bullimore, 1993).

Disability glare is usually encountered in scotopic light conditions as pupil dilation allows more intraocular scatter to enter from the glare source (Allen *et al.*, 2009). Dim light makes

contrast loss more significant as rod photoreceptors need larger contrast differences for target detection than cones (roughly 20 % vs 1 %, respectively; Smith, 2002, Schreuder, 2008, Wordenweber, 2010, Mainster and Turner, 2012). The term disability glare gives an understanding of the patient's actual experience of the visual impairment (Vos, 2003b, Aslam *et al.*, 2007b, Schreuder, 2008), inducing an almost complete blindness close to the light source whilst only hampering visual performance when further away (Vos, 1984, van den Berg, 1995, Vos and van den Berg, 1999).

Discomfort glare is caused by illumination that is too intense for an individual; classed as a normal response to abnormal illumination. Discomfort glare causes an annoyance resulting in squinting, distraction, blinking, tearing and light aversion (Bullough, 2009, Fekete *et al.*, 2010). The threshold for discomfort glare varies considerably between individuals as it depends on a person's adaptation luminance and the characteristics of surrounding natural and artificial light sources (luminaires). Glare is intensified by increasing the number and luminance of light sources, or by decreasing the angular separation between glare sources and the visual axis (Narisada and Schreuder, 2004, Wordenweber, 2010, Mainster and Turner, 2012). Light source spectrum affects visual discomfort, with recent data showing that the sensitivity spectra for discomfort glare peak between 510 and 550 nm (green) for light exposures within 5 degrees of the visual axis (Bullough, 2009, Fekete *et al.*, 2010). In general, the relative contributions of rod, cone, and retinal ganglion photoreceptors to visual discomfort probably vary considerably for different people and glare situations (Mainster and Turner, 2012).

For people with normal binocular vision, shutting one eye decreases binocularly summed retinal illuminance, therefore reducing discomfort glare, photophobia and dazzle (Bourassa and Wirtschafter, 1966, Wirtschafter and Bourassa, 1966, Plainis *et al.*, 2006). Conversely, if someone with normal binocular vision views a scene with a neutral-density filter over one eye, shutting that eye increases image brightness even though total retinal illuminance has decreased (a phenomenon known as Fechner's paradox; Mainster and Turner, 2012). Thus, emphasizing that discomfort glare does not depend on brightness (Bourassa and Wirtschafter, 1966, Wirtschafter and Bourassa, 1966, Plainis *et al.*, 2006), and that there is a difference between brightness perception and the luminance of light sources (Hopkinson, 1957, Lennie *et al.*, 1993, Rea *et al.*, 2011). Discomfort glare varies little with age (Narisada and Schreuder, 2004), unlike disability glare (Wolf, 1960, Elliott and Bullimore, 1993, Vos and van den Berg, 1999).

The term dysphotopsia encompasses more phenomena than glare alone. There are currently ten different types that are recognised: dark arc, bright arc, bright room, night

halos, night starburst, day halos, day starburst, central flash, streaks of light and ripple effect (Aslam *et al.*, 2004a). A commonly reported complaint is halos; the subjective perception of a bright ring around a light source (Aslam *et al.*, 2007b, Buznego and Trattler, 2009). The effect is regularly perceived when looking at a bright light source in the dark, such as when looking at street lamps on a foggy night. This type of dysphotopsia is formed by light rays that are scattered outside the focussed image creating a dim disc of light around the light source (Allen *et al.*, 2009). Although visual acuity is normal, the effect of the bright headlight causes such a severe detriment to the vision of some that it causes individuals to stop driving, which in turn reduces quality of life (Ranney *et al.*, 2000, Theeuwes *et al.*, 2002).

In the field of ophthalmic science the key scattering component to analyse is the forward scattering, which occurs when light is incident to the retina causing a veiling luminance superimposed on the retinal image reducing retinal contrast (Dewaard *et al.*, 1992, Aslam *et al.*, 2007b, van den Berg *et al.*, 2013). Backward scatter is the dispersion of light reflected out of the eye and is typically used in slit lamp examination to assess the quality of ocular tissues (McCally *et al.*, 2007, Patel *et al.*, 2007). Back scattered light is not a cause of any photic effects as it only reduces the amount of light reaching the retina (Atchinson and Smith, 2000).

1.3. Light scattering theory

The initial light scattering theory was that of Rayleigh light scattering in which forward scatter was said to be equal to backward scatter, however, it was only applicable to small spherical particles with a diameter of less than one tenth of the wavelength of the incident light (Hahn, 2006, Piñero *et al.*, 2010, van de Hulst, 2012). Blue light is scattered more than red as according to Rayleigh scattering, it is more effective at short wavelengths (Aslam *et al.*, 2007b).

The theory of Mie light scattering however, accounts for general scattering independent of particle size. Intensity and direction of scattered light are a function of the scattering properties of the media and the wavelength of the incident light (van de Hulst, 2012). According to the Mie theory, the intensity and direction of scattered light by an isotropic, homogeneous and spherical particle can be calculated using the following mathematical relationship, assuming a flat monochromatic incident wavefront and homogeneous surrounding medium (van de Hulst, 2012):

$$I_s(x, m, \theta) = s^2(x, m, \theta)\frac{I_0\lambda^2}{4\pi^2 d^2}$$

Equation 1.1

Where I_s is the intensity of scattered light, s, the scattering coefficient of the particle for which Mie derived exact formulas, I_0, the intensity of incident light, λ, the wavelength of light, and d, the position where the scattering is measured. Therefore, increased light scatter occurs for longer wavelengths, higher intensities and with light sources that are closer to the eye.

I_s and s parameters are a function of three parameters, the angle of incident light (θ), x and m. x and m are calculated with the following expressions (Piñero *et al.*, 2010):

$$x = \frac{\pi D}{\lambda}; m = \frac{n_1}{n_2}$$

Equation 1.2

Where D is the diameter of the spherical particle, n_1, the index of refraction of the particle, and n_2, the index of refraction of the surrounding media. Equation 1.1 is therefore dependent on the size of the particle and the wavelength of the light, where a larger particle would cause more scattering as would short wavelength light. A greater difference between the refractive index of the particle and the surrounding media would also cause increased scattering.

In the eye, most light scatter is not wavelength dependent, and thus Mie's theory stands (Wooten and Geri, 1987, Holden *et al.*, 1993). Mie scattering of light is of important use as it predicts that assessment of back scatter during slit lamp examination, does not necessarily equate to the amount of forward scatter on the patient's retina (Bettelheim and Ali, 1985, Weale, 1986, Dewaard *et al.*, 1992, Holden *et al.*, 1993, Donnelly *et al.*, 2004, Aslam *et al.*, 2007b).

In an ideal eye with optically-clear media and perfect optical surfaces, no back and forward scatter would occur. However, the human eye is imperfect and each of the various structures within the eye contributes to the amount of light scatter through diffraction and aberration (see Fig 1.1 and Table 1.1). In normal individuals, previous authors have estimated that the cornea accounts for about 30 %, the lens 40 % and retina approximately 20 % of scattered light (Yuan *et al.*, 1993). Similarly, Vos (2003a) approximated that 20 %

of the glare veil is caused by the retina, when it comes to scattering from the fovea towards the periphery; the cornea and lens together make up about 60 % of the veiling luminance.

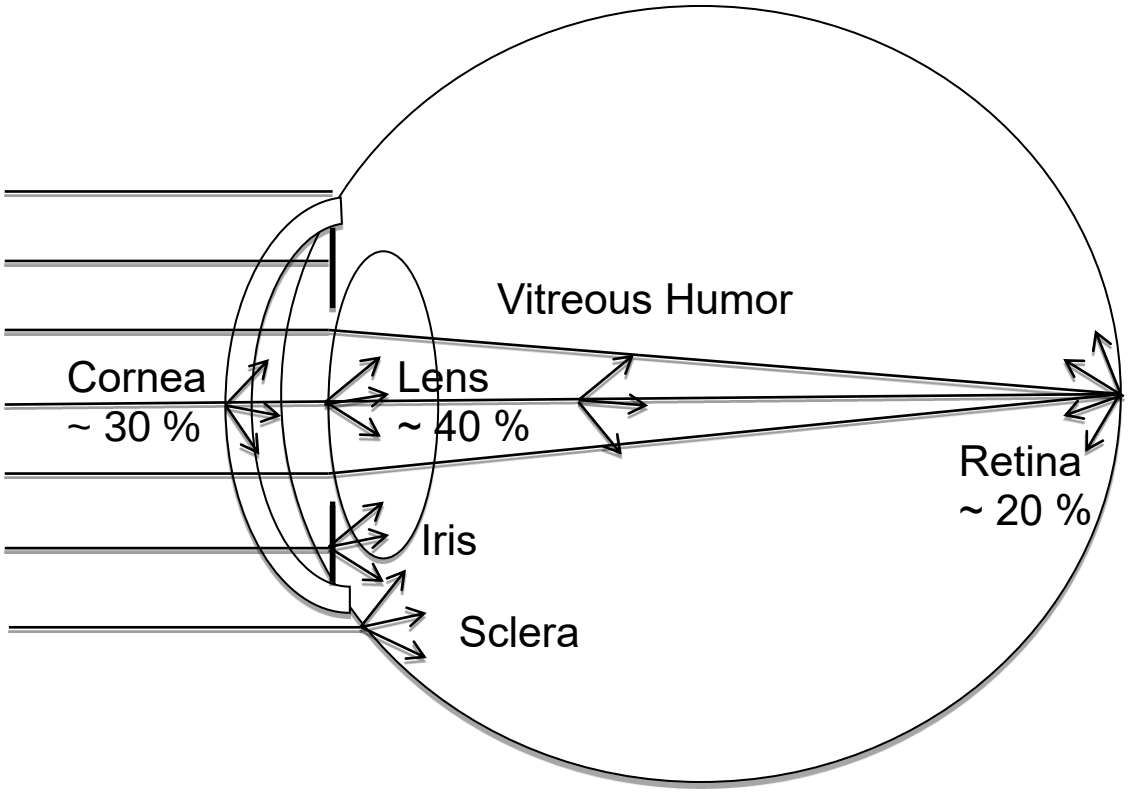


Figure 1.1: Sources of ocular scatter, values from Yuan et al. (1993)

The cornea (McCally and Farrell, 1982, Olsen, 1982, Lohmann *et al.*, 1993, Patel *et al.*, 2007) and crystalline lens (Bettelheim and Ali, 1985, Weale, 1986, Smith *et al.*, 1992, Whitaker *et al.*, 1993, Qian *et al.*, 1994, Yaroslavsky *et al.*, 1994, Fujisawa and Sasaki, 1995, van den Berg and Ijspeert, 1995, Hemenger, 1996, Wegener *et al.*, 1999, Thaung and Sjostrand, 2002, Tang *et al.*, 2003) cause scattering when their transparency is reduced by corneal haze (Lohmann *et al.*, 1991, Braunstein *et al.*, 1996, Corbett *et al.*, 1996, Wang *et al.*, 2004, De Brouwere *et al.*, 2008), dystrophy (van den Berg *et al.*, 1993), keratoconus, corneal surgery (Lohmann *et al.*, 1993, Jain *et al.*, 1995, Chang *et al.*, 1998, Wang *et al.*, 2006, Fankhauser, 2007, Hindman *et al.*, 2007, Kymionis *et al.*, 2007, McCally *et al.*, 2007, Patel *et al.*, 2008), normal age related lenticular changes (Puell *et al.*, 2014) and cataract (Delaye *et al.*, 1982, Whitaker *et al.*, 1993, Qian, 2000, Gilliland *et al.*, 2001, Donnelly *et al.*, 2004, Costello *et al.*, 2007, Gilliland *et al.*, 2008). Within the lens, different light scattering processes govern forward scatter compared to backward scatter (Bettelheim and Ali, 1985). Both the iris and sclera are partially responsible for intraocular scattering as they are not completely opaque, and therefore allow some light to pass through (Ijspeert *et al.*, 1990,

van den Berg *et al.*, 1991). The amount of light that can pass through is dependent on the level of pigmentation, whereby blue/green eyes with lower amounts of pigmentation would transmit and scatter more light than dark brown eyes (van den Berg *et al.*, 1991). When light reaches the retina, some of it is absorbed, whilst some is reflected back contributing to the intraocular scattering (van den Berg *et al.*, 1991); this type of scattering is also dependent on the subjects' level of pigmentation. The vitreous humour is usually a transparent gel due to the regular structure of its fibrils. The transparency of this element may be severely affected by the presence of blood or cells in pathological conditions such as vitreous haemorrhage or posterior uveitis (Piñero *et al.*, 2010).

Source	Key Points
Cornea	- Increased scattering when transparency is reduced. - Corneal Surgery – Photorefractive Keratectomy/Radial Keratotomy/LASEK/LASIK. - Corneal Haze – Oedema/Dystrophies/Wounds. - Contact lens induced corneal oedema.
Crystalline Lens	- Increased scattering when transparency is reduced. - Cataract. - Posterior Capsular Opacification.
Iris	- Allows some light to pass through from outside the eye when not completely opaque. - Fuchs' heterochromic cyclitis (iris translucency). - Reduced pigmentation in albinism allows more light to pass through. - Blue/green eyes have less pigmentation, so would transmit and scatter more light than highly pigmented brown eyes.
Sclera	- Allows light to partly pass through from outside the eye when not completely opaque. - Reduced pigmentation allows more light to pass through, again blue/green eye have less pigmentation, so would transmit and scatter more light than highly pigmented brown eyes.
Retina	- Some incident light is absorbed, whilst some is reflected back, contributing to intraocular scatter. - Reduced pigmentation will result in less absorption, and more light will be reflected back.
Vitreous Humour	- The presence of blood or cells creates irregularities in the transparent media off which more scatter occurs. - Posterior Uveitis. - Vitreous Haemorrhage. - Floaters.
Intraocular Lenses	- Increased ocular scattering with multifocal IOLs as they produce two or more focal points simultaneously.
Age	- Increase with age due to lenticular changes, such as increased density and increased homogeneity, causing more scatter.
Pathology	- Choroideremia. - Retinitis Pigmentosa. - Hereditary Corneal Dystrophies. - Keratoconus.
Angle of incidence of glare source	- Smaller angle between glare source and visual axis results in increase scattering.
Uncorrected Astigmatism	- Especially for higher cylinders (>1.00 DC).

Table 1.1: Summary of keys causes of straylight.

Stiles (1929) and Holladay (1926) used the idea of veiling light falling on the retina from a bright light source reducing the contrast of the retinal image in the formulation of the disability glare equation (Cobb, 1911). The Stiles-Crawford effect states that light entering the eye via the centre of the pupil is about five times more effective than light entering the periphery of the pupil (Snyder and Pask, 1973, Marcos and Burns, 2000). In the eye the strength of this veiling light (equivalent veiling luminance) can be calculated and used as a measure of glare. The value found is dependent on the angular distance (θ) of the glare light from the object being viewed (Vos, 2003a) and the strength of light falling in the plane of the eye (veiling luminance):

$$L_V(\theta) = [10E/\theta^2] \text{ for } 1° < \theta < 30°$$

Equation 1.3

Where L_V = luminance of the veiling background (cd/m^2), E = illumination (lux) incident on the cornea and θ = the angle between the line of sight and glare source (°). Thus, a greater veiling glare luminance shall be experienced as the incident angle of the glare source approaches the visual axis (θ). Extensive studies reviewed by Vos (2003a) have validated this formula for angles between 1 - 30°.

The Commission Internationale de l'Eclairage (CIE) modified this expression to take into account the age of the subject, the level of pigmentation and angles outside 1 - 30° range (Aslam *et al.*, 2007b). When adapted for age, the new version of the equation shows that disability glare tends to increase rapidly beyond the age of 60 years. A simplified version is (Vos and van den Berg, 1999):

$$\left(\frac{L_{veil}}{E_{glare}}\right) = 10\left(1 + \left[\frac{Age}{70}\right]^4\right)\frac{1}{\theta^2}$$

Equation 1.4

Where L_{veil} = luminance of the veiling background (cd/m^2), E_{glare} = illumination (lux) incident on the cornea, and θ = the angle between the line of sight and glare source (°).

The initial Rayleigh light scattering theory was dependent on short wavelength light, and only held true for small particles. Mie scattering, however, could be used for particle of any size, and was independent of the wavelength of the incident light. The veiling luminance equation was limited to glare sources less than 30° from the line of sight. The CIE modified the veiling luminance equation to take into account further factors that cause glare including

age and level of pigmentation, as well as standing true for angles outside the 30° range. The latter is the most commonly used theory when looking at glare now.

1.4. Why measure dysphotopsia?

An increase in intraocular straylight may be one of the most important causes of photic complaints because it results in a visual handicap of much more than the general nature of glare alone (Piñero *et al.*, 2010, van den Berg *et al.*, 2013). Patient complaints include problems of 'hazy vision', difficulties in recognising faces when looking against the light, and halos around bright lights in low light conditions. Even in photopic conditions, loss of contrast and colour can occur (Piñero *et al.*, 2010). These effects are further enhanced when a driver tries to identify low contrast objects, such as unilluminated obstacles or pedestrians along the roadside at night time (Theeuwes *et al.*, 2002); highlighting why measurements of glare sensitivity are considered important for the assessment of drivers (Mantyjarvi and Tuppurainen, 1999).

Dysphotopsia is a well-known complaint after refractive surgery or cataract surgery (Tester *et al.*, 2000, Souza *et al.*, 2006, Woodward *et al.*, 2009, Chang *et al.*, 2012, de Vries and Nuijts, 2013). Such surgeries are becoming increasingly common since the introduction of multifocal IOLs, which allow patients spectacle independence as good distance and near visual acuity are achieved (Schwiegerling, 2006, Calladine *et al.*, 2012). Multifocal IOLs create two or more focal points focused at different planes. For distance viewing, the distance focal point produces a spot image with the near focal point creating an out of focus blur circle on the retina. The surrounding blur results in the retinal image having less contrast against its background and therefore, also results in the halo phenomenon (Buznego and Trattler, 2009). Previously published work report dysphotopsia such as glare and halos as being the most common cause of dissatisfaction (Tester *et al.*, 2000, Souza *et al.*, 2006, de Vries and Nuijts, 2013). Various studies have reported on the amount of patients implanted with IOLs that complain of dysphotopic symptoms (see Table 1.2). Souza *et al*. (2006) reported values of 13 % and 20 % of glare and halos respectively in 30 eyes fitted with monofocals; these values increase to 40 % and 50 % of 50 eyes, respectively with multifocals. Woodward *et al*. (2009) discovered 42 % of 43 eyes fitted with multifocal IOLs complained of photic phenomena, although 8 of these 18 eyes effects were attributed to posterior capsular opacification. In a study by de Vries *et al*. (2011), a value of 38.2 % of 76 eyes receiving multifocal IOL implantations had dysphotopsia. Chang *et al*. (2012) investigated 45 eyes for complaints of halo, night glare, and starburst; with 48 %, 15 % and 22 %, respectively, experiencing moderate to severe symptoms. A 2006 Cochrane review of multifocal IOLs found that photic phenomena

are 3.5 times more likely with multifocal IOLs than with monofocal IOLs (Leyland and Pringle, 2006). The subjective complaints of glare and halos can vary greatly from mild, to quite severely debilitating, to the extent that a patient requests IOL explantation; which in itself carries inherent risks (Tester *et al.*, 2000, Pepose, 2008). A retrospective review of 44 patients dissatisfied with visual outcomes after multifocal IOL implantation aimed to devised a symptom-specific treatment algorithm to maximise post-operative outcomes with minimally invasive treatment strategies (Woodward *et al.*, 2009), highlighting the need to avoid explantation and if possible distinguish those potentially problematic patients pre-operatively.

Author and key features of the study	**Proportion of patients experiencing dysphotopsia**
Souza *et al*. (2006) n = 30 eyes of 15 patients in monofocal group, 50 eyes of 25 patients in multifocal group	• 13 % and 20 % reported of glare and halos respectively with monofocal IOLs • 40 % and 50 % respectively with multifocal IOLs
Woodward *et al*. (2009) n = 43 eyes of 32 patients	• 42 % of the multifocal IOLs patients complained of photic phenomena
de Vries *et al*. (2011) n = 76 eyes of 49 patients	• 38.2 % of multifocal implantations had dysphotopsia
Chang *et al*. (2012) n = 45 eyes from 29 patients	• Complaints of halo, night glare, and starburst were 48 %, 15 % and 22 %, respectively with multifocal IOLs

Table 1.2: Summary of reports on the proportion of patients implanted with IOLs that complain of dysphotopsia.

Cataract surgery techniques have improved with the use of phacoemulsification and small incision surgery that now with careful biometry, refractive outcomes can be predicted. This has led to clear lens extraction or refractive lens exchange as a method of refractive surgery, especially in older patients or higher refractive errors. The need to measure glare is becoming ever more important as patients are being fitted successfully with multifocal IOLs, not only in cataract surgery but also with refractive lens exchange as an alternative to laser eye surgery in presbyopia (Barisic *et al.*, 2008, Chang *et al.*, 2012). Refractive lens exchange is becoming increasing popular as it is an easy procedure that addresses both

refractive error and presbyopia (Goes, 2008). Multifocal IOLs now increases the likelihood of spectacle independence (Pager, 2004, Hawker *et al.*, 2005, Munoz *et al.*, 2011, Ferrer-Blasco *et al.*, 2012). Previous presbyopic correction options with laser included PresbyLasik and monovision; however these were not commonly recommended procedures due to the variable outcomes. With refractive lens exchange, the goal after IOLs implantation has altered, it is no longer accepted to simply remove the cataractous lens, replacing it with an IOL of a close pre-operative refractive error (Lichtinger and Rootman, 2012); it also comes with increased patient expectation of the achievement of the best possible refractive outcome with restoration of vision for near and distance without spectacles (Aslam *et al.*, 2004a, Pager, 2004, Hawker *et al.*, 2005, Munoz *et al.*, 2011, Braga-Mele *et al.*, 2014). It has become increasingly common that a lot refractive lens exchange patients have no refractive error for distance pre-operatively, and have the surgery simply to be rid of their reading spectacles (Schena, 2005). In these cases, it is more evident that patients with moderate visual acuity pre-operatively are less happy with making the trade-off of good visual acuity at the cost of troublesome glare and loss of contrast sensitivity (Aslam *et al.*, 2007b). Chang *et al*. (2012) found that the most satisfied patients were those who underwent bilateral refractive lens exchange and were habitual spectacle wearers pre-operatively. Considering that dysphotopsia is a chief complaint after otherwise successful cataract surgery (Tester *et al.,* 2000, Welch *et al.,* 2010, Kinard *et al.,* 2013); there are few studies that have investigated the change in objective and subjective measures of dysphotopsia in response to cataract surgery. Whilst some studies have reported post-operative effects, they are rarely on a longitudinal basis (Aslam *et al.,* 2007) with no pre-operative measures for comparison.

One of the biggest challenges is that there is currently no evidence based approach used pre-operatively to attempt to identify individuals who might be most severely affected subjectively; with some surgeons suggesting that prospective patients who have a Type A personality or simply ask too many questions should be refused multifocal IOLs (Pepose, 2008, Braga-Mele *et al.*, 2014). Patients who do happen to suffer from dysphotopsia post-refractive surgery are often told that it will reduce over time, with very little evidence in place to support whether it does in fact reduce (Arnold, 1994, Davison, 2000). Whilst anecdotal evidence suggests that subjective photic effects reduce with time following laser refractive surgery, there is a lack of empirical data to support this viewpoint past 6 months. It is also unclear how much of the apparent improvement is due to a subjective acceptance of the disturbances (by neural adaptation) or an actual physical reduction in halo area (Fan-Paul *et al.*, 2002) and straylight. A subjective study which examined pseudophakic patients at 12 to 18 months after surgery found that 17 of 55

patients still complained of symptoms of halos and glare at night and day, although arc effects and central flash seemed to be less common (Aslam *et al.*, 2007a).

Various methods developed to quantify the amount of light scatter experienced by an individual, such as representative pictures (Hunkeler *et al.*, 2002, Aslam *et al.*, 2004a), subjective questionnaires (Shoji and Shimizu, 1996, Jacobi *et al.*, 2003, Kohnen *et al.*, 2006, Harman *et al.*, 2008), glare testers (measuring the size of halo; Miller *et al.*, 1972, Bores, 1983, Holladay *et al.*, 1987, Bailey and Bullimore, 1991, Gutierrez *et al.*, 2003, Allen *et al.*, 2008, Babizhayev *et al.*, 2009) and psychophysical techniques (van den Berg, 1986, Cervino *et al.*, 2008). Several instruments provide coefficients that indirectly measure ocular scattering, but most do not have clinical validation. Currently there is still no widely accepted test for glare (Rubin, 1990, van den Berg, 1991, Elliott and Bullimore, 1993), as there is no standard definition for the parameters that should be used to characterise ocular scattering (Aslam *et al.*, 2007b). There is no consensus regarding the size, intensity and location of the glare source (van den Berg *et al.*, 2003). An even bigger problem is the lack of consensus about the relation between glare sensitivity and difficulties as experienced during daily activities (van den Berg *et al.*, 2003). The likely reason for this is due the fact that it manifests in many forms, which are difficult to measure and differ between patients (Aslam *et al.*, 2007b). Whilst there are various objective and subjective measures of dysphotopsia, most studies report the use of one or the other; the link between the two is unknown in a pre-operative cohort.

1.5. Effect of intraocular lens design on dysphotopsia

Although multifocal IOLs have become popular, the commonest cause of dissatisfaction is due to dysphotopsia (Tester *et al.*, 2000, Souza *et al.*, 2006, de Vries and Nuijts, 2013). The multifocal IOLs design creates two or more focal points focused at different planes (see Fig 1.2). For distance viewing, the distance focal point produces a focused image with the near focal point creating an out of focus blur circle on the retina. The surrounding blur results in the retinal image having less contrast against its background and therefore, also results in the halo phenomenon (Gil-Cazorla *et al.*, 2016).

Many different designs of multifocal IOLs have been developed over the years to improve both distance and near vision but also to combat unwanted side effects such as glare and halos. The design of the lens affects the light distribution, the number of focal points, the distance of their separation, and ultimately the quality of the images.

There are various designs of multifocal IOLs, a full review of all designs is beyond the scope of this literature review, thus a brief overview is given. Multifocal IOLs can be divided into refractive and diffractive designs. Refractive designs can be subdivided into concentric and sectorial, while diffractive designs can be categorised as fully diffractive or partially diffractive.

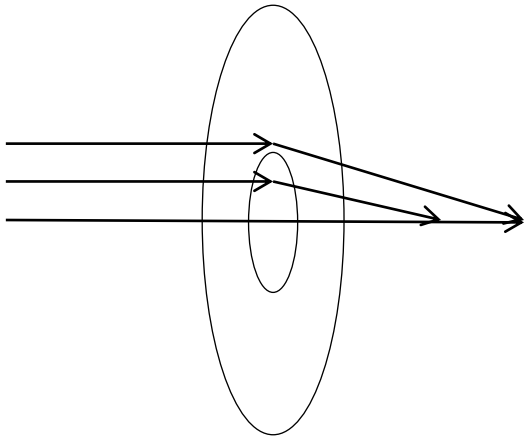


Figure 1.2: The multifocal IOLs design creates two or more focal points focused at different planes.

1.5.1. Refractive multifocal intraocular lenses

1.5.1.1. Concentric refractive multifocal intraocular lenses

In refractive multifocal IOLs, refractive power changes from centre to the periphery of the lens and produces many foci (see Fig 1.3; Barisic *et al.*, 2008). Concentric refractive multifocal IOLs have several concentric zones that differ in curvature, creating two or more refractive powers. The *Array* (Abbott Medical Optics, Inc., Santa Ana, CA, USA), *ReZoom* (Abbott Medical Optics, Inc., Santa Ann, CA, USA), and *MFlex* (Rayner Intraocular Lenses Ltd, Hove, UK) are all five-zone concentric refractive multifocal IOLs; alternating near and distance zones surround the central distance zone. The *Array* and *ReZoom* are similar in design as both have a near addition equivalent to + 3.50 D at the IOL plane (approximately + 2.60 D at the spectacle plane). The posterior surface of the *Array* optic is spherical, however, the *ReZoom* incorporates an aberration reducing aspheric posterior surface optic. The *ReZoom* has three zones, including the central that is for distance vision, the other two are for near; it distributes 10 – 11 % of light to intermediate focus by contributions from the defocus characteristics of both primary lens powers (Davison and Simpson, 2006, Barisic *et al.*, 2008). The *MFlex* multifocal is available with either a

+ 3.00 D or a + 4.00 D addition and with four or five refractive zones depending on the base power of the IOL; the *MF-4* is a four-zone concentric refractive multifocal IOL with a centre near zone surrounded by alternating distance and near zones. Due to the refractive zones in all refractive multifocal IOLs being relatively large, the design is pupil size dependent. Centre distance designs ensure preservation of distance vision even with the smallest of pupil (Kawamorita *et al.*, 2009); however, those with small pupils are likely to struggle with reading.

Rau *et al*. (2003) noted a relatively high level of spectacle independence with the *MF-4*, but a prevalence of dysphotopsia of 45 %. Perez *et al*. (2003) reported that visual acuities with the *MF-4* were inferior when compared with a diffractive multifocal IOL with an equivalent addition. Optical bench studies were unable to determine the disparity between the IOLs as they both produce equivalent image formations (Gobbi *et al.*, 2007). Whilst very few studies have been done on the *MF-4* IOL, the *Array* and *ReZoom* five-zone, refractive multifocal IOLs have been extensively evaluated in both *in vivo* and *in vitro* studies. Such studies have reported reduced contrast sensitivity in lower lighting conditions and lower spatial frequencies with the five-zone refractive multifocal IOLs (Montes-Mico *et al.*, 2004, Cillino *et al.*, 2008), whilst the prevalence of dysphotopsia is higher than with a monofocal IOL (Haring *et al.*, 2001, Pieh *et al.*, 2001, Cillino *et al.*, 2008). In regards to near vision (Cillino *et al.*, 2008), spectacle dependence (Fujimoto *et al.*, 2010) and reading ability (Harman *et al.*, 2008) the five-zone refractive multifocal IOLs are superior in comparison with a monofocal IOL.

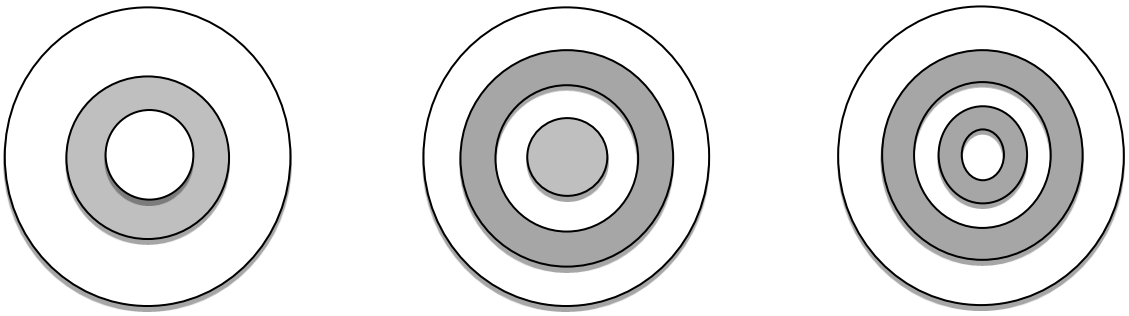


Figure 1.3: Optics of a three, four, and five zone refractive multifocal IOLs, i.e. *Array* or *ReZoom*. In the three zone lens, the centre distance zone supports distance vision in bright light conditions such as daylight driving with constricted pupils. The surrounding near zone provides good near vision in moderate to low light conditions. The outer distance zone provides additional distance vision support in dim light conditions, such as night driving when pupils are dilated. In the four and five zone lenses, the extra zones provide good vision in differing light conditions. Shaded regions = near power, non-shaded regions = distance power.

1.5.1.2. Sectorial refractive multifocal intraocular lenses

In contrast to concentric refractive multifocal IOLs, these lenses are rotationally asymmetrical. Sectorial refractive multifocal IOLs have the reading addition in a specific region of the lens; similar to the appearance of a bifocal spectacle lens. The mechanism of action, like all other multifocal IOLs, is simultaneous rather than translating vision.

The *Lentis MPlus* (Oculentis/Topcon Europe, Capelle a/d Ijssel, The Netherlands) has the appearance of a C-type bifocal spectacle lens; the near segment covers 100° of the inferior IOL and has a small in-cove for distance vision (see Fig 1.4). The near portion of the IOL has an addition of 3.00 D over the distance refractive correction of the IOL. The manufacturers of this lens recommend placing the IOL with the near segment inferiorly.

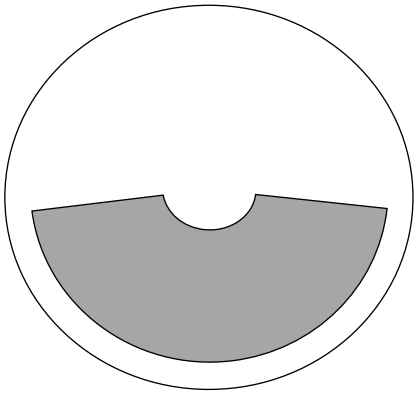


Figure 1.4: Optic of the *Lentis MPlus*, a sectorial multifocal IOL; the inferiorly placed near segment (shaded) covers 100° of the lower IOL and the small in-cove allows good undisrupted distance vision.

Sectorial multifocal IOLs are dependent on IOL centration. The amount of light dedicated to distance or near is dependent on the proportion of the near segment occupying the pupil. A sectorial multifocal IOL requires the central radius points of the distance and near portions of the IOL to run along the same optical path, therefore negating image jump (Maxwell and Nordan, 1991). The sectorial multifocal IOL has the advantage that it is not pupil dependent. It also has reduced photic phenomena as glare and halos are confined to the area corresponding to the near segment, although not completely eliminated (Munoz *et al.*, 2011).

1.5.2. Diffractive multifocal intraocular lenses

Diffractive multifocal IOLs are based on the Huygens-Fresnel principle, in which concentric rings on the optic surface typically generate two foci (distance and near; Slagsvold, 2000,

Davison and Simpson, 2006, Barisic *et al.*, 2008, de Vries *et al.*, 2008, Sheppard *et al.*, 2013). A diffractive pattern is created by light diffracted by a boundary; this creates an interference pattern and results in multiple orders of light. The separation between these orders of light determines the IOL addition (Davison and Simpson, 2006). The distance between the ring edges determines the order separation and thus the effective addition (Davison and Simpson, 2006). However, not all of the light is distributed to the desired light orders and some is spread diffusely to the higher orders (Sheppard *et al.*, 2013). In the case of a + 4.00 D diffractive multifocal IOL, designed to separate the light equally between two orders, 18 % of the light is lost to higher orders (Davison and Simpson, 2006, Huetz *et al.*, 2006). Chromatic aberration occurs as a consequence of both refraction and diffraction; however, the spread of light into different colours occurs in the opposite direction to the spread through refraction (Maxwell and Nordan, 1991).

1.5.2.1. Fully diffractive multifocal intraocular lenses

Fully diffractive multifocal IOLs have concentric rings that cover the entire optic of the IOL (see Fig 1.5). These lenses are therefore pupil-independent and the split of light is maintained regardless of pupil size (Valle *et al.*, 2005). The *Tecnis ZM900* (Abbott Medical Optics, Inc., Santa Ana, CA, USA) has a silicone fully diffractive multifocal optic with the diffractive pattern on the posterior surface. It has an aspheric anterior surface that acts to suppresses spherical aberrations. The effective addition of the IOL is + 4.00 D at the IOL plane; this IOL also has an equal split of light towards the distance and near focal points. There is also an acrylic version of the IOL, the *Tecnis ZA900*.

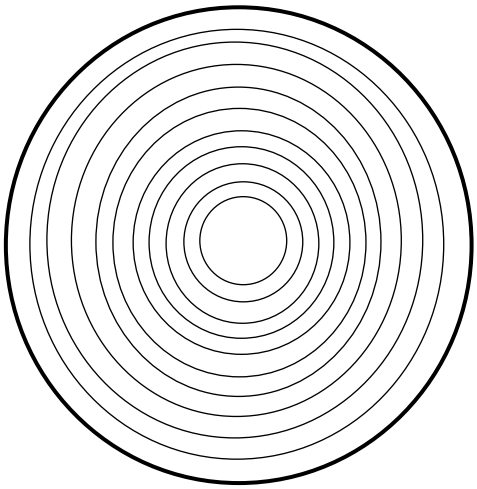


Figure 1.5: Optic of *Tecnis ZM900*, a fully diffractive multifocal IOL with alternating distance and near zones allows an equal split for distance and near vision despite the pupil size.

Equal split fully concentric multifocal IOLs offer a high level of near acuity and spectacle independence in comparison with a monofocal IOL and refractive concentric multifocal IOLs (Cillino *et al.*, 2008, Packer *et al.*, 2010). The literature is equivocal in regards to the quality of intermediate vision with the equally split fully concentric multifocal IOLs: defocus curve profiles (Schmidinger *et al.*, 2006), and optical bench tests (Terwee *et al.*, 2008) have demonstrated a reduction in intermediate vision whilst a study measuring visual acuity at an intermediate distance has not corroborated these findings (Packer *et al.*, 2010). Distance visual acuity is superior with the distance dominant lens; the reverse is true for near visual acuity. Binocularly the vision is summated providing relatively good distance and near vision (Jacobi *et al.*, 1999). Optical bench studies (Gobbi *et al.*, 2007) and clinical studies (Alio *et al.*, 2004) have highlighted the presence of dysphotopsia. Moreover on assessment of distance contrast acuity via optical bench testing, contrast acuity has been found to be improved with the distance dominant multifocal IOL when compared to an equal split fully diffractive multifocal IOL (Gobbi *et al.*, 2007).

1.5.2.2. Partially diffractive multifocal intraocular lenses

Unlike fully diffractive multifocal IOLs, partially diffractive multifocal IOLs only have the diffractive pattern over a specific area of the optic (see Fig 1.6). *AcrySof ReSTOR* apodized diffractive IOL (Alcon Laboratories Inc., Fort Worth, TX, USA) has a single piece biconvex optic. The optic is composed of the same proprietary acrylic material that has been used in *ReSTOR* lenses since 1995. This material has been shown to provide excellent clinical benefits through its high refractive index (1.55), flexibility, ultraviolet wavelength-absorbing properties and biocompatibility. The lens can be folded before insertion, allowing placement through an approximately 3.5 mm incision. The *ReSTOR* MA60D3 has a 6.0 mm diameter biconvex optic and an overall length of 13.0 mm. Twelve diffractive zones in the central 3.6 mm region divide light between two foci. The diffractive steps gradually reduce in height and spacing from the lens centre to the edge of the diffractive region (apodization); distributing the light for a full range of vision. Step heights decrease smoothly from 1.3 μm in the central zone to 0.2 μm at the diffractive periphery. The outer refractive region has no diffractive zones and is strictly refractive dedicated to distance vision. Therefore the lens is pupil-dependent: the larger the pupil the greater the distribution of light to the distance. The lens incorporates a + 4.00 D add at lens plane equal to a + 3.2 D at spectacle plane (Kohnen *et al.*, 2006, Souza *et al.*, 2006) and is also available in a + 3.00 D near addition.

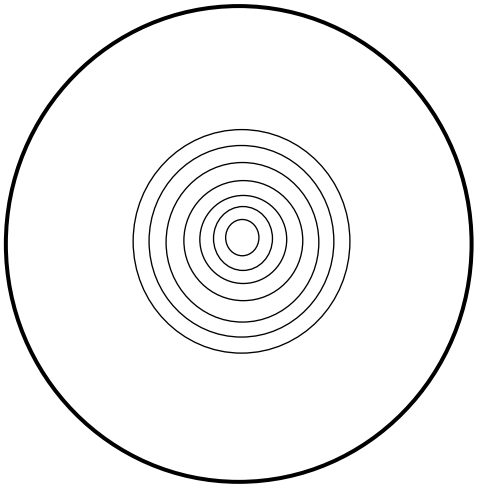


Figure 1.6: Optic of *ReSTOR*, a partially diffractive multifocal IOL. Only the centre region has the diffractive zones, whereby the outer refractive region is for distance vision only, giving those with larger pupils a greater distribution of light to distance.

The *ReSTOR* has been extensively examined in optical and clinical studies. Near visual acuity and spectacle independence is better in comparison with a monofocal IOL, distance visual acuity is comparable, however, contrast sensitivity with the + 4.00 *ReSTOR* is reduced (Vingolo *et al.*, 2007, Cionni *et al.*, 2009, Hayashi *et al.*, 2009b). Interestingly Hayashi *et al*. (2009a) concluded that the + 3.00 version of the multifocal IOL produced similar contrast sensitivity levels in comparison with a monofocal IOL. However, de Vries *et al*. (2010) found no difference in contrast sensitivity between the + 4.00 and + 3.00 versions of the *ReSTOR*. A significant limitation of the + 4.00 *ReSTOR* multifocal IOL is its ineffectiveness at providing intermediate vision (Blaylock *et al.*, 2006, Pepose *et al.*, 2007). This is less of a problem with the + 3.00 D *ReSTOR* multifocal IOL which provides a longer working distance for the patient hence improving intermediate vision (Maxwell *et al.*, 2009).

1.5.3. Trifocal multifocal intraocular lenses

A trifocal multifocal IOL is a lens that supports good intermediate vision. A combination of 2 diffractive profiles can provide 3 foci for distance, near and intermediate distance (Gatinel *et al.*, 2011). *FineVision* IOL (PhysIOL, Belgium) is a single-piece aspheric fully diffractive trifocal IOL, allowing for an improved intermediate vision. It is composed of 25 % hydrophilic acrylic material and the overall diameter is 10.75 mm and the optic 6.15 mm. It features two diffractive profiles consisting of alternating diffractive steps of different heights on the anterior surface, resulting in three foci: one for distance, one for intermediate (+ 1.75 D add), and one for near (+ 3.00 D add). It also has an apodized optic with

decreasing step height from the centre to the periphery, resulting in variable distribution of light energy to far, intermediate, and near vision with changing pupil diameters. The proportion of incident light directed to far vision is greater than for near or intermediate vision at all pupil diameters and rises with pupil size to increase distance-vision dominance. For a 20 D IOL and a 3.0 mm pupil diameter, the light-energy distribution to distance, near, and intermediate vision is 42 %, 29 %, and 15 %, respectively (Gatinel *et al.*, 2011). Approximately 14 % of light energy is lost at higher orders of diffraction with this IOL compared with 18 % with IOLs of a typical bifocal refractive design (Davison and Simpson, 2006).

Sheppard *et al.* (2013) reported a good standard of distance visual acuity and intermediate and near visual function with the *Finevision* trifocal IOL, in a prospective interventional study on 15 patients after bilateral IOL implantation. The increasing far-vision dominance of the IOL as pupil size increases may be effective in reducing the photic phenomena frequently associated with multifocal IOLs (Sheppard *et al.*, 2013), especially in night time conditions where photic phenomena are most prominent.

A theoretical study on model eyes showed that diffractive multifocal IOLs are superior to refractive multifocal IOLs for near vision, whereas for distance vision they are comparable (Pieh *et al.*, 2002). Clinical studies also confirm the superiority of the diffractive over the refractive principle for near vision (Knorz, 1993, Weghaupt *et al.*, 1996, Walkow *et al.*, 1997, Steinert *et al.*, 1999) and have shown that refractive multifocal IOLs are significantly more pupil dependent (Koch *et al.*, 1991, Knorz, 1993, Hayashi *et al.*, 2001). A pupil diameter of less than 4.5 mm cannot provide useful near visual acuity (Hayashi *et al.*, 2001); therefore mean pupillary size in a normal cataract population needs to be considered. A study by Weghaupt *et al*. (1998) showed that results for distance and near visual acuities are very satisfactory with a diffractive multifocal IOL, whereas for intermediate distances visual acuity may be limited to activities that do not require optimal vision.

In various studies evaluating diffractive (Rossetti *et al.*, 1994) and/or refractive (Dick *et al.*, 1999, Javitt and Steinert, 2000, Pieh *et al.*, 2001) multifocal IOLs, visual phenomena, mainly glare and halos, have been proven to be increased relative to monofocal IOLs; however, rates of self-reported patient satisfaction remain high with simultaneous vision IOLs. Steinert *et al*. (1999) observed statistically significant differences in rating of visual symptoms reported by subjects implanted with the *Array* zonal-progressive multifocal IOL in comparison to the monofocal control. Difficulties with halos, glare/flare, and blurred far vision were reported most frequently, and at higher proportions in the zonal multifocal IOL subjects than in the monofocal subjects.

Javitt *et al*. (2000) also reported a significantly higher degree of problems with glare, halos, or rings around lights for the multifocal *Array* IOL subjects versus monofocal IOL subjects. The study involved bilateral implantation; with 127 participants receiving multifocal IOLs and 118 participants receiving monofocal IOLs. In comparison, lower proportions of these symptoms were reported as severe by the *ReSTOR* IOL subjects in a study by Kohnen *et al.* (2006), evidenced by 8.5 % for glare/flare and 4.2 % for halos. Kohnen *et al.* (2006) successfully observed 117 participants for 330 to 420 days after bilateral multifocal IOL implantation. Conversely, glare and halos have been reported not to differ statistically significantly between a monofocal IOL and a zonal-progressive multifocal IOL (Dick *et al.*, 1999), after monocular implantation of a monofocal IOL in 28 subjects and multifocal IOL in 28 subjects. In a study by Pieh *et al.* (2001), halos were detected in all 24 patients with a refractive multifocal IOL under clinical setting conditions, and 23 patients reported seeing halos at night, whereas only one patient was disturbed by this phenomenon. Patients receiving refractive multifocal IOLs (*Array*) were more likely to report halos, although their overall visual function and satisfaction were rated higher than those in the monofocal control group (Javitt and Steinert, 2000).

Visual phenomena have been reported to be more severe with diffractive IOLs than with monofocal IOLs, but not leading to less patient satisfaction (Rossetti *et al.*, 1994, Leyland and Zinicola, 2003, Montes-Mico *et al.*, 2004). Kohnen *et al*. (2006) reported that the *AcrySof ReSTOR* IOL provided clear vision, with a low incidence of severe visual disturbances. The favourable performance of the *AcrySof ReSTOR* might be attributed to the sophisticated technology it employs, apodization, which renders to the diffractive portion of the optic gradual decreases in step height and spacing, allowing for a smooth transition of the distribution of light energy between distance and near focal points. The blend of near and distance vision reduces the potential for glare, halos, and other visual disturbances. Mean low-contrast distance visual acuity with *AcrySof* IOL improved during binocular testing; compared with monocular testing providing evidence that binocular implantation is beneficial for the patient.

1.5.4. Intraocular lens material and edge design

In pseudophakic dysphotopsia, the design and material of the IOL are typically responsible for redirecting the unwanted light to the retina. IOLs have made significant advances in achieving superior vision following the removal of cataract. One of the drawbacks of IOLs has been posterior capsular opacification. Acrylic square-edge IOLs were introduced to reduce the incidence of posterior capsular opacification and seemed to provide a significant step forward towards eliminating it. Both material and mechanical design offered

advantages. However, the lenses resulted in an increase in dysphotopsia (Schwiegerling, 2006). Holladay *et al.* (1999b) compared the edge glare caused by sharp and rounded edge designs using non-sequential ray tracing techniques. Both square and round-edged IOLs produce straylight, but only the square-edged design concentrated the light into a well formed arc on the retina. Round-edge designs tended to disperse the straylight over a much larger portion of the retina.

Ellis (2001) presented several case studies of patients with dysphotopsia following the implantation of acrylic IOLs. Of the 543 eyes examined, 1.5 % provided unsolicited complaints of positive dysphotopsia. The number of problems was fairly small, but these patients were unhappy with their visual results. Several IOL exchanges were performed in this group. Polymethyl methacrylate (PMMA) IOLs were used as replacements and glare problems did not recur with this lens material. The visual side effects are attributed to the edge designs of the implanted lenses and the high refractive index of acrylic (Ellis, 2001).

Farbowits *et al.* (2000) performed a retrospective study of acrylic IOL explantations performed at two clinical sites. The incidence of exchange is not given, but nine eyes of eight patients were described over a 2 year period. Glare and starbursts were the dominant complaints. The dysphotopsia subsided following the removal of the acrylic IOLs and replacement with silicone or PMMA IOLs. This group offers two possible explanations for the straylight effects; the first is the traditional square-edge effects suggested in other reports previously and the second is a double reflection that occurs at the faces of the IOL. The higher surface reflectance of acrylic when compared to silicone and PMMA is suggested as the difference (Schwiegerling, 2006).

Davison (2002) presented results of 2630 consecutive cases of acrylic lens implantation over a 1.5 year period. In this study, the acrylic lenses had been modified by the manufacturer to address some of the concerns that had arisen previously. The modifications were designed to retain the material and sharp edge design to keep the incidence of posterior capsular opacification low. Specifically, the edges of these lenses were textured to reduce their reflectance. Furthermore, the unequal proportions of the surface curvatures were adjusted to address the reflection issue. Davison (2002) found that 0.2 % (4) of patients had positive dysphotopsia and 0.5 % (14) had negative dysphotopsia. This rate of incidence was considerable lower than that reported by Ellis (2001).

Meacock *et al*. (2002) performed a prospective study of 60 patients split between acrylic lenses with textured and non-textured edges. By prospectively analysing the two groups, the advantages of textured edges were assessed. One month post-operatively, 67 % of the

non-textured IOL patients and 13 % of the textured IOL patients had glare symptoms. The textured edges provided a statistically significant reduction in glare symptoms.

Diffractive multifocal IOLs enable excellent near and far vision and have no restriction on pupil size as well as reducing night visual issues, but exhibit poor intermediate vision. Refractive lenses give excellent far vision, good near and intermediate images but their disadvantages are problems with halo and glare. Acrylic square edge designs reduce posterior capsular opacification but result in increased dysphotopsia. IOLs of PMMA and silicone with rounded edges, along with square-edge acrylic IOLs with non-reflective surfaces, appear less likely to cause clinically significant pseudophakic dysphotopsia (Davison, 2000).

1.5.5. Intracorneal inlays

Intracorneal inlays are an additional method for presbyopic patients; placed in the non-dominant eye, implanted under a LASIK style flap or more commonly into a corneal pocket created by a femtosecond laser (Greenwood *et al.,* 2016). A variety of light focusing principals are employed. Inlays such as Raindrop utilise corneal curvature alteration whereas, KAMRA uses small aperture pinhole principals to increase depth of focus and reduce blur (Naroo and Bilkhu, 2016).

1.6. Laser refractive surgery and dysphotopsia

The excimer laser became commercialised for refractive surgery after Trokel *et al.* (1983) found it to be a precise corneal cutting device, where tissue is ablated rather than burnt. The 193 nm ultraviolet wavelength Argon-Fluoride (ArF) laser is the most commonly used in ophthalmology (Basting *et al.,* 2002). Photorefractive keratectomy (PRK) was the first successful (and now least used) excimer laser refractive surgery technique (Munnerlyn *et al.,* 1988), after excimer laser keratotomy failed due to different corneal healing processes (Marshall *et al.,* 1986). In PRK, the corneal epithelium is completely removed and discarded manually, mechanically or more commonly with dilute alcohol, before the corneal stroma is reshaped to the predetermined profile. After surgery, a protective bandage lens is used whilst the epithelium regrows naturally (Yu & Jackson, 1999).

Compared with PRK, in laser-assisted sub-epithelial keratectomy (LASEK), the epithelium is retained; it is simply moved out of the way usually after alcohol softening.

One of the most common procedure performed to ideally abolish refractive error by administrating laser to corneal tissue is laser in situ keratomileusis (LASIK) surgery

(Holladay *et al.,* 1999a). Generally a 160 micrometre (µm) corneal flap is created with a microkeratome or more recently with a solid state femtosecond laser. The flap is pulled back so the corneal stroma can be sculpted with the excimer laser. The corneal flap is then repositioned and the epithelium continues to regenerate as normal (Yu & Jackson. 1999). LASIK technique provides improved clinical outcome success (Hersh *et al.,* 1998) and healing pattern compared to its predecessor; PRK (Chang *et al.,* 1998). Following successful PRK and LASIK, some patients will complain of the occurrence of glare and halos; the prevalence of which lies within 3 – 40 % (Obrart *et al.,* 1994).

The study by Lackner *et al*. (2003) examined the glare and halo size experienced under mesopic lighting by computer simulation prior to LASIK and 1, 3 and 6 months after surgery. At each of the post-operative stages, the glare and halo sizes observed by patients were significantly greater than the measures taken pre-operatively. There was a peak at one month, which was followed by a decrease in glare. It is thought that the peak occurrence of glare increase at one month post-LASIK may be due to the subsequent use of an excimer laser, where interruption to the arrangement of corneal collagen fibrils and increase interfibrillar spacing when compared to an unoperated eye, is so extensive that obliteration of scattered light no longer occurs by the process of destructive interference (Kaji *et al.,* 1998). The ocular surface healing leads to corneal haze and corneal oedema, which peaks at 4 weeks (Kaji *et al.,* 1998) and lessens with time (Chang *et al.,* 1998), thus reducing glare and halo size as observed at 3 and 6 months post-operation (Lackner *et al.,* 2003). Therefore, it has been suggested that LASIK increases manifestation of dysphotopsia, correlating with the elevation of light scatter from corneal healing. A more recent study by Pop and Payette (2004) agrees with the finding.

1.7. Measurement of dysphotopsia

The measurement of visual acuity alone cannot be used as an indicator of disability glare as it has been shown that disability glare and visual acuity are poorly correlated with cataract and aphakic patients (Le Claire *et al.*, 1982, Abrahamsson and Sjostrand, 1986, van den Berg, 1986). Many attempts have been made to establish an instrument that could be used clinically to assess the amount of glare. Unfortunately many of these have had limited success as they do not directly assess the straylight or glare, and no single device is in wide spread clinical use as there currently is no gold standard available for the clinical evaluation of dysphotopsia.

Both psychophysical and optical methodologies have been developed to measure intraocular forward scattering. In psychophysical procedures, the assessment is dependent on the participant's performance, and therefore, relates to their actual visual function

(Piñero *et al.*, 2010). In contrast, the optical methods are less dependent on patient response and have the limitation of providing estimations of scattering for a small angle domain, where the level of scattering is minimal; this provides a less functional measure (Piñero *et al.*, 2010).

1.7.1. Early methods

One of the earliest methods to measure halos involved drawing the outline of the halo created from a candle on a cardboard strip with a pencil; this method was clumsy and unsatisfactory (Elliot, 1924). Another used a device that had two points of light at a fixed distance showing through a metal disc; a large one for the creation of the halo, and a small one whereby any particular ring can be located. The technique had a great disadvantage as the smaller light aperture itself gives rise to halos and can confuse the patient (Elliot, 1924).

1.7.2. Elliot halometer

Elliot (1924) developed a halometer comprising of a circular wooden box containing a 4-volt tungsten lamp creating the principal light seen through a 7 mm aperture. Attached to the box is a ruler with a sliding box; the observer is required to slide this up and down until it corresponds with the outer rim of the halo to provide an outline of the photopic scotoma surrounding the light source. The ruler has an inch scale in numerals, corresponding to the radius of the glare circle; the value is converted to the angle subtended at the eye using the Tan equation together with the distance of the eye from the source of light. Elliot (1924) calculated the angle subtended for each radius on the rule for a viewing distance of 100 inches, and noted these on the ruler for ease of use without need for calculation if used at 100 inches.

1.7.3. Miller-Nadler glare tester

The Miller-Nadler glare tester was introduced by Miller *et al.* (1972) and later modified by Le Claire *et al*. (1982). The instrument presents a series of constant sized, randomly orientated Landolt rings of progressively reduced contrast (92 to 2 %) surrounded by a broad glare source of constant luminance with a viewing distance of 40 cm. The disability glare score is recorded as the last correctly identified slide. The Miller-Nadler glare tester was used to asses 32 eyes with IOLs (Nadler *et al.*, 1984) and it was discovered that glare score correlated with the percentage of capsular opacification as estimated by an independent observer. Outdoor visual acuity (with subjects facing the sun) was poorly predicted by consulting room measures of acuity ($r = 0.57$) but better predicted by their glare

scores (r = 0.80; Hirsch *et al.*, 1984). Disadvantages of the Miller-Nadler glare tester include difficulty in controlling the density of the target slides and the directional properties of the screen make the test sensitive to the positioning of the patient. For example, a patient moving 10 cm off line experiences a 50 % reduction in the effective intensity of the glare source (van der Heijde *et al.*, 1985). It has been reported that results obtained with this device showed no significant differences between radial keratotomy patients and normal even though radial keratotomy patients reported symptoms of difficulty with night driving (Waring *et al.*, 1985). Elliott and Bullimore (1993) stated poor repeatability of the test when three subject groups (young normals, n = 24; older normals, n = 22 and early cataract, n = 33) were evaluated on two visits. Another study using a different technique to evaluate glare sensitivity showed radial keratotomy patients did have increased susceptibility to glare (Applegate and Wolf, 1987), after which Bailey and Bullimore (1991) speculated that it raised questions about the sensitivity of the Miller-Nadler test.

1.7.4. The Vistech MCT8000

The targets and glare sources of the Vistech MCT8000 are contained within a portable unit (Bores, 1983, Olsen and Andersen, 1991, Elliott and Bullimore, 1993, Fan-Paul *et al.*, 2002). A console provides control of target presentation, luminance, and glare source position. The unit allows contrast sensitivity measurements at 1.5, 3, 6, 12 and 18 cycles/degree under night-time (3 cd/m^2) and day time (125 cd/m^2) luminance conditions with or without a central or peripheral glare source. Each target consists of seven circular discs, each containing a sine-wave grating of a fixed spatial frequency. The gratings are either vertical or tilted 15° to the right or left, and the contrast of the grating progressively decreases from disc one to seven. Starting at disc on, the subject is asked to indicate the orientation of each grating or to respond ‘blank’ when nothing is seen. The last disc whose orientation is correctly identified determines the contrast sensitivity score. Measurement of contrast sensitivity at 6 cycles/degrees with and without glare is described as a functional disability test (FDT) and is recommended as an initial screening technique (Vistech Consultants Inc.). The chart and glare source luminance levels can be checked using the internal calibration feature before any measurements are taken. It is recommended that night-time measurements should be made first (Vistech Consultants Inc.). The ability to vary luminance has been helpful to test for glare disability post-refractive keratotomy (Bores, 1983). Neumann *et al*. (1988) found it to be lacking in validity and to have difficult testing times. Similar tests include the Vistech chart 6500 (Reeves *et al.*, 1991) and the CSV 1000 (Ghaith *et al.*, 1998).

1.7.5. Simple pen torch glare assessment

In this most simple and accessible test, the patient reads a vision chart to distinguish their visual acuity without any glare source, and then repeats the test in the presence of a glare source, for example, a pen torch. Such methods have been found to provide a rapid test of glare (Williamson *et al.*, 1992). The test may be subject to inaccuracies caused by pupil miosis (Tan *et al.*, 1998, Boxer-Wachler *et al.*, 1999) and the difficulties in standardising the glare source distance.

1.7.6. Brightness Acuity Tester

The Brightness Acuity Tester (BAT) was introduced by Holladay *et al*. (1987) and consists of an internally illuminated white hemispherical bowl, 60 mm in diameter with a 12 mm central aperture (see Fig 1.7). It is a relatively cheap and simple to use handheld device, that the patient holds to their eye to view a visual acuity chart through the aperture. The luminance of the internal surface of the hemisphere may be varied. Elliott *et al*. (1993) used the medium intensity setting (measured to be 345 cd/m^2 using a spot photometer) when testing reliability. The high intensity setting has been reported to give inappropriately high prediction of disability glare (Neumann *et al.*, 1988, Prager *et al.*, 1989) and can reduce contrast beyond a chart's limits with some early cataract patients (Elliott and Hurst, 1990, Regan, 1991). Holladay *et al*. (1987) and Mantyjarvi *et al*. (1999) used the BAT with an ETDRS high contrast acuity chart but variable or low contrast charts, such as the Pelli-Robson contrast sensitivity or Regan visual acuity charts, can be used.

The Pelli-Robson chart is an 86 x 63 cm chart that contains 16 triplets of 4.9 x 4.9 cm letters (Pelli *et al.*, 1988). At a test distance of 1 m, these letters correspond to spatial frequencies of about 1 - 2 cycles/degree. Within each triplet, the letters have the same contrast, and the contrast in each successive triplet decreases by a factor of 0.15 log units. A by-letter scoring system that gives credit (0.05 log units) for each letter read correctly was used. This has been shown to provide more reliable test scores that the originally recommended scoring rule (Elliott *et al.*, 1991). The chart is illuminated to 100 cd/m^2. Contrast sensitivity can then be measured with and without the BAT.

The Regan Charts are logMAR (Logarithm of the Minimum Angle of Resolution) acuity charts of varying contrast. Elliott and Bullimore (1993) used the BAT with the 25 % and 11 % contrast charts, as well as the traditional high-contrast 96 % chart. The 25 % and 11 % have been discovered to be the most useful for disability glare evaluation in older patients and those with cataract (Regan, 1991). By the letter scoring method of 0.0125 log units per letter was adopted. The chart was illuminated to 100 cd/m^2, and the recommended

viewing distance of 3 m was used. Visual acuity was measured with and without the BAT for each of the three charts.

Figure 1.7: Brightness Acuity Tester consists of an internally illuminated bowl white hemispherical bowl. The patient holds the device to their eye and views a visual acuity chart through the aperture. Image from Marco Ophthalmic Inc. website.

Neumann *et al*. (1988) reported that the BAT was an excellent predictor of outdoor visual acuity and in this respect it was superior to the Miller-Nadler glare tester; it was also the quickest, least expensive and most simple of tests used. Holladay *et al*. (1987) compared normal and cataract patients' visual acuity inside with the BAT and these results were compared to visual acuities measured outside in bright sunlight. The BAT correlated extremely well ($r = + 0.84$, $P < 0.0001$) with acuities measured outside. There was no decrease in visual acuity in the 14 normal patients, but there was a one to ten line decrease in vision among the cataract patients. Mantyjarvi *et al*. (1999) wanted to investigate the use of contrast sensitivity and visual acuity in glare as a predictor of those drivers with cataracts who are likely to struggle in traffic. Using the BAT with an Early treatment diabetic retinopathy study (ETDRS) chart, none of the control eyes lost any of the lines the visual acuity chart, whereas in the cataract eyes, the loss of lines with highest glare varied from 0 to 6 lines (mean 1.4 ± 1.5). Elliott *et al*. (1990) also demonstrated its sensitivity in registering glare disability in patients with cataract who were subject to a battery of tests and to a visual ability questionnaire. Magno *et al*. (1997) looked at improvements in glare after laser capsulotomy using a BAT. Wilkins *et al*. (1996) similarly showed that the

strongest improvements in vision after Neodymium-doped yttrium aluminium garnet (Nd:YAG) laser were in contrast sensitivity with glare.

The results obtained with the BAT will depend on the design, luminance, and contrast of the test chart and some standardisation will be necessary to allow meaningful comparison of results (Bailey and Bullimore, 1991). As the patient holds the instrument, frequently over spectacles, the angular size of the aperture and its position relative to the test target is variable and this could have some influence on results (Bailey and Bullimore, 1991). Elliott *et al*. (1993) proved it to be a very repeatable test. However, more recent experimenters report the BAT device to have poor sensitivity and validity because of the pupil miosis that it induces (Tan *et al.*, 1998, Boxer-Wachler *et al.*, 1999). Another study by Rubin *et al*. (2001), the relationship between psychophysical measures and self-reported difficulty with everyday tasks was assessed in individuals of age 65 and over. The association of visual disability with glare sensitivity with BAT was the most tenuous of all the visual function links (Rubin *et al.*, 2001). Such conflicting arguments with the BAT has led to some doubts being raised over the lack of evidence for its validity, despite its ease of use and low expense (Aslam *et al.*, 2007b).

1.7.7. The Berkeley glare test

The Berkeley glare test consists of a reduced low contrast Bailey-Lovie letter chart (Weber's contrast = 18 %) mounted on a triangular opaque panel in the centre of a 30 x 27 cm opal Plexiglas panel (see Fig 1.8; Bailey and Bullimore, 1991). The chart is front illuminated (80 cd/m^2), and the glare source is provided by transillumination of the Plexiglas panel at the medium setting (750 cd/m^2). Low contrast visual acuity (VA) is measured at 1 m with and without the glare source, with credit (0.02 logMAR units) given for each letter read correctly.

Figure 1.8: Berkeley glare test with mounted Bailey-Lovie test chart. The VA is measured with the low contrast chart under different glare conditions. Images reproduced with permission from BMJ Publishing Group (Niesen *et al.*, 1997).

1.7.8. Perimetry glare test

Namiki and Tagami (1993) attached a glare source within an Octopus 500E (Haag-Streit, Koeniz, Switzerland) automated perimeter to determine the extent of visual field loss surrounding a central glare source. Twelve normal control phakic eyes together with a number of other pseudophakic groups each consisting of 6 eyes were enrolled in this study. These groups were a 6 mm no hole lens group, a 6 mm 4 hole lens group, a 5.5 times 6.5 mm 2 hole lens group, a 5.0 times 6.0 mm no hole lens group and a diffractive multifocal group. There were minimum glare disabilities in the visual field in the control group. The 6 mm no hole lens group and the diffractive multifocal group showed no statistical

significance compared to the control group. Groups with the two types of ovoid lens and the 6 mm 4 hole lens group showed a statistically higher degree and a greater extent of glare disabilities in the static visual field than the control group. Careful selection of appropriate patients to receive implants of small efficient optic IOLs, such as IOLs with positioning holes and ovoid lenses, according to the pre-operative pupil size under scotopic or mesopic condition and efficient lens optic size are important in order to reduce hole and edge glare. The diffractive multifocal IOLs group showed a slightly higher degree and a greater extent of glare than the control group and the 6 mm no hole monofocal lens group but the difference was very small and statistically insignificant. Therefore the effects of diffractive microstructure on glare disabilities were considered to be slight and clinically acceptable.

1.7.9. van den Berg Straylight meter

Initial attempts to measure ocular straylight using the equivalent veiling luminance theory required measurements of two types of thresholds; in the presence of a distant glare source, and in the presence of a homogeneous background luminance. The equivalent luminance could be derived from these measurements, defined as the luminance yielding identical thresholds as the glare source (equivalent veil method; Vos, 1984). van den Berg (1991) compared results from various groups, all using this method, and concluded that these results varied considerably. The method was not widely used as it was not easily accessible for clinical application (Franssen *et al.*, 2006).

In 1986, a new psychophysical method was designed to overcome the problems experienced with glare testers, called the Direct Compensation technique (van den Berg, 1986). A bright ring shaped flickering light source around a dark test field is presented. Due to intraocular scatter, part of the light from the bright ring shaped source will be projected on the retina at the location of the test field, inducing a weak flicker in the test field. To determine the exact amount of straylight, a variable amount of counter phase compensation light is presented in the test field. By adjusting the amount of compensation light, the flicker perception in the test field can be extinguished. In this way, the straylight modulation caused by light scattered from the glare source is ‘directly compensated for’.

In 1990, van den Berg and Ijspeert introduced a small portable device to implement the Direct Compensation method, called the Straylight meter (Ijspeert and van den Berg, 1992, van den Berg and Ijspeert, 1992). Subsequently, many studies on ocular straylight have been published using the Direct Compensation method, such as on normal population ageing effects where straylight was shown to increase with age (Ijspeert *et al.*, 1990, Hohberger *et al.*, 2007). A study exploring the relationship between straylight and the translucency of the ocular wall noted that straylight values increase a more translucent

ocular wall (van den Berg *et al.*, 1990, Lahey *et al.*, 1993). Increased ocular pigmentation resulted in a decrease in ocular straylight (van den Berg *et al.*, 1991). Dewaard *et al*. (1992) investigated the effects on straylight on populations with different kinds of cataract. It was used as a gold standard to assess the validity of glare tests (Elliott and Bullimore, 1993).

The method has some major drawbacks for routine clinical or large-scale use (Franssen *et al.*, 2006): (1) Judgement of the weak flicker in the test field often appeared to be difficult for untrained subjects; this seemed to be caused by the presence of the strong flicker of the straylight source. (2) Usually, visual tests are based on what subjects actually see. On the contrary, in the direct comparison method, the subjects have to indicate whether the flicker perception has disappeared. The continuous flickering of the straylight source in the periphery made this contra intuitive task even more difficult. (3) The accuracy of the measurement seemed to depend on the adjustment strategy, which could differ considerably between subjects, and on proper explanation of the test. (4) There was no control over an individual's measurement reliability. (5) Subjects had the ability to influence the test outcome. As a result of these drawbacks, the straylight meter largely remained limited to laboratory use.

1.7.10. Glare and Halo test

The Glare and Halo test is a standardised commercially available computerised test used to measure the size of photopic phenomena. A central white target 15 mm in size is displayed on the screen and the subject is required to place a mark at the boundary of the photopic phenomenon for 12 equidistant orientations separated by 30 degrees surrounding the glare source. The central glare area in degrees is then calculated in accordance with the working distance of the subject. The Glare and Halo test has been used in three studies examining the difference in halo area between a monofocal IOL and the Array refractive multifocal IOL; Pieh *et al*. (2001) discovered a significant difference in dysphotopsia between the two types of pseudophakic correction, however, two further studies did not find a significant difference (Eisenmann *et al.*, 1996, Dick *et al.*, 1999). The Glare and Halo test has also been used to assess photopic phenomenon in post-LASIK subjects (Lackner *et al.*, 2003). Repeatability studies have not been conducted using this instrument.

1.7.11. *C-Quant*

One of the most used clinical psychophysical procedures for measuring intraocular forward scattering was defined in 2003 and implemented in the commercially available *C-Quant* (Oculus Optikegerate GmbH, Wetzlar-Dutenhofen, Germany); this uses the compensation comparison method. Compensation comparison was developed to overcome the limitations

of the direct compensation method (van den Berg and Ijspeert, 1992). The main advantage of the compensation method is that the two central stimuli are compared simultaneously, in contrast to the direct compensation method where the subject has to compare different stimuli sequentially. The new approach enabled control over the reliability of the assessment (van den Berg *et al.*, 2013). It was no longer possible to influence the measurement outcome, and quality control factors could be defined (van den Berg *et al.*, 2013).

The task involves the patient viewing a central circular stimulus that is split into two hemispheres, and is surrounded by a larger annulus of bright light, with a radius of 5 to 10 degrees resulting in an effective average of angular value of 7 degrees (see Fig 1.9; van den Berg, 1995). The straylight is caused by presenting a flickering light in the peripheral ring of the stimuli, which is scattered by the ocular structures.

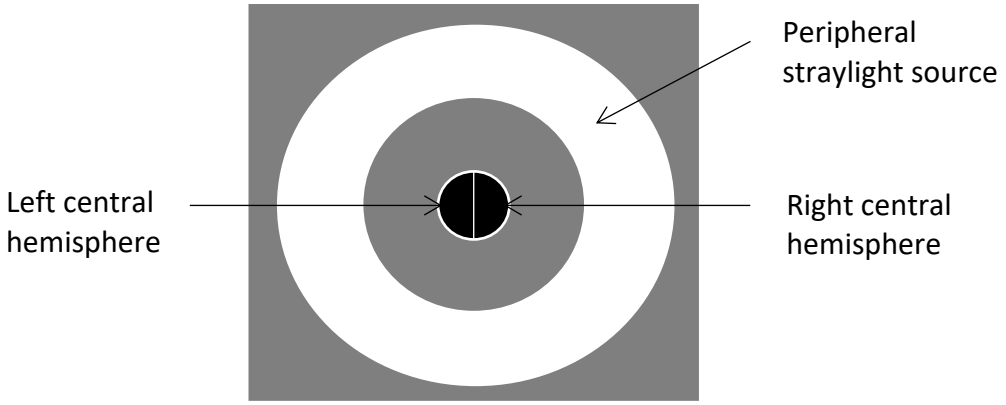


Figure 1.9: Diagram of stimulus seen when using *C-Quant*.

The compensation light is presented in one of the two randomly chosen central halves (referred to as field B); the resultant flicker is a combination of straylight and compensation light modulated at the same frequency in counter phase with the straylight source (Franssen *et al.*, 2006). No compensation light is presented in the other half (referred to as field A) so the perceived modulation comes from straylight alone (Franssen *et al.*, 2006). During the test, differing amounts of the compensation light are presented in field B, making its half appear to flicker more or less than the unmodulated half, depending on the brightness of the modulation (Franssen *et al.*, 2006). A 2-alternative forced choice psychophysical method (2AFC) is used, where the subject has to decide which of the two hemispheres flickers stronger. The subject's responses are recorded by means of two push buttons, representing the left and right test fields. With this method, the subject indicates a choice even when there is no perceived difference between the two halves, and as the

number of trials increases each half will be chosen about 50 % of the time (Piñero *et al.*, 2010).

1.7.12. Halometers

Various types of halometers have been developed over the years in attempt to outline the size of halos. A gross estimation halometer technique involved a central light source with an overlaying neutral density filter being place 3 m from the subject. The subjective measure required instructing the examiner to move their hands until they intersected with the outer rim of the photic phenomena. The distance between the examiner's hands was taken as the representation of the size of the photopic scotoma. The technique failed to identify any difference between a multifocal IOL and monofocal IOL; no validation studies have been conducted using this technique (Hunkeler *et al.*, 2002).

The halometer described by Gutierrez *et al*. (2003) was designed to measure post-LASIK dysphotopsia in subjects. The halometer comprises of a board with a central hole through which a light emitting diode (LED) is placed to provide the glare source. To create the targets, a series of holes radiating away from the central light also have LEDs shining through them. These LEDs flash in sequence, similar to a visual field screening test allowing the area of glare scotoma to be mapped. No repeatability studies have been conducted using this instrument.

Allen *et al*. (2008) measured the halo using a red fixation cross within a white ring (luminance of 86.6 cd/m^2), which generated the halo source on a black background. The subject, at a distance of 100 cm, positions a marker at the outer limit of the halo using a computer mouse, thus recording the side of the halo around the ring at 30 degree intervals. It has been used to assess dysphotopsia following multifocal implantation. The design used for examining multifocal IOLs was not assessed for repeatability and was found to show similar results with both multifocal and monofocal IOLs (Allen *et al.*, 2009).

Babizhayev *et al.* (2009) later described a halometer with a central light source with a variable intensity control. A luminous optotype of a set size and brightness is moved horizontally towards and away from the glare source until it is just distinguishable. The working distance is set as 30 cm and the distance between the optotype and the glare source are recorded. The halometer was validated on phakic subjects with and without cataracts (Babizhayev *et al.*, 2009).

1.7.12.1 Vision Monitor

Halo radius has been measured using the Vision Monitor and low luminance optotypes presented at 2.5 m (Puell *et al.,* 2014). An off axis light source was used, with the participant's head positioned with centre of monitor, whilst the LED glare source is at the edge of the screen. Optotypes arranged in three radial lines of letters appear from the periphery, moving towards the glare source. Each line contains 10 letters forming 10 rings at intervals of 33 arc min. Each letter subtends 15 arc min and corresponds to 0.5 logMAR. The Vision Monitor only quantifies the halo extent in 3 meridians, and from these halo radius values, the overall halo map is approximated (Puell *et al.,* 2013). However, it has been reported that halos are not perfectly circular (Castro *et al.,* 2011, Meikies *et al.,* 2013); accentuating the importance of measuring the halo in multiple meridians.

1.7.12.2 Aston Halometer

Buckhurst (2011) developed a new halometer; consisted of a display screen presenting a series of dots, of varying contrasts, radiating away from a central LED, which was controlled by a single battery. The design was inspired by that of Gutierrez *et al*. (2003). Subjects were requested to count the number of dots seen in each direction. Subsequently, the dot targets were changed to letters as keeping track of the number of dots observed with the central glare was a difficult task for the participant. It became apparent that in its current form, results would be unreliable and not sensitive enough to detect differences in glare profiles (Buckhurst, 2011). Instead of using a static display, a bespoke computer programme was developed for the Aston halometer that allowed a changing letter to move away and towards the glare source in 8 meridians separated by 45 degrees. The letter targets were designed to have multiple contrast levels. A letter size equivalent to 0.3 logMAR was selected. The letters 'D', 'E', 'F', 'H', 'N', 'U' and 'Z' were chosen due to their similar legibility (Bailey and Lovie, 1976).

The program is designed so that the letter size and its position on the screen were controllable. The letter size is displayed in degrees subtended at the eye in the corner of the screen. The programme is based around a turtle graphics design; the left/right arrow moved the letter towards or away from the centre of the screen 0.05° at a time. The letter can be randomised at the press of a button.

To ensure the repeatability and validity of the test, it was important to ensure that the glare source retained a constant brightness. A warm white luxeon emitter white star LED was mounted at the end of a telescopic arm so it could be attached to the edge of a flat screen and the light positioned in the centre (see Fig 1.10). The LED has a correlated colour

temperature of 3200 K, whilst maintaining 70 % lumen over 50,000 hours of operation. The telescopic arm was shrink-wrapped in a black matt plastic to ensure non-reflectance. The halometer was connected to a 18 pin board designed to provide protection against a drop in output by running the current through 10 K, 47 K, 100 R and 22 L resistors; this was then connected to a mains output with a consistent voltage, the current was limited to 5 V and 100 mA (full load 1 W).

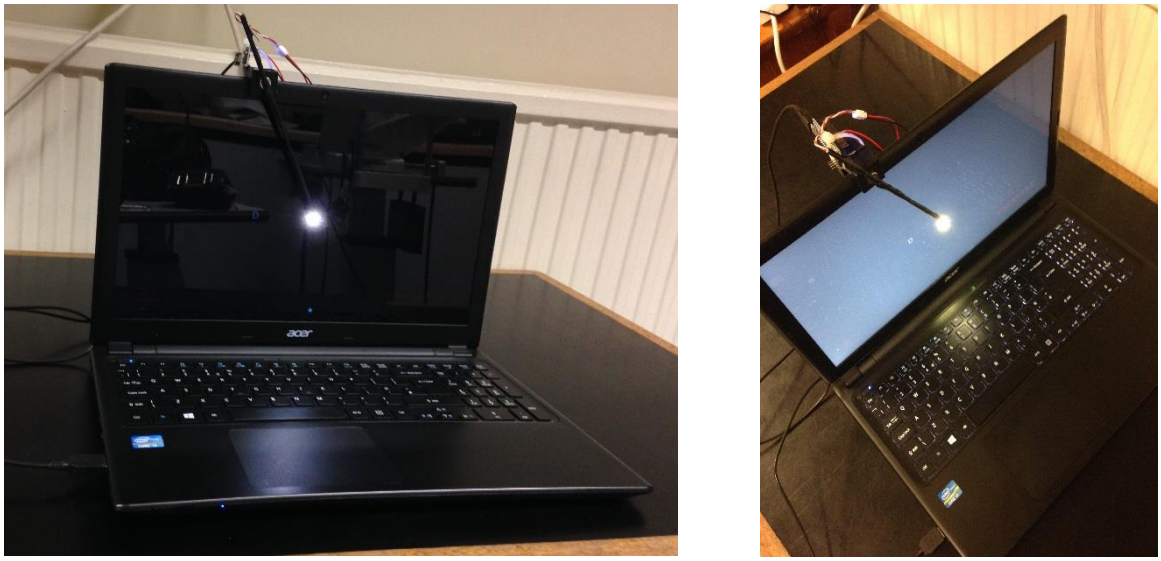


Figure 1.10: Set up of the halometer device involves attaching a telescopic arm to the edge of the flat screen with a LED mounted at the end so that the light can be positioned in the centre.

Buckhurst *et al.* (2015) reported the halometer to demonstrate good inter- and intra-repeatability for the measurement of dysphotopsia with and without Bangerter foil. The intraclass correlation co-efficient (ICC) based on a two-way mixed ANOVA model with a 95 % confidence interval. Intra-observer variability can be seen in Table 1.3 and inter-observer variability is displayed in Table 1.4.

	Contrast of the Optotype target			
	1000 C_W	**500 C_W**	**100 C_W**	**25 C_W**
Control Lens	0.876	0.843	0.775	0.806
0.8 Bangerter foil	0.979	0.929	0.874	
0.6 Bangerter foil	0.929	0.840		

Table 1.3: Intra-observer variability of halometer with each *Bangerter foil* and at each contrast level (n=20).

	Contrast of the Optotype target			
	1000 C_W	**500 C_W**	**100 C_W**	**25 C_W**
Control Lens	0.776	0.729	0.632	0.675
0.8 Bangerter foil	0.696	0.675	0.532	
0.6 Bangerter foil	0.576	0.529		

Table 1.4: Inter-observer variability of the halometer with each *Bangerter foil* and at each contrast level (n=20).

The halometer is also available as a tablet app version for easier clinical application. The software works in the same way, but on an iPad. It has a custom built attachment and arm to create the central light source (see Fig 6.1). Intra-observer repeatability was good for the iPad halometer (ICC = 0.89; Buckhurst *et al.,* 2017).

1.7.13. Questionnaires

Quality of life surveys are gaining acceptance as effective evidence-based methods of measuring patient visual well-being (Aslam *et al.*, 2004b). The underlying reason for using quality of life questionnaires in clinical practice is to ensure that treatment plans are centred on the patient rather than the disease. Questionnaires used to assess vision with presbyopic correcting IOLs are mainly bespoke and few have been validated using either classic test theory (CTT) or with Rasch analysis. Questionnaires should be validated on the target group for the questionnaire, however, rarely have the questionnaires been validated with multifocal IOLs.

1.7.13.1. Kohnen questionnaire

To assess the incidence and impact of visual phenomena such as glare and halos, subjects were asked to rate the impact of any observed phenomena. The subjects were specifically queried about glare (trouble seeing street signs due to bright light or oncoming headlights), halos (rings around lights), distorted near vision (straight lines looking crooked close up), distorted far vision (straight lines looking crooked at distance), blurred near or far vision, problems with night vision, double vision with both eyes or with other (non-operated eye) closed, and problems with colour perception. Patients rated the effect of each phenomenon on a scale from 0 to 7, with 0 meaning not observed; 1 is easily tolerated; and 7 is incapacitating. A rating of 1 to 2 was interpreted as mild, a rating of 3 to 5 was defined as moderate, and a rating of 6 to 7 was defined as severe. Kohnen *et al*. (2006) enrolled 127

patients and for glare at 120 to 180 days after the second implant, of the 118 patients who answered the question 8.5 % (n = 10) rated their observation as severe in effect, 24.6 % (n = 29) rated it as moderate, and 66.9 % (n = 79) rated it as none or mild. Halos were reported as severe by 4.2 % of patients, moderate by 16.1 %, and absent or mild by 79.7 % of patients.

Apart from halos (which slightly increased), the mean rating of the visual disturbances decreased after second eye implantation compared with assessment after first eye implantation. The results of the subjective questionnaire on perceived optic phenomena and quality of life in this study of the *AcrySof ReSTOR* IOL MA60D4 demonstrated lower rates of visual symptoms in comparison to published values from multifocal studies, and high rates of patient satisfaction consistent with other studies (Steinert *et al.*, 1999, Javitt and Steinert, 2000). The questionnaire has not be validated.

1.7.13.2. Cataract TyPE Specification questionnaire

The Cataract TyPE Specification questionnaire is a 13-item questionnaire developed to determine the patient's outcome after cataract surgery in five dimensions: distance vision, near vision, day-time driving, night-time driving and glare (Javitt *et al.*, 2003). It has been validated for this purpose in monofocal and multifocal pseudophakic subjects demonstrating high Cronbach's alpha and good correlation with visual acuity. Gothwal *et al*. (2009) validated the questionnaire in subjects with cataracts using Rasch analysis, they reduced the questionnaire to a 12 item questionnaire, which demonstrated good measures of visual function within this group. The questions cover assessment of vision and glare. The questionnaire was internally valid (Cronbach alpha = 0.94), both on self-administration in the patient care setting and upon mailed survey administration and across patient race and gender (Javitt *et al.,* 2003).

1.7.13.3. Quality of Vision questionnaire

The Quality of Vision questionnaire was designed to measure the overall subjective perception of vision. It is a 30 item questionnaire, 9 questions specific to dysphotopsia, 12 enquire about blurred, distorted and hazy vision and 9 are specific to focussing and depth perception. Rasch analysis was used to validate the questionnaire in a study involving 900 subjects (including correction with monofocal, multifocal and accommodative IOLs; Mcalinden *et al.*, 2010).

1.7.13.4. Self-Perceived Quality of Vision questionnaire

The Self-Perceived Quality of Vision questionnaire was designed to assess vision post IOL implantation. It contains 17 questions detailing perception of satisfaction, photopic phenomena and ability to perform visually dependent tasks. The questionnaire was validated for monofocal pseudophakic subjects using CTT and by examination of Cronbach's alpha and repeatability (Aslam *et al.*, 2004b). Subsequently, the questionnaire was used to assess subjects implanted with multifocal and single optic accommodative IOLs (Harman *et al.*, 2008).

1.7.13.5. Welch's questionnaire

A study carried out by Welch *et al*. (2010) investigated the causes in dissatisfaction after uncomplicated cataract surgery. Sixty-one patients had uncomplicated cataract surgery, and there was forty control patients.

The patient was asked questions dealing with dysphotopsia:

1. Do you experience glare when looking into light (ranked no, hardly ever, more often than not, or always)?
2. Do you experience sensitivity to light (ranked no, hardly ever, more often than not, or always)?
3. Do you see flashes of light (yes or no)?
4. Do you see haloes around lights (yes or no)?

A dysphotopsia score was calculated by adding the scores for all 4 questions where no equals 0, hardly ever equals 1, more often than not equals 2, and always equals 3. For the two yes and no questions, no equals 0 and yes equals 2.

Overall satisfaction with vision after surgery was scored as very satisfied equals 0, satisfied equals 1, no change since before surgery equals 2, dissatisfied equals 3, and very dissatisfied equals 4 (Welch *et al.*, 2010). The only significant correlation with dissatisfaction was dysphotopsia ($r = 0.602$, $P < 0.0001$). Highlighting that whilst satisfaction with cataract removal and IOL placement is high, dysphotopsia is the most important contributor to dissatisfaction and is relatively common (Welch *et al.*, 2010). No validation has been carried out for this questionnaire.

1.7.13.6. The Perceived Visual Disability questionnaire

The Perceived Visual Disability (PVD) questionnaire was designed to determine the effect of cataract on lifestyle. The questionnaire consists of 20 items, the results of which were correlated against measures of glare, visual acuity, and contrast sensitivity (Elliott *et al.*, 1990). The questionnaire has not been validated on pseudophakic subjects.

1.7.13.7. Photographic questionnaires

Hunkeler *et al*. (2002) developed a series of images simulating night time visual phenomena that are often experienced, alongside 12 illustrations of visual phenomena under high contrast conditions varying in terms of detail, brightness and thickness (see Fig 4.1 and Fig 4.2). Of 22 patients that had bilateral implantation of Array multifocal, on the images most patients chose the clear starburst (image 4 on Fig 4.1) and blurred starburst (image 5) as representative of their visual sensations. None chose double ring halos (image 3) or cataract-like glare (image 6). Most patients picked the starburst illustrations in the third column (31, 32, and 33 on Fig 4.2) and fourth column (41, 42, and 43) as representative of their visual phenomena. No patients picked the bright-light illustrations in the first column (11, 12, and 13). Some of the participants stated that the images were a good match.

Aslam *et al*. (2004a) developed a similar style of questionnaire with images depicting different types of dysphotopsia and varying severities of each (see Fig 3.3). Aslam and Dhillon (2004) stated that questionnaire assessments provide scores that are perhaps closest to patient's perceived morbidity but have poor specificity and are subject to interpretation errors, ambiguity, use of jargon and biases in responding. The images were developed to avoid these problems. The photographic images of photic phenomena (*PIPP*) provided a range of glare conditions including dark arc, bright arc, serrated arc, night halos, night starburst, day halos, day starburst, central flash (glare from the sun causing excessively bright light), streams of light and ripple effect; which participants would be able to relate to. The images showed good repeatability when tested on 22 patients and good reliability when two examiners tested 12 patients on 2 separate intervals.

1.7.13.8. Other questionnaires

Sedgewick survey instrument that only asks a single question about glare; Are you bothered by glare, halos, or rings around lights? Response options are never, occasionally, about half the time, often or always (Sedgewick *et al.*, 2002). The Javitt questionnaire is a detailed quality of life questionnaire, with respect to dysphotopic symptoms (Javitt *et al.*, 1997). It

involves questions related to spectacle wearing habits, self-reported rating of vision (zero to 10) and eight further sets of questions related to symptoms of glare and halo occurring during activities of daily life, scored on a scale of zero to four. The questionnaire was validated using 100 subjects implanted bilaterally with a silicone optic foldable zonal progressive IOL. The questionnaire was valid with a Cronbach's alpha of 0.94.

The Winther-Nielson questionnaire involves questions relating to necessity for wearing sunglasses, a comparison of pre- and post-operative vision, and some very specific questions pertaining to the type of dysphotopic symptoms that were originally volunteered with the early multifocal lens types (Allen *et al.*, 2009). The answers were weighted and given a score on a scale of zero to 10 for their relative importance.

The Tester questionnaire was designed to determine whether a patient was experiencing any form of dysphotopsia (Tester *et al.*, 2000). Patients who do experience dysphotopsia are then asked more about the nature of the symptoms. The questionnaire is structured around six stems, with the first three questions on dysphotopic symptoms being graded on a scale of zero to three. Overall satisfaction with vision is scored on a scale of zero to five.

1.8. Aims of thesis

To summarise, glare tests that were introduced often consisted of either visual acuity charts including ETDRS (Holladay *et al.*, 1987, Prager *et al.*, 1989, Mantyjarvi and Tuppurainen, 1999), Ferris-Bailey (Elliott *et al.*, 1990), Bailey-Lovie (Bailey and Bullimore, 1991, Elliott and Bullimore, 1993), or Regan (Elliott and Bullimore, 1993) or contrast sensitivity charts including sinusoidal gratings (Ginsburg *et al.*, 1987, Neumann *et al.*, 1988, Prager *et al.*, 1989, Dewaard *et al.*, 1992, Elliott and Bullimore, 1993), Landolt rings (Hartmann and Wehmeyer, 1980, Le Claire *et al.*, 1982, Prager *et al.*, 1989, van Rijn *et al.*, 2005), Pelli-Robson (Elliott *et al.*, 1990, Elliott and Bullimore, 1993), with and without a glare source presented at some angular distance in the visual field (van den Berg *et al.*, 2013). Some studies utilised a laboratory setup, with and without glare source present, with visual field stimuli (Verriest and Uvijls, 1989), a flashing test field (Yuan *et al.*, 1993), sinusoidal gratings (Harrison *et al.*, 1993), or low contrast letters (Hard *et al.*, 1990) as targets, and also for specific night time conditions (Rubin *et al.*, 1993). The repeatability and discriminative ability of the glare tests studied were found to be inadequate (Elliott and Bullimore, 1993, van den Berg *et al.*, 2003, van Rijn *et al.*, 2005). A large multicentre Prospective Evaluation of Radial Keratotomy (PERK) study omitted glare test data from the final results (Waring *et al.*, 1990), as the glare tester was not sufficiently sensitive to detect small but significant amounts of light scattering (Waring *et al.*, 1985, Elliott and Bullimore, 1993, Veraart *et al.*, 1993). Due to these issues, a standard glare

measurement test was never adopted, and papers discussing glare test problems emerged (Prager *et al.*, 1988, Rubin, 1990, van den Berg, 1991, Elliott, 1993, van den Berg, 1994, Aslam *et al.*, 2007b). However, Cervino *et al*. (2008) showed high repeatability of the *C-Quant*, suggesting that the system is reliable and useful for detecting clinically significant stray light values. Although there are various questionnaires available, they don't seem to be in wide use. Photographic questionnaires depicting various types of dysphotopsia have the potential for clinical use due to the quick and easy nature of use. When investigating dysphotopsia in a normal population, each study reports either objective measures or subjective complaints. It is therefore unknown how both measures are linked, if they are.

The aims of this thesis are:

- Describe the relationship between objective measures and subjective complaints of dysphotopsia and to establish a normal range of values for the first time representing the subjective grade divided by the objective grade (the glare effect ratio).
- Compare binocular and monocular halometry measures to ascertain if there is a significant difference.
- Establish how objective measures and subjective complaints of dysphotopsia change with age in healthy eyes, whilst defining a normal range of values for halometry halo area over a wide age range.
- Establish if pupil size has an effect on the halo area measured by the Aston halometer.
- Measure longitudinal changes in halo area, straylight and subjective photic effects following LASIK refractive surgery, and to determine whether both objective and subjective measures return back to normal values.
- Determine how cataract surgery impacts on objective and subjective photic effects, and to track longitudinal changes in response to cataract surgery.

CHAPTER 2

A NOVEL GLARE EFFECT RATIO TO DESCRIBE THE RELATIONSHIP BETWEEN OBJECTIVE AND SUBJECTIVE MEASURES OF DYSPHOTOPSIA

2.1. Introduction

Cataract surgery is the most commonly performed surgical procedures with approximately 19 million operations carried out per year globally (Donaldson *et al.*, 2013). Cataract is the leading cause of avoidable blindness (World Health Organisation, 2007). In developed countries, a routine and cost-effective procedure (Asbell *et al.*, 2005) can be carried out in which the cataract is extracted followed by implantation of an IOL within the capsule. Monofocal IOLs are currently the most commonly implanted lens type (Hovath *et al.*, 2014), designed to provide good vision at a single focal point, typically distance, often leaving patients with poor unaided near vision, thus corrective lenses must be worn. In the UK, cataract surgery is the most frequently undertaken procedure within the National Health Service (NHS) with an estimated 330,000 operations undertaken annually in England (Trikha *et al.*, 2013, Donachie *et al.*, 2016). The volume of cataract surgery has increased dramatically since the 1980s (Taylor, 2000) due to growth and ageing of the population. As cataract surgery has improved, it is now offered as clear lens exchange as a refractive surgery option.

Dysphotopsia is a well-known complaint after refractive and cataract surgery (Tester *et al.*, 2000, Souza *et al.*, 2006, Aslam *et al.*, 2007b, Woodward *et al.*, 2009, Chang *et al.*, 2012, de Vries and Nuijts, 2013). Such surgeries are becoming increasingly common since the introduction of multifocal IOLs (Davison and Simpson, 2006, Alfonso *et al.*, 2008, van der Linden *et al.*, 2012, Aychoua *et al.*, 2013), which usually allow patients spectacle independence as good distance and near visual acuity are achieved. Despite good scores on traditional measures of visual acuity, patients may report poor vision or light sensations in everyday situations (Nadler *et al.*, 1990). Multifocal IOLs create two or more focal points at different planes. For distance viewing, the distance focal point produces a spot image with the near focal point creating an out of focus blur circle on the retina. The surrounding blur results in the retinal image having less contrast against its background and therefore, also results in the halo phenomenon (Buznego and Trattler, 2009). It is recognised that patients with cataract or individuals fitted with multifocal IOLs may demonstrate excellent high contrast visual acuity, but suffer from undesirable photic phenomena such as halos and disabling glare (Schwiegerling, 2006, Aslam *et al.*, 2007b, Calladine *et al.*, 2012). Halos are a major cause of dissatisfaction following multifocal IOL implantation and may necessitate explantation if the effects are

severe and persistent (Galor *et al.*, 2009, Kamiya *et al.*, 2014). It has been reported that up to 40 % of those fitted with multifocal IOLs complain of dysphotopsia, compared to only 20 % with monofocal IOLs (Souza *et al.*, 2006, Woodward *et al.*, 2009, de Vries *et al.*, 2011, Chang *et al.*, 2012). However, a 2006 Cochrane review found that photic phenomena are 3.5 times more likely with multifocal IOLs than monofocal IOLs (Leyland and Pringle, 2006). Dysphotopsia (Tester *et al.*, 2000) also increases naturally with age due to greater light scattering by the optical media.

The need to measure photic phenomena is becoming ever more important as patients are being fitted successfully with multifocal IOLs, and these have become increasingly popular amongst patients (Davison and Simpson, 2006, Alfonso *et al.*, 2008, van der Linden *et al.*, 2012, Aychoua *et al.*, 2013). Hovath *et al*. (2014) reported that in 2011, 7.8 % of European cataract surgery patients opted to receive a premium IOL, defined as multifocal, multifocal toric or accommodative IOL, compared to 14.7 % in the United States. Whilst monofocal IOLs are the most commonly implanted IOL type currently, it is envisaged that the trajectory of premium IOLs, specifically multifocal IOLs, will increase at a significantly faster rate in comparison to the steady increase of monofocal IOLs.

Multifocal IOLs are not only used in cataract surgery but are becoming a common first choice for refractive lens exchange as an alternative to laser eye surgery in presbyopia (Barisic *et al.*, 2008, Chang *et al.*, 2012). Refractive lens exchange is becoming increasingly popular, as it is a relatively uncomplicated procedure that addresses both ametropia and presbyopia (Goes, 2008). Multifocal IOLs increase the likelihood of spectacle independence compared to monofocal designs (Pager, 2004, Hawker *et al.*, 2005, Munoz *et al.*, 2011, Ferrer-Blasco *et al.*, 2012). In the UK, multifocal IOLs are a part of the private sector and are not available on the NHS unless under a clinical trial.

Since the introduction of refractive lens exchange, the purpose of the procedure is no longer to simply remove the cataractous lens and replace it with an IOL of a close pre-operative refractive error (Lichtinger and Rootman, 2012); it also comes with increased patient expectation of the best possible refractive outcome with restoration of vision for near and distance without spectacles (Aslam *et al.*, 2004a, Pager, 2004, Hawker *et al.*, 2005, Munoz *et al.*, 2011, Braga-Mele *et al.*, 2014). It has become increasingly common for emmetropic presbyopes to undergo refractive lens exchange simply to be rid of reading spectacles (Schena, 2005). In these cases, it is more evident that patients with moderate visual acuity pre-operatively are less happy with making the trade-off of good visual acuity at the cost of troublesome glare and loss of contrast sensitivity (Aslam *et al.*, 2007b).

Chang *et al*. (2012) found that the most satisfied patients were those who underwent bilateral refractive lens exchange and were habitual spectacle wearers pre-operatively.

A number of halometers have been developed to measure the size of the photic scotoma (halo) surrounding a glare source (Pieh *et al.*, 2001, Babizhayev *et al.*, 2009, Puell *et al.*, 2013, Buckhurst *et al.*, 2015). Such devices allow objective quantification of halos, with newer halometers typically controlled using computer programmes, providing a high level of accuracy and avoiding the previous limitation of patients having to manually indicate the halo boundary. Halo area increases with age in healthy eyes (Puell *et al.*, 2013) and may also be greater for cataract patients (Babizhayev *et al.*, 2009, Palomo-Álvarez and Puell, 2015), those fitted with multifocal IOLs (Zhang *et al.*, 2011) and following corneal refractive surgery procedures, depending on factors such as pupil diameter and ablation zone (Lackner *et al.*, 2003, Valverde and Gonza, 2003).

Measurement of intraocular forward-scattered light, using a straylight meter such as the *C-Quant* (Oculus Optikgeräte, Wetzlar, Germany) represents a further objective clinical approach to evaluate visual quality. Retinal straylight, caused by light scattering in the ocular media, increases with age (van den Berg, 1995, Guber *et al.*, 2011) and measurements may aid the diagnosis of cataract (Palomo-Álvarez and Puell, 2015) and surgical decision-making processes (van der Meulen *et al.*, 2012), alongside conventional visual acuities. It has been suggested that straylight values could be used as an indicator for fitness to drive (van Rijn *et al.*, 2011) in cataract patients, even when visual acuity is within acceptable limits.

Subjective dysphotopsia assessment techniques are also available; these include simple numerical scales of severity (Hofmann *et al.*, 2009), more detailed complaint questionnaires (Arnold, 1994, Dick *et al.*, 1999) and grading of various photic effects with reference to simulated photographs (Aslam *et al.*, 2004a). Subjective evaluation of photic complaints may be valuable in addition to objective measures as the experience of dysphotopsia is believed to have a significant psychological component (Aslam *et al.*, 2007a), with some surgeons recommending or making decisions regarding refractive procedures on the basis of patient personality traits (Dick *et al.*, 1999, Pepose, 2008, Braga-Mele *et al.*, 2014).

Although the subjective experience of dysphotopsia has a significant impact on both post-operative patient satisfaction and the need for subsequent corrective procedures, e.g. lens explantation, subjective findings are not routinely considered in light of objective measures. That is despite the fact that one study by Dick *et al*. (1999), which examined both objective and subjective measures of photic phenomena after monofocal and multifocal lens implantation, found a positive correlation. However, no previous study has investigated the

typical relationship between newer objective measures, such as Aston halometer and *C-Quant*, and subjective complaints of photic complaints using images across a broad age range prior to any refractive surgery. Such information could be clinically valuable at the pre-operative stage in the identification of individuals at risk of the worst subjective problems post-operatively, that is, those with a high level of subjective grievance in comparison to objective findings are most likely to experience extreme dissatisfaction with any undesirable photic phenomena.

The aims of this prospective study are:

- Describe the relationship between objective measures and subjective complaints of dysphotopsia.
- Establish a normal range of values for the first time representing the subjective grade divided by the objective grade (the glare effect ratio).
- Compare binocular and monocular halometry measures to see if there is a significant difference as typically, previous studies state monocular values only (Bailey and Bullimore, 1991, Pieh *et al.*, 2001, Lackner *et al.*, 2003, Puell *et al.*, 2013). Binocular measures may be more representative of an individuals' visual experience.
- Use *Bangerter* foils (Haag-Strait, Koeniz, Switzerland) to simulate glare conditions, such as those that would be experienced in a 'cataractous' eye, to permit assessment of the relationship of objective and subjective measures in these conditions.

2.2. Subjects and methods

All procedures were conducted in the Ophthalmic Research Group laboratories at Aston University, Birmingham, UK. Risk assessment was conducted as part of the ethics application. The study was reviewed by the Aston University Life and Health Sciences Research Ethics Committee (Application number 595). A copy of this approval can be found in appendix A1. The study was conducted in accordance with the tenets of the Declaration of Helsinki and all subjects gave their informed consent to take part.

Power calculations, made using GPower (version 3.1.9.2), showed that 93 participants were required to enable Spearman correlation to detect statistically significant medium size (0.3) effect at the 5 % significance level ($\alpha = 0.05$) with 80 % power. One hundred participants were recruited from the staff and student body in the Optometry department at Aston University subject to the following criteria:

Inclusion Criteria

- Healthy subjects under 35 years old as it is known that glare increases with age (Bailey and Bullimore, 1991, Vos, 2003a).
- Corrected visual acuity of logMAR 0.1 or better in the eye to be tested, and logMAR 0.3 or better in the weaker eye to allow easy viewing of the logMAR 0.4 letter on the halometer.
- Participants who are able to understand and undertake the informed consent process.

Exclusion Criteria

- Any history of ocular surgery, including laser refractive surgery as it could increase the magnitude of the glare effect (Lackner *et al.*, 2003, Valverde and Gonza, 2003, Zhang *et al.*, 2011).
- Participants with any pre-diagnosed ocular conditions.
- Any participants with a history of using drugs that are known to affect the eye.
- Any participants with a systemic health problem that may result in ocular complications.

Unaided visions were measured and a full subjective refraction was performed at 3 m using the *Thomson Test Chart 2000* (Thomson Software Solutions, Hatfield, Herts, UK). If the participant for distance wore a habitual refractive correction, then this refractive correction was used for halometry. An *Oculus Universal* trial frame (Keeler Ltd, Windsor, UK) was used to house the manifest refraction; adjusted to ensure a 12 mm back vertex distance. The full aperture trial lenses (one spherical lens and one cylindrical lens, if required) were cleaned before insertion into the trial frame to ensure that they did not increase the amount of glare experienced.

A short pilot study (n = 5) was carried out to check that the trial lens did not affect the *C-Quant* measurements. The investigator took 2 repeated measures for each condition: without a lens, with a dirty lens (a trial lens with any visible marks present, e.g. fingerprints), and with a lens that had been cleaned with lens cleaner solution. Dirty lenses were found to increase straylight readings compared to without a lens, whilst clean lenses did not have any effect (see Table 2.1). A one-way repeated measures ANOVA was conducted to compare the effect of a lens on straylight using no lens, a clean lens, and a dirty lens. There was a significant difference between these three conditions [$F_{(2, 8)} = 52.98$, $P < 0.001$]. Post hoc comparison using the Tukey test indicated that the mean score for the dirty lens condition (mean 1.50 ± 0.10) was significantly different than the no lens condition

(mean 1.17 ± 0.17; $P < 0.001$) and clean lens condition (mean 1.06 ± 0.07; $P < 0.001$). However, the clean lens condition did not significantly differ from the no lens condition ($P = 0.079$). The findings were supported by results from a previous study by de Wit (2003), who found that fingerprints, dirt, and dust increased the straylight value. The no lens condition appears to have a higher mean and SD than the clean lens condition. The cause of this could be a learning effect as the no lens condition was carried out first, which may have led to the greater variability whilst the participant adjusted to carrying out the test.

Habitual contact lens wearers kept their lenses in throughout. The lens type was not recorded, however, the lenses were inspected on the eye with a slit lamp prior to assessment to ensure the lenses were not heavily deposited. It was ensured that the participant had visions/VAs better than 0.1 logMAR in the monocular eye to be tested. The *C-Quant* guidelines suggest that it is difficult to perform the test with visual acuities of worse than 0.1 logMAR (van den Berg, 2004).

	Mean Log(s)
No lens	1.17 ± 0.17
Clean lens	1.06 ± 0.07
Dirty lens	1.50 ± 0.10

Table 2.1: Pilot study (n = 5) comparing the straylight measurements with no lens, with a dirty lens, and with a clean lens in place. Log(s) is the straylight value, where the average of 2 readings were taken. One-way RM ANOVA showed that straylight values in the clean lens and no lens conditions were not significantly different.

As participants were selected to have no history of ocular problems or surgery, dysphotopsia assessment was undertaken under normal viewing conditions and under simulated glare conditions using a *Bangerter* foil. *Bangerter* foils are an effective tool for increasing light scatter due to their effect on the point spread function simulating different levels of light spread on the retina (Perez *et al.*, 2010). *Bangerter* foils are available in a range of density levels (1.0, 0.8, 0.6, 0.4, 0.3, 0.2 and 0.1) that are intended to provide a graded amount of blur, and are imprinted on to a self-adhesive plastic foil for ease of application (see Fig 2.1). *Bangerter* foils are designed to induce mild to moderate degradation in visual acuity making them useful in the treatment of diplopia and amblyopia (Odell *et al.*, 2008).

Figure 2.1: *Bangerter* foil was pressed on to the wet surface of a clean +0.12 D trial lens and left to dry until there were no air bubbles

Perez *et al*. (2010) measured microbubble density at each *Bangerter* filter level. It was expected that a higher microbubble density level would result in more severe image degradation (Perez *et al.*, 2010). The density of bubbles (bubbles/mm^2) in the selected field was 1.5 in the 0.8 foil, 1.7 in the 0.6 foil, 2.4 in the 0.4 foil, and paradoxically, 1.7 in the 0.3 foil (Perez *et al.*, 2010). Perez *et al*. (2010) identified that both the physical structure and optical properties were similar and not necessarily ordinal for their samples of the 0.3, 0.4, and 0.6 filters; only the 0.8 filter was substantially different. Odell *et al.* (2008) similarly stated that the amount of visual degradation did not correspond well with the density designation of the *Bangerter* foil. Odell *et al*. (2008) found that the 1.0, 0.8, and 0.4 filters degraded distance acuity to a similar degree (mean 0.22, 0.23, and 0.28 logMAR); the 0.6 filter was not selected as initial pilot testing showed it did not degrade visual acuity differently from the 0.8 filter.

A *Bangerter* foil was required which would cause an increase in straylight without reducing the VA to worse than 0.4 logMAR as this would cause difficulties with distinguishing the letter on the halometer. Therefore, two filters were chosen to pilot as previous research has indicated that *Bangerter* filters do not always degrade visual acuity consistently to the manufacturer's specified levels (Odell *et al.*, 2008, Perez *et al.*, 2010). The 0.4 foil was

chosen as the website of the manufacturer states that it degrades to approximately 0.4 logMAR (Haag-Strait), whilst Odell *et al.* (2008) found it has an actual visual acuity of 0.3 logMAR which would be the ideal VA for this study. The 0.8 foil was chosen as it is significantly different from 0.4; whilst 0.4 and 0.6 are both physically and optically the same (Perez *et al.*, 2010). The 0.8 foil was found to cause the least impairment but is still considerably worse than the reference Modular Transfer Function (MTF; Perez *et al.*, 2010).

Initial work in the laboratory involved comparing the results for the halometer and *C-Quant* without a lens, with the 0.4 *Bangerter* and with the 0.8 *Bangerter* for two participants. It immediately became apparent that with the 0.4 *Bangerter* in place, the visual acuity dropped to 0.6 logMAR making it impossible to distinguish the letter on the halometer. The participant could only note when the letter was seen, removing the accuracy of determining the glare scotoma size. With the 0.8 *Bangerter*, visual acuity was better at 0.12 logMAR but distinguishing the letter was still quite difficult due to the drop in visual acuity. It was found that the participant had an unaided vision of - 0.08 logMAR, therefore, there was a respective drop in visual acuity of 0.24 logMAR. To make the task of halometry consistent in difficulty with the 0.8 *Bangerter* as it is without a lens, the target letter was made 0.24 logMAR bigger, equivalent to approximately 0.6 logMAR; this improved the participants' accuracy when distinguishing the letter, whilst still showing an increase in the glare scotoma with the 0.8 *Bangerter*.

2.2.1. Objective assessment of dysphotopsia

The Aston halometer device which has been described and used in previously published studies (Sheppard *et al.*, 2013, Buckhurst *et al.*, 2015) was used to measure monocular and binocular halo area, under natural viewing conditions and with a *Bangerter* foil *in situ*. Subjects were positioned at 2.0 m from the halometer screen with their eyes aligned with the centre of the screen and the light path of the glare source. Halometry was carried out in scotopic light conditions; the emergency light in the room was covered with a black cloth to ensure the halometer was the only light source. Prior to the examination, the halometer was switched on allowing sufficient 'warm up' time of 5 minutes for the output of the LED light to stabilise. During this period the subject was allowed to dark-adapt before halometry was undertaken.

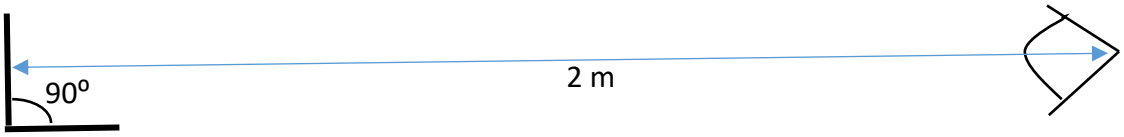


Figure 2.2: Ray diagram of the experimental set-up of the halometer. The participants' eye was aligned with the centre of the screen. The screen is always set at a 90 º angle.

Binocular and monocular measures (on a randomly selected eye (Armstrong, 2013)) were carried out in a random order. The participant was instructed to look at the halometer screen, which has a central bright light source, attached to a wand (see Fig 1.10) acting as the glare source. The laptop screen was always placed at a 90 º angle. The halometer uses a letter height of 0.21°, equivalent to a visual acuity of 0.4 logMAR at 2 m. 0.4 logMAR or Snellen 6/15 is the visual acuity required to distinguish a 79.4 mm high letter on a number plate viewed at a distance of 20.5 m (Charman, 1997); the minimum driving requirement for the UK (Kiel *et al.*, 2003). A letter emerges from behind the glare source (in 0.05 degree increments) in one of eight directions, and the participant was asked to focus on the letter and to distinguish the character at the earliest point. From this point, the character was moved progressively closer to the glare source- the letter was changed with each incremental movement. The closest point at which the subject could correctly identify the letter was recorded as the boundary of the halo for that meridian. The remaining 7 meridians were assessed in the same way to allow the size and shape of the glare scotoma to be determined (See Fig 2.9).

The commercially available *C-Quant* was used to measure the amount of straylight falling on the retina in the monocular eye as chosen previously (see Fig 2.3). *C-Quant* readings were taken under natural viewing conditions and with *Bangerter* foil *in situ*. Franssen *et al*. (2006) noted that refractive correction is not critical for the measurement; only spherical errors over 2.00 D required correction and cylindrical errors of up to 3.00 D may be corrected with the spherical equivalent (van den Berg, 2004). It is recommended to use only one trial lens for refractive correction, to reduce the possible effect on straylight readings (van den Berg, 2004). Following these guidelines, low myopes (up to -2.00 D) did not have a lens inserted. However, for hyperopes, a single lens was used where the patient habitually wore spectacles for near vision to allow for comfortable viewing of the stimulus screen at a distance of 32 cm (Franssen *et al.*, 2006). If a cylindrical correction was required then spectacles were worn as only one trial lens fitted into the lens holder with the *Bangerter* foil. The spectacles were cleaned before starting the test.

The participant was directed to look at the central circular stimulus, which is split into two hemispheres, surrounded by a larger ring of bright light causing the straylight. Both of the

hemispheres flash alongside the glare source with different intensities, and the subject pressed a button corresponding to the side appearing to flash the brightest. Two repeats were taken (Coppens *et al.*, 2006, Cervino *et al.*, 2008). If the two values differed by greater than 0.1 log units, then a third reading was taken and averaged. A limit value of 0.1 was applied to the GLARE study when testing for reliability on 2422 patients using 2 measures and a clinically relevant limit value of 0.1 was assumed (Coppens *et al.*, 2006). Franssen *et al*. (2006) found an overall SD of repeated measures between 0.06 and 0.1 log units, and Cervino *et al*. (2008) had findings of SD between 0.04 and 0.13 log units. The measurement of straylight was considered reliable if the estimated standard deviation (ESD) was below 0.8 and the quality factor for the psychometric sampling (Q) was above 1.00 (Coppens *et al.*, 2006, Cervino *et al.*, 2008). The *C-Quant* software highlights values considered as unreliable by displaying them in red (van den Berg, 2004).

Figure 2.3: Set up of *C-Quant*

2.2.2. Subjective assessment of dysphotopsia

Subjective grading of dysphotopsia was performed using the photographic images of photic phenomena (*PIPP*) plates developed by Aslam *et al*. (2004a) which were shown to have excellent repeatability and reliability. Eight images depict 10 types of dysphotopsia: dark arc, bright arc, serrated arc, night halos, night starburst, day halos, day starburst, central flash (glare from the sun causing excessively bright light), streams of light and ripple effect (see Fig 2.4 – 2.6). Participants are presented with the first board with a set introduction: 'Some people can get problems in their vision with light effects or glare at different times in different places. These are pictures of the problems some people have.' The participant is asked which, if any of the problems shown they experience. If the participant points to any particular plate they are then presented with the grading scale of four stages of severity for that plate (see Fig 2.8). The individual is then informed: 'Some patients only get this problem in a mild form (pointing to plate 1) and some will get very severe forms (pointing to plate 4). How bad on this scale would you say you experience this?' The score for that particular phenomenon was recorded 1 to 4, depending on the plate that they point out most appropriately correlated with the severity of their symptoms. Participants were returned to the first board and asked if they had any other visual phenomena. A grade of 0 was given to any image that they did not feel they experience; thus a scale of 0 to 4 was determined to grade the severity of each phenomenon. All of these 10 values were summed to give the overall subjective grade between 0 – 40, where 0 indicated no dysphotopsia and 40 indicated severe photic impairment.

The original document containing the images was obtained from Dr. Aslam, and with permission, the images were printed on to matt finish photographic paper. The images were mounted onto 9 A3 sized cards; the first of which displayed 8 images portraying the different types of glare most commonly experienced (see Fig 2.7).

A

B

C

Figure 2.4: *PIPP* plates (A – dark arc, B – bright arc and C – serrated arc). Images supplied and reproduced with permission from Karger Publishers.

D

E

Figure 2.5: *PIPP plates* (D - night halos and night starburst and E - day halos and day starburst). Images supplied and reproduced with permission from Karger Publishers.

F

G

H

Figure 2.6: *PIPP plates* (F - central flash, G - streaks of light and H - ripple effect). Images supplied and reproduced with permission from Karger Publishers.

Figure 2.7: Image to show the layout of the first board of *PIPP* images with the most severe of each of the 10 photic phenomena.

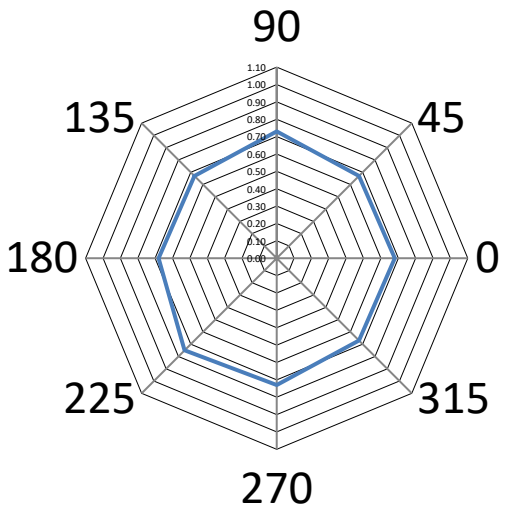
Figure 2.8: Night halo *PIPP* board showing the 4 severities of night halos that the participant may select from if they report experiencing this effect.

2.3. Data and statistical analysis

The data was stored in a password protected Excel 2016 Spreadsheet document (Microsoft, Redmond, WA). All statistical tests were performed using *SigmaPlot* graphing and statistical software (Version 12.0, Systat Software Inc., Chicago, Illinois, USA). The one-sample Kolmogorov-Smirnov test was used to determine if results from each measurement followed a normal distribution. All data sets deviated from a normal distribution, thus, median and range are reported and the following non-parametric statistical analyses were utilised:- Wilcoxon Signed Rank Test was used when comparing two related samples; Spearman's Rank Correlation was used to investigate the strength of association between 2 variables. Although the data are not normally distributed, a one-way ANOVA was used to compare the 8 triangle areas from halometry, as the test is not highly sensitive to deviations from the assumption of normality (McDonald, 2014). In all cases, a *P* value of < 0.05 was considered statistically significant.

2.3.1. Calculation of halo area from halometer

The halometer output displays the angle in degrees subtended at the eye for each of the 8 meridians (see Fig 2.9).



90	45	0	315	270	225	180	135
0.73	0.67	0.68	0.67	0.73	0.75	0.68	0.67

Figure 2.9: Example of raw halometer output when measuring monocular halo area. Table represents the angle in degrees subtended at the eye for each of the 8 meridians.

To report a single value that encompasses the whole glare scotoma, the area of glare scotoma was calculated. Thereby, allowing more accuracy in comparison than visual inspections of the plots. The glare scotoma was split into the 8 triangles that are made up from the measurements of the 8 meridians (see Fig 2.10).

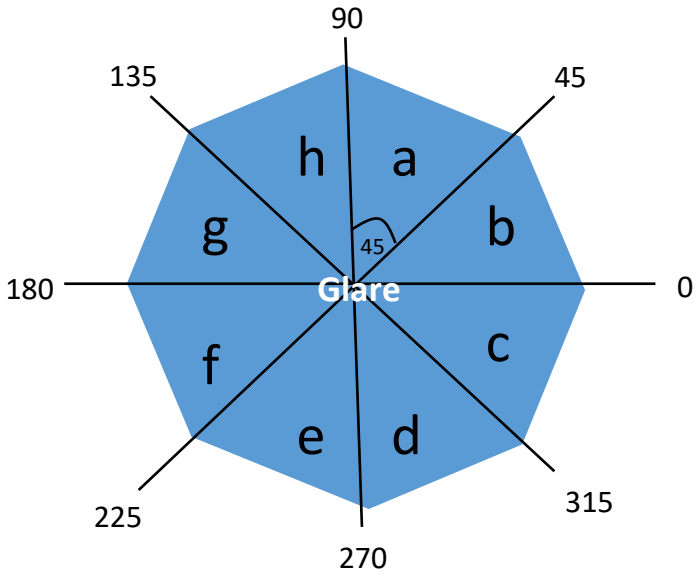


Figure 2.10: The total halo area is the sum of the 8 triangles labelled a-h.

To calculate the area (cm^2) of these triangles, the distance, *D*, from the glare source in the centre of the screen to the centre of the letter at the edge of the glare scotoma (equivalent to the radius of the glare scotoma) was required. Equation 2.1 was used to convert the angle given by the halometer to the distance (see Fig 2.11).

$$D\ (\mathrm{cm}) = 200 * \tan(x)$$

Equation 2.1

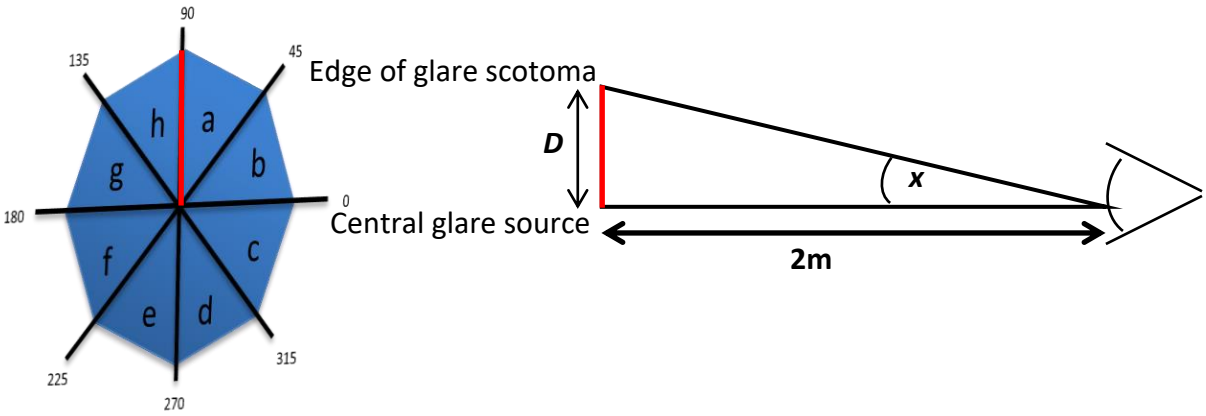


Figure 2.11: The relationship between the angular output by the halometer, *x*, and the distance, *D*, from the glare source in the centre of the screen to the centre of the letter at the edge of the glare scotoma.

D values were used to calculate total areas; the areas of each of the triangles were calculated using the lengths of two adjacent meridians. For example, *area a* was calculated

by inserting *D*(90) and *D*(45) (see Fig 2.10) into Equation 2.2. All areas were summed together to give the total glare scotoma area value.

$$Area = \frac{1}{2} \times D_1 \times D_2 \times \sin 45$$

Equation 2.2

A single value was used for the total area of the glare scotoma as glare scotomas measured with the halometer were found to be symmetrical in shape in this cohort, despite present literature showing a debate that halos may not be perfectly circular (Castro *et al.*, 2011, Meikies *et al.*, 2013). The 8 triangular areas of the glare scotoma were analysed using a one-way ANOVA (McDonald, 2014). For the 8 triangular areas, no significant difference was found for either the binocular or monocular measurements ([$F_{(7, 792)}$ = 1.799, *P* = 0.084] and [$F_{(7, 792)}$ = 1.098, *P* = 0.363], respectively).

As previous studies have stated halo area using mean radii in arc min (Puell *et al.*, 2013) and mean area in square degrees (Allen *et al.*, 2008, Buckhurst *et al.*, 2015), both of these were calculated for the present data. To calculate the mean radii in arc min, first, the mean radii in degrees was calculated. *x,* in Fig 2.11, shows the radii in degree, the mean of this for each of the 8 meridians was calculated. The value was converted to arc min using the following formula:

$$Mean\ Radii\ (arc\ \min) = Mean\ Radii\ (\deg)/(1/60)$$

Equation 2.3

The area in square degrees was calculated using the following formula:

$$Mean\ Area\ (sq\ deg) = \pi(Mean\ Radii\ (\deg))^2$$

Equation 2.4

These parameters are used further in chapter 3 and subsequent chapters.

A glare effect ratio was calculated to encompass the objective results with subjective complaints by means of the following formula:

$$Glare\ Effect\ Ratio = \frac{Subjective\ Grade}{Objective\ Measure}$$

Equation 2.5

A glare effect ratio was calculated separately for objective measures using halometer and *C-Quant*. A low glare effect ratio would indicate a low level of subjective effect compared to

objective measure; whilst a high glare effect ratio indicates an individual who is more subjectively affected by a given objective measure. It is expected that the glare effect ratio could be used pre-operatively to ascertain those who are most likely to suffer from subjective complaints post-operatively. Individuals with higher glare effect ratio may suffer and complain of more dysphotopic effects post-surgery.

The interquartile range (IQR) was calculated for the glare effect ratio using the following formula (Simmons, 2000):

$$IQR = Third\ Quartile - First\ Quartile$$

Equation 2.6

As the glare effect data were non-parametric, *SigmaPlot* was used to calculate the median, and the 25th (first quartile) and 75th (third quartile) percentiles. The IQR was then used to calculate outliers in the data by the following formula (Simmons, 2000):

$$Upper\ Outliers > Third\ Quartile + (1.5\ x\ IQR)$$
$$Lower\ Outliers < First\ Quartile - (1.5\ x\ IQR)$$

Equation 2.7

2.4. Results

One hundred participants aged 18.0 – 33.0 years (median age 21.0 years) were recruited. The cohort consisted of 65 female and 35 male volunteers. Eleven of these participants wore soft contact lenses during the assessments. Table 2.2 provides summary descriptive statistics for the entire cohort.

Participant data	**Median halo radius (range)**	**Median halo area (range)**	**Median straylight score (range)**	**Median subjective complaint score (range)**	**Median GE ratio based on binocular halo area (range)**	**Median GE ratio based on straylight score (range)**
n = 100 (65 female) **Median age:** 21.0 years (range 18.0 – 33.0 years)	**Monocular:** 21.0 (14.4 – 45.3) arc min **Binocular:** 18.4 (13.1 – 29.5) arc min	**Monocular:** 4.25 (1.97 – 19.61) cm^2 **Binocular:** 3.24 (1.64 – 8.26) cm^2	0.90 (0.62 - 1.56) log(s)	4.0 (0.0 – 13.0)	1.03 (0.0 – 4.06)	4.97 (0.0 – 15.29)

Table 2.2: Summary descriptive statistics for the whole cohort (n = 100). GE = Glare Effect Ratio.

Monocular halo areas (median = 4.25 cm^2; range 1.97 to 19.61 cm^2) were significantly larger than the binocular halo areas (median = 3.24 cm^2; range 1.64 to 8.26 cm^2) with halometry ($P < 0.001$). The median radius in arc min (median = 21.0; range 14.4 to 45.3) and median area in square degrees (median = 0.39; range 0.18 to 1.79) was calculated for monocular data to compare with previously published results. The median straylight score was 0.90 (range 0.62 – 1.56) log(s). The median subjective complaint score was 4.0 (range 0.0 – 13.0). A summary of the subjective grading for each dysphotopic condition is shown in Table 2.3.

There was no significant relationship between binocular halo area and subjective grade using Spearman correlation ($r_s = - 0.072$, $r_s^2 = 0.005$, $P = 0.478$); monocular halo area and subjective grade ($r_s = - 0.013$, $r_s^2 = 0.0002$, $P = 0.896$); *C-Quant* and subjective complaints ($r_s = 0.153$, $r_s^2 = 0.023$, $P = 0.128$; see Fig 2.12); halometer and *C-Quant* ($r_s = 0.121$, $r_s^2 = 0.015$, $P = 0.229$; see Fig 2.13).

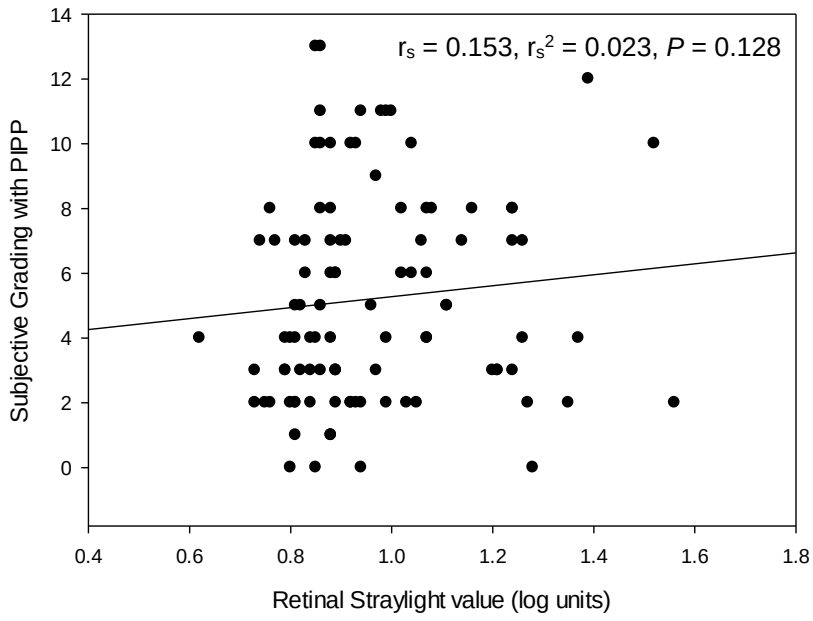


Figure 2.12: Retinal straylight values determined with *C-Quant* versus subjective grading with PIPP (n = 100).

Dysphotopic Condition	Grade				
	0	**1**	**2**	**3**	**4**
Dark Arc	100	0	0	0	0
Bright Arc	98	1	1	0	0
Serrated Arc	96	2	0	2	0
Night Halo	25	60	15	0	0
Night Starburst	25	60	15	0	0
Day Halo	48	14	25	10	3
Day Starburst	48	14	25	10	3
Central Flash	39	27	25	8	1
Streams of Light	88	10	2	0	0
Ripple Effect	100	0	0	0	0

Table 2.3: Summary of the number of participants and the subjective grade of severity given to each dysphotopic condition (n =100).

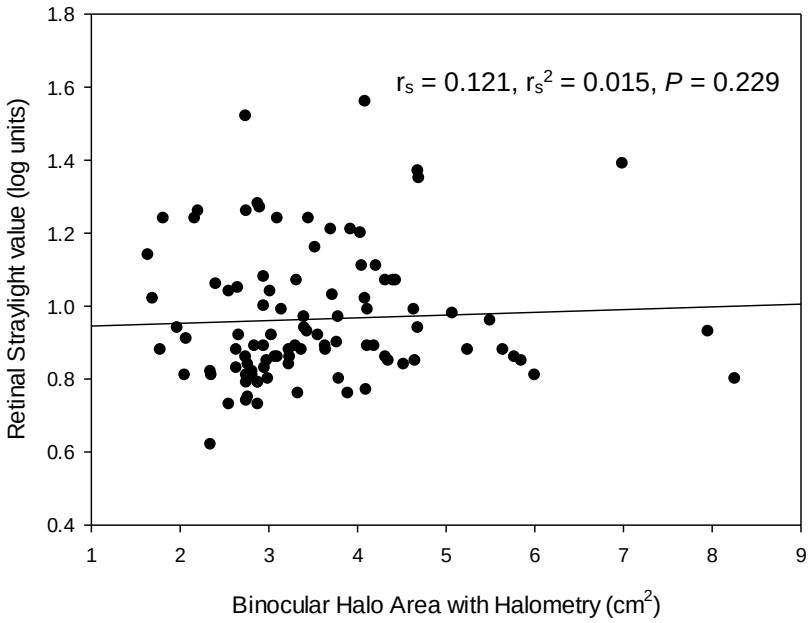


Figure 2.13: Binocular halo area determined with halometry versus retinal straylight measured with *C-Quant* (n = 100).

The normal range for the glare effect ratio was calculated for binocular halometry (median = 1.03; range 0 – 4.06; IQR 0.55 – 1.76; see Fig 2.14) and for *C-Quant* (median = 4.97; range 0 – 15.29; IQR 2.50 – 7.76; see Fig 2.15). Seven outliers were identified for normal binocular halometry glare effect ratio with the following characteristics summarised in Table 2.4. No outliers were identified for the *C-Quant* glare effect ratio.

Age	Sex	Monocular halo area (cm^2)	Subjective grade	Glare effect ratio	Bangerter halo area (cm^2)	Bangerter subjective grade	Monocular halo area proportional increase
22	F	3.88	13	4.01	22.39	19	5.8 x
24	F	2.99	10	3.75	14.06	16	4.7 x
23	M	3.00	7	4.26	12.84	18	4.3 x
22	F	2.36	8	4.41	14.84	12	6.3 x
18	M	3.60	10	3.92	11.19	19	3.1 x
18	F	2.76	7	3.93	15.16	17	5.5 x
24	M	5.47	10	3.65	17.01	12	3.1 x

Table 2.4: Summary of characteristics for participants who were outliers in the binocular glare effect ratio category (n = 7).

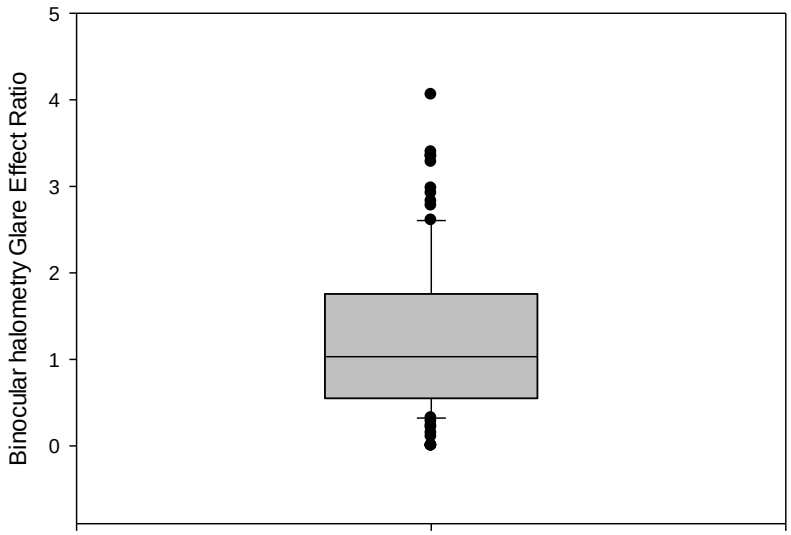


Figure 2.14: Box-and-whisker plot to show the interquartile range of the glare effect ratio with binocular halometry (n = 100). Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

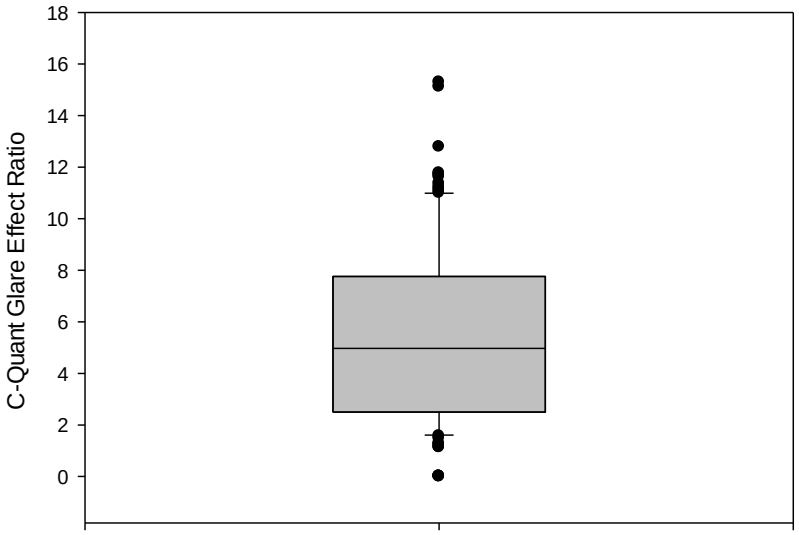


Figure 2.15: Box-and-whisker plot to show the interquartile range of the glare effect ratio with *C-Quant* (n = 100). Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

Data collected using *Bangerter* filters were assessed (see Table 2.5). The median *Bangerter* halo area was 17.25 cm^2 (range 10.27 - 40.45 cm^2) and the median straylight score was 1.43 (range 1.29 - 1.77) log(s). The subjective score with *Bangerter* filter *in situ* was evaluated (median = 12.0; range 2.0 – 21.0; IQR 9.0 – 16.0; see Fig 2.16). A summary of the number of participants and the severity that each dysphotopic condition was graded is shown in Table 2.6. The *Bangerter* monocular halometry glare effect ratio median was 0.63 (range 0.06 – 1.70).

	Halo Area (range)	**C – Quant (range)**	**Subjective Grade (range)**	**Glare Effect Ratio Monocular Halometry (range)**	**Glare Effect Ratio *C-Quant* (range)**
With *Bangerter*	17.25* (10.27 – 40.45) cm^2	1.43* (1.29 – 1.77) log(s)	12.0* (2.0 – 21.0)	0.63* (0.06 – 1.70)	8.01* (1.47 – 14.93)
Without *Bangerter*	4.25 (1.97 – 19.60) cm^2	0.90 (0.62 – 1.56) log(s)	4.0 (0.0 – 13.0)	1.36 (0.0 – 4.41)	4.97 (0.0 – 15.29)

Table 2.5. Summary of data collected with and without *Bangerter* filters. * indicates a significant difference between normal and *Bangerter* conditions (n = 100).

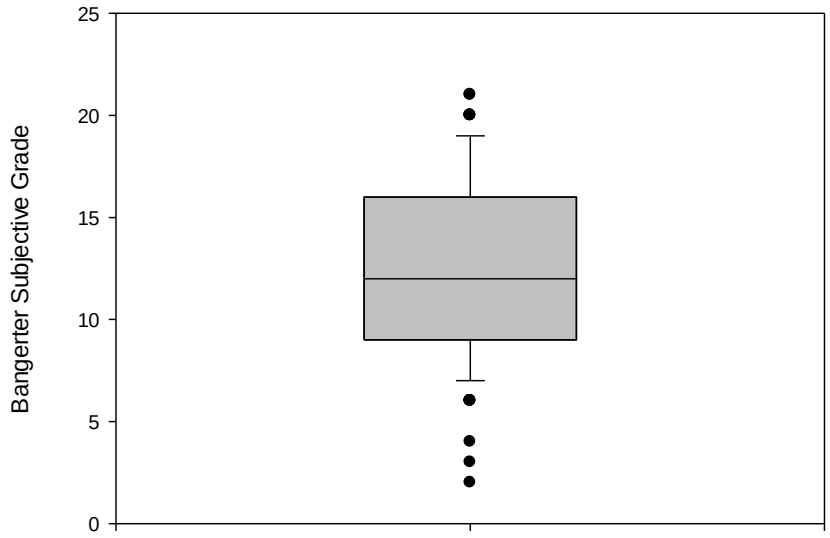


Figure 2.16: Box-and-whisker plot to show the interquartile range of the *Bangerter* subjective grading (n = 100). Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

Dysphotopic Condition	Grade				
	0	**1**	**2**	**3**	**4**
Dark Arc	98	1	1	0	0
Bright Arc	91	1	7	1	0
Serrated Arc	85	2	8	4	1
Night Halo	11	9	37	37	6
Night Starburst	11	9	37	37	6
Day Halo	26	1	22	31	20
Day Starburst	26	1	22	31	20
Central Flash	36	7	16	30	11
Streams of Light	54	9	27	9	1
Ripple Effect	96	3	1	0	0

Table 2.6: Summary of the number of participants and the subjective grade of severity given to each dysphotopic condition with *Bangerter* foil *in situ* (n = 100).

No relationship was found when the glare effect ratios from normal binocular halometry readings were compared with subjective grades from participants with the *Bangerter* foil (r_s = - 0.054, r_s^2 = 0.003, *P* = 0.594). However, when normal binocular halometry glare effect ratio was compared to halometry measurements with the *Bangerter* foil in place, a significant relationship was found (r_s = - 0.215, r_s^2 = 0.046, *P* = 0.032; see Fig 2.17).

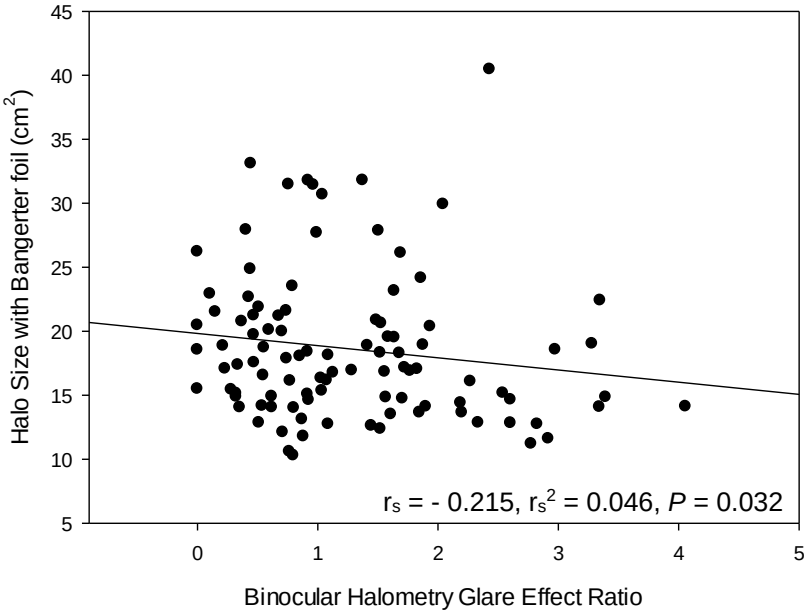


Figure 2.17: Binocular halometry glare effect ratio versus binocular halo area with *Bangerter foils* (n = 100).

The difference in halo area caused by the *Bangerter* filter was calculated for halometry by subtracting the monocular normal halo area from the *Bangerter* halo area. No significant relationship was found when binocular halo area was compared to the increase in halo area (r_s = 0.103, r_s^2 = 0.011, *P* = 0.305). However, the proportional change, calculated by dividing the *Bangerter* glare area by the normal halo area, showed a weak significant correlation (r_s = - 0.477, r_s^2 = 0.228, *P* < 0.001). A similar result was found when normal monocular halo areas were compared to the increase in halo area (r_s = 0.130, r_s^2 = 0.017, *P* = 0.199) and proportional change (r_s = - 0.706, r_s^2 = 0.498, *P* < 0.001). The *C-Quant* showed no relationship with the increase in straylight score (r_s = - 0.028, r_s^2 = 0.0008, *P* = 0.780) and proportional increase (r_s = - 0.090, r_s^2 = 0.008, *P* = 0.372).

2.5. Discussion

The present study set out to determine the typical relationship between the most common objective measures of photic effects (halo area and retinal straylight) and subjective complaints of dysphotopsia. Previous studies in the field of photic phenomena have generally reported either objective or subjective measures only (Arnold, 1994, van den Berg, 1995, Dick *et al.*, 1999, Pieh *et al.*, 2001, Aslam *et al.*, 2004a, Puell *et al.*, 2013), largely without consideration of normal values in healthy eyes. That is despite Dick *et al*. (1999) having investigated both objective and subjective measures after monofocal and multifocal lens implantation, and a positive association between subjective

reports of halos and the objective quantification of halo area being discovered for both lens types. Dick *et al*. (1999) used a method of moving a small mark from outside the central round source of light to the outer part of the halo using a computer mouse and computer program called 'glare and halo'. The method is prone to inaccuracies as marking the edge of the halo could lead to some difficulties and thus, seems a rather crude way to measure halo area. The subjective measure is by means of a questionnaire, the modified Arnold questionnaire, targeted at post-cataract surgery patients (see section 1.6.13). It simply asks participants whether they have 'noticed light flashes or streaks after cataract surgery not noticed before'. The question is followed up with 'what did your light flash seem the most like', and were given options of: a curved streak of light, a halo of light, a flare of light, a flash of light, or glare. It is arguable that a participant may not be aware of using these terms to describe the types of dysphotopsia they are experiencing. Also, those who experienced 'light flashes or streaks' prior to cataract surgery are omitted from being able to say whether they still experience them, whether they are worse or no longer experience symptoms of dysphotopsia. For this reason, it was decided that the relationship between newer objective measures of dysphotopsia, such as Aston halometer and *C-Quant*, should be investigated with an alternative subjective measure of dysphotopsia using simulated images.

Dysphotopsia is a complaint often reported by patients after corneal refractive surgery or cataract surgery/refractive lens exchange. Some patients find the symptoms reduce their quality of life with problems such as being unable to drive at night due to the glare. Such patients may request for the multifocal IOL to be removed, which in itself carries inherent risks. Since refractive surgery is becoming more common, it is important to be able to assess glare and to be able to predict those who will likely experience the adverse effect of glare. Currently, no clinical approach is in use pre-operatively to attempt to identify individuals who might be most severely affected subjectively with some surgeons refusing IOL implantation on personality traits alone in otherwise healthy individuals (Pepose, 2008, Braga-Mele *et al.*, 2014).

Binocular and monocular measures were taken with halometry as all previous papers have taken monocular readings only and binocular measures may best represent natural viewing conditions. Monocular halo area was found to be significantly larger (31.2 %) than the binocular area in this study, indicating the effect of binocular summation on objective measures of halo area. Thus, a potential limitation of many previous studies e.g. Puell *et al*. (2013) and Pieh *et al*. (2001), is reporting of monocular halo area values only, which are not representative of an individual's normal binocular visual experience, and may over-estimate the effects of dysphotopsia. Indeed, the correlation between subjective

complaint score and halo radius was found to be weaker for monocular, compared to binocular area.

Using the *PIPP* plates to grade subjective complaints of dysphotopsia found that the higher values came from day halos, day starburst, night halos, night starburst and central flash. Aslam *et al*. (2007a) reported a similar finding with a predominance of halos and starburst effects but also substantial symptoms of arc effect, streams of light, and central flash. These were also the more common complaint with the *Bangerter* lens in situ.

Despite Dick *et al.* (1999) finding a correlation between subjective reports of halos and halo area, this study found a lack of relationship between subjective and objective measures highlighting the difficulties in being able to predict the potential subjective complaints a patient may experience from an objective measure alone. From this, it is clear that the perception of dysphotopsia is individual to each person. Some have a high objective measure of glare, however subjectively they give a low score for glare effects. It is possible that these individuals have adapted to the glare that they experience and as such have no complaints of glare, or are less troubled by photic effects. Dick *et al.* (1999) did not state the r-value for the association found, and possibly related it to the complaints of halos alone rather than any dysphotopic complaint. The number of participants was only 28 in each for the monofocal and multifocal group. The study was also carried out 5 months after refractive surgery took place, which is known to increase dysphotopsia, and only those with new complaints of dysphotopsia post-surgery are included in the subjective complaints. Thus, a relationship may have been found as there were 24 monofocal and 19 multifocal participants that answered no to noticing photic phenomena not noticed before, which therefore may include participants who have dysphotopsia but had experienced it prior to surgery. In this study any dysphotopic complaint made up the subjective complaint score, which evidently varies from objective measures. The cohort in this study were mainly young, who are likely to have smaller halos. With the expected larger halo area in older individuals, it is possibly that a relationship may exist, which will be explored in the next chapter.

Puell *et al*. (2014) found a significant correlation between halo radius and straylight ($r = 0.45$, $r^2 = 0.203$, $P = 0.001$) in a cohort of similarly aged participants to the present study. However, no relationship between halometry and *C-Quant* measurements was found here and it is likely to be due to the fact that both machines measure different aspects of glare; the *C-Quant* measures the amount of straylight in the eye (van den Berg, 1995), whereby, the halometer measures the actual size of the disability glare area experienced and is not based on forward scatter within the eye alone. Again, this would indicate that using one objective measure alone may not be enough to distinguish those who struggle

with dysphotopsia. The subjective/objective ratio (glare effect ratio) was calculated to give a single value that combined both measurements. Seven outliers were identified for binocular halometry glare effect ratio. Perhaps surprisingly, the outliers had a range of monocular halo areas, with only one participant having an area larger than the median monocular halo area, however, all of them had higher than the median subjective grade of 4. Supporting the fact that objective measures alone are not enough to predict the possibility of dysphotopsia after refractive surgery. These participants had an average proportional increase of 4.7 times, and had a *Bangerter* subjective grade of between 12 and 19, which is above the median *Bangerter* subjective grade for the whole cohort. A finding that supports the idea that those with higher glare effect ratios are more likely to suffer with dysphotopic complaints post-surgery. It could be possible that in this scenario, using the usual equation to calculate the upper outlier by Q3 + 1.5*IQR may not be appropriate. Only seven outliers were identified, yet a significant proportion, about 20 %, of monofocal IOL patients end up dissatisfied (Souza *et al.*, 2006). A suggestion would be to consider anyone above the upper quartile (Q3) as suspicious. Further experimental investigation would be required to confirm this.

There were 11 participants who wore contact lenses during the assessment of halo area and straylight. The lens type was not recorded, however, all wore soft contact lenses. The lenses were assessed at the start of the examination to ensure that there were no significant deposits on the lenses as this would have caused an increased in straylight. Of the 11 contact lenses wearers, the powers were as follows: 3 x < - 2 D, 3 x – 2 D to – 4 D, 2 x – 4 D to – 6 D and 3 x > - 6 D. In this cohort, there were only 3 high myopes. However, in future studies it may be worthwhile investigating whether high powered plus and negative lenses cause increased intraocular scatter due to the edge of the optic and given that the pupils will be dilated in the dark. A limitation of this study is that participants were able to carry out the assessment either with no lenses, with trial lenses or with contact lenses. Whilst, the lenses were cleaned and contact lenses were checked for deposits, in future studies it may be wise to carry out the assessment with trial lenses for all including using plano lenses for those with no refractive error.

Simulating glare conditions using *Bangerter* foils meant that an estimate of subjective performance if a participant was to develop a cataract or perhaps have refractive surgery could be achieved. Glare effect ratios from binocular halometry readings (under normal viewing conditions) were plotted against subjective grading with *Bangerter* foils *in situ*, and no relationship was found. However, when glare effect ratio was compared to halometry with *Bangerter* foils in place, a weak negative relationship was found. Both of these findings support the fact that the glare effect ratio could be a good indicator of those who are likely

to suffer with increased dysphotopsia post-surgery. It would appear that those with a low glare effect ratio have the larger halo area with *Bangerter*, which may be due to them having both a high subjective and objective measure in normal viewing conditions giving a low glare effect ratio value, but a large halo area.

The normal range of subjective/objective ratios that have been found could be used for comparison purposes pre- and post-refractive surgery. It is expected that those with the highest subjective/objective ratios are most likely to perform poorly with multifocal IOLs – further studies seeing cataract patients both pre-operatively and post-operatively will be required to test this hypothesis. Having this information would be valuable to IOL manufacturers, as distance and near vision is good in multifocal IOLs with the main complaint being glare. If there is a way to reduce the number of patients who suffer from these glare effects, there may be 100 % patient satisfaction.

The next chapter will investigate both objective and subjective changes over a wider age group, as this data set was a fairly young cohort, to give normative data for halo area and glare effect ratio.

CHAPTER 3

EFFECT OF AGE ON SUBJECTIVE AND OBJECTIVE MEASURES OF DYSPHOTOPSIA

3.1. Introduction

As detailed in section 1.2, dysphotopsia is a term used to denote any light-related visual phenomenon experienced by both phakic and pseudophakic patients (Tester *et al.*, 2000). Dysphotopsia includes flashes of light, increased light sensitivity, glare and haloes (Tester *et al.*, 2000). Although dysphotopsia is one of the most common causes of dissatisfaction in an otherwise satisfied pseudophakic population (Schwiegerling, 2006, Galor *et al.*, 2009, Calladine *et al.*, 2012, Kamiya *et al.*, 2014), it is also a common occurrence in the ageing phakic population (van den Berg, 1995, Vos, 2003a).

In an ideal eye with optically clear media and perfect optical surfaces, no backward or forward scatter would occur. However, the human eye is imperfect and each of its structures contributes to the amount of light scatter through diffraction and aberration (Piñero *et al.*, 2010). In normal individuals, previous authors have estimated that the cornea accounts for about 30 %, the lens 40 % and retina approximately 20 % of scattered light (Yuan *et al.*, 1993, Vos, 2003a). The cornea and crystalline lens cause scattering when their transparency is reduced by conditions including corneal haze (Lohmann *et al.*, 1991, Braunstein *et al.*, 1996, Corbett *et al.*, 1996, Wang *et al.*, 2004, De Brouwere *et al.*, 2008), dystrophy (van den Berg *et al.*, 1993), keratoconus, corneal surgery (Lohmann *et al.*, 1993, Jain *et al.*, 1995, Chang *et al.*, 1998, Wang *et al.*, 2006, Fankhauser, 2007) and cataracts (Delaye *et al.*, 1982, Whitaker *et al.*, 1993, Qian, 2000, Gilliland *et al.*, 2001, Donnelly *et al.*, 2004, Costello *et al.*, 2007). Both the iris and sclera are partially responsible for intraocular scattering as they are not completely opaque, and allow some incident light to pass through (Ijspeert *et al.*, 1990, van den Berg *et al.*, 1991). When light reaches the retina, some of it is absorbed, whilst some is reflected back contributing the intraocular scattering (Vos, 1984, van den Berg, 1995). The vitreous humour is usually a transparent gel due to the regular structure of its fibrils. The transparency of this element may be severely affected by the presence of blood or cells in pathological conditions such as vitreous haemorrhage or posterior uveitis (Piñero *et al.*, 2010).

The resultant increase in intraocular light scatter or straylight from a bright light source causes a veiling glare and a loss of contrast across the retinal image (Vos, 1984, van den Berg, 1995, Aslam *et al.*, 2007b, Allen *et al.*, 2009). A loss in contrast typically reduces the observer's ability to distinguish detail within a visual scene. Disability glare is

usually encountered in scotopic light conditions as pupil dilation allows more intraocular scatter to occur from the glare source (Allen *et al.*, 2009). The term dysphotopsia encompasses more phenomena than glare alone- a commonly reported complaint is halos; the subjective perception of a bright ring around a light source (Aslam *et al.*, 2007b, Buznego and Trattler, 2009). The effect is regularly perceived when looking at a bright light source in the dark, such as street lamps on a foggy night. The halo is formed by light rays that are scattered outside the focussed image creating a dim disc of light around the light source (Allen *et al.*, 2009).

Dysphotopsia is widely accepted to increase with age (van den Berg, 1995, Tester *et al.*, 2000, Vos, 2003a, Puell *et al.*, 2013), and complaints of halos with night driving are more frequent in older patients. Although visual acuity may be normal, the effect of the bright headlight can cause such a severe detriment to the vision of some that it causes individuals to stop driving, which in turn reduces quality of life (Dewaard *et al.*, 1992, Ranney *et al.*, 2000, Theeuwes *et al.*, 2002). Individuals affected by dysphotopsia may complain of 'hazy vision', difficulties in recognising faces when looking into the light, and halos around bright lights in low light conditions (van den Berg *et al.*, 2007). Even in photopic conditions, loss of contrast and colour can occur (Piñero *et al.*, 2010). The age-related increase in dysphotopsia is attributable to natural ageing changes increasing ocular media irregularities such as lens opacities and vitreous floaters, and therefore increasing the amount of scatter (Wolf, 1960, Vos, 1984, Bailey and Bullimore, 1991, Dewaard *et al.*, 1992, Elliott, 1993). The resultant increase in intraocular light scatter from a bright light source causes a veiling glare and a loss of contrast across the retinal image (Vos, 1984, van den Berg, 1995, Aslam *et al.*, 2007b, Allen *et al.*, 2009).

Previous studies have used different devices to study changes in dysphotopsia with age; these have been summarised in Table 3.1. One of the earlier methods of measuring straylight was the direct compensation method, as used by Ijspeert *et al*. (1990; n = 129, range = 20 – 82 years). The observer monocularly views a screen at a distance of 45 cm. A 1 degree radius circular test field is in the centre, surrounded by a ring shaped field with an outer radius of 1.5 cm (2 deg) of steady, homogeneous, luminance of 30 cd/m^2, called the separation ring. On the screen, one of four ring shaped straylight sources were projected with effective angular radii of 3.5, 7.0, 13.6 and 25.4 deg. The straylight source was intermittent at a frequency of 8 Hz by means of a chopper. The intraocular light scattering between 3.5 and 25 deg of scattering angle was determined using direct compensation method. The authors reported that straylight increased significantly (to the power of 4.3 ± 0.2) with age, and after 70 years the straylight doubled.

Bailey *et al*. (1991) used the Berkeley glare test to determine Disability Glare Index (DGI) as a measure of dysphotopsia in younger versus older individuals (Younger cohort: n = 28**,** mean age = 28.4 ± 7.0 years, range = 15 – 41 years; Older cohort: n = 47, mean age = 64.9 ± 9.2 years, range = 50 – 82 years). The Berkeley glare test is a low contrast (10 %) letter chart surrounded by a white background which may be transilluminated to serve as the glare source. The chart is front-illuminated by lamps to a level of 80 cd/m^2. The surrounding luminance can be set at 300 (low glare), 800 (medium glare) and 3000 (high glare) cd/m^2. Visual acuity is measured at 1 m from the chart. DGI is calculated as the difference between VA scores in the no glare and high glare conditions. In this study, a strong positive correlation between DGI values and age was found (r = 0.75).

Since the development of the psychophysical compensation comparison method, it has been favoured over the previous direct compensation method (Coppens *et al.*, 2006, Franssen *et al.*, 2006), and can be performed using the commercially available *C-Quant*. To date two studies have used the *C-Quant* to measure the effect of age on straylight (Rozema *et al.*, 2010b, Puell *et al.*, 2014). Rozema *et al*. (2010b) found that straylight remained constant until the age of 45 years, after which it gradually increased (n = 518 eyes of 277 subjects, mean age = 39.7 ± 13.2 years, range = 8.5 – 78 years). Puell *et al*. (2014), described no significant effect of age on straylight in their study cohort (n = 51, mean age = 29.3 ± 7.5 years, range = 20 – 43 years), although the age range was more limited. Thus, there is no clear consensus on the effect of age on straylight measured with the *C-Quant*, although it may increase beyond the middle of the fifth decade.

Measurement of halo area with age has been carried out in just two previously published studies, from the same research team (Puell *et al.*, 2013, Puell *et al.*, 2014). Both measured halo radius using the Vision Monitor and low luminance optotypes presented at 2.5 m. An off axis light source was used, with the participant's head positioned with centre of monitor, whilst the LED glare source is at the edge of the screen. Optotypes arranged in three radial lines of letters appear from the periphery, moving towards the glare source. Each line contains 10 letters forming 10 rings at intervals of 33 arc min. Each letter subtends 15 arc min and corresponds to 0.5 logMAR. Monocular testing in a dark room with best spectacle correction was performed in both studies. Puell *et al.* (2013) investigated the change in halo radius over a range of age groups (n = 147, mean age = 48.2 ± 16.2 years, range = 20 – 77 years; 20 – 29 years n = 28; 30 - 39 years n = 17; 40 – 49 years n = 25; 50 – 59 years n = 31; 60 – 69 years n = 34; 70 – 79 years n = 12) using an optotype luminance of 5 cd/m^2. Mean halo radius was found to be 111.6 ± 39.8 arc min (range 66 – 220 arc min). A significant relationship between halo area and age was established (r = 0.65, r^2 = 0.42, $P < 0.0001$). Halo areas were similar in the 20 – 29, 30 – 39

and 40 - 49 age groups, and then increased beyond the age of 50 years. There was a mean halo radius difference of 72 arc min between the youngest (88.4 ± 22.1 arc min) and the oldest (160.4 ± 35.5 arc min) age groups. A limitation of this study is that the test was conducted monocularly, and as found in chapter 2, monocular glare areas are larger than binocular glare areas. Therefore, an overestimation of halo areas, as experienced by the participant, may have occurred. An off-axis light source was used, with halo radius estimated from just 3 radius measurements as only a semi circle of the halo is measured. An assumption of halo area being symmetrical has been made, despite existing literature showing a debate that halos may not be perfectly circular (Castro *et al.*, 2011, Meikies *et al.*, 2013). In 2014, Puell *et al*. conducted a further study (n = 51, mean age = 29.3 ± 7.5 years, range = 20 – 43 years) using the Vision Monitor but with a reduced optotype luminance of 1 cd/m^2. The lower optotype luminance meant the mean halo radius of 201.6 ± 42.7 arc min was almost double that reported in the previous study. However, no significant effect of age on halo radius was observed in this younger study sample.

The previous studies described have failed to provide information on how individuals are affected by dysphotopsia, as no subjective measures were included. It might be anticipated that both subjective and objective measures increase with age. The previous chapter highlighted the lack of a relationship between objective measures and subjective complaints of dysphotopsia. The use of the 'glare effect ratio' to combine the two measurements, and its potential use as a pre-operative assessment was introduced in chapter 2. The effect that the increase in both objective and possibly subjective complaints will have on the 'glare effect ratio' with age is unknown. The previous chapter also described normal values for halometry in a 'young' cohort, however, further investigation of the normative data over a wider age range would be useful when carrying out pre- and post-operative examination on the likely older cohort with cataract.

Parameter Measured	Author and Technique	Cohort Characteristics	Mean Value	Effect of Age
Straylight	Puell *et al*. (2014) Straylight measured using *C-Quant*.	n = 51 Mean age = 29.3 ± 7.5 years Range 20 – 43 years	Straylight 0.95 ± 0.12 (range 0.64 – 1.21) log units	No significant effect of age on straylight was observed. Highest age was 43 years.
	Rozema *et al*. (2010b) Straylight measured using *C-Quant*.	n = 518 eyes of 277 subjects (257 right and 261 left) 90 male and 198 female Mean age = 39.7 ± 13.2 years Range 8.5 – 78 years	N/A	Straylight remained constant until the age of 45 years, after which it gradually increased.
	Vos (2003) Theoretical study linked to disability glare	N/A	N/A	Introduced age dependence into the Stiles-Holladay disability glare equation. For ages under 35 years old, the change in glare is negligible. Disability glare rapidly increases beyond the age of 60 years; it doubles by 70 years and triples by 83 years.

Bailey *et al.* (1991) Berkeley Glare Test- low contrast (10 %) letter chart surrounded by a white background which may be transilluminated to serve as the glare source. Visual acuity is measured at 1 m from the chart. DGI calculated as the difference between VA scores in the no glare and high glare conditions.	**Younger cohort** n = 28 Mean age = 28.4 ± 7.0 years Range 15 – 41 years **Older cohort** n = 47 Mean age = 64.9 ± 9.2 years Range 50 – 82 years	**Younger cohort** Mean DGI value = 2.3 ± 1.9 **Older cohort** Mean DGI value = 10.2 ± 4.8	Linear regression analysis showed a correlation coefficient of r = 0.75 between DGI values and age.
Ijspeert *et al.* (1990) Monocular observation of a screen at 45 cm. A 1 degree radius circular test field was in the centre, surrounded by a ring shaped field with an outer radius of 1.5 cm (2 deg). Direct compensation method determined the intraocular light scattering between 3.5 and 25 deg of scattering angle.	n = 129 Range 20 – 82 years 20 – 30 years n = 20 (40 eyes) 30 – 40 years n = 21 (42 eyes) 40 – 50 years n = 20 (40 eyes) 50 – 60 years n = 20 (40 eyes) 60 – 70 years n = 20 (40 eyes) 70 – 80 years n = 8 (13 eyes)	N/A	Straylight increased to the power of 4.3 ± 0.2 with age. It doubled from the age of 70
Vos (1984) Assessment of straylight using the equivalent veil method.	N/A	N/A	Straylight increases with age by a factor of 3 between 20 and 80 years.

Halo Area	Puell *et al*. (2014) Monocular halo radius measured using the Vision Monitor and low luminance (1 cd/m^2) optotypes presented at 2.5 m. Off axis light source used. Optotypes arranged in three radial lines of letters appearing from the periphery towards the glare source.	n = 51 Mean age = 29.3 ± 7.5 years Range 20 – 43 years	Halo Radius 201.6 ± 42.7 arc min / 3.4 ± 0.7 º	No significant effect of age on halo radius was observed in this study sample. Oldest participant was 43 years old.
	Puell *et al.* (2013) Halo radius measured using the Vision Monitor as described above. However, optotype used had a luminance of 5 cd/m^2.	n = 147 Mean age = 48.2 ± 16.2 years Range 20 – 77 years 20 – 29 years n = 28; 30 - 39 years n = 17; 40 – 49 years n = 25; 50 – 59 years n = 31; 60 – 69 years n = 34; 70 – 79 years n = 12.	Halo Radius 111.6 ± 39.8 (range 66 – 220) arc min	Relationship between halo area and age ($r = 0.65$, $r_2 = 0.42$, $P < 0.0001$) Halo areas were similar in the 20 – 29 / 30 – 39 / 40 - 49 age groups, and then increased beyond the age of 50 years. Mean halo radius difference of 72 arc min between the youngest (88.4 ± 22.1 arc min) and the oldest (160.4 ± 35.5 arc min) groups.

Table 3.1: Summary of studies that have investigated the changes in dysphotopsia with age.

The effect of age on halo area is unknown, and there is a lack of information about subjective changes in dysphotopsia with age. Therefore, the aims of this prospective study are to:

- Establish how objective measures and subjective complaints of dysphotopsia change with age in healthy eyes.
- Determine how the “glare effect ratio”, introduced in chapter 2, changes with age
- Define a normal range of values for halometry glare area and “glare effect ratio” over a wide age range to facilitate an evidence-based approach to assist with the selection, and counselling of candidates for refractive procedures which may induce post-operative photic effects.

3.2. Subjects and methods

All procedures were conducted in the Ophthalmic Research Group laboratories at Aston University, Birmingham, UK. The study was reviewed by the Aston University, Life and Health Sciences Research Ethics Committee (Application number 595). A copy of this approval can be found in appendix A1. The study was conducted in accordance with the tenets of the Declaration of Helsinki and all subjects gave their written informed consent to take part after explanation of the nature and consequences of the study.

Power calculations, made using GPower (version 3.1.9.2), showed that 135 participants were required to enable Spearman correlation to detect statistically significant medium size (0.25) effect at the 5 % significance level ($\alpha = 0.05$) with 80 % power. One hundred and forty-one subjects were recruited from staff and student body and Aston Research Centre for Healthy Ageing (ARCHA).

Inclusion Criteria

- Corrected distance visual acuity (CDVA) of 0.0 logMAR or better binocularly, with at least 0.1 logMAR monocularly in the better eye.
- Clear ocular media or with normal age related media changes on slit lamp examination; classed as posterior capsular cataract, cortical or nuclear opacities less than LOCS III classification grade 1.5 (Chylack *et al.*, 1993, van den Berg *et al.*, 2007, Puell *et al.*, 2013).

Exclusion Criteria

- Any history of ocular surgery, including laser refractive procedures.
- Participants with any pre-diagnosed ocular conditions.
- Any participants with a history of using drugs that are known to affect the eye.
- Any participants with a systemic health problem that may result in ocular complications.

Unaided visions were measured and a full subjective refraction was performed at 3 m using the *Thomson Test Chart 2000.* Where the participant wore a distance habitual refractive correction, then this refractive correction was used for halometry and *C-Quant*. An *Oculus Universal* trial frame was used to house the manifest refraction; adjusted to ensure a 12 mm back vertex distance. The full aperture trial lenses were cleaned before insertion into the trial frame to ensure that they did not increase the amount of glare experienced.

As described in sections 2.2.1 and 2.2.2, objective and subjective measures of dysphotopsia were conducted in a random order. Halometry was carried out both binocularly and monocularly, with the eye for monocular measurement selected using a randomisation table (Armstrong, 2013). The *C-Quant* was used to quantify intraocular light scatter in the same eye used for monocular halometry reading. Subjective complaints of dysphotopsia were recorded using the *PIPP* plates to give a grade between 0 – 40, where 0 = no dysphotopsia experienced, and 40 = severe complaints in all forms of photic effects (Aslam *et al.*, 2004a).

3.3. Data and statistical analysis

The data was stored in a password-protected Excel 2016 Spreadsheet document (Microsoft, Redmond, WA). All statistical tests were performed using *SigmaPlot* graphing and statistical software (Version 12.0, Systat Software Inc., Chicago, Illinois, USA). The data was checked for normality using the one-sample Kolmogorov-Smirnov test; only *C-Quant* glare effect ratio did not deviate significantly from a normal distribution (all $P < 0.05$). Therefore, median and range values are reported for all parameters. Monocular and binocular halo areas were compared using Wilcoxon signed rank test. Spearman's correlation was used to determine the relationship between objective measures of dysphotopsia / subjective gradings and age. In all cases, a P value of < 0.05 was considered statistically significant.

3.3.1. Calculation of halo area from halometer

The halo radius in degrees for each of the 8 meridians was recorded, and these were used to calculate the area of the triangle that is created by two adjoining meridians (see Fig 2.11). The total area of the glare scotoma was calculated. To calculate total halo area, the sum of the areas of 8 triangles resulting from the 8 medians was calculated as previously described in section 2.3.1 (see Fig 2.10). The halo radius was converted from degrees subtended to arc min using Equation 2.3. The median and range for halo radius was calculated. Glare area was also calculated in square degrees using mean radii in degrees described in Equation 2.4.

The glare effect ratio was calculated by dividing subjective grading by the objective area found for binocular halometry. In addition, a similar calculation was carried out for *C-Quant* measures. The glare effect ratio provides a single value to represent the combination of subjective and objective measures. A low ratio indicates a low level of subjective effect compared to the objective measure, whilst a high glare effect ratio indicates an individual who is more subjectively affected by a given objective measure. Median and IQRs glare effect ratios were calculated. The IQR was then used to calculate outliers in the data by adding 1.5 x IQR to Q3 (the upper value of the interquartile range) and by subtracting 1.5 x IQR from Q1 (the lower value of the interquartile range).

A power function was fitted using *SigmaPlot* graphing software (Version 12.0) to model the relationship between halo area and age.

3.4. Results

One hundred and forty one healthy volunteers aged 18.0 – 82.0 years (median age 23.0 years) participated in the study. Table 3.2 provides summary descriptive statistics for the entire cohort. It was not possible to include straylight readings for 3 participants due to the poor reliability of their readings, other data from these individuals were included in the analyses.

Participant data	Median halo radius (range)	Median glare area (range)	Median straylight score (range)	Median subjective complaint score (range)	Median GE ratio based on binocular halo area (range)	Median GE ratio based on straylight score
n = 141 (86 female) **Median age:** 23.0 years (range 18.0 – 82.0 years)	**Monocular:** 22.7 (14.4 – 46.7) arc min **Binocular:** 19.8 (13.1 – 35.6) arc min	**Monocular:** 4.87 (1.97 – 20.87) cm^2 **Binocular:** 3.77 (1.64 – 12.11) cm^2	0.99 (0.62 - 1.56) log(s) N = 138	5.0 (0.0 – 20.0)	1.28 (0.0 – 4.41)	5.63 (0.0 – 17.17) N = 138

Table 3.2: Summary descriptive statistics for the whole cohort. N = 141. GE = Glare Effect Ratio.

The cohort of 141 participants consisted of 86 females and 55 males (see Table 3.2). Monocular halo areas (median = 4.87 cm^2; range 1.97 to 20.87 cm^2) were significantly larger than binocular halo areas (median = 3.77 cm^2; range 1.64 to 12.11 cm^2) with halometry ($P < 0.001$). The median radius in arc min (median = 22.7; range 14.4 to 46.7) and median area in square degrees (median = 0.45; range 0.18 to 1.91) was calculated for monocular data to allow comparison with previously published results. Binocular and monocular halo areas both increased with age ($r_s = 0.449$, $r_s^2 = 0.202$, $P < 0.001$ and $r_s = 0.403$, $r_s^2 = 0.162$, $P < 0.001$, respectively; see Fig 3.1). Monocular mean radii increase with age ($r_s = 0.405$, $r^2 = 0.162$, $P < 0.001$). A power function was fitted to the halo radius data plotted against age (see Fig 3.2), to enable comparison with that plotted by Puell *et al*. (2013). Straylight measured with the *C-Quant* also increased significantly with age ($r_s = 0.457$, $r_s^2 = 0.209$, $P < 0.001$; see Fig 3.3).

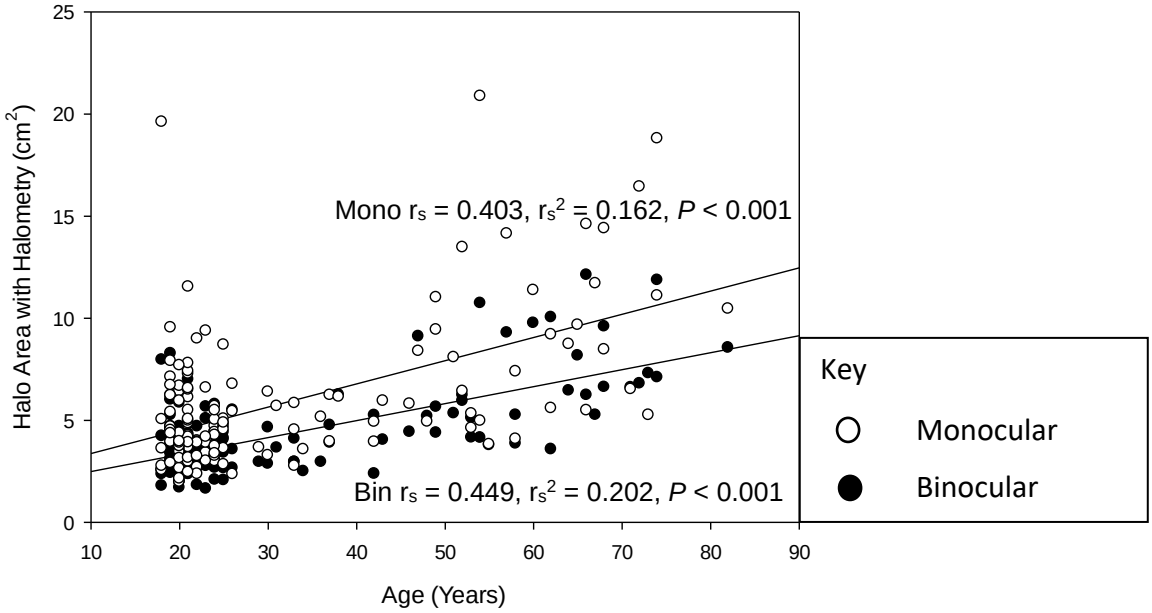


Figure 3.1: Binocular and monocular halo area measured with halometry versus age (n = 141).

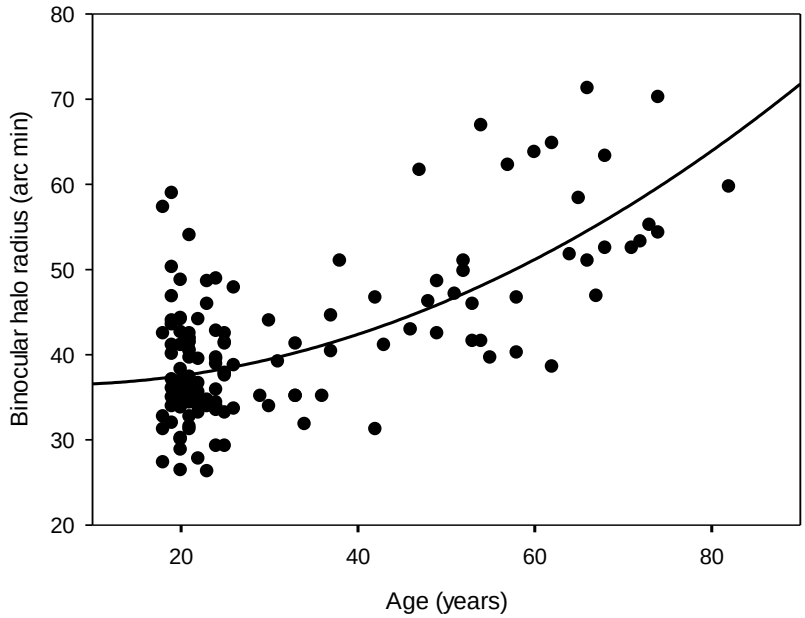


Figure 3.2: Power function fitted to halo radius data plotted against age (n = 141).

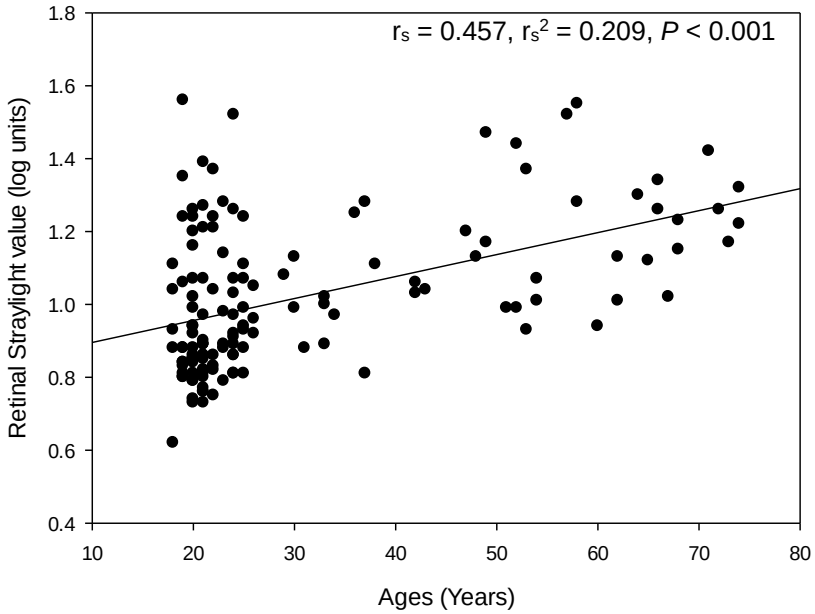


Figure 3.3: *C-Quant* straylight values plotted against age (n = 138).

The median subjective complaint score was 5.0 (range 0.0 – 20.0). A summary of the subjective grading for each dysphotopic condition is shown in Table 3.3.

	Grade				
Dysphotopic Condition	**0**	**1**	**2**	**3**	**4**
Dark Arc	140	1	0	0	0
Bright Arc	136	2	1	0	2
Serrated Arc	137	2	0	2	0
Night Halo	27	77	31	5	1
Night Starburst	27	77	31	5	1
Day Halo	73	18	29	15	6
Day Starburst	73	18	29	15	6
Central Flash	58	31	33	14	5
Streams of Light	117	15	3	4	2
Ripple Effect	139	0	1	1	0

Table 3.3: Summary of the number of participants and the subjective grade of severity given to each dysphotopic condition (n = 141).

No relationship was exhibited between objective binocular halo area and subjective grade (r_s = 0.132, r_s^2 = 0.017, *P* = 0.119; see Fig 3.4); and between monocular halo area and subjective grade (r_s = 0.148, r_s^2 = 0.022, *P* = 0.08; see Fig 3.5). However, a weak correlation was found when binocular halo area was compared to subjective night halo complaints (r_s = 0.330, r_s^2 = 0.109, *P* < 0.001; see Fig 3.6). There was no relationship between any of the other PIPP plate conditions with either monocular or binocular halo area (see Table 3.4). A weak relationship was shown between *C-Quant* and subjective complaints (r_s = 0.268, r_s^2 = 0.072, *P* = 0.002; see Fig 3.7). Binocular halometry and *C-Quant* also

exhibited a weak relationship (r_s = 0.337, r_s^2 = 0.114, P < 0.001, N = 138; see Fig 3.8). Overall, a weak relationship was seen between age and subjective grade (r_s = 0.314, r_s^2 = 0.099, P < 0.001; see Fig 3.9); night halo complaints specifically increased with age, again only a weak but significant relationship (r_s = 0.356, r_s^2 = 0.127, P < 0.001; see Fig 3.10).

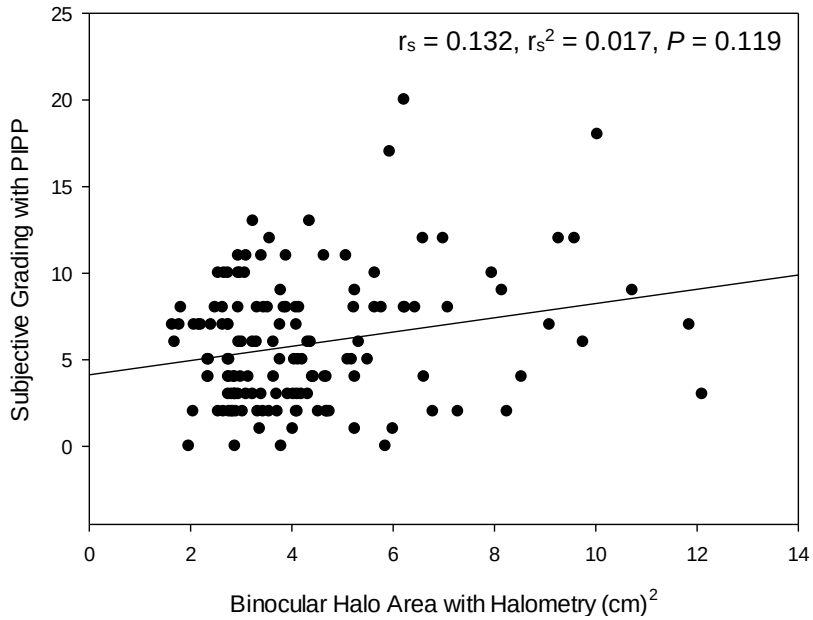


Figure 3.4: Binocular halo area measured with halometry versus subjective grading with PIPP (n = 141).

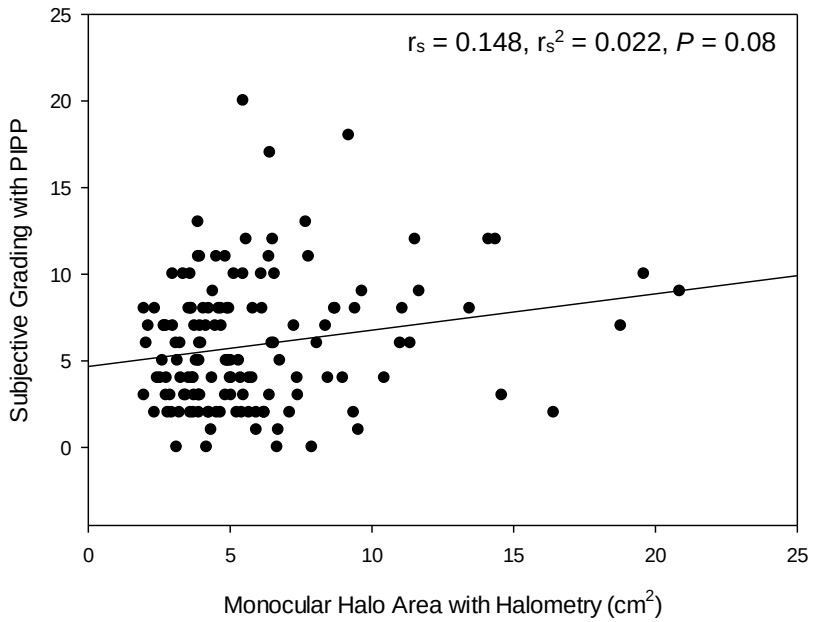


Figure 3.5: Monocular halo area determined with halometry versus subjective grading with PIPP (n = 141).

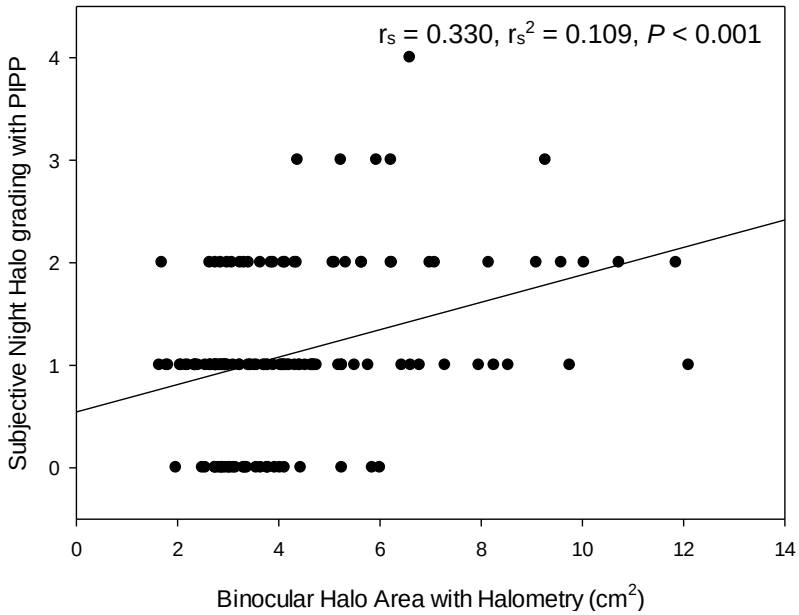


Figure 3.6: Binocular halo area measured with halometry plotted against subjective night halo complaints with *PIPP* (n = 141).

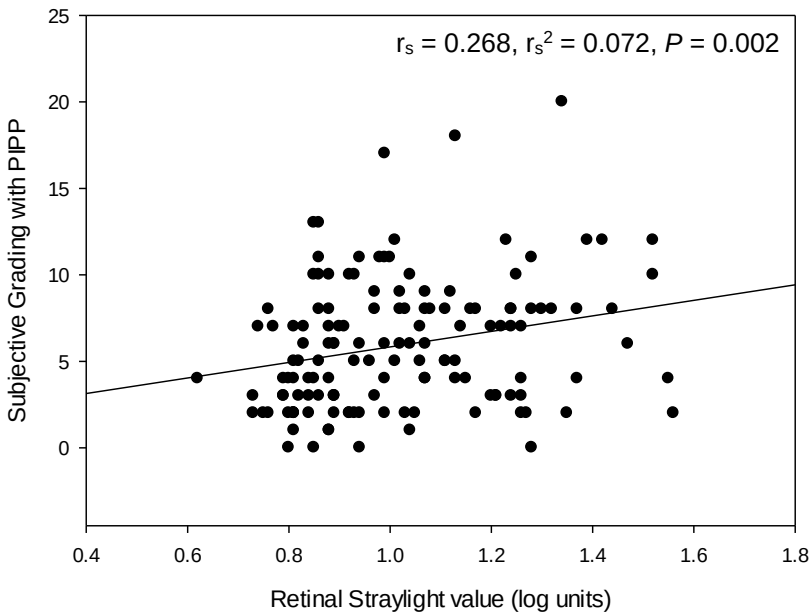


Figure 3.7: Retinal straylight values with *C-Q*uant versus subjective grading with *PIPP* (n = 138).

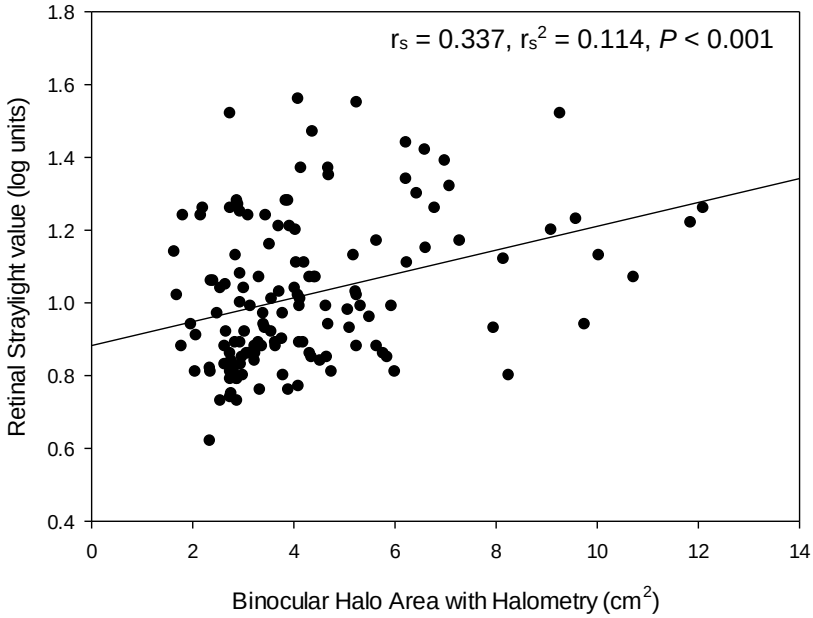


Figure 3.8: Binocular halo area determined with halometry versus retinal straylight measured with *C-Quant* (n = 138).

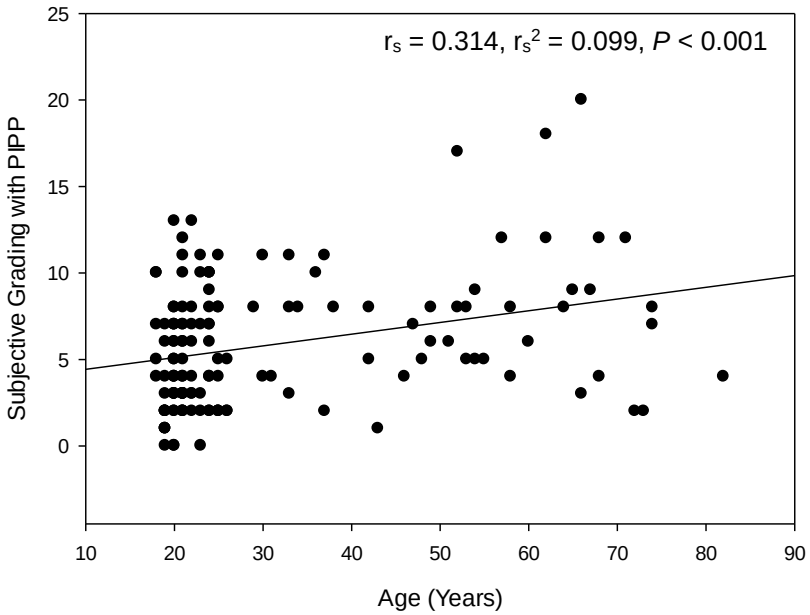


Figure 3.9: Subjective grading with *PIPP* against age (n = 141).

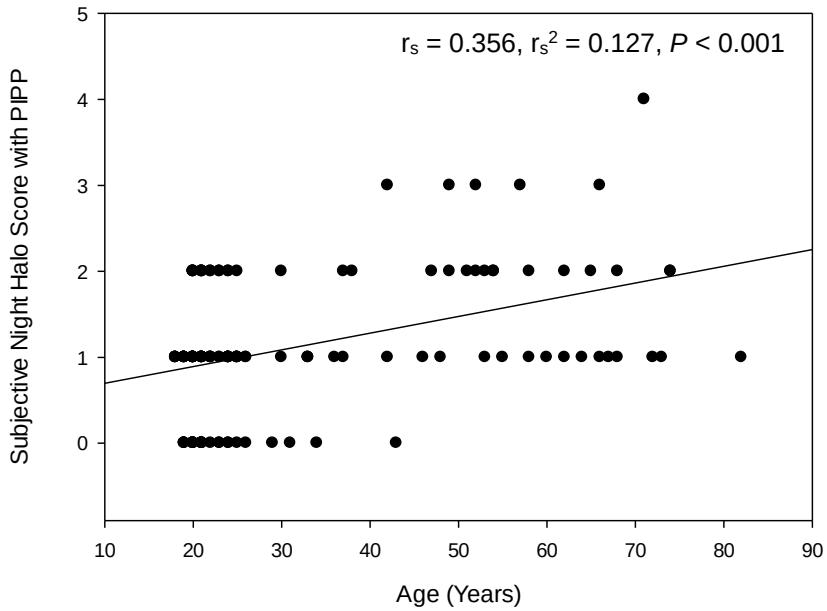


Figure 3.10: Subjective night halo complaints on PIPP against age (n = 141).

Dysphotopic Condition	Binocular halo area	Monocular halo area
Dark Arc	r = 0.075, r^2 = 0.0056, *P* = 0.378	r = 0.004, r^2 < 0.001 , *P* = 0.961
Bright Arc	r = 0.123, r^2 = 0.015, *P* = 0.146	r = 0.091, r^2 = 0.008, *P* = 0.284
Serrated Arc	r = - 0.054, r^2 = 0.003, *P* = 0.524	r = - 0.142, r^2 = 0.020, *P* = 0.094
Night Halo	r = 0.330, r^2 = 0.109, *P* < 0.001	r = 0.227, r^2 = 0.052, *P* = 0.007
Night Starburst	r = 0.330, r^2 = 0.109, *P* < 0.001	r = 0.227, r^2 = 0.052, *P* = 0.007
Day Halo	r = - 0.131, r^2 = 0.017, *P* = 0.122	r = - 0.044, r^2 = 0.002, *P* = 0.604
Day Starburst	r = - 0.131, r^2 = 0.017, *P* = 0.122	r = - 0.044, r^2 = 0.002, *P* = 0.604
Central Flash	r = 0.087, r^2 = 0.008, *P* = 0.305	r = 0.055, r^2 = 0.003, *P* = 0.514
Streams of Light	r = 0.092, r^2 = 0.008, *P* = 0.276	r = 0.108, r^2 = 0.012, *P* = 0.201
Ripple Effect	r = 0.155, r^2 = 0.024, *P* = 0.067	r = 0.162, r^2 = 0.026, *P* = 0.055

Table 3.4: Spearman correlation values for monocular and binocular halometry versus the 8 dysphotopic conditions on the PIPP plates.

The normal range for the glare effect ratio was calculated for binocular halometry (median = 1.28; range 0.0 – 4.41; IQR 0.75 – 2.15; see Fig 3.14) and for *C-Quant* (median = 5.63; range 0.0 – 17.17; IQR 2.72 – 7.97; see Fig 3.15). There was no significant relationship found between age and the binocular glare effect ratio for halometry (r_s = 0.0002, r_s^2 < 0.001, *P* = 0.998; see Fig 3.11); monocular halometry glare effect ratio (r_s = - 0.003, r_s^2 < 0.001, *P* = 0.969; see Fig 3.12); however, a weak relationship was found with *C-Quant* glare effect ratio (r_s = 0.199, r_s^2 = 0.040, *P* = 0.020, N = 138; see Fig 3.13).

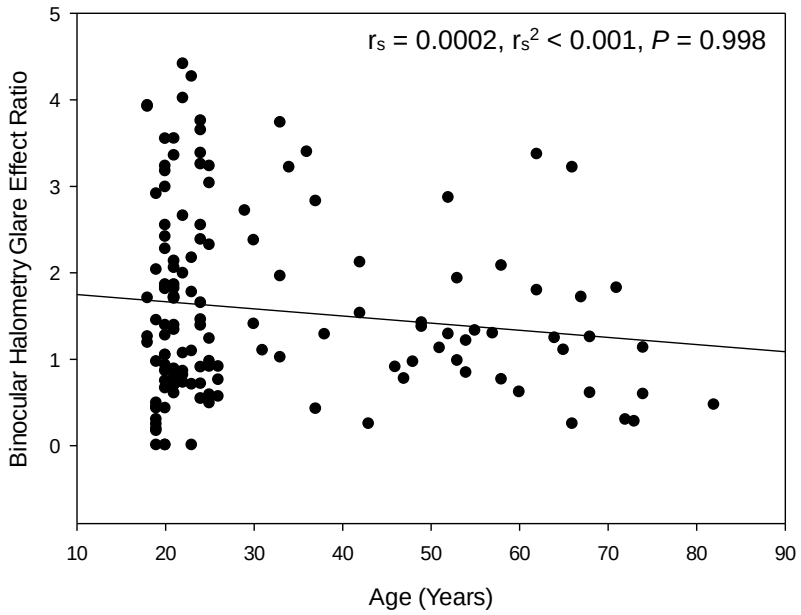


Figure 3.11: Binocular halometry glare effect ratios against age (n = 141).

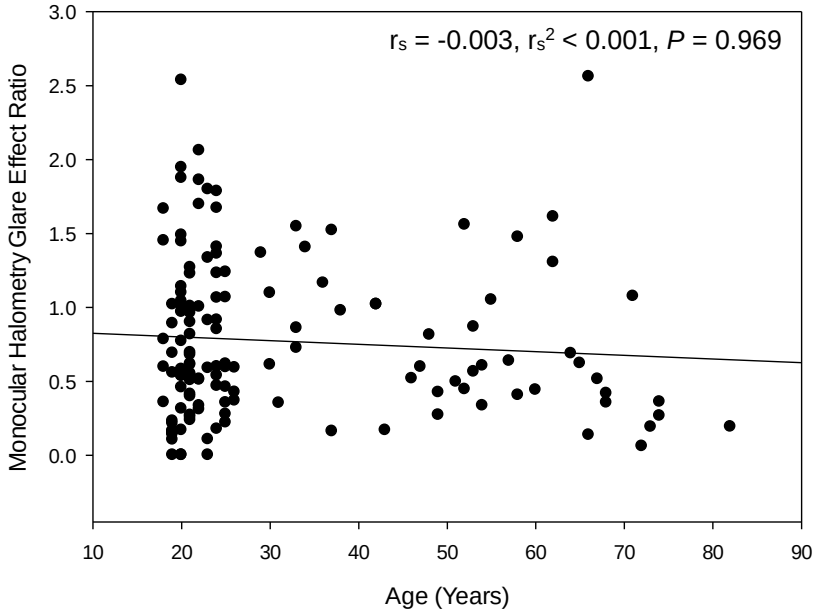


Figure 3.12: Monocular halometry glare effect ratios against age (n = 141).

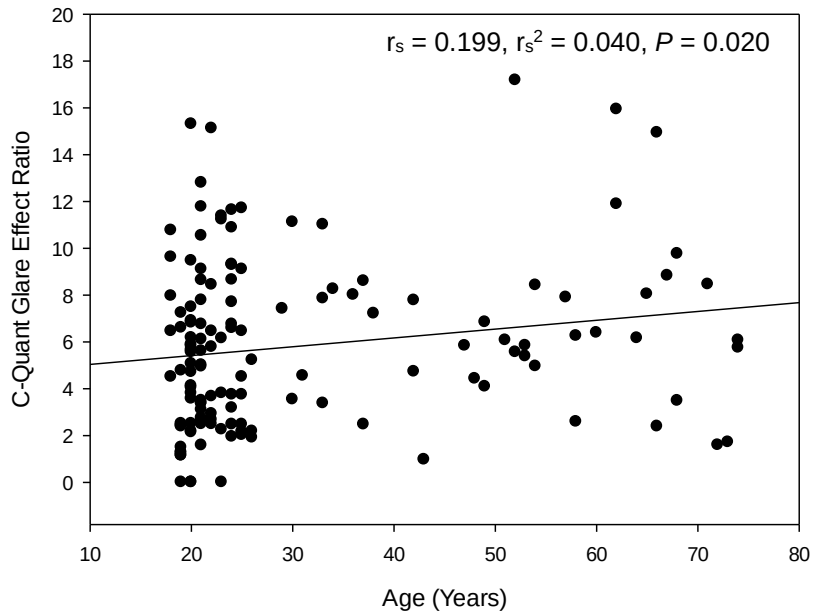


Figure 3.13: *C-Quant* glare effect ratios against age (n = 138).

As with chapter 2, the box-and-whisker plot shows the median, 25th percentile and 75th percentile (see Fig 3.14 and Fig 3.15). Outliers are calculated by adding 1.5 x IQR to the upper value of the interquartile range. For binocular halometry, glare effect ratios above 4.25 would be classed as outliers; in this cohort there were 2 outliers (see Table 3.5), according to this calculation. For *C-Quant*, glare effect ratios above 15.85 are outliers. Two outliers were identified in this cohort and their characteristics are summarised in Table 3.6**.**

Sex	**Age**	**RE Rx**	**LE Rx**	**Subjective Grade**
M	23	Plano	Plano / -0.50 x 180	7
F	22	+1.00 / - 0.50 x 100	+ 1.00 / - 0.50 x 70	8

Table 3.5: Summary of characteristics of outliers for the binocular halometry glare effect ratio (n = 2).

Sex	**Age**	**RE Rx**	**LE Rx**	**Subjective Grade**
M	62	+ 0.25 / -1.25 x 50	+ 0.50 / -1.00 x 20	18
F	52	- 2.00 DS	- 3.00 DS	17

Table 3.6: Summary of characteristics of outliers for the *C-Quant* glare effect ratio (n = 2).

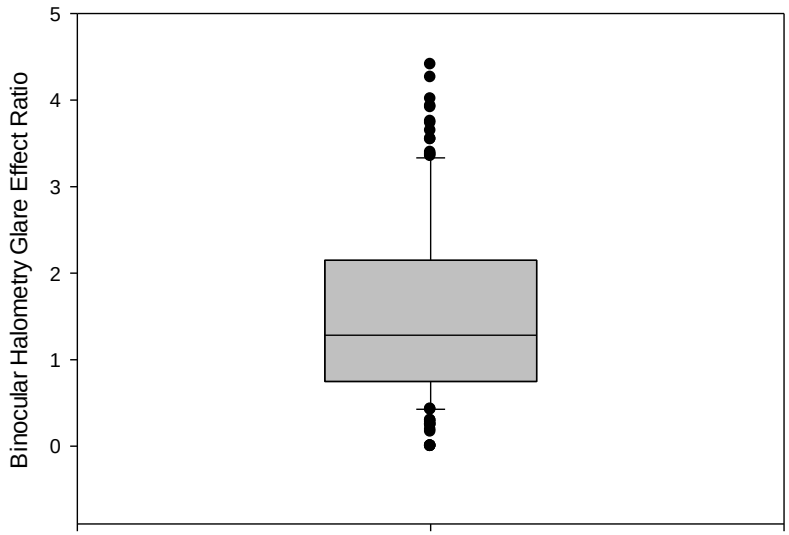


Figure 3.14: Box-and-whisker plot to show the interquartile range of the glare effect ratio with binocular halometry (n = 141). Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

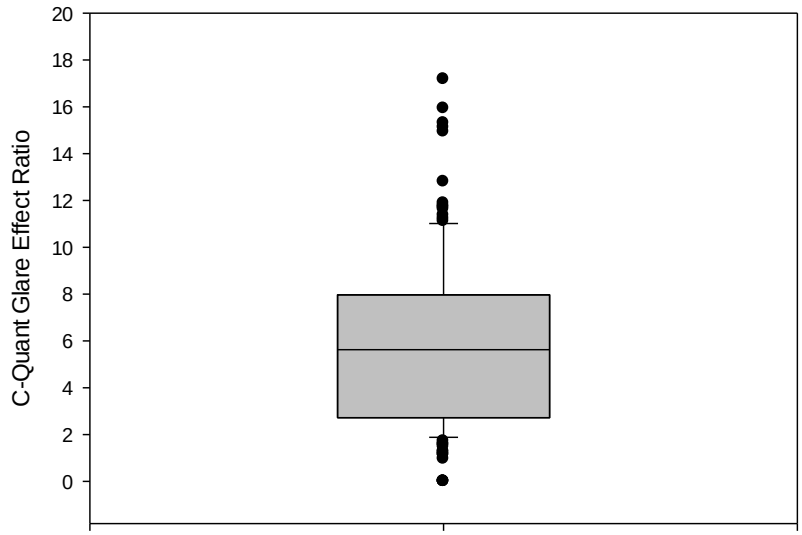


Figure 3.15: Box-and-whisker plot to show the interquartile range of the glare effect ratio with *C-Quant* (n = 138). Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

3.5. Discussion

The present study set out to determine how halo area, measured with the Aston halometer, changes with age in a large cohort. The effect of age on objective measures of retinal straylight was also established, as well as the effect on subjective complaints. The influence that age has on 'glare effect ratio', which was introduced in chapter 2, was investigated for the first time.

Dysphotopsia is a complaint often reported by patients after corneal refractive surgery or cataract surgery/refractive lens exchange, but it is also a common occurrence in the healthy aging population (van den Berg, 1995, Vos, 2003a). Dysphotopsia is widely accepted to increase with age (van den Berg, 1995, Tester *et al.*, 2000, Vos, 2003a, Puell *et al.*, 2013), with frequent complaints from older patients about halos around light when driving at night. Individuals may have good visual acuity, and still find the glare to be bothersome (Dewaard *et al.*, 1992, Ranney *et al.*, 2000, Theeuwes *et al.*, 2002). Some patients find the symptoms causes such a severe detriment to their vision that it reduces their quality of life, as they lose the confidence to drive at night. The literature presently concludes that straylight increase with age (Wolf, 1960, Ijspeert *et al.*, 1990, Bailey and Bullimore, 1991, Dewaard *et al.*, 1992, Elliott and Bullimore, 1993, Vos, 2003a, van den Berg *et al.*, 2007, Rozema *et al.*, 2010b, Puell *et al.*, 2014). Only two studies have investigated how halo area

changes with age, and whilst one found a significant relationship with age ($r = 0.65$, $r^2 = 0.42$, $P < 0.0001$) and that it rapidly increased beyond 50 years old (Puell *et al.*, 2013). The second study by Puell *et al*. (2014) found no effect with age in that cohort (range 20 – 43 years old). However, no studies to date have described how subjective complaints of dysphotopsia change with age.

Consistent with the findings of chapter 2, monocular halo area was also found to be significantly larger than binocular halo area in this cohort including a much wider age range. The difference was approximately 29 %, similar to the 31.2 % difference found in chapter 1. Thus, a potential limitation of previous studies, such as Puell *et al*. (2013) and Pieh *et al*. (2001), is reporting of monocular halo area values only, which are not representative of an individual's normal visual experience, and may over-estimate the level of dysphotopsia.

It is widely accepted that even in the absence of ocular disease, normal age-related changes in dysphotopsia occur due to an increase in intraocular scatter (Ijspeert *et al.*, 1990, Bailey and Bullimore, 1991, Vos, 2003a, Rozema *et al.*, 2010b, Puell *et al.*, 2014) and the current data also demonstrate an increase in straylight with age ($r_s = 0.457$, $r_s^2 = 0.209$, $P < 0.001$). Bailey *et al*. (1991) found a correlation coefficient of $r = 0.75$ between age and straylight, however a low contrast letter chart was used to assess the DGI. The difference between VA in no glare and high glare (3000 cd/m^2) conditions was used to calculate the DGI. The compensation comparison method uses a different technique to assess straylight, thus these values would not be comparable to *C-Quant* straylight values.

The results of the present study indicate that binocular halo area increases with age ($r_s = 0.449$, $r_s^2 = 0.202$, $P < 0.001$) in individuals with healthy eyes. The finding compares favourably with studies that have used alternative halometers such as the Vision monitor (Puell *et al.*, 2014), although the raw data values are not comparable to this data set, an issue which is discussed further later on in this section. Puell *et al*. (2013) reported a similar correlation for halo radius and age ($r = 0.65$, $P < 0.001$) as the monocular halometry results in the current study ($r_s = 0.405$, $r^2 = 0.162$, $P < 0.001$). Puell *et al*. (2013) stated that this increase in halo area with age could be due to changes in the transparency of the ocular media.

Halometry is used to establish the limit in the visual field at which the subject is unable to identify a letter around a central light source, thus, allowing the extent of the halo to be plotted. Identifying letters is more accurate than attempting to mark on the score the limit of

a diffuse halo produced by a central glare source, which has to be viewed by the subject. In several previous studies, the task for the subject was to report when a red spot touched the edge of a possible halo at a 2 m distance (Pieh *et al.*, 2001, Lackner *et al.*, 2003). Alternatively, the subject had to place a marker at the outer limit of the halo using a computer mouse at a 1 m distance (Allen *et al.*, 2008). A limitation of these methods is that if the subject does not see a defined halo or does not understand what a halo is, identification of its margin could be difficult. Differences in methodology, luminance of the glare source, distance, and measurement units make it difficult to compare the findings of the few studies that have examined halo area. In one study, halo area has been reported as its radius (mm) at 30 cm (Babizhayev *et al.*, 2009). In others, halo area values are given in square degrees (sqd; Lackner *et al.*, 2003, Allen *et al.*, 2009). In LASIK patients younger than 50 years, mean pre-operative halo area was 1.97 ± 1.20 sqd. (Lackner *et al.*, 2003). Puell *et al*. (2013) found a mean halo area in subjects younger than 50 years of 6.9 ± 0.4 sqd. Allen *et al*. (2009) found larger values of 61.3 ± 6.5 sqd, which could be due to the very close proximity of the glare source to the participant at 1 m. The limit of the halo was also defined by placing a marker at the outer limit using a computer mouse, which could have led to a gross overestimation. The median halo area in the present study was 0.45 sqd (range 0.18 – 1.91). Puell *et al*. (2013) recorded mean halo radii in arc min and found a mean of 100 ± 43 and 93.4 ± 41.6 for their first and second sessions, whilst the median radii in the present study was 22.7 arc min (range 14.4 – 46.7). The difference could be explained by the difference in light brightness, light source size, test distance or the position of glare source as Puell *et al*. (2013) positioned it peripherally. Puell et al. (2013) also had intervals of 33 min of arc that is the equivalent of 0.55 degree steps, whilst the Aston halometer uses increments of 0.05 degrees, making it more sensitive to small differences in halo area. Halo radius is estimated from only 3 radius measurements as only a semi circle of the halo is measured. An assumption of the halo area being symmetrical has been used, despite present literature showing a debate that halos may not be perfectly circular (Castro *et al.*, 2011, Meikies *et al.*, 2013).

Similar to findings in chapter 2, no relationship was exhibited between objective binocular halo area and subjective grade ($r_s = 0.132$, $r_s^2 = 0.017$, $P = 0.119$); and between monocular halo area and subjective grade ($r_s = 0.148$, $r_s^2 = 0.022$, $P = 0.08$). However, a weak correlation was found when binocular halo area was compared to subjective night halo complaints ($r_s = 0.330$, $r_s^2 = 0.109$, $P < 0.001$); whilst no other dysphotopic conditions exhibited a relationship. It may be that the night halo image on the PIPP plates is most similar to the appearance of the halo, and therefore, some correlation lies there for the measurement of similar photic phenomena.

Subjective grading showed only a weak relationship with age (r_s = 0.314, r_s^2 = 0.099, P < 0.001), indicating that although both objective measures of dysphotopsia increased with age, subjective complaints do not concur with this finding. Substantially highlighting the fact that it is possible for individuals to have high objective measures but not have significant complaints of glare. Night halo complaints had a slightly stronger relationship with age, again only a weak but significant relationship (r_s = 0.356, r_s^2 = 0.127, P < 0.001); it may be that it is a specific complaint that individuals feel they can relate to. In chapter 2, the glare effect ratio was introduced as a way of incorporating objective and subjective measures of dysphotopsia. Both binocular and monocular halometry glare effect ratios displayed no relationship with age (r_s = 0.0002, r_s^2 < 0.001, P = 0.998 and r_s = - 0.003, r_s^2 < 0.001, P = 0.969, respectively); and *C-Quant* glare effect ration presented a very weak relationship with age (r_s = 0.199, r_s^2 = 0.040, P = 0.020). It is widely accepted that objective measures increase with age, therefore, it can be difficult to establish if an older patient has a high objective measure due to age alone. The glare effect ratio is independent of age, and as suggested in chapter 2, a high glare effect ratio would indicate an individual more subjectively affected by a given objective measure. Along with the two outliers on halometry according to the IQR formula, those at the top of the box and whisker plot would be more susceptible to subjective effects. The outlier formula may not be appropriate here, as it is known that up to 50 % of patients may complain of dysphotopsia post-operatively, therefore, in a cohort of 141, a significant number of outliers would have been expected. So, whilst those that are classed as outliers would be most problematic, it is likely that there are others who would also be troubled by dysphotopsia. In the current cohort, 2 participants were also identified as outliers for the *C-Quant* glare effect ratio. Looking at the characteristics of all the individuals, there were 2 males and 2 females; who had a subjective grade from 7 to 18. There was no obvious trend of refractive error with the outliers.

Factors such as translucency of the wall of the eye can allow straylight to enter the eye depending on the individuals' pigmentation. Therefore, a potential limitation of this study was not recording the ethnicity or iris colour of the participants. However, many papers have evaluated glare and they have not considered ethnicity or iris colour, despite the likelihood that it would impact on the levels of ocular pigmentation (Puell *et al.*, 2013, Buckhurst *et al.,* 2017, Pieh *et al.,* 2001). The point is explored further in chapter 7.

In summary, this study has found that monocular and binocular halo area increases with age. Subjective complaints were only very weakly associated to age. Glare effect ratio was also independent of age. Indicating that the use of glare effect ratio may be a more suitable pre-operative test to establish those likely to suffer from complaints of dysphotopsia. A future study described in this thesis will examine glare effect ratios measured

pre-operatively in cataract patients, and compare them to subjective complaints post-operatively.

CHAPTER 4

HOW DOES PUPIL DIAMETER IMPACT ON HALO AREA?

4.1. Introduction

As detailed in earlier chapters, dysphotopsia describes unwanted light sensations, and including glare and halos. The scatter of intraocular straylight from the various surfaces within the eye, such as the cornea, lens and vitreous, is the cause of dysphotopic effects. Dysphotopsia can cause severe problems for people when driving at night due to the bright light source of car headlights and streetlamps (Dewaard *et al.*, 1992, Ranney *et al.*, 2000, Theeuwes *et al.*, 2002). Many different techniques exist to measure the amount of glare or straylight; although currently there is no gold standard (Neumann *et al.*, 1988, Elliott and Bullimore, 1993, Aslam *et al.*, 2007b). Often dysphotopsia is measured by placing a bright light source in the subjects' field of view (Williamson *et al.*, 1992, Elliott and Bullimore, 1993), and pupil diameter is known to decrease with increasing luminance (Laughlin, 1992, Winn *et al.*, 1994, Loewenfeld, 1999, Watson and Yellott, 2012, Orr *et al.*, 2015). Therefore, one might argue that pupil size will be affected in these assessments of dysphotopsia, as less retinal illuminance will occur. It leads to the question of whether pupil size should be measured or controlled in the measurement of dysphotopsia.

The iris is a thin, contractile, pigmented, disc-shaped diaphragm (Snell and Lemp, 1997). The iris is suspended in the aqueous humour between the cornea and crystalline lens and is attached to the anterior surface of the ciliary body (Zinn, 1972, Pipe *et al.*, 1997, Snell and Lemp, 1997, Kaufman *et al.*, 2003; see Fig 4.1). The pupil is an aperture located in the centre of the iris of the eye that allows light to strike the retina. It appears black because light rays entering the pupil are either absorbed by the tissues inside the eye directly, or absorbed after diffuse reflections within the eye that mostly miss exiting the narrow pupil.

The anterior surface of the iris is divided into a central pupillary zone and a peripheral ciliary zone (Pipe *et al.*, 1997, Snell and Lemp, 1997). Muscles control the size of the pupil. Fig 4.2 shows that the sphincter pupillae muscle is located in the pupillary zone of the iris (Pipe *et al.*, 1997, Snell and Lemp, 1997). It forms a ring of smooth muscle fibres running parallel to the pupil margin, measuring about 1 mm wide, and is located in the stromal layer. When the sphincter pupillae contracts, the iris diaphragm reduces in size making the pupil constrict (Snell and Lemp, 1997). The nerve supply of the sphincter pupillae is from the parasympathetic postganglionic fibres in the short ciliary nerves; derived from the autonomic Edinger-Westphal nucleus of the third cranial nerve.

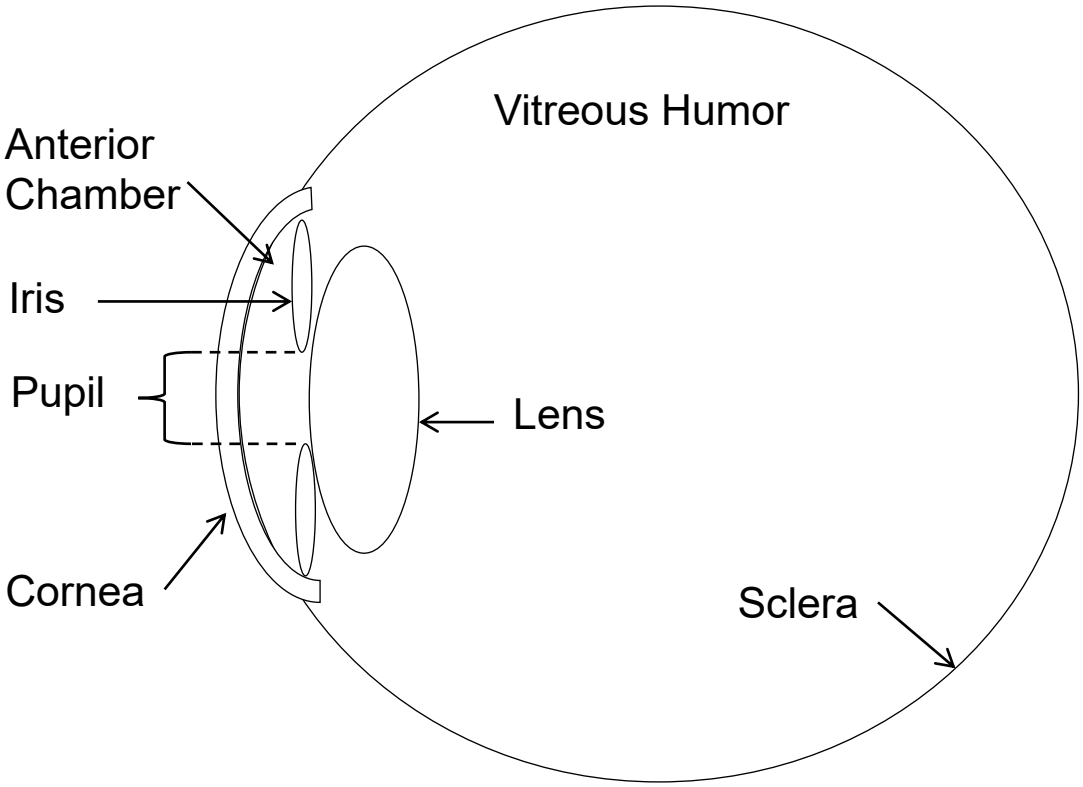


Figure 4.1: Anatomical section through the globe showing the relative position of the iris and pupil.

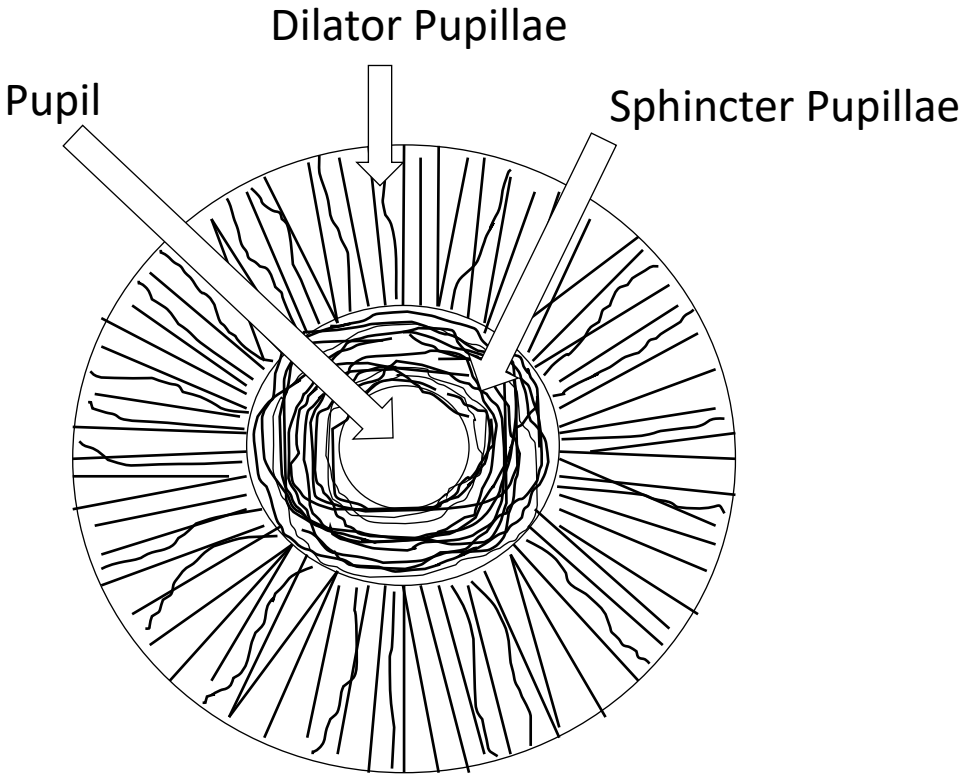


Figure 4.2: Diagram showing the arrangement of the fibres of the dilator pupillae and the sphincter pupillae of the iris.

The dilator pupillae, shown in Fig 4.2, is a thin layer of myo-epithelium that extends from the iris root as far as the sphincter pupillae (Pipe *et al.*, 1997, Snell and Lemp, 1997). When the dilator pupillae contracts, the pupil dilates (Snell and Lemp, 1997). The nerve supply of the dilator pupillae is from the postganglionic fibres of the superior cervical sympathetic ganglion via the long ciliary nerves (Pipe *et al.*, 1997).

Changes in pupil diameter are under the control of the two branches of the autonomic nervous system (Alexandridis *et al.*, 2012). As with other autonomically-innervated muscles, the pupil cannot be controlled voluntarily, although it is susceptible to the influence of the central nervous system (Pipe *et al.*, 1997). The iris muscles are innervated by the sympathetic and parasympathetic pathways (Alexandridis *et al.*, 2012). The dilator muscles of the iris are part of the sympathetic innervation pathway, whilst the sphincter muscles are para-sympathetically innervated.

There are three reflex pupil responses; known as the light reflex, the near reflex and psycho-sensory reflex (Walker *et al.*, 1983). The main function attributed to the pupillary light reflex is regulating the amount of light reaching the retina (Woodhouse and Campbell, 1975). Therefore, the light reflex regulates retinal illumination to minimise disabling effects on vision, caused by excessive bleaching of the photoreceptors at high luminances, and to facilitate retinal adaptation following rapid changes in incident light levels (Woodhouse and Campbell, 1975). In accordance with this theory, it is known that pupil size decreases with increased retinal illumination (Watson and Yellott, 2012, Orr *et al.*, 2015), and as such, it is important to know whether the pupil size affects halo area measurements.

The near reflex involves constriction of the pupil, which occurs when viewing close objects. A smaller pupil diameter increases the depth of focus of the eye, reducing the detrimental effects of the optical aberrations (Westheimer, 1964, Loewenfeld, 1999, Atchison and Smith, 2000). The near pupil reflex occurs simultaneously with accommodation and convergence (Loewenfeld, 1999). Lastly, psycho-sensory reflex describes when intense emotion can produce mydriasis (Alexandridis *et al.*, 2012). Loud noises can cause dilation of the pupil along with strong emotional or physical stimuli and states of heightened central nervous system arousal (Loewenfeld, 1999).

Normal pupil size has been reported to be 2 to 4 mm in diameter in bright light and 4 to 8 mm in the dark (Walker *et al.,* 1983). The pupil diameter also decreases with increasing age (Kadlecova *et al.*, 1958, Schaeffel *et al.*, 1993, Winn *et al.*, 1994, Watson and Yellott, 2012). As halometry is used to measure halo area, and this is a common problem in the ageing population (van den Berg, 1995, Puell *et al.*, 2013); it is

likely that many participants will have senile miosis. When pupils are small, vision may be adversely affected by loss of retinal illumination (Campbell and Gubisch, 1966). Equally, a smaller pupil can have a positive effect on visual acuity as it may result in less retinal illumination, and thus, VA improves with small pupils (Atchison *et al.*, 1979).

The existing literature shows debate on whether pupil size affects the amount of dysphotopsia that is measured (summarised in Table 4.1). It could be reasoned that in darkness, pupil dilation allows more glaring light to enter the pupil and scatter on the retina. Franssen *et al*. (2007) believed this argument was misleading, as larger pupils also allow more of the dark scenery to reach the retina, thus counteracting the effect of the glaring light. The more likely reason for increased glare with large pupils could be due to the impact of the extreme periphery of the lens (Cahane *et al.*, 1993, Franssen *et al.*, 2007) - previous work has demonstrated that for pupil diameters greater than 8 mm, the zonular area scatters light much more than the central parts of the lens (van den Berg, T, unpublished data, 1992 as cited in Franssen *et al*. 2007). Franssen *et al*. (2007) showed that for pupil diameters between 2 and 7 mm, straylight measured with *C-Quant* weakly but not significantly depended on pupil size. On average, the change was + 0.025 log units per mm of pupil diameter increase. The authors concluded that straylight values measured with photopic pupils are also valid under mesopic and scotopic pupils, such as night driving. Whitaker *et al*. (1994) hypothesised that there should not be an increased amount of forward light scatter related to a larger pupil diameter as pupil size change affects retinal illuminance of the stimulus and the glare source equally. Contrarily, Masket (1992) used the *Miller–Nadler* glare tester (Miller *et al.*, 1972, Nadler *et al.*, 1984) to measure glare before and after dilation. The results indicated that pupillary enlargement is associated with increased glare disability.

Due to the nature of most the tests, it might be expected that the bright glare source used would cause pupil constriction. Investigators found that the reduction in disability glare results produced by the *BAT* were possibly due to pupil miosis from the increased illumination from the glare source (Tan *et al., 1998)*. The study measured glare with the *BAT* before and after Nd:YAG capsulotomy for posterior capsule opacification (PCO). It is therefore possible that pupil miosis caused some PCO to be excluded from the pupil, effectively reducing glare, thus, potentially giving an underestimate of the amount of glare experienced. However, Whitaker *et al*. (1994) postulated that the decrease in pupil size with a bright glare source would mean that the PCO would take up a much greater proportion of the pupillary area, therefore, increasing the glare experienced. Boxer-Wachler *et al*. (1999) found a similar improvement in visual acuity and contrast threshold measures with a glare source. The VectorVision CSV-1000 (VectorVision, Dayton, Ohio) used to measure VA and

contrast sensitivity simulates mesopic conditions, which allows natural pupil dilation. It is a self-calibrated, internally illuminated light box. In this scenario, it could be argued that the ablation zone would be between 4.5 – 5 mm in size. Thus, the non-operated area outside of the ablation zone will have an increased power, and therefore, increase peripheral spherical aberrations. However, when the glare source is present in the field of view, the pupil size reduces, masking the transition zone and decreasing the visual degradation, leading to improved vision or less dysphotopsia.

Author and methods	Effect of pupil size
Franssen *et al*. (2007) n = 5; 31 – 59 years old. Straylight was measured using the *C-Quant* as a function of pupil diameter ranging from 1.3 mm to > 8 mm.	For pupil diameters of 2 - 7 mm, straylight weakly (but not significantly) depends on pupil diameter. On average, the change was + 0.025 log units per mm of pupil diameter increase. In normal eyes, straylight values measured with photopic pupils are by approximation also valid for mesopic and scotopic pupils (e.g. night driving).
Boxer-Wachler *et al*. (1999) Photorefractive keratectomy (PRK), n = 13, median age = 39 years, range 27 – 50 years; Radial keratotomy (RK), n = 20, median age = 41 years, range = 28 – 53 years. Measured visual acuity and contrast sensitivity with VectorVision CSV-1000 in glare and no-glare conditions.	Reported an increase in both measures when tested under a glare condition. Visual acuity under glare conditions was significantly higher in the photorefractive keratectomy group by one letter ($P = 0.02$). Pupils were significantly smaller under glare conditions (PRK, $P = 0.002$; RK, $P < 0.001$). Hypothesised that the glare source reduced the pupil size, masking the transition zone in the entrance pupil and accounted for results of improved visual acuity and contrast sensitivity with glare testing.
Tan *et al*. (1998) n = 19; mean age 72 years ± 6.3; age range 60 – 80 years. *Brightness Acuity Tester* and Straylightmeter used pre- and post-Nd:YAG capsulotomy.	Glare was significantly improved (Straylightmeter, $P < 0.001$; *BAT*, $P < 0.014$) following capsulotomy. *BAT* – 18.8% of patients with PCO had improved VA with glare testing prior to capsulotomy. Aberrant disability glare results produced due to pupil miosis from the bright light source.
Masket (1992) n = 40. *Miller–Nadler* glare testing was performed before and after dilation.	Pre-dilation mean pupillary size of 2.8 mm, and Miller-Nadler glare disability score of 15 %. Post-dilation mean pupillary size of 5.4 mm and Miller-Nadler glare disability score of 28.1 %. Difference in pupil size and glare disability were statistically significant (pupil size $P < 0.001$; glare score $P < 0.004$).

Table 4.1: Summary of previous work investigating the effect of pupil size on glare and measurements of dysphotopsia.

There is a lack of consensus over whether pupil size affects the amount of glare measured. It seems that it may be dependent on which device is used to measure glare; whilst, *C-Quant* results are not affected by pupil size, *BAT* and *Miller–Nadler* results are affected. No previous study has investigated whether pupil size needs to be controlled when assessing the size of the halo area using halometry. Halometry plays an important part in accurately assessing the size of a glare scotoma, and is becoming a popular choice (Pieh *et al.*, 2001, Sheppard *et al.*, 2013, Puell *et al.*, 2014, Buckhurst *et al.*, 2015). It has easy clinical use in the assessment of dysphotopsia post-refractive surgery, both laser and IOLs (Sheppard *et al.*, 2013). Therefore, it is essential to know whether results are robust without controlling the pupil size.

The aim of this prospective study was to establish whether pupil size impacts on halo area (measured using the Aston halometer), and if necessary, determine how pupil diameter should be controlled during the technique.

4.2. Subjects and methods

All procedures were conducted in the Ophthalmic Research Group laboratories at Aston University, Birmingham, UK. Risk assessment was conducted as part of the ethics application. An amendment was made to the ethical application (Number 595) to allow the use of mydriatic drugs to dilate the pupil for halometry measures. The principal investigator was a UK registered Optometrist and followed the College of Optometrist's guideline on dilation (College of Optometrists, 2015). The amendment was reviewed by the Aston University Life and Health Sciences Research Ethics Committee (Application number 595). A copy of this approval can be found in the appendix A2. The study was conducted in accordance with the tenets of the Declaration of Helsinki and all subjects gave their written informed consent to take part.

Power calculations, made using GPower (version 3.1.9.2), showed that 24 participants were required to enable Friedman repeated measures ANOVA on Ranks to detect statistically significant large size (0.7) effect at the 5 % significance level ($\alpha = 0.05$) with 80 % power. Twenty-five participants were recruited from the staff and student body in the Optometry department at Aston University subject to the following criteria:

Inclusion Criteria

- Corrected visual acuity of logMAR 0.1 or better in the eye to be tested, and logMAR 0.3 or better in the weaker eye to permit easy viewing of the logMAR 0.4 letter targets on the halometer.
- Participants who are able to understand and undertake the informed consent process.

Exclusion Criteria

- Any history of ocular surgery, including laser refractive surgery as it may increase the magnitude of the glare effect (Gutierrez *et al.*, 2003, Lackner *et al.*, 2003).
- Participants with any pre-diagnosed ocular conditions.
- Any participants with a history of using drugs that are known to affect the eye.
- Any participants with a systemic health problem that may result in ocular complications.

Unaided visions were measured and a full subjective refraction was performed at 3 m using the *Thomson Test Chart 2000*. Where the participant wore a distance habitual refractive correction, then this refractive correction was used for halometry. An *Oculus Universal* trial frame was used to house the manifest refraction; adjusted to ensure a back vertex distance as small as possible to allow the pupil aperture to be close to the eye. The full aperture trial lenses were cleaned before insertion into the trial frame to ensure that they did not increase the amount of glare experienced.

Initially, halometry was carried out monocularly on a randomly selected eye (using a randomisation table) in its undilated state. Subjects were positioned at 2.0 m from the halometer screen. Halometry was conducted in scotopic light conditions. The technique is described in full in Section 2.2.1.

Tropicamide is a drug commonly used in practice to dilate patients' pupils. Prior to dilation, intraocular pressures (IOPs) were measured using Reichert 7 (Haag-Streit, UK). Van Herrick's angle was assessed and any history of previous reactions was established. If deemed safe to do so, the participant was dilated, and warned not to drive for 6 hours post–dilation. One drop of 0.5 % tropicamide was used for light irides, whilst, one drop of 1 % was used for dark irides as per College of Optometrists guidance. Participants were also advised of the possibility of an adverse effect, and that in the case of a red or painful eye, a visit to eye casualty would be required. IOPs were also checked at the end of the data collection to check for the occurrence of an adverse reaction, and a College of

Optometrists leaflet on Tropicamide was given (College of Optometrists). Participants waited 20 minutes for dilation to occur, and following this; dilation was classed as complete when the pupil size was greater than 7.5 mm measured with a ruler, as this was the largest pupil size tested.

Pupil size was controlled by exact diameter holes being drilled into occluders. The same method has been used to simulate different pupil size in the clinical evaluation of the WAM-5500 (Sheppard and Davies, 2010; see Fig 4.3). 3 pupil sizes were chosen: 4.5 mm, 6.0 mm and 7.5 mm. Previous studies have found the mean night time driving pupil diameter at 2.5 cd/m^2 was 5.76 mm (Guillon *et al.*, 2016). The mean scotopic pupil diameter was 6.61 ± 0.92 mm when measured with Wavescan, and 6.40 ± 0.90 mm with Procyon pupilometer (Wickremasinghe *et al.*, 2005). The scotopic pupil size of 6.0 mm was chosen to replicate night-time driving, as it is when most people complain of glare problems. A pupil size of 4.5 mm was chosen as pre–presbyopic individuals (18 – 39 years; n = 166) have a mean pupil diameter of 4.21 ± 1.61 mm (Guillon *et al.*, 2016). The largest pupil diameter of 7.5 mm was chosen based on the study of MacLachlan and Howland (2002), which reported a typical pupil size of 7.5 mm in 15 – 18 year olds. The chosen pupil sizes allow a linear increase and decrease around the scotopic pupil diameter.

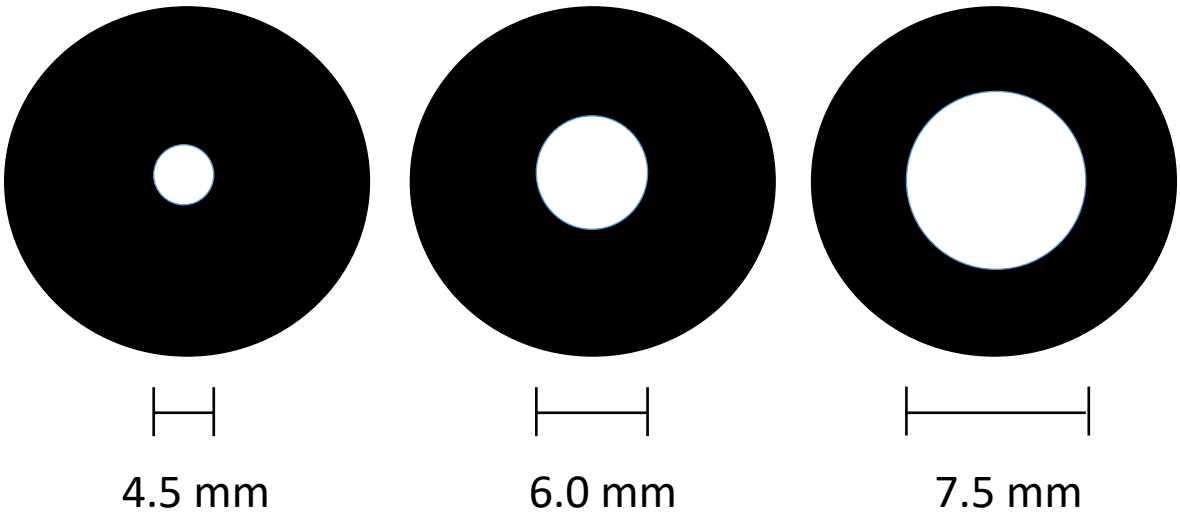


Fig 4.3: Image to show the pupil size difference by creating exact 4.5 mm, 6.0 mm and 7.5 mm holes in occluders.

Halometry was conducted for each of the 3 pupil sizes in a random order. A randomisation table was used to decide which of the pupil sizes would be tested first, secondly and thirdly for each participant. The participant wore a trial frame, set up to ensure central positioning of any lenses or occluders to the eye, both vertically and horizontally. The occluder with the fixed pupil size hole was placed in front the eye to be tested. It was inserted in to the back

cell, to minimise the back vertex distance without touching the eyelashes. The fellow eye was occluded to allow for monocular testing. Subjects were given a break (5 minutes) between halometry measurements to enable recovery from the glare source.

4.3. Data and statistical analysis

The data was stored in password-protected Excel 2016 Spreadsheet document (Microsoft, Redmond, WA). All statistical tests were performed using *SigmaPlot* graphing and statistical software (Version 12.0, Systat Software Inc., Chicago, Illinois, USA). The one-sample Kolmogorov-Smirnov test was used to determine if results from each measurement followed a normal distribution. Only the pre-dilation halo area followed a normal distribution, therefore, to aid comparison, median and range are reported for all data sets. Due to the non-parametric data sets, to compare the halo area from the different pupil sizes, a Friedman repeated measures ANOVA on Ranks was used. In all cases, a *P* value of < 0.05 was considered statistically significant.

4.4. Results

Twenty-five participants aged 18.0 – 41.0 years (median age 20.0) were recruited. Summary descriptive data are detailed in Table 4.2. The summary details of the median refraction results for the eye that was tested are displayed in Table 4.3. No adverse effects occurred with dilation of the pupil. The median halo area for each of the pupil conditions were calculated: pre-dilation 4.47 cm^2 (range 2.28 – 11.94); 4.5 mm pupil 4.07 cm^2 (range 1.64 – 11.90); 6.0 mm pupil 3.89 cm^2 (range 1.70 – 11.45); 7.5 mm pupil 4.19 cm^2 (range 1.78 – 9.51). The median and IQR of halo areas for each pupil size are shown in Table 4.4 and Fig 4.4.

Number of Participants	Median Age (Years)	Age Range (Years)	Gender
25	20.0	18.0 – 41.0	16 females; 9 males

Table 4.2: Summary descriptive data for cohort.

Tested Eye Median Sph Rx (range)	Tested Eye Median Cyl Rx (range)	Tested Eye Median Axis (range)	Median unaided vision or VA of eye when tested (range)
0.00 (- 6.25 – 5.50) D	-0.50 (- 2.75 – 0.00) D	130 (5 – 180) deg	0.00 (- 0.10 - 0.30) logMAR

Table 4.3: Summary of median refraction results for cohort.

Pupil Size	Median Halo Area (range)	Median Halo Radius (range)
Natural – Pre-dilation	4.47 (2.28 – 11.94) cm^2	21.6 (15.4 – 35.4) arc min
4.5 mm	4.07 (1.64 – 11.90) cm^2	20.6 (13.1 – 35.4) arc min
6.0 mm	3.89 (1.70 – 11.45) cm^2	20.3 (13.2 – 34.5) arc min
7.5 mm	4.19 (1.78 – 9.51) cm^2	20.7 (13.7 – 31.5) arc min

Table 4.4: Median halo area for the various pupil conditions: natural pupil, 4.5 mm, 6.0 mm and 7.5 mm simulated artificial pupils. N = 25.

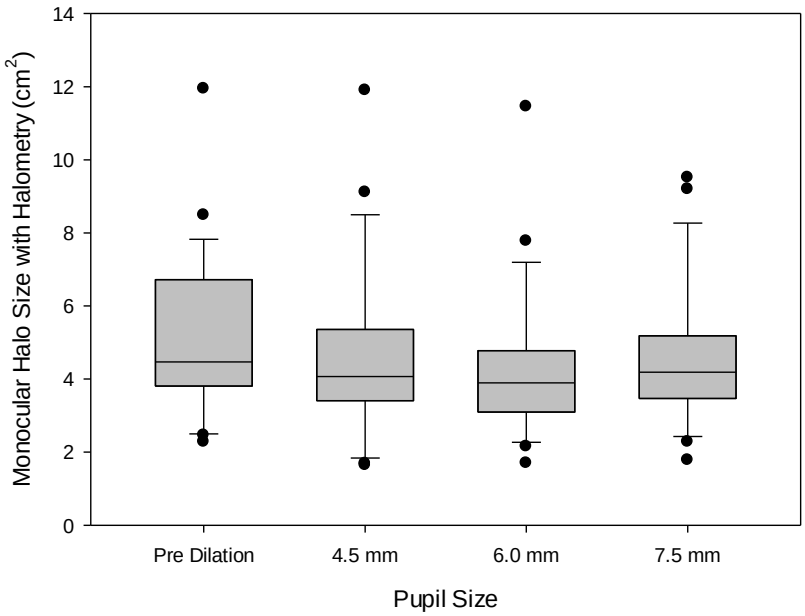


Figure 4.4: Box-and-whisker plot to show the interquartile range of halo area with halometry for each of the set pupil diameters (n = 25). Line within box = median, upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

No significant relationship was found between the pre-dilation halo area and unaided vision or VA in the eye used for halometry assessment (r_s = 0.09, r_s^2 = 0.008, *P* = 0.665). There was also no relationship between the mean equivalent sphere and the pre-dilation halo area (r_s = 0.10, r_s^2 = 0.010, *P* = 0.630). The simulated artificial pupil size was compared to the halo area, which found no significant relationship (r_s = 0.03, r_s^2 = 0.001, *P* = 0.769).

A non-parametric Friedman test of differences amongst repeated measures was conducted to compare the effect of pupil size on halo area with natural pupil size, 4.5 mm, 6.0 mm and 7.5 mm pupils (see Table 4.5 for descriptive statistics used). There was no significant difference between these four conditions ($\chi^2_{(3)}$ = 7.56, *P* = 0.056).

	N	**Percentiles**		
		25th	**50th (median)**	**75th**
Pre-dilation	25	3.81	4.47	6.72
4.5 mm	25	3.41	4.07	5.36
6.0 mm	25	3.10	3.89	4.78
7.5 mm	25	3.47	4.19	5.18

Table 4.5: Descriptive statistics used for the non-parametric Friedman test, showing the median and IQR for halo area.

4.5. Discussion

It is becoming more important to measure dysphotopsia due to the relatively high prevalence of complaints (10 – 50 %) linked to the phenomena in post-refractive surgery eyes (Applegate and Gansel, 1990, Aslam *et al.*, 2007b). Despite it being imperative to be able to measure dysphotopsia, currently a gold standard does not exist. Many techniques, including *C-Quant*, *Miller–Nadler* glare tester and halometry, are carried out in a dark room, potentially increasing pupil size, but use a bright light source in visual field, causing constriction of the pupil. There is likely to be an effect on the measurement, as individuals will have a different pupil size, which is true even in mesopic conditions without a bright light source. The present literature shows debate on whether pupil size affects the amount of dysphotopsia measured. With *C-Quant*, straylight was not significantly, dependent on pupil size (Franssen *et al.*, 2007), with an average change of + 0.025 log units per mm of pupil diameter increase. Whilst, Masket (1992) found an increase in glare disability with pupillary enlargement, using the *Miller–Nadler* glare tester. Thus, with halometry becoming a more popular choice in the assessment of dysphotopsia (Pieh *et al.*, 2001, Sheppard *et al.*, 2013, Puell *et al.*, 2014, Buckhurst *et al.*, 2015), it leads to the question of whether the pupil size should be measured or controlled in the assessment of dysphotopsia with halometry. This is the first study to report empirical data on whether pupil size impacts on halo measurements.

The median halo area pre-dilation was 4.47 cm^2 (range 2.28 – 11.94 cm^2) in this cohort, which is in line with the median for monocular halometry previously reported in chapter 3 of 4.87 cm^2 (range 1.97 – 20.87 cm^2) and within the IQR of 3.70 – 6.62. From this, it could be said that the cohort in this study are a good representation of ‘normal’ values of halo area. No significant relationship was found between the pre-dilation halo area and the unaided vision or VA used for halometry assessment (r_s = 0.09, r_s^2 = 0.008, *P* = 0.665). There was also no relationship between the mean equivalent sphere and the pre-dilation halo area (r_s = 0.10, r_s^2 = 0.010, *P* = 0.630). Therefore, confirming that there is no secondary effect influencing the halo area in this cohort.

The simulated artificial pupil size was compared to the halo area, with no significant relationship identified (r_s = 0.03, r_s^2 = 0.001, *P* = 0.769). From Fig 4.2, it is apparent that there is a wide spread of halo areas for each pupil size. The non-parametric Friedman test of differences amongst repeated measures showed no significant difference in halo area with the different pupil sizes. Assessment with halometry is carried out in a dark room. Pupil dilation occurs in darkness, and therefore, could potentially allow more glaring light to enter the eye and cause more scatter on the retina. The results here appear to support the

argument that whilst a larger pupil allows more glaring light from the glare source to enter, the retinal illuminance is also changed by the stimulus (Whitaker *et al.*, 1994, Franssen *et al.*, 2007). More dark scenery enters the eye, thus counteracting the effect of the glaring light. Franssen *et al*. (2007) indicated that the pupil size would affect the overall light intensity, but not the quality of the retinal image. Therefore, the amount of glare that is experienced is more dependent on the individual and the optics of their eye creating the straylight, such as cornea, crystalline lens and vitreous rather than the pupil size alone. The more likely reason of increased glare with large pupils may be due to the extreme periphery of the lens (Cahane *et al.*, 1993, Franssen *et al.*, 2007). This hypothesis is supported by previous work by van den Berg *et al.* (1992; cited in Franssen *et al.*, 2007), which demonstrated that for pupil diameters of greater than 8 mm, the zonular area scatters light much more than the central region of the lens.

Factors such as translucency of the wall of the eye can allow straylight to enter the eye depending on the individuals' pigmentation. Franssen *et al.* (2007) reported a translucency value average of 0.30 mm^2 in four more lightly pigmented subjects, compared to 0.00 mm^2 in the brown-eyed individual. The effect of translucency was more apparent for small pupil sizes when the scattering angle increases (Franssen *et al.*, 2007), thus, negating the expected reduction in glare entering the eye. Franssen *et al.*, (2007) measured the pupil reflex in the presence of 1-second flashes of glaring light. The investigators found that the glare effect invokes significant pupillary contraction, and that the contraction makes the pupil size approach daylight situations.

Whilst most studies of conventional and wavefront-guided LASIK have not shown a relationship between the diameter of the low light pupil and night vision symptoms post-operatively (Schallhorn *et al.*, 2003, Pop and Payette, 2004, Tuan and Liang, 2006, Villa *et al.*, 2007, Chan and Manche, 2011), Tan *et al.* (1998) and Boxer-Wachler *et al.* (1999) reported unusual findings where both found an improvement in measurements when the glare source was present. An explanation of these findings is due the presence of PCO, where the pupil miosis has excluded some of the PCO area from the pupil, effectively reducing the amount of source for light scatter to occur. Boxer-Wachler *et al.* (1999) investigated individuals post-laser surgery. The ablation zone is likely to be more exposed when in mesopic conditions; therefore, increased light scatter would occur at the periphery of the pupil where the remaining spherical error is still present. Pupil miosis due to the glare source would have masked the transition zone, and thus reduced the visual degradation.

The use of artificial pupil holes creates a limitation in this study, despite ensuring that the artificial pupil was central, and in the closest cell of the trial frame to the eye. There is debate about whether the centre of a pharmacologically-dilated pupil corresponds to the centre of the undilated pupil (Yang *et al.,* 2002), therefore having the artificial pupil central to the real pupil may not have been effective. A contact lens to act as a pupil block may be a good alternative, but that also brings its own problems due to movement of the lens on the eye.

The pre- and post-dilation pupil size was not measured. Instead, before starting the assessment, the pupil was measured to ensure it was bigger than 7.5 mm as that is the largest pin hole being used. Having the pupil sizes could have been useful. Measuring the pupils with a ruler was a limitation, and perhaps an infrared pupilometer could be used in future studies for this task to increase accuracy.

The results of the present study indicate that the pupil size has no effect on the glare area measured with the Aston halometer, analogous to findings when straylight is measured with *C-Quant* (Franssen *et al.*, 2007). Thus, similarly as the authors concluded that straylight values measured with photopic pupils are also valid under mesopic and scotopic pupils, such as night driving, this stands true for the Aston halometer. The likely cause for this is because both the direct light from the scenery and scattered light veil from a headlamp would increase in direct proportion to each other with increasing pupil size. In other words, the ratio between the useful and disturbing light, and thus the contrast in the scenery, would remain constant. The Aston halometer is a robust way to measure dysphotopsia without measuring or controlling the pupil size.

CHAPTER 5

A COMPARISON OF POST-OPERATIVE PHOTIC EFFECTS IN LASIK PATIENTS VERSUS NORMAL CONTROLS

5.1. Introduction

Refractive surgery encompasses various elective procedures that modify the optical status of the eye. Procedures that involve altering the cornea may be referred to as keratorefractive surgery, refractive keratoplasty, or corneal refractive surgery (American Academy of Ophthalmology, 2013). The most frequently performed procedures for low to moderate myopia utilise the excimer laser (Sakimoto *et al.*, 2006, American Academy of Ophthalmology, 2013), with millions of procedures performed worldwide each year (Market Scope, 2016). The US FDA first approved the excimer laser for this purpose in 1995 (Bailey and Zadnik, 2007).

A surface ablation technique, PRK, was the first excimer laser refractive procedure performed (Marshall *et al.,* 1985). It uses a non-thermal ultraviolet wavelength excimer laser to reshape corneal tissue following removal of the epithelium. LASIK surgery has since overtaken PRK to become one of the most common operations performed worldwide (Sekundo *et al.*, 2003, O'Doherty et al., 2006). LASIK utilises the excimer laser to reshape the cornea beneath its surface after a superficial corneal flap is fashioned using either a femtosecond laser or a manual microkeratome. Both make corneal flaps of very high quality and consistency, approximately 100 – 140 µm in thickness (Ruth *et al.*, 2008, Ahn *et al.*, 2011). Although both PRK and LASIK use the excimer laser to ablate the cornea, they differ in the layers of corneal tissue remaining after ablation. PRK removes the epithelium and Bowman layer, whereas in LASIK, these layers are preserved with the repositioning of the corneal flap (Ivarsen *et al.*, 2009). Replacing the epithelium post-operatively is thought to be the cause of decreased pain and faster visual recovery in LASIK procedures (Ambrosio and Wilson, 2003). PRK declined in popularity during the late 1990s, however, the use of surface ablation has seen a partial resurgence in patients with thinner corneas and low to moderate myopia, due to the avoidance of lamellar flap creation and associated risks (Sakimoto *et al.*, 2006). Other keratorefractive procedures to correct low to moderate myopia include variations of PRK such as LASEK (Tobaigy *et al.*, 2006) and epi-LASIK (American Academy of Ophthalmology, 2013).

Approximately 1.4 million patients undergo corneal refractive surgery each year in the United States alone (Harmon, 2011), whilst an estimated 8.5 million people in the United States underwent refractive surgery between 1995 and 2010 (Market Scope, 2010: cited by

American Academy of Ophthalmology, 2013). A survey based study examining trends in the UK in 2009 reported that Optimax surgeons have performed over 300,000 procedures since 1991 whilst Ultralase, the UK's longest established provider, quoted in 2008 that they had carried out 175,500 treatments to date. Optical Express reports its surgeons have a combined experience of over 600,000 procedures (Ewbank, 2010).

Refractive error affects approximately 60 – 80 % of the adult population in the United States (Vitale *et al.*, 2008, Solomon *et al.*, 2009), with a similar proportion of UK adults likely to be affected. Refractive surgery may be considered when an individual wishes to be less dependent on spectacles or contact lenses. It may also enable people to enter occupations previously closed to them because of their ametropia. A meta-analysis of outcomes of treatments with US FDA approved LASIK platforms reported that 93.1 % of patients achieved monocular uncorrected visual acuity (UCVA) of 20/40 and 62.5 % of patients achieved monocular UCVA of 20/20 (Bailey and Zadnik, 2007); whilst about 20 % complained of glare, halos and night driving problems post-operatively. Research released by the American Society of Cataract and Refractive Surgeons analysed 19 studies from 13 countries involving 2198 subjects who underwent LASIK from 1988 to 2008; 95 % of patients were satisfied with the results (Solomon *et al.*, 2009). Patient satisfaction is linked to the ease and comfort of the procedure for the patients, the excellent UCVA outcomes, and the relatively low complication rate, with complications leading to permanent visual loss occurring very rarely (Sugar *et al.*, 2002, Varley *et al.*, 2004, Schallhorn *et al.*, 2017). The excimer laser seems set to continue to be a primary means of refractive surgery, despite phakic and accommodative IOLs growing in popularity and clinical use (Sakimoto *et al.*, 2006).

Although high contrast visual acuity outcomes following refractive surgery are usually excellent, problematic photic effects may occur. Even after uneventful surgery, glare sensitivity is increased (Veraart *et al.*, 1992, Butuner *et al.*, 1994, Niesen *et al.*, 1997, Ghaith *et al.*, 1998, Katlun and Wiegand, 1998, Fan-Paul *et al.*, 2002). Whilst anecdotal evidence suggests that subjective photic effects reduce with time following laser refractive surgery, there is a lack of empirical data to support this viewpoint past 6 months. It is also unclear how much of the apparent improvement is due to a subjective acceptance of the disturbances (by neural adaptation) or an actual physical reduction in halo area (Fan-Paul *et al.*, 2002) and straylight.

Studies acquiring objective measures of straylight using the *C-Quant* following laser refractive surgery have provided conflicting evidence regarding whether there is an increase or decrease in values post-operatively (see Table 5.1). Overall, Lapid-Gortzak *et al*. (2010b)

found no significant increase in straylight at 3 months, compared to pre-operative levels in a LASIK group of 39 eyes and in a LASEK group of 26 eyes. However, in some individuals, notable increases in straylight occurred. In some affected eyes, haze or debris could be seen, whilst in others, the cause could not be determined. A second report from the same research group examining myopic eyes found on average, a significant improvement in straylight values post-operatively (Lapid-Gortzak *et al.*, 2010a). The mean decrease was -0.016 log(s) in the LASIK group and -0.026 log(s) in a LASEK group. Straylight improved in 62 of 102 eyes in a LASIK group ($P < 0.001$) and 78 of 137 eyes in the LASEK group ($P < 0.02$) and deteriorated in 35 eyes and 58 eyes, respectively. Rozema *et al*. (2010a) found a significant decrease in base and age-corrected straylight from 0.15 ± 0.14 log units to 0.00 ± 0.14 log units in a LASEK group. The base and age corrected (BAC) straylight subtracts a reference value of 0.931 from the measured straylight to compensate for the base constant and the effect of the age-related increase in straylight. Lorente-Velazquez *et al*. (2010) reported an initial improvement in straylight values post-surgery, which later worsened. Straylight values (mean ± SD) were 0.99 ± 0.03, 0.88 ± 0.03, and 0.93 ± 0.03 log(s) before, 15 days and 6 months after LASIK surgery, respectively. The 15 days values were significantly better than pre-operatively, although at 6 months, there was no difference compared to the pre-operative measures.

LASIK is undoubtedly a very successful refractive procedure, however, it may be associated with unwanted and disabling dysphotopsia. There has been limited research to date on longitudinal photic effects post-laser refractive surgery. Those that have reported on post-operative effects have typically used the *C-Quant* and report conflicting findings, usually following participants for a maximum of 6 months. Some authors report an improvement in straylight post-surgery, although usually by just a small amount and it is debatable how clinically significant these improvements may be. No previous studies have investigated longitudinal changes in subjectively reported and objectively measured (including halometry) photic effects following refractive surgery.

Author and study details	Key results
He and Manche (2014) n = 71 (142 eyes). Post PRK. Patients answered questionnaires on their visual symptoms and quality of vision pre-operatively and at 1, 3, 6, and 12 months after surgery.	Patients experienced less night-time glare from 6 months onward (P <0.03). Halos, double vision, and visual clarity were initially worse (P < 0.025) but not significantly different after 1 month.
Lapid-Gortzak *et al*. (2010a) n = 39 eyes for LASIK, n = 26 eyes for LASEK. Straylight levels measured before and 3 months after LASIK and LASEK in hyperopic eyes.	No significant increase in straylight at 3 months, compared to pre-operative levels in the LASIK and LASEK group.
Lapid-Gortzak *et al*. (2010b) n = 102 eyes for LASIK, n = 137 eyes for LASEK. Straylight levels measured before and 3 months after LASIK and LASEK in myopic eyes.	On average, there was a significant improvement in straylight values post-operatively. Straylight improved in 62 eyes in the LASIK group (P < 0.001) and 78 eyes in the LASEK group (P < 0.02) and deteriorated in 35 eyes and 58 eyes, respectively.
Lorente-Velazquez *et al.* (2010) n = 20. Straylight measured before, 15 days and 6 months after LASIK.	Straylight values significantly improved from pre-operative levels to those recorded 15 days after LASIK (P = 0.03), although values at 6 months failed to differ from baseline (P > 0.05).
Rozema *et al.* (2010) n = 49 (86 eyes). Straylight measured using *C-Quant* before and 6 months after LASEK in myopic patients.	After LASEK a significant decrease in base and age-corrected straylight, corrected to negate the effect of increasing straylight with age.

Table 5.1: Previous studies available at the time of writing that have reported longitudinal changes in dysphotopsia after laser refractive surgery.

The aims of this prospective study are:

- To measure longitudinal changes in halo area, straylight and subjective photic effects following bilateral LASIK refractive surgery in young adults.
- To compare results obtained with those of an age-matched control group.

5.2. Subjects and methods

All procedures were conducted in the Ophthalmic Research Group laboratories at Aston University, Birmingham, UK. Risk assessment was conducted as part of the ethics application. The study was reviewed by the Aston University Life and Health Sciences Research Ethics Committee (Application number 595). A copy of this approval can be found in appendix A1. The study was conducted in accordance with the tenets of the Declaration of Helsinki and all subjects gave their written informed consent to take part.

Power calculations, made using GPower (version 3.1.9.2), showed that 16 participants were required to enable Friedman repeated measures ANOVA on ranks to detect statistically significant large size (1.0) effect at the 5 % significance level ($\alpha = 0.05$) with 80 % power. Sixteen participants (32 eyes) were recruited from the student body at Aston University subject to the following criteria:

Inclusion Criteria

- Underwent uncomplicated bilateral LASIK refractive surgery within the last 3 months.
- Uncorrected visual acuity of logMAR 0.1 or better in both eyes to allow easy viewing of the logMAR 0.4 letter on the halometer.
- Able to understand and undertake the informed consent process.

Exclusion Criteria

- Any history of ocular surgery other than recent LASIK.
- Participants with any pre-diagnosed ocular conditions.
- Any participants with a history of using drugs that are known to affect the eye.
- Any participants with a systemic health problem that may result in ocular complications.

The LASIK patients came from a cohort of ‘pick and mix’ surgeries, where there was no access to key surgery information such as flap diameter, flap thickness, and pre-op information. Participants were seen at the following time points; within 3 months, 6 months

and 12 months post-surgery. At the < 3 months visit, unaided visions were measured and a full subjective refraction was performed at 3 m using the *Thomson Test Chart 2000*. All had unaided visions of 0.00 logMAR or better monocularly and required no spectacle correction for distance tasks.

Objective Measures

As described in section 2.2.1, objective measures of dysphotopsia were acquired in a random order from participants. Halometry was carried out both binocularly and monocularly, with the eye for monocular measurement selected using a randomisation table (Armstrong, 2013). The *C-Quant* was used to quantify intraocular light scatter in the same eye used for the monocular halometry reading.

Subjective Assessment

Subjective complaints have been measured using questionnaires in previously published studies (Arnold, 1994, Dick *et al.*, 1999, Aslam *et al.*, 2004a, Pepose *et al.*, 2007, Hofmann *et al.*, 2009), however, there is questionable value in simple questionnaires which may just ask individuals, 'do you suffer from glare?', or to grade severity on a scale of 1 - 10. Aslam *et al*. (2004a) stated that questionnaire assessments provide scores that are perhaps closest to patient's perceived morbidity but have poor specificity and are subject to interpretation errors, ambiguity, use of jargon and biases in responding. Hunkeler *et al.* (2002) developed a series of images and illustrations that depict various night-time visual phenomena including halo and starburst (see Fig 5.1 and Fig 5.2). The images have been successfully used in a previously published study, and received good feedback as participants felt they could relate to the images (Hunkeler *et al., 2002*). Based on previous chapters, of the 10 types of dysphotopsia shown, most were reported only at a low level. The Hunkeler images are in line with the night halos most reported. In the present study, with reference to the Hunkeler images (shown in Fig 5.1), the participant was asked which image best related to how they perceive the headlights of oncoming traffic. A value ranging from 1 – 6 was recorded. With Hunkeler illustrations (shown in Fig 5.2), the participant was asked which image best represented the way that a point source light would look. For these images a 2 digit number is recorded, the first of which is from 1 – 4 and represents the type of glare experienced. The second number from 1 – 3 indicates the severity of the symptom. A final subjective score was calculated from the sum on the Hunkeler image grade, and the second number for Hunkeler illustration, giving a value between 1 and 9; where 1 indicates no problems, and 9 indicates severe dysphotopsia.

Figure 5.1: Hunkeler images grading halo effects as seen around car headlights. Images supplied and reproduced with permission from Elsevier Ltd.

Figure 5.2: Hunkeler Illustrations depicting varying levels of halos and starburst experienced from a point source light. Images supplied and reproduced with permission from Elsevier Ltd.

Participants returned for repeat measures within 6 months and 12 months after their surgery date. At these visits, unaided visions were checked, and if there was a reduction in vision of 0.1 logMAR or more, a full subjective refraction was carried out. Repeat measures were taken with the halometer, *C-Quant* and subjective images as per the first visit.

5.2.2. Age matched control group

An age-matched control group underwent the same procedures outlined above at a single visit, for comparison with the treatment group.

5.3. Data and statistical analysis

The data was stored in a password protected Excel 2016 Spreadsheet document (Microsoft, Redmond, WA). All statistical tests were performed using *SigmaPlot* graphing and statistical software (Version 12.0, Systat Software Inc., Chicago, Illinois, USA). The one-sample Kolmogorov-Smirnov test was used to determine if results from each measurement followed a normal distribution; results for binocular halo area at visit 2, monocular halo area at visit 1, *C-Quant* at visit 3, subjective grading at visit 1, control group age, control group binocular halo area and control group subjective grading. Where data followed a normal distribution, the following parametric analyses were performed: - paired t-test was used when comparing two related samples, and t-test for comparing the control group to the laser group. For those data sets where one or both groups deviated from a normal distribution, Mann-Whitney Rank Sum Test was used for comparing the control group to the laser group. As there were some non-normally distributed data sets, median and range are reported for all data sets allowing for comparison between groups. Although the data are not normally distributed, a one-way ANOVA was used to compare the 8 triangle areas from halometry, as the test is not highly sensitive to deviations from the assumption of normality (McDonald, 2014). For repeated measures, due to some non-parametric data sets, to compare the halo area, straylight values and subjective grade over time, a Friedman repeated measures ANOVA on Ranks was used. In all cases, a P value of < 0.05 was considered statistically significant.

5.3.1. Calculation of halo area from halometer

Halo area was calculated in cm^2 as described in Section 2.3.1 and to aid comparison with published data on halo area, halo radius in arc min was also calculated.

Although it was previously determined (see Section 2.3.1) that a single halo area would suffice for the normal participants, due to the nature of refractive laser surgery and the possibility of it inducing asymmetry in monocular halo area; the 8 triangular areas of the glare scotoma were analysed using a one-way ANOVA (McDonald, 2014). For the

8 triangular areas, no significant difference was found for either the binocular or monocular measurements ([$F_{(7, 120)}$ = 0.137, *P* = 0.995] and [$F_{(7, 120)}$ = 0.101, *P* = 0.998], respectively), suggesting symmetry in glare scotoma shape.

5.4. Results

Sixteen refractive surgery patients and 16 control participants took part in the study. The median age of the control group was 22.0 years (range 20.0 – 29.0 years); this was not significantly different from the age of the laser group (median 21.5 years; range 18.0 – 31.0 years; *P* = 0.410). The cohort descriptive data is summarised in Table 5.2. The data collected from the control group is summarised in Table 5.3**.**

Group Type	Number of Participants	Median Age (Years)	Age Range (Years)	Gender
Laser	16	21.5	18.0 – 31.0	12 females; 4 males
Control	16	22.0	20.0 – 29.0	10 females; 6 males

Table 5.2: Summary descriptive data for entire cohort.

Median Binocular Halo Area (range)	Median Binocular Halo Radius (range)	Median Monocular Halo Area (range)	Median Monocular Halo Radius (range)	Median *C-Quant* (range)	Median Subjective Grade (range)
3.13 (2.64 – 5.50) cm^2	18.1 (16.6 – 23.9) arc min	4.28 (2.69 – 6.76) cm^2	21.2 (16.8 – 26.6) arc min	0.86 (0.76 – 1.21) log(s)	5.0 (2.0 – 6.0)

Table 5.3: Summary descriptive statistics for age-matched control group. N = 16.

Twelve of sixteen participants returned for the all visits; one participant did not attend the 6 month visit, but did the 12 month visit, and 4 were unable to return for the 12 month visit. Objective and subjective data from the laser group from the < 3 months, 6 months and 12 months are summarised in Tables 5.4, 5.5, and 5.6, respectively.

Median Binocular Halo Area (range)	Median Binocular Halo Radius (range)	Median Monocular Halo Area (range)	Median Monocular Halo Radius (range)	Median *C-Quant* (range)	Median Subjective Grade (range)
5.93* (2.79 –17.91) cm^2	24.8 (16.8 – 43.1) arc min	7.35* (3.99 – 27.86) cm^2	27.7 (20.3 – 53.9) arc min	0.93 (0.72 – 1.35) log(s)	5.0 (2.0 – 7.0)

Table 5.4: Summary descriptive statistics for laser group at visit 1 (< 3 months post-operatively). N = 16. * indicates significant difference compared to the age-matched control group.

Median Binocular Halo Area (range)	Median Binocular Halo Radius (range)	Median Monocular Halo Area (range)	Median Monocular Halo Radius (range)	Median *C-Quant* (range)	Median Subjective Grade (range)
3.52 (1.88 – 6.42) cm^2	19.2 (14.0 – 25.9) arc min	6.32* (2.75 – 8.07) cm^2	25.7 (17.0 – 29.0) arc min	0.93 (0.75 – 1.49) log(s)	5.0 (2.0 – 7.0)

Table 5.5: Summary descriptive statistics for laser group at visit 2 (6 months post-operatively). N = 15. * indicates significant difference compared to the age matched control group.

Median Binocular Halo Area (range)	Median Binocular Halo Radius (range)	Median Monocular Halo Area (range)	Median Monocular Halo Radius (range)	Median *C-Quant* (range)	Median Subjective Grade (range)
2.97 (1.78 – 7.19) cm^2	17.7 (13.7 – 27.2) arc min	4.14 (2.07 – 11.0) cm^2	20.3 (15.0 – 32.6) arc min	0.90 (0.74 – 1.46) log(s)	5.0* (3.0 – 8.0)

Table 5.6: Summary descriptive statistics for laser group at visit 3 (12 months post-operatively). N = 12. * indicates significant difference compared to the age matched control group.

5.4.1. Monocular halo area

A non-parametric Friedman test of differences amongst repeated measures was conducted to compare the halo area at < 3 months, 6 months and 12 months post-operatively. There was a significant difference between these three conditions ($\chi^2_{(2)}$ = 13.17, P < 0.001). Post hoc Tukey test showed monocular halo area significantly reduced between visits 1 and 3 (P = 0.009), and between visits 2 and 3 (P = 0.027). There was no significant difference between visits 1 and 2 (P = 0.051). For monocular halo area, a significant difference was found at 3 months (median 7.35 cm^2; range 3.99 – 27.86; P < 0.001, N = 16), and at 6 months (median 6.32 cm^2; range 2.75 – 8.07; P = 0.027, N = 15) compared to the control group. At 12 months post-operatively, no significant difference was found.

Consistent with previous findings, in chapter 2 and chapter 3, monocular halo area is greater than binocular halo area in both the laser group and the control group (Wilcoxon Signed Rank Test P = 0.018 and P < 0.001).

5.4.2. Binocular halo area

A non-parametric Friedman test of differences amongst repeated measures was conducted to compare the halo area at < 3 months, 6 months and 12 months post-operatively. There was a significant difference between these three conditions ($\chi^2_{(2)}$ = 16.17, P < 0.001). Post hoc Tukey test shows binocular glare area significantly reduces between visits 1 and 2 (P = 0.003), and between visits 1 and 3 (P < 0.001). There was no significant difference between visit 2 and 3 (P = 0.880).

In the laser group, the binocular halo area at 3 months (median 5.93 cm^2; range 2.79 – 17.91) was significantly larger than the control group (median 3.13 cm^2; range 2.64 – 5.50; P = 0.001, N = 16). However, by 6 months there was no significant difference in binocular halo area between the laser group and control group (P = 0.199, N = 15).

5.4.3. *C-Quant*

A one-way repeated measures ANOVA was conducted to compare the effect of time on straylight at < 3 months, 6 months and 12 months post-operatively. There was a significant difference between these three conditions [$F_{(2, 15)}$ = 5.91, P = 0.008]. Post hoc comparison using the Tukey test indicated that there was significant difference between visits 1 and 3 (P = 0.009). However, straylight was not significantly different between visits 1 and 2 (P = 0.051) and visits 2 and 3 (P = 0.658). The *C-Quant* values did not vary significantly from the control group for any of the visits.

5.4.4. Subjective grading

A one-way repeated measures ANOVA was conducted to compare the effect of time on subjective complaints of dysphotopsia at < 3 months, 6 months and 12 months post-operatively. There was no significant difference in subjective score between these three visits [$F_{(2, 15)} = 0.107$, $P = 0.899$]. Subjective complaints at visits 1 and 2 do not show a significant difference between the laser and control group. At 12 months, the median subjective grade in the laser group was significantly greater than the control group.

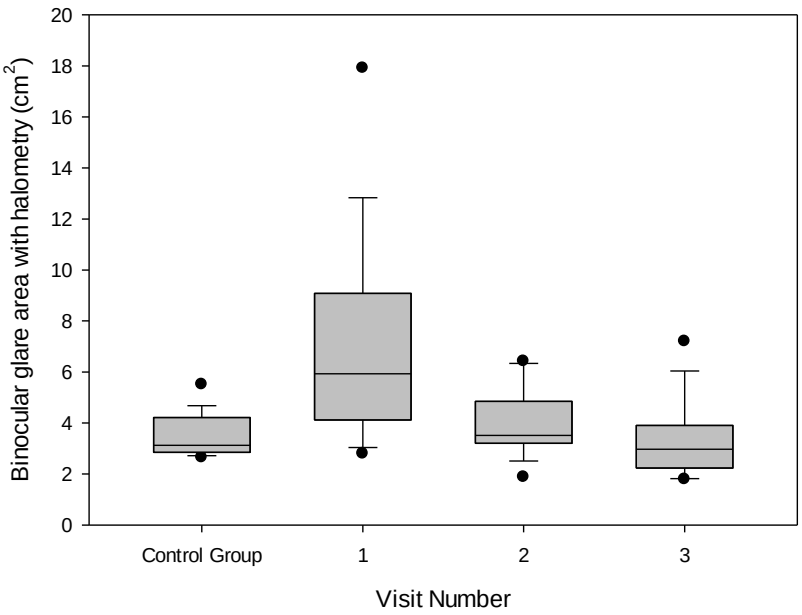


Figure 5.3: Box-and-whisker plot to show the magnitude of the binocular glare area measured with halometry at visits 1, 2 and 3. N = 16. Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

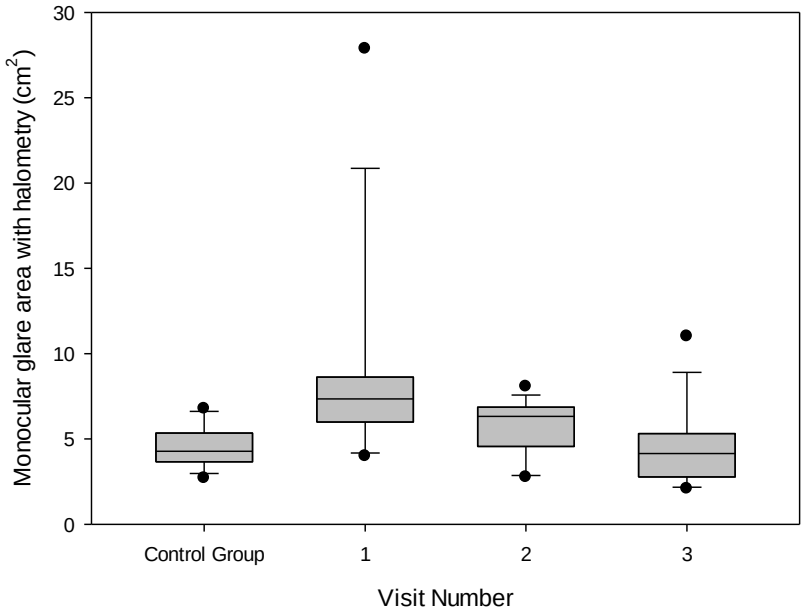


Figure 5.4: Box-and-whisker plot to show the magnitude of the monocular glare area measured with halometry at visits 1, 2 and 3. N = 16. Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

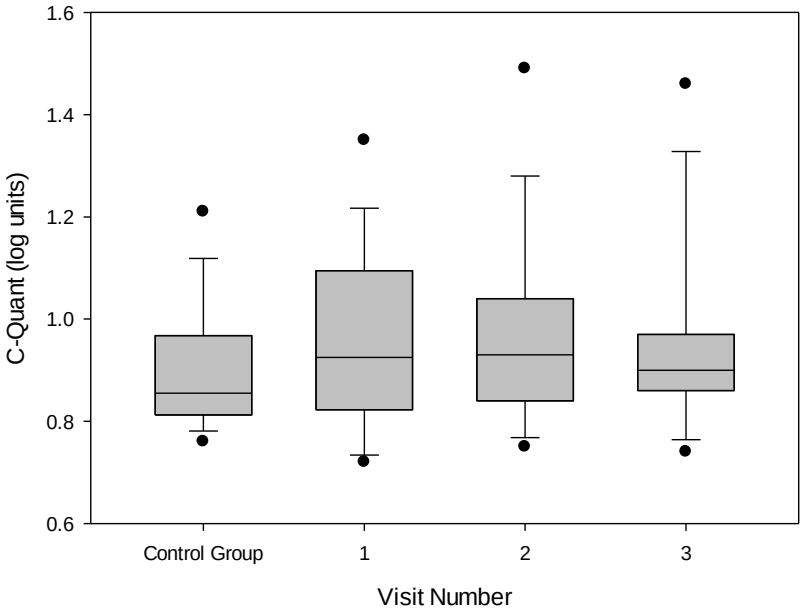


Figure 5.5: Box-and-whisker plot illustrating *C-Quant* values at visits 1, 2 and 3. N = 16. Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

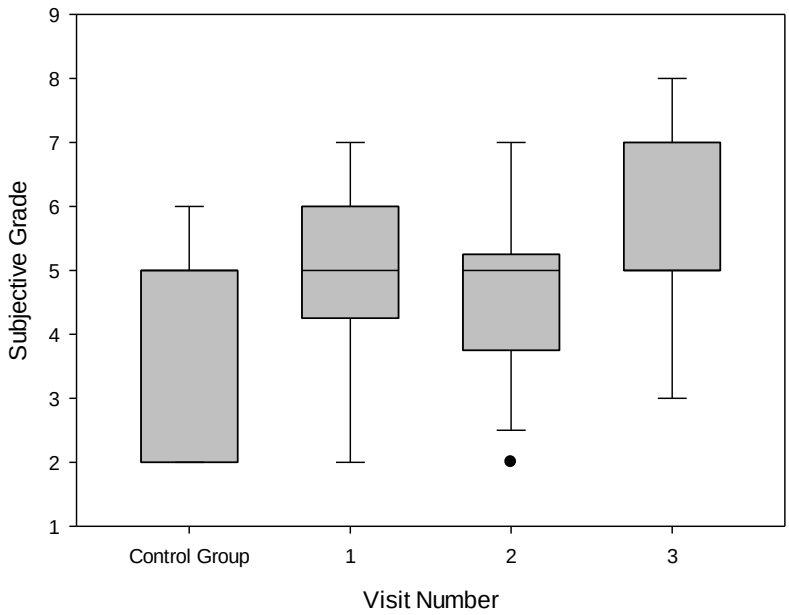


Figure 5.6: Box-and-whisker plot illustrating subjective grading at visits 1, 2 and 3. N = 16. Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

5.5. Discussion

LASIK is widely used across the world in the correction of different degrees of ametropia (Sekundo *et al.*, 2003, O'Doherty *et al.*, 2006). It usually provides patients with excellent visual acuity (Bailey and Zadnik, 2007), however, a well-known complaint is disappointment due to unwanted glare and halos around lights when driving at night (Veraart *et al.*, 1992, Butuner *et al.*, 1994, Niesen *et al.*, 1997, Ghaith *et al.*, 1998, Katlun and Wiegand, 1998, Fan-Paul *et al.*, 2002). Light scattering within the eye causes such complaints. The light spreading can have two origins (van den Berg *et al.*, 2009), a refractive one, caused by wave front aberrations spreading light over small angular distances, and a diffractive one, due to small irregularities in the ocular media scattering light over large angular distances. Many conditions can cause this diffractive process, such as the corneal epithelial healing process, corneal haze, superficial scars, and post-operative flap positioning (Rozema *et al.*, 2010a).

Previous studies have tracked changes in straylight up to 6 months post-surgery, and only one study has looked at subjective complaints by questionnaire up to a year after surgery (He and Manche, 2014). There appears to be debate on how straylight values are affected with one study finding no significant difference between pre-operative and 3 month post-surgery values (Lapid-Gortzak *et al.*, 2010b), whilst the same research group found an

improvement in straylight between pre-operative and 3 months post-surgery (Lapid-Gortzak *et al.*, 2010a). Another study by Lorente-Velazquez *et al*. (2010) found an initial improvement 15 days after surgery, which reduces back to baseline by 6 months post-surgery. The present study is the first time that a longitudinal investigation has used simulated images to monitor changes in subjective complaints, and measured objective halo area up to a year after refractive laser surgery. The aim of the study was to measure longitudinal changes in halo area, straylight and subjective photic effects following bilateral LASIK refractive surgery in young adults. These values were then compared to an age-matched control group to ascertain when it returns back to normal levels.

Similar to chapter 2, when comparing the 8 triangular areas, no significant difference was found for both binocular and monocular measurements (P = 0.995 and P = 0.998, respectively). It indicates that despite corneal surgery, there is a symmetrical halo shape, which may be expected with a regular, circular flap. Also, consistent with findings in chapter 2 and 3, binocular glare areas were approximately 24 % smaller than monocular measurements due to the effects of binocular summation.

At the 3 month post-operative visit, median binocular and monocular halo areas (5.93 cm^2 and 7.35 cm^2, respectively) are significantly larger than the control group median (3.13 cm^2 and 4.28 cm^2, respectively). By 6 months, the binocular glare area is not significantly different from the control group, however, monocular glare is, further evidence that binocular summation is present and able to reduce the effects of dysphotopsia. There is a reduction in halo area over time, so that by 12 months, there is no significant difference to the control group. The median binocular halo area is 2.97 cm^2 and median monocular area is 4.14 cm^2, which also compares well to median data in chapter 2 (3.24 cm^2 and 4.25 cm^2, respectively).

The other objective assessment, *C-Quant*, showed no significant difference between visits 1 and 2, and between 2 and 3. However, there was a small but significant reduction in straylight between visits 1 (median 0.93 log(s)) and 3 (median 0.90 log(s)), suggesting a gradual reduction in straylight in the 12 months following laser refractive surgery. Consistent with Lapid-Gortzak *et al.* (2010b), where a significant difference was not found between pre-operative levels and 3 months after surgery in hyperopic eyes. The same research group did find a significant reduction at 3 months compared to pre-operative levels in a myopic group (Lapid-Gortzak *et al.*, 2010a).

Subjective findings by 3 months (median 5.0) are the same as the control group (median 5.0), indicating that laser patients are no more bothered by dysphotopsia than

normal individuals of the same age soon after surgery. These results tie in with previous work by He and Manche (2014) where halos significantly reducing by 1 month post-surgery. The authors found that night-time glare was experienced less from 6 months onwards. It is likely that a neural adaptation is occurring post-surgery (Fan-Paul *et al.*, 2002).

An unusual finding is present in the subjective grading at 12 months as there is a significant increase. The anomaly could be due to the visit being in December/January time. At this time of year, it gets darker earlier and therefore, night driving issues would become more apparent. Participants would also be more familiar with the images at the final visit, so they may be more aware of the symptoms. The cohort is smaller by 4 participants so any small differences would have more of an effect. In this cohort, at visit 3, 3 participants reported a value of 8.

Due to the nature of the recruitment, the participants came from a cohort of 'pick and mix' surgeries. Little pre-operative information was known, and that information could have been useful. For example, pre-operative glare effect ratio could not be calculated, and flap diameter and thickness were unknown. A limitation was that a control group had to be used to ascertain when halo area and subjective complaints reduced back to normal levels.

The study findings indicate that the halo shape is symmetrical even after laser refractive surgery. Both halo area and *C-Quant* increase post-laser surgery, but this effect reduces over 12 months. Subjective results, however, are comparable to the control group by 3 months. In patients undergoing uneventful bilateral LASIK refractive surgery, a transient increase in objectively measured dysphotopsia occurs. It reduces over time and does not seem to cause significant subjective complaints for patients.

CHAPTER 6

A LONGITUDINAL EVALUATION OF CHANGES IN PHOTIC PHENOMENA FOLLOWING CATARACT SURGERY

6.1. Introduction

Cataract is a common problem in the ageing eye; according to the World Health Organisation (WHO; Pascolini and Mariotti, 2012), age-related cataract is responsible for 51 % of world blindness, which represents about 20 million people. Straylight increases with age in the perfectly healthy eye, but to a greater extent with disturbances to the optical media, including cataract (Vos, 1984, van den Berg, 1986, Elliott and Bullimore, 1993). Quality of vision loss because of media disturbances is not limited to visual acuity reduction, but includes other effects such as those caused by straylight (van den Berg *et al.*, 2007). Straylight is the known cause of disability glare (Vos, 1984, van den Berg, 1986, Elliott and Bullimore, 1993), leading to problems with glare while driving at night, hindrance from a low sun during the daytime, facial recognition difficulties, reports of hazy vision and colour and contrast loss (van den Berg *et al.*, 2007).

Undesirable optical phenomena such as negative and positive dysphotopsia are also a well-known side effect following modern cataract surgery (Tester *et al.*, 2000, Mamalis, 2010, Hood and Sugar, 2015). Previous studies have reported the primary cause of post-surgical dissatisfaction in a normal pseudophakic population was dysphotopsia (Welch *et al.*, 2010, Kinard *et al.*, 2013). Negative dysphotopsia is defined as the perception of a shadow obscuring the temporal field of vision, while positive dysphotopsia is characterized as halos, arcs or streaks around point light sources (Davison, 2000, Mamalis, 2010). It is difficult to gauge the prevalence of dysphotopsia- studies report a range from as low as 1.5 % up to 67 % for positive dysphotopsia, with most authors identifying more moderate values of 12 % to 35 % (Tester *et al.*, 2000, Ellis, 2001, Meacock *et al.*, 2002). Negative dysphotopsia is less common and estimated to occur in only 0.5 % to 2.4 % of patients (Meacock *et al.*, 2002, Osher, 2008). In the majority of cases, dysphotopsia resolves or diminish over time (Makhotkina *et al.*, 2015). It has been suggested that this is due to neuroadaptation (Kershner, 2011) although, in 0.2 % to 1 % of pseudophakic patients severe symptoms will persist (Davison, 2000) and additional surgery may be required.

For negative dysphotopsia implantation of a secondary IOL in the bag or in the ciliary sulcus has been proposed as an option to alleviate the problem (Masket and Fram, 2011, Zeldovich, 2012). Other available treatment options for severe and persistent negative

dysphotopsia include implantation of a supplementary IOL, reverse optic capture and Nd:YAG laser anterior capsulectomy (intended to eliminate a sector along the nasal aspect of the anterior capsule overlying the IOL optic); however, in some cases the symptoms may persist after treatment (Davison, 2000, Trattler *et al.*, 2005, Masket and Fram, 2011, Weinstein, 2012, Zeldovich, 2012, Cooke *et al.*, 2013, Folden, 2013, Burke and Benjamin, 2014). Successful treatment of positive dysphotopsia appears less common, despite it being the more frequent form of photic effect. There is currently no widely accepted management strategy for positive dysphotopsia (Chandramani and Riaz, 2017). If severe symptoms persist after four to six weeks, IOL exchange may be considered; however, it should be the last resort (Sukhovolskiy, 2015). The IOL may develop a strong adherence to the capsule, making it difficult to dissect it from the capsular bag (Leysen *et al.*, 2009). Therefore, there is an importance in being able to distinguish those individuals who are more likely to encounter subjective problems prior to surgery.

Dysphotopsia occurs with IOLs of different materials (Davison, 2000) with either rounded or squared edges (Davison, 2000, Trattler *et al.*, 2005). PMMA was the first widely used IOL material (Chehade and Elder, 2009). PMMA lenses cause little or no dysphotopsia, which is supported by the fact that dysphotopsia were virtually unknown when PMMA was the IOL material of choice (Schwiegerling, 2006), although at the time designs were all monofocal which have less incidence of photic effects. The lack of foldability of PMMA, requiring a large incision during surgery, and the high rate of PCO due to the round edge design has resulted in these lenses rarely being used today (Cheng *et al.*, 2007). Flexible acrylic and silicone materials with vertical, sharp-edged designs were introduced with great success (Sukhovolskiy, 2015). The sharp edge design greatly reduced the rate of PCO (Hollick *et al.*, 1999, Yan *et al.*, 2005). However, acrylic lens materials increased the incidence of dysphotopia (Schwiegerling, 2006). IOLs of PMMA and silicone with rounded edges, along with square-edge acrylic IOLs with non-reflective surfaces, appear less likely to cause clinically significant pseudophakic dysphotopsia (Davison, 2000).

Lens design also affects the amount of dysphotopsia experienced. Multifocal IOLs are significantly more likely to induce photic phenomena than monofocal IOLs (Leyland and Pringle, 2006). Souza *et al*. (2006) reported values of 13 % and 20 % of glare and halos respectively in 30 eyes fitted with monofocals; these values increased to 40 % and 50 % of 50 eyes, respectively with multifocals. Woodward *et al*. (2009) reported 42 % of 43 eyes fitted with multifocal IOLs complained of photic phenomena, although in 8 of these 18 eyes effects were attributed to posterior capsular opacification. In a study by de Vries *et al*. (2011), 38.2 % of 76 eyes receiving multifocal IOL implantations had dysphotopsia. Chang *et al*. (2012) investigated 45 eyes for complaints of halo, night glare

and starburst; with 48 %, 15 % and 22 %, respectively, experiencing moderate to severe symptoms. A 2006 Cochrane review of multifocal IOLs found that photic phenomena are 3.5 times more likely with multifocal IOLs than with monofocal IOLs (Leyland and Pringle, 2006).

van den Berg *et al*. (2007) measured visual acuity using logMAR, straylight using *C-Quant* and scored lens opacity using the Lens Opacities Classification System III (LOCS III; Chylack *et al.*, 1993) in 220 pseudophakic eyes, 3182 non cataractous eyes (average LOCS III score < 1.5) and 134 cataractous eyes (average LOCS III score > 3) of 2422 subjects aged between 20 and 90 years. Participants were recruited among drivers in a wide area around five participating clinics in Amsterdam, Salzburg, Tubingen, Barcelona, and Antwerp. The investigators reported that pseudophakic eyes performed better on *C-Quant* than the cataract eyes, as expected, as well as the age-normal eyes. The study, however, did not look at pre- and post-operative changes in the same group; it compared a cataract group to a different group that underwent cataract surgery and did not report any longitudinal effects.

Bournas *et al*. (2007) assessed the risk of dysphotopsia after phacoemulsification with the use of four different IOLs in 600 individuals (mean age 70.48 years, range 58 – 84 years). In week 1, 117 participants (19.5 %) reported dysphotopsia. The number of individuals still reporting phenomena declined to 15, 12 and 7 (1.52 %) at 1, 3, 6 months, respectively, indicating a reduction in symptoms over time. However, this study only takes in to account subjective complaints, there is a lack of objective measures to support the findings.

Buckhurst *et al*. (2017) investigated 45 patients (aged 61.8 ± 8.9 years) 4 – 6 months after bilateral implantation with Tecnis ZM900 (diffractive multifocal), Lentis MPlus MF30 (segmented refractive multifocal) or Softec-1 (monofocal) IOLs (each n = 15). Each reported their dysphotopsia symptoms subjectively, identified its form (EyeVisPod illustrations), quantified retinal straylight (*C-Quant*) and halo area (Aston halometer). There was no significant correlation between the subjective dysphotopsia severity and the straylight (r_s = - 0.103, *P* = 0.503). Similarly, no significant correlation was found between the subjective scores and the monocular (r_s = 0.246, *P* = 0.103) and binocular (r_s = 0.241, *P* = 0.111) halometry scores. There was also no significant correlation found between the straylight scores and the halometry area both monocularly (r = 0.051, *P* = 0.739) and binocularly (r = 0.153, *P* = 0.315). The findings from this study are comparable to the findings in chapter 2 with the young normal cohort. Whilst these results indicate that subjective and objective measures do not relate post-operatively, there was no consideration of pre-operative values to understand how they change in response to

surgery. Aslam *et al*. (2007a) similarly reviewed 55 individuals more than a year after cataract surgery to assess subjective complaints using photographic images (*PIPP* plates). Dysphotopsia in the operated eye was still common more than a year later, with 18 participants (32.7 %) complaining of some level of dysphotopsia, mainly halos and starburst effects. However, the authors also did not assess participants prior to surgery to get baseline data.

Although phacoemulsification cataract surgery has improved visual outcomes and patient satisfaction, some patients with excellent acuity report that they are unhappy even with uncomplicated surgical results (Tester *et al.*, 2000, Radmall *et al.*, 2015). There is limited published data regarding changes in objective and subjective measures in response to cataract surgery. Numerous studies have reported post-operative effects, but are lacking pre-operative measures and are usually not on a longitudinal basis (Aslam *et al.*, 2007a).

The aims of this prospective study are:

- To determine how cataract surgery impacts on objective and subjective photic effects.
- To track longitudinal photic effects in response to cataract surgery for the first time with halometry and subjective assessment.

6.2. Subjects and methods

This prospective study included patients undergoing routine cataract surgery and implantation of the Rayner 600S monofocal IOL (described in section 6.2.1) between March 2016 and January 2017. All study procedures were performed in the Ophthalmology Outpatients clinic at Queen Elizabeth Hospital, Birmingham, United Kingdom. The University Hospitals Birmingham (UHB) Research and Development Governance Office of the UHB NHS Foundation Trust reviewed the study (UHB Ref: RRK5260; see appendix A3 and A4). The study was conducted in accordance with the tenets of the Declaration of Helsinki. After receiving an explanation of the nature and possible consequences of the study, all subjects gave their written informed consent to take part.

Power calculations, made using GPower (version 3.1.9.2), showed that 30 participants were required to enable Friedman repeated measures ANOVA on ranks to detect statistically significant large size (0.6) effect at the 5 % significance level ($\alpha = 0.05$) with 80 % power. Thirty-nine patients with bilateral visually significant cataract scheduled for routine phacoemulsification cataract surgery and IOL implantation at the Queen Elizabeth Hospital were enrolled in the study, subject to the following criteria:

Inclusion Criteria

- Over 18 years of age.
- Cataract for which phacoemulsification extraction and posterior IOL implantation has been planned for the operative eye.
- Listed for monocular surgery, or it is the first eye of those requiring binocular treatment.
- Calculated IOL power requirement within the range of + 8.0 to + 34.0 D.
- Clear intraocular media other than cataract.
- Able to understand and undertake the informed consent process.
- Able to perform halometry at 2 metres.

Exclusion Criteria

- Prior surgery on the selected eye, glaucoma-filtering surgery, retinal detachment surgery or laser treatment.
- Previous uveitis or trauma to the selected eye, anterior or posterior synechiae.
- Previous eye trauma.
- Potential for best-corrected visual acuity worse than logMAR 0.30.
- Partial or total paralysis, Parkinson syndrome, cerebrovascular accident or other condition that could impact on the results of the study.
- Insufficient physical and/or mental condition to allow participation.
- Participants with any pre-diagnosed ocular condition other than cataract.
- Any participants with a history of using drugs that are known to affect visual function measures.

6.2.1. Intraocular lens

The IOL used in the study is based on the traditional Rayner C-flex design and material but has a 6.00mm platform diameter. Other lens features include:

- Hydrophilic acrylic aspheric monofocal IOL.
- 360 degree square edge.
- Aberrations neutral aspherical lens.
- Square edge is on both anterior and posterior surfaces.
- Available in powers from + 8.0 D to + 34.0 D.
- Can be delivered through a 2.2 mm mini incision.

6.2.2. Surgical technique

All patients were having monocular surgery, or it was the first eye of binocular surgery. All patients had cataract surgery under topical anaesthesia performed by the same experienced surgeon (S.K.). A standard suture less micro incision phacoemulsification technique was used. The IOL was implanted in the capsular bag with a single-use injection system. Post-operatively, topical therapy included a standard combination of antibiotic and steroidal agents.

6.2.3. Assessments

At the pre-operative assessment, an optometrist and ophthalmologist examined participants to judge their suitability for cataract surgery. A slit-lamp examination of the anterior segment and funduscopy of the optic nerve head and macular region were performed. The condition of the lens was scored using the LOCS III system (Chylack *et al.*, 1993). Unaided vision or visual acuity in their current spectacles or with pinhole was recorded using a LogMAR chart.

Objective measures of dysphotopsia were acquired using a newer halometer comparable to that described in section 2.2.1, but using an iPad (Apple Inc, California, USA) to run the software, with the light source mounted directly to the tablet screen (see Fig 6.1). An iPhone (Apple Inc, California, USA) acted as the remote to control the movement and randomization of the letter. Halo radius was measured in 8 directions monocularly in the eye to be operated on. The images used to subjectively grade dysphotopsia were also installed on to a programme on the iPad, and measurements were conducted as described in 2.2.2. The Aslam *PIPP* plates provide an overall subjective grade between 0 (no dysphotopsia) – 40 (most severe dysphotopsia).

In addition to routine post-operative assessments, participants were evaluated at 1 month and 3 - 6 months post-surgery. Unaided visions or best-corrected visual acuity were recorded at these visits, along with objective and subjective assessments of dysphotopsia, as outlined above.

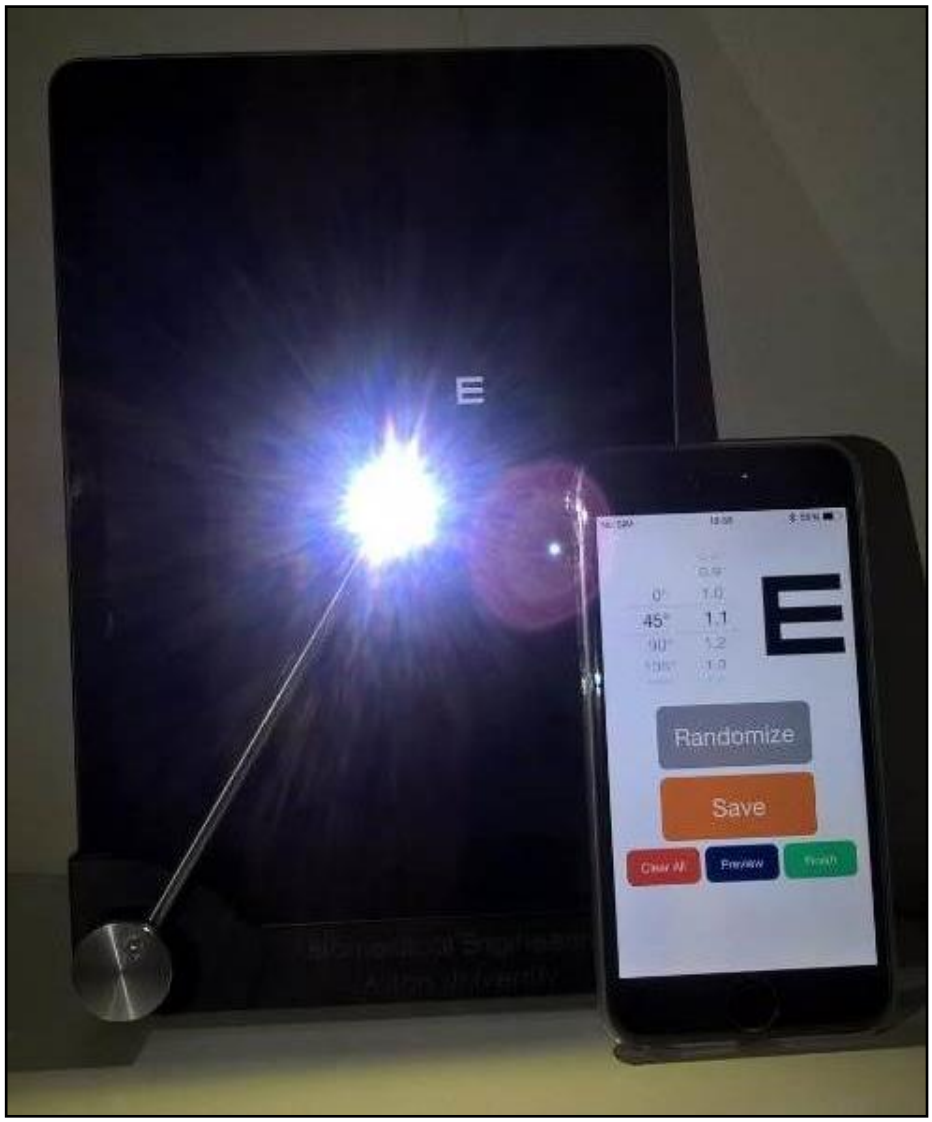


Figure 6.1: iPad halometer with custom built attachment and arm for the central light source. iPhone with a program to control the direction and distance that the letter moves, with the ability to randomise the letter.

6.3. Data and statistical analysis

The data was stored in a password protected Excel 2016 Spreadsheet document (Microsoft, Redmond, WA). All statistical tests were performed using *SigmaPlot* graphing and statistical software (Version 12.0, Systat Software Inc., Chicago, Illinois, USA). The one-sample Kolmogorov-Smirnov test was used to determine if results from each measurement followed a normal distribution. As there were some non-normally distributed data sets (e.g. halo area in cm^2 and halo radii in arc min at 3 – 6 month visit and subjective grading at all 3 visits), median and range are reported for all data sets allowing for comparison. For correlation between two data sets, if both data sets followed a normal distribution, Pearson's Correlation was used. For those data sets where one or both groups deviated from a normal

distribution, Spearman's Correlation was used. To track changes in objective and subjective measures over time, for parametric data sets a one-way repeated measures ANOVA was used, and for non-parametric data sets a Friedman repeated measures ANOVA on Ranks was used. In all cases, a *P* value of < 0.05 was considered statistically significant.

6.3.1. Calculation of halo area from halometer

The halo radius in degrees for each of the 8 meridians was recorded, and these were used to calculate the area of the glare scotoma as previously described in section 2.3.1. The halo radius was converted from degrees subtended to arc min. The median and range for halo radius and halo area were calculated.

6.4. Results

All patients underwent uncomplicated phacoemulsification extraction and IOL implantation. Table 6.1 provides descriptive statistics for the entire cohort.

No of Participants	Median Age (Years)	Age Range (Years)	Gender	Median pre-operative VA in operative eye	Median final VA in operative eye
39	74.3	52.8 – 86.3	25 female; 14 male	0.50 (range 0.20 – 1.0)	0.00 (range – 0.10 – 0.30)

Table 6.1: Summary descriptive data for the cohort.

Participants were assessed prior to surgery, and at 1 month and 3 - 6 months post-operatively. One participant missed the 1 month visit, but returned for the 3 - 6 month visit. Four participants were unable to attend the 3 – 6 month visit.

Median halo area pre-operatively was 190.29 cm^2 (range 63.74 – 297.86), and 66.33 cm^2 (range 22.71 – 117.69) and 32.49 cm^2 (range 15.08 – 107.48) at the 1 month and 3 – 6 month post-operative stages, respectively. Median halo radius was 141.0 arc min (range 81.75 – 176.25) pre-operatively, 83.25 arc min (range 48.75 – 111.0) at 1 month and 57.75 arc min (range 39.75 – 104.25) at 3 – 6 month visit.

The median overall subjective grade was 3.0 (range 0.0 – 12.0) pre-operatively, 0.0 (range 0.0 – 6.0) at 1 month and 0.0 (range 0.0 – 8.0) at 3 – 6 month. The median halo

area, halo radius and subjective grade pre-operatively, and at 1 month and 3 - 6 months post-surgery are recorded in Tables 6.2, 6.3 and 6.4. Box-and-whisker plots show the median and interquartile ranges at each visit halo area (Fig 6.2) and subjective grade (Fig 6.3).

Median Halo Area (range)	**Median Halo Radius (range)**	**Median Overall Subjective Grade (range)**
190.29 (63.74 – 297.86) cm^2	141.0 (81.75 – 176.25) arc min	3.0 (0.0 – 12.0)

Table 6.2: Summary descriptive statistics for the cohort at the pre-operative assessment (n = 39).

Median Halo Area (range)	**Median Halo Radius (range)**	**Median Overall Subjective Grade (range)**
66.33 (22.71 – 117.69) cm^2	83.25 (48.75 – 111.0) arc min	0.0 (0.0 – 6.0)

Table 6.3: Summary descriptive statistics for the cohort 1 month post-surgery (n = 38).

Median Halo Area (range)	**Median Halo Radius (range)**	**Median Overall Subjective Grade (range)**
32.49 (15.08 – 107.48) cm^2	57.75 (39.75 – 104.25) arc min	0.0 (0.0 – 8.0)

Table 6.4: Summary descriptive statistics for the cohort 3 - 6 month post-surgery (n = 35).

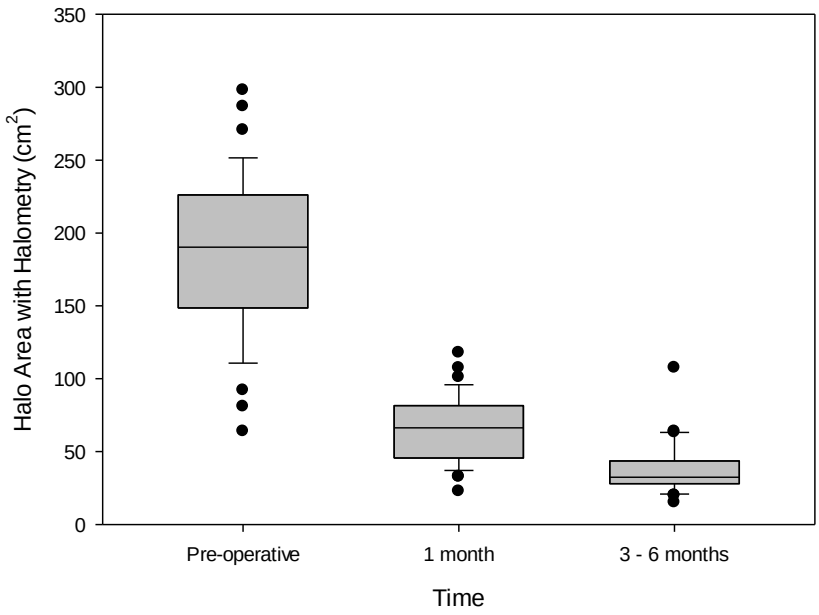


Figure 6.2: Box-and-whisker plot to show the interquartile range of the halo area at the three time points. n = 39 at pre-operative, 38 at 1 month and 35 at 3 – 6 months. Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

A non-parametric Friedman test of differences amongst repeated measures was conducted to compare the median halo area at the three time points used in the study. There was a significant difference in halo area between these three time points ($\chi^2_{(2)} = 58.69$, $P < 0.001$). Post hoc comparison using the Tukey test indicated that halo area pre-operatively (median 190.29 cm^2, IQR 148.54 – 226.18 cm^2) was significantly greater than at one month post-surgery (median 66.33 cm^2, IQR 45.55 – 81.55 cm^2) and 3 - 6 month post-surgery (median 32.49 cm^2, IQR 28.01 – 43.65 cm^2). There was also a significant reduction in halo area between one month and 3 - 6 month post-operatively ($P < 0.05$).

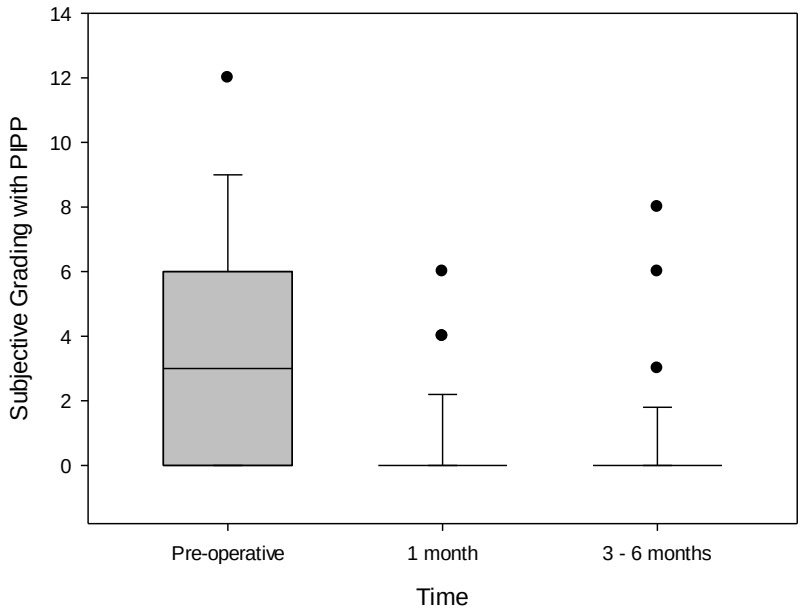


Figure 6.3: Box-and-whisker plot to show the interquartile range of the subjective grading at the three time points. n = 39 at pre-operative, 38 at 1 month and 35 at 3 – 6 months. Line within box = median; upper limit of box = 75th percentile; lower limit of box = 25th percentile; upper error bar = 90th percentile; lower error bar = 10th percentile; points = outliers in the upper and lower 10th percentile.

A non-parametric Friedman test of differences amongst repeated measures was conducted for the same time intervals for subjective complaints of dysphotopsia. There was a significant difference between the three time points ($\chi^2_{(2)}$ = 40.96, P < 0.001). Post hoc comparison using the Tukey test indicated that the subjective complaints scores pre-operatively (median 3.0, IQR 0.0 – 6.0) was significantly greater than one month post-operatively (median 0.0, IQR 0.0 – 0.0; P < 0.001) and 3 - 6 month post-operatively (median 0.0, IQR 0.0 – 0.0; P < 0.001). There was no significant difference between one month and 3 - 6 months post-operatively (P = 0.997). Fig 6.4 and 6.5 show the proportion of participants complaining of each type of dysphotopsia pre-operatively and 1 month post-operatively, respectively.

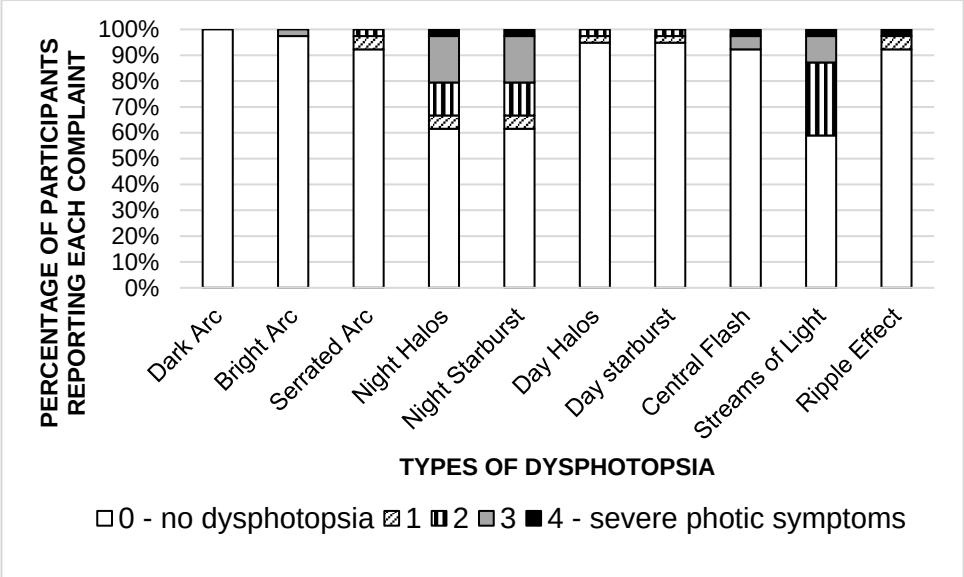


Figure 6.4: Diagram showing the proportion of participants complaining of each type of dysphotopsia using *PIPP* plates pre-operatively, where 0 indicates no dysphotopsia and 4 indicates severe photic symptoms.

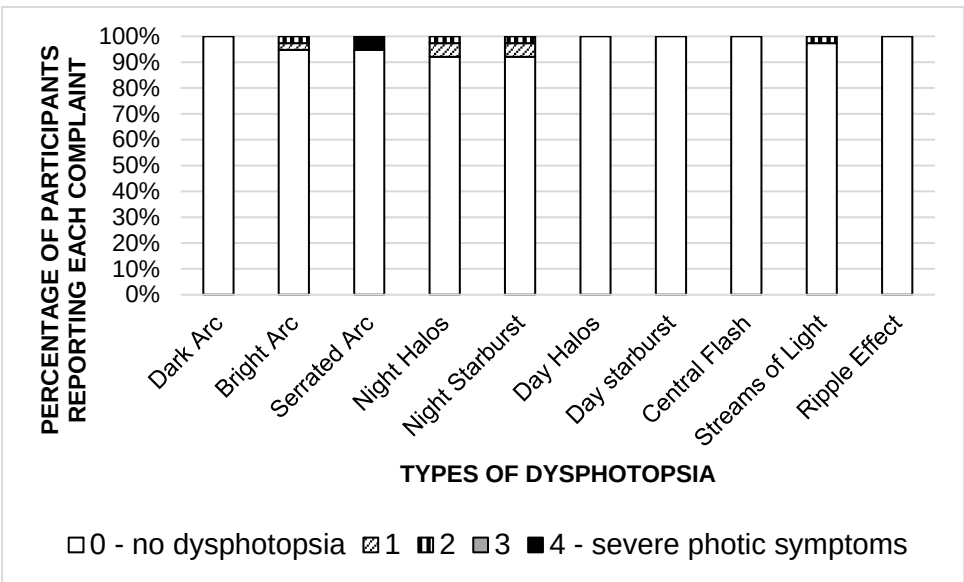


Figure 6.5: Diagram showing the proportion of participants complaining of each type of dysphotopsia using *PIPP* plates 1 month post-operatively, where 0 indicates no dysphotopsia and 4 indicates severe photic symptoms.

Pre-operatively there was no relationship between VA and halo area ($r_s = 0.140$, $r_s^2 = 0.020$, $P = 0.391$). Subjective grade was also not related to VA ($r_s = - 0.062$, $r_s^2 = 0.004$, $P = 0.705$).

Pearson's correlation exhibited no relationship between age and halo area prior to surgery ($r = 0.152$, $r^2 = 0.023$, $P = 0.355$); whilst at 1 month post-surgery a weak relationship was found ($r = 0.339$, $r^2 = 0.115$, $P = 0.035$; see Fig 6.6).

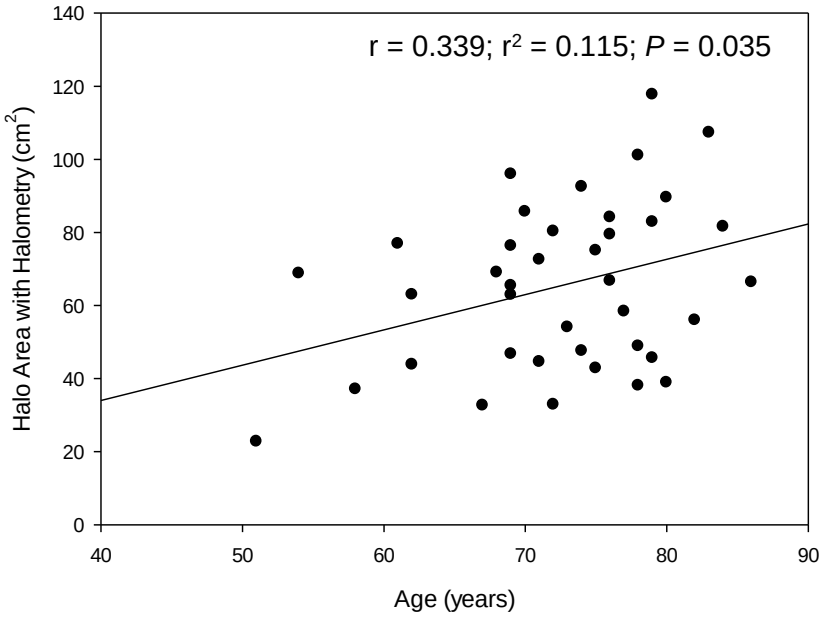


Figure 6.6: Monocular halo area determined with halometry 1 month post-surgery plotted against age (n = 38).

No relationship was shown between halo area and subjective grade prior to surgery ($r_s = -0.054$, $r_s^2 = 0.003$, $P = 0.741$) or at 1 month ($r_s = -0.124$, $r_s^2 = 0.015$, $P = 0.454$) and 3 – 6 month post-surgery ($r_s = 0.002$, $r_s^2 < 0.001$, $P = 0.993$).

There was no correlation between pre-operative halo area and halo area at the 3 – 6 months visit ($r_s = 0.198$, $r_s^2 = 0.039$, $P = 0.253$). However, a weak relationship was found between pre-operative subjective complaints and those at the 3 – 6 months visit ($r_s = 0.401$, $r_s^2 = 0.161$, $P = 0.017$).

The glare effect ratio was calculated at the pre-operative appointment (median 0.0151, range 0.0 – 0.141). No significant relationship was found between the glare effect ratio and the halo area at one month ($r_s = 0.006$, $r_s^2 < 0.001$, $P = 0.971$) or the halo area at the 3 – 6 month visit ($r_s = -0.132$, $r_s^2 = 0.017$, $P = 0.448$). However, a weak association was found between the pre-operative glare effect ratio and the 1 month subjective grading ($r_s = 0.419$, $r_s^2 = 0.176$, $P = 0.009$; see figure 6.7). It was also related to the 3 – 6 month subjective grading ($r_s = 0.366$, $r_s^2 = 0.134$, $P = 0.031$; see figure 6.8).

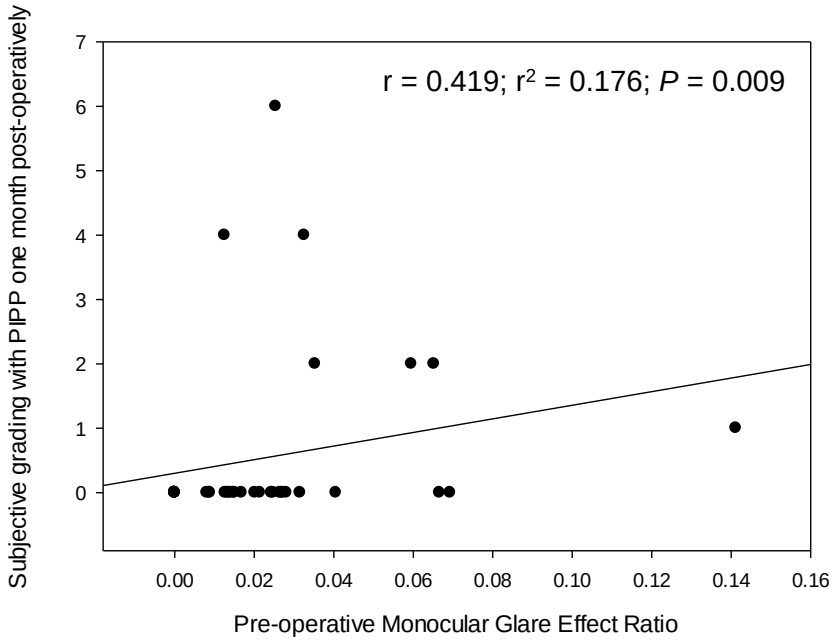


Figure 6.7: Pre-operative monocular halometry glare effect ratio against subjective grading with PIPP one month post-operatively.

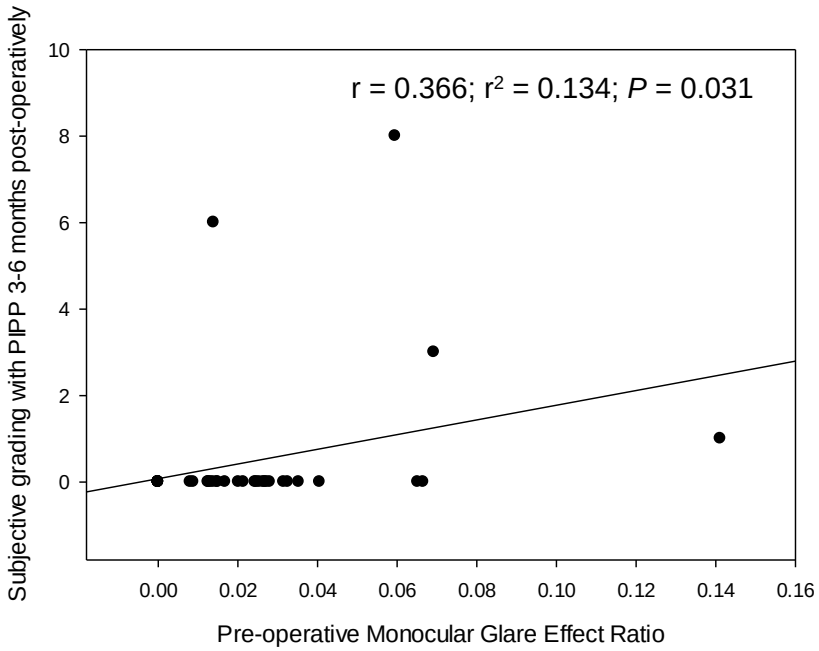


Figure 6.8: Pre-operative monocular halometry glare effect ratio against subjective grading with PIPP 3 – 6 months post-operatively.

6.5. Discussion

Modern cataract surgery is extremely successful at improving patients' vision and quality of life. However, there are a small percentage of patients who remain dissatisfied after the procedure, even with good visual acuity. Dysphotopsia is a chief complaint after otherwise successful cataract surgery (Tester *et al.*, 2000, Welch *et al.*, 2010, Kinard *et al.*, 2013). Considering this, there are few studies that have investigated the change in objective and subjective measures of dysphotopsia in response to cataract surgery. Whilst some studies have reported post-operative effects, they are rarely on a longitudinal basis (Aslam *et al.*, 2007a) with no pre-operative measures for comparison.

There is some evidence that glare improves after surgery presented by van den Berg *et al*. (2007), who assessed straylight in pseudophakic eyes, non-cataractous eyes and cataractous eyes. It was previously known that straylight increases with age. The cataract eyes had a relatively mild increase in straylight compared to non-cataract eyes. Surprisingly, in pseudophakia, straylight values were better than in the non-cataract group. However, the study did not compare the pre- and post-operative measures in the same participants, but instead compared a group with cataract to a different post-cataract surgery group. The lens starts to change colour from colourless at age 20 to 25 years, to slight yellow, up to brown at around 65 years and over (van den Berg *et al.*, 2007). The lens continues to grow throughout life, creating more and more optical distortions (Augusteyn, 2010). The retained anatomic layers of the crystalline lens from the embryonic stage to the adult may be one of the causes of light scattering in the eye (Michael and Bron, 2011). A likely reason why pseudophakic participants performed better than the non-cataractous group is that even without the presence of a significant cataract there will be some degree of normal age-related scattering occurring compared to the colourless IOL.

Participant halometry data from chapter 3 was converted to match the iPad halo values; by multiplying each angle subtended by 2 as recommended by the developers of both the Aston halometer and the iPad version. Therefore, based on the converted participant data from chapter 3, a median halo area of 34.87 cm^2 (IQR 22.10 – 50.30 cm^2) was calculated for participants aged between 51 and 82 years to provide an indication of expected normal values for an older age group. Perhaps unsurprisingly, the pre-operative halo areas (median 190.29 cm^2) were almost 5.5 times larger than the older age group values from chapter 3. The presence of cataract causes more scattering of light as it enters the eye (Vos, 1984, van den Berg, 1986, Elliott, 1993). The halo area significantly reduces during the month after surgery (66.33 cm^2), and return to values of over 55 year olds, from chapter 3, by 3 - 6 months (32.49 cm^2).

Subjective complaints significantly reduced from the pre-operative visit (median 3; range 0.0 – 12.0) to 1 month post-surgery (median 0.0; range 0.0 – 6.0) as may be expected. There was no significant difference between 1 month and 3 – 6 months post-surgery (median 0.0; range 0.0 – 8.0), indicating that all subjective complaint improvements occur within the first month. There may be an aspect of neuroadaptation as the subjective grade reduces by 1 month, whereas it takes 3 – 6 months for the objective measures to return to normal. The subjective values post-surgery were generally low with many participants reporting zero complaints, which could be a consequence of dramatic and sudden improvement in visual quality after cataract surgery meaning participants are on the whole very happy with their quality of vision. Due to patient expectations, in cases of clear lens exchange there may be higher values for subjective grading post-surgery for a longer duration. Bournas *et al*. (2007) reported from a group of 600 who had undergone cataract surgery, 117 participants (19.5 %) reported some level of dysphotopsia in week 1. There was a significant reduction to only 7 (1.52 %) complaining at 6 months post-surgery.

Relatively little work to date has used simulated images to grade types and severity of subjective photic complaints following cataract surgery with monofocal IOL implantation. Aslam *et al*. (2007a) reported higher levels of post-operative photic effects in monofocal IOL recipients at a minimum of 12 months post-surgery. The types of effects reported were more diverse than in the present study, whilst the severity was also greater, with around 20 % of individuals affected by each of night halos, night starburst, day starburst, day halos and central flash. The reasons for this difference may be due to the longer time interval post-operatively used by Aslam *et al.* (2007a), meaning that posterior capsular opacification may have a greater effect, or the initial elation following a substantial improvement in visual quality with cataract surgery declines and individuals become aware of undesirable photic effects.

Pre-operatively, there was a lack of relationship between VA and measured dysphotopsia, both objective halo area (P = 0.391) and subjective grade (P = 0.705). This finding is concurrent with several previously published studies reporting that the two measures are independent of each other with dysphotopsia often present despite excellent visual acuity (van den Berg *et al.*, 2007, Welch *et al.*, 2010, Kinard *et al.*, 2013).

It is well documented that straylight increases with age (Ijspeert *et al.*, 1990, Bailey and Bullimore, 1991, Vos, 2003a, Puell *et al.*, 2014). Presumably due to cataracts increasing halo area, there was no correlation between age and halo area pre-operatively (r = 0.152, r^2 = 0.023, P = 0.355). However, 1 month after the cataract surgery, a weak but significant relationship was established between age and halo area (r = 0.339, r^2 = 0.115, P = 0.035)

indicating that even without the presence of lens opacities, other ocular media changes with age cause an increase in straylight.

Objective and subjective grades do not exhibit a relationship at any time interval pre- (P = 0.741) or post-surgery (P = 0.454 and P = 0.993). The findings are similar to those reported in chapter 2. Recently, Buckhurst *et al*. (2017) also described no relationship between subjective scores and straylight (P = 0.503), subjective scores and monocular halo area (P = 0.103). Therefore, glare effect ratio may be a better predictor of outcomes, as it will identify those with high subjective complaints compared to objective metrics.

There appears to be a weak relationship between glare effect ratio pre-operatively, and subjective complaints post-operatively. Indicating that indeed high glare effect ratios prior to surgery are likely to indicate higher subjective complaints post-operatively and vice versa.

The participants were only seen up to 3 – 6 months after their surgery in this study. To see how things continue to change, tracking these patients further would be useful. Also, a limitation was the fact that the participants seen received monofocal IOLs of a particular material, edge design and optic zone size. For future studies, investigating post-operative effects after multifocal IOLs would be interesting, as well as comparing different lens materials or edge designs.

To conclude, this study has shown that both objective and subjective measures of dysphotopsia improve significantly in the month after uncomplicated cataract surgery. Halo area continues to reduce up to 6 months post-operatively. Objective and subjective measures are not related in participants with cataracts or after cataract surgery. The proposed glare effect ratio may be used to highlight individuals with a significantly high subjective complaint score compared to objective measures; these individuals may need additional counselling prior to surgery or recommendation of alternative procedures.

CHAPTER 7

GENERAL CONCLUSIONS AND PLANS FOR FUTURE WORK

7.1. General conclusions

The central experimental theme of the thesis has been objective and subjective assessment of dysphotopsia. Dysphotopsia is still only vaguely familiar to optometrist; however, with the incidence on the rise (Sukhovolskiy, 2015) and occurrence with normal ageing, it is important that the condition is more widely understood. Tester *et al.* (2000) first used the term *dysphotopsia* in 2000 to describe the visual phenomena encountered by phakic and pseudophakic patients, including flashes of light, glare, and light sensitivity. Dysphotopsia is generally divided into two categories: positive and negative. Positive visual changes involve symptoms of bright artefacts, whilst negative dysphotopsia are perceived as shadows or dark areas in the visual field (Hood, 2015). Patients may report glare, starbursts, halos or shadows when describing their visual symptoms (Sukhovolskiy, 2015).

Dysphotopsia is widely accepted to increase in the ageing phakic population (van den Berg, 1995, Tester *et al.*, 2000, Vos, 2003a, Puell *et al.*, 2013). The age-related increase in dysphotopsia is attributable to natural ageing changes increasing ocular media irregularities such as lens opacities and vitreous floaters, and therefore increasing the amount of scatter (Wolf, 1960, Vos, 1984, Bailey and Bullimore, 1991, Dewaard *et al.*, 1992, Elliott, 1993). The resultant increase in intraocular light scatter from a bright light source causes a veiling glare and a loss of contrast across the retinal image (Vos, 1984, van den Berg, 1995, Aslam *et al.*, 2007b, Allen *et al.*, 2009). The direct compensation method and the *Berkeley Glare* Test have been reported to show an increase in glare (Ijspeert et al., 1990, Bailey et al., 1991). However, the *C-Quant* has been shown to remain stable until the age of 45 years and then gradually increase (Rozema et al., 2010) in one study, and is not related with age in another (Puell et al., 2014). Thus, there is no clear consensus on the effect of age on straylight measured with the *C-Quant*, although it may increase beyond the middle of the fifth decade. The data presented in chapter 3, demonstrated a significant increase in straylight with age ($r = 0.457$, $r^2 = 0.209$, $P < 0.001$). Chapter 3 also investigated the effect of age on halo area using the Aston halometer for the first time. The results indicate that binocular halo area increases with age ($r = 0.449$, $r^2 = 0.202$, $P < 0.001$) in individuals with healthy eyes. The finding compares favourably with studies that have used alternative halometers such as the Vision monitor (Puell et al., 2014). Puell et al. (2013) reported a similar correlation for halo radius and age ($r = 0.65$, $r^2 = 0.42$, $P < 0.001$) as the monocular halometry mean radii results in the current study ($r_s = 0.405$,

$r^2 = 0.162$, $P < 0.001$). In chapter 3, subjective grading exhibited only a weak relationship with age ($r = 0.314$, $r^2 = 0.099$, $P < 0.001$), indicating that although both objective measures of dysphotopsia increased with age, subjective complaints do not concur with this finding. This important finding highlights the fact that photic effects may not subjectively trouble individuals with significant objective measures of dysphotopsia.

Dysphotopsia is a common cause of dissatisfaction after both corneal refractive surgery (Veraart *et al.*, 1992, Butuner *et al.*, 1994, Niesen *et al.*, 1997, Ghaith *et al.*, 1998, Fan-Paul *et al.*, 2002), and cataract surgery/refractive lens exchange (Tester *et al.*, 2000, Mamalis, 2010). Even after uneventful surgery, glare sensitivity is increased. For pseudophakic patients, multifocal IOLs cause increased complaints compared to monofocal IOLs (Leyland and Zinicola, 2003, Souza *et al.*, 2006, Woodward *et al.*, 2009, de Vries *et al.*, 2011, Chang *et al.*, 2012). There is a lack of data showing the time frame for improvement in visual quality after the various types of refractive surgery, with most studies only tracking changes to 6 months (Bournas et al., 2006, Lapid-Gortzak et al., 2010a, Rozema et al., 2010). In chapter 5, post-corneal refractive surgery, the data presented indicate that objectively, the process takes 12 months to recover (to levels observed in age-matched controls), whilst subjective recovery occurs in only 3 months. It is likely that a neural adaptation is occurring post-surgery (Fan-Paul et al., 2002). Clinically, the findings indicate that patients could be informed that by 3 months post-surgery, they are likely to be completely happy with their visual quality. In chapter 6, participants' halo area was assessed pre- and post-cataract surgery. As expected, there was a significant improvement in objective and subjective measures following cataract surgery with improvements in halo area continuing up to 6 months.

Despite the availability of many objective and subjective methods to measure dysphotopsia, no single method is in common use, nor are photic effects commonly measured prior to cataract or refractive surgery. The chapters in this thesis predominantly used *C-Quant* to measure straylight and the Aston halometer to quantify the size of the halo area. Where many previously published studies have carried out monocular halometry (Pieh *et al.*, 2001, Puell *et al.*, 2013), in chapters 2 and 3, both binocular and monocular measures were taken with halometry. Monocular halo area was found to be significantly larger (approximately 29 %) than the binocular area in this programme of research, indicating the effect of binocular summation on objective measures of halo area (chapter 2 and 3). Binocular measures may be more appropriate and representative of an individual's typical visual experience.

Often dysphotopsia is measured by placing a bright light source in the subjects' field of view (Williamson *et al.*, 1992, Elliott and Bullimore, 1993), and pupil diameter is known to decrease with increasing luminance (Laughlin, 1992, Winn *et al.*, 1994, Loewenfeld, 1999, Watson and Yellott, 2012, Orr *et al.*, 2015). Therefore, one might argue that pupil size will affect the assessments of dysphotopsia, as less retinal illuminance will occur. The pupil diameter also decreases with increasing age (Watson and Yellott, 2012; Kadlecova et al., 1958; Schaeffel et al., 1993; Winn et al., 1994). Many of the participants that will undergo dysphotopsia assessment are likely to be older adults, and will therefore be affected by senile miosis. When pupils are small, vision may be adversely affected by loss of retinal illumination (Campbell and Gubisch, 1966; Donnelly and Roorda, 2003). Equally, a smaller pupil may result in less retinal illumination, and VA improves with small pupils (Atchinson et al., 1979). This led to the question of whether pupil size should be measured or controlled in the measurement of dysphotopsia. The existing literature showed debate on whether pupil size affects the amount of dysphotopsia that is measured (Masket, 1992, Cahane et al., 1993, Whitaker et al., 1994, Franssen et al., 2007). It was apparent that it may be dependent on the device that is used to measure glare. In Chapter 4, for the first time, the study investigated whether pupil size has an effect on the size of the halo area when measured using halometry. No significant difference in halo area with the different simulated pupil sizes was detected. The results support the assertion that whilst a larger pupil allows more glaring light from the glare source to enter, the retinal illuminance is also changed by the stimulus (Whitaker *et al.*, 1994, Franssen *et al.*, 2007). More dark scenery enters the eye, thus counteracting the effect of the glaring light. The Aston halometer is a robust way to measure dysphotopsia without measuring or controlling pupil size. The findings are also likely to be more widely applicable to other halometers, which work on the principle of measuring the size of the glare scotoma arising from a glare source.

Subjective complaints of dysphotopsia were assessed using PIPP plates in the studies described in chapters 2, 3, 4 and 6. Using the PIPP plates to grade subjective experience of dysphotopsia found that the most common complaints were day halos, day starburst, night halos, night starburst and central flash (chapter 2). Aslam et al. (2007) reported a similar finding with a predominance of halos and starburst effects but also substantial symptoms of arc effect, streams of light, and central flash. The types of effects reported were more diverse than in chapter 2, whilst the severity was also greater. The reasons for this difference may be due to the longer time interval post-operatively used by Aslam *et al.* (2007), meaning that posterior capsular opacification may have a greater effect,

or the initial elation following a substantial improvement in visual quality with cataract surgery declines and individuals become aware of undesirable photic effects.

Previous studies in the field of photic phenomena have generally reported either objective or subjective measures only (Arnold, 1994, van den Berg, 1995, Dick *et al.*, 1999, Pieh *et al.*, 2001, Aslam *et al.*, 2004a, Puell *et al.*, 2013), largely without consideration of normal values in healthy eyes. The relationship between objective measures and subjective complaints is unknown in a normal population; despite conflicting evidence post IOL exchange where Dick *et al*. (1999) reported a correlation between subjective reports of halos and halo area, although very recently Buckhurst *et al*. (2017) stated that there is no correlation in pseudophakes. Chapter 2 established a lack of relationship between subjective and objective measures highlighting the difficulties in being able to predict the potential subjective complaints a patient may experience from an objective measure alone. Chapter 3 reported a weak relationship between halo area and grading of night halos severity. From this, it is clear that the perception of dysphotopsia is individual to each person. Some have a high objective measure of glare, however subjectively they may give a low score for glare effects. It is possible that these individuals have adapted to the glare that they experience and as such have no complaints of glare, or are less troubled by photic effects.

No relationship between halometry and *C-Quant* measurements was discovered in chapter 2, and it is likely to be due to the fact that both machines measure different aspects of glare; the *C-Quant* measures the amount of straylight in the eye (van den Berg, 1995), whereby, the halometer measures the actual size of the disability glare area experienced and is not based on forward scatter within the eye alone. Again, this would indicate that using one objective measure alone may not be enough to distinguish those who struggle with dysphotopsia. However, Puell *et al*. (2014) found a significant correlation between halo radius and straylight ($r = 0.45$, $r^2 = 0.203$, $P = 0.001$) in a cohort of similarly aged participants to the present study. This finding could be due to the fact that they measure halo area monocularly, or due to the difference in taking measurements of halo area, such as size of glare source, size of target and distance from glare source.

The subjective/objective ratio (glare effect ratio) was calculated to give a single value that combined both forms of measurement and indicated the level of subjective complaint compared to an objective measure. It is widely accepted that objective measures increase with age, therefore, it can be difficult to establish if an older patient has a high objective measure due to age alone. The glare effect ratio is independent of age, and as suggested

in chapter 2, a high glare effect ratio would indicate an individual more subjectively affected by a given objective measure.

The normal range of glare effect ratios that have been found could be used for comparison purposes pre- and post-refractive surgery as suggested in chapter 2 and 6. A larger study on subjective satisfaction after cataract surgery may be required as the individuals in chapter 6 were all very happy post-operatively. Further studies would confirm if this is a typical finding across NHS cataract patients. If cataract severity is graded at the pre-operative appointments, then it could be established whether there is a relationship between severity and subjective complaints post-surgery, as there is likely to be a larger improvement in symptoms for individuals with severe cataracts. Additionally, further work on how disabling photic effects due to cataracts are would provide valuable information. Therefore, clinically expected values of dysphotopsia with different types or varying levels of cataract could be complied and would provide additional information to VA measures. How photic effects change as cataracts develop is currently not well understood.

It has been noted that both the iris and sclera are partially responsible for intraocular scattering as they are not completely opaque, and allow some light to pass through (Ijspeert *et al.*, 1990, van den Berg *et al.*, 1991). The amount of light that can pass through is dependent on the level of pigmentation, whereby blue/green eyes with lower amounts of pigmentation would transmit and scatter more light than dark brown eyes (van den Berg *et al.*, 1991). When light reaches the retina, some of it is absorbed, whilst some is reflected back contributing to the intraocular scattering (van den Berg *et al.*, 1991); this type of scattering is also dependent on the subjects' level of pigmentation. This would lead you to believe that a participant's ethnicity or iris colour would affect the level of straylight and therefore, dysphotopsia experienced. Many papers have investigated dysphotopsia and glare, but they have not recorded nor taken into account ethnicity or iris colour. It could be said that ethnicity would likely impact on the levels of ocular pigment, but I would say that iris colour is the important detail to note as a few ethnicities may have brown or blue eyes. Franssen *et al.* (2007) reported a translucency value average of 0.30 mm^2 in four more lightly pigmented subjects, compared to 0.00 mm^2 in the brown-eyed individual. However, it was noted that the effect of translucency was more apparent for small pupil sizes when the scattering angle increases. Due to this, as we carry out halometry in the dark, and pupil sizes would be larger, the translucency may not have an effect. A future study comparing the levels of dysphotopsia in various coloured eyes or ethnic backgrounds would be interesting to ascertain if an effect is present.

A further study using multifocal IOLs may be a good comparison, as the cohort in chapter 6 were implanted with monofocal IOLs, and it is known that multifocal IOLs cause more dysphotopsia, therefore a comparison with monofocal IOLs may be nice. An alternative is to investigate the efficacy of the glare effect ratio in predicting post-operative dissatisfaction is by using multifocal contact lenses; this way glare effect ratios could be determined prior to lens wear and could be compared to subjective complaints of dysphotopsia with multifocal contact lens *in situ*. Therefore, allowing for a larger cohort as the effects will be reversible, unlike with multifocal IOL implantation.

Various limitations were present amongst the studies that were carried out. In future studies, it would be wise to avoid the use of contact lenses amongst glasses wearers when taking measurements, and perhaps, all should wear a trial frame, using plano lenses for those with no refractive error. A study investigating high powered contact lenses and their effect on measurements of dysphotopsia would be useful to find if there is an effect caused by the edge of the optic. If pupil sizes are to be controlled, then perhaps occluding contact lenses may work, but this is dependent on them sitting stably on the eye. It also suggested to measure the pupil size pre- and post-dilation, as it may give another dimension of analysis, and these should be measured with a pupilometer.

The glare effect ratio concept could be used by other researchers, if they establish normal values dependent on the objective measure (e.g. type of halometer) they employed.

7.2. Concluding statement

The investigations detailed in the thesis have explored some of the various ways to measure dysphotopsia both objectively and subjectively, which remain poorly understood, despite vast literary coverage of the subject. There is currently no gold standard to quantify dysphotopsia. Whilst this is the case, halometers are soon becoming a popular choice to calculate amounts of dysphotopsia objectively (Pieh *et al.*, 2001, Puell *et al.*, 2013, Sheppard *et al.*, 2013, Buckhurst *et al.*, 2015). The Aston halometer is a robust, relatively quick and easy to perform technique. The use of simulated images of dysphotopsia proved favourable amongst patients to establish their subjective complaints.

New information regarding linking objective and subjective grades to give a glare effect ratio could be useful to predict outcomes of refractive surgery if measures are taken pre-operatively. Using a combination of objective and subjective grades removes the variability in measurements that are associated with using subjective measures alone. Those with the highest glare effect ratios are most likely to perform poorly with multifocal IOLs. Having this information would be valuable to IOL manufacturers as distance and near

vision is good in multifocal IOLs, the only problematic effect is glare. Glare effect ratio can be used to predict subjective outcomes post-surgery; this could be an effective tool for surgeons. If there is a way to reduce the number of patients who suffer from these glare effects, there could be almost 100 % patient satisfaction. Subjective complaints reduce by 3 months post-refractive surgery, objective halo area take 6 months to resolve post-cataract surgery and up to 12 months post-corneal surgery. In addition to providing greater insight into several aspects of dysphotopsia associated with refractive surgery which are not fully understood, the findings detailed form a platform for numerous future investigations in an exciting and expansive field of research, the ultimate goal of which is the prediction of dysphotopsia complaints post-surgery and to better provide information on time scale of resolution of symptoms.

REFERENCES

Abrahamsson, M. and Sjostrand, J. (1986). Impairment of Contrast Sensitivity Function (CSF) as a Measure of Disability Glare. *Investigative Ophthalmology & Visual Science* **27**(7): 1131-1136.

Ahn, H., Kim, J. K., Kim, C. K., Han, G. H., Seo, K. Y., Kim, E. K. and Kim, T. I. (2011). Comparison of Laser in Situ Keratomileusis Flaps Created by 3 Femtosecond Lasers and a Microkeratome. *Journal of Cataract and Refractive Surgery* **37**(2): 349-357.

Akutsu, H., Legge, G. and Luebker, A. (1993). Multifocal Intraocular Lenses and Glare. *American Academy of Optometry* **70**(6): 487-495.

Alexandridis, E., Telger, T. and Blodi, F. C. (2012). *The Pupil*. New York, Springer.

Alfonso, J. F., Fernández-Vega, L., Valcárcel, B. and Montés-Micó, R. (2008). Visual Performance after Acrysof Restor Aspheric Intraocular Lens Implantation. *Journal of Optometry* **1**(1): 30-35.

Alio, J. L., Tavolato, M., De la Hoz, F., Claramonte, P., Rodriguez-Prats, J. L. and Galal, A. (2004). Near Vision Restoration with Refractive Lens Exchange and Pseudoaccommodating and Multifocal Refractive and Diffractive Intraocular Lenses: Comparative Clinical Study. *Journal of Cataract and Refractive Surgery* **30**(12): 2494-2503.

Allen, R., Ho-Yen, G. O., Beckingsale, A. B., Fitzke, F. W., Sciscio, A. G. and Saleh, G. M. (2009). Post-Capsulotomy Dysphotopsia in Monofocal Versus Multifocal Lenses. *Clinical and Experimental Optometry* **92**(2): 104-109.

Allen, R. J., Saleh, G. M., Litwin, A. S., Sciscio, A., Beckingsale, A. B. and Fitzke, F. W. (2008). Glare and Halo with Refractive Correction. *Clinical and Experimental Optometry* **91**(2): 156-160.

Ambrosio, R., Jr. and Wilson, S. (2003). LASIK Vs LASEK Vs PRK: Advantages and Indications. *Seminars in Ophthalmology* **18**(1): 2-10.

American Academy of Ophthalmology. (1993). Radial Keratotomy for Myopia. . *Ophthalmology* **100**(7): 1103-1115.

American Academy of Ophthalmology. (2013) "Refractive Errors & Refractive Surgery PPP - 2013." *AAO Refractive Management/Intervention PPP Panel.*

Applegate, R. A. and Gansel, K. A. (1990). The Importance of Pupil Size in Optical Quality Measurements Following Radial Keratotomy. *Journal of Refractive Surgery* **6**(1): 47-54.

Applegate, R. A. and Wolf, M. (1987). Disability Glare Increased by Hydrogel Lens Wear. *American Journal of Optometry and Physiological Optics* **64**(5): 309-312.

Armstrong, R. A. (2013). Statistical Guidelines for the Analysis of Data Obtained from One or Both Eyes. *Ophthalmic and Physiological Optics* **33**(1): 7-14.

Arnold, P. N. (1994). Photic Phenomena after Phacoemulsification and Posterior Chamber Lens Implantation of Various Optic Sizes. *Journal of Cataract and Refractive Surgery* **20**(4): 446-450.

Asbell, P. A., Dualan, I., Mindel, J., Brocks, D., Ahmad, M. and Epstein, S. (2005). Age-Related Cataract. *The Lancet* **365**(9459): 599-609.

Aslam, T. M. and Dhillon, B. (2004). Principles of Pseudophakic Photic Phenomena. *Ophthalmologica* **218**(1): 4-13.

Aslam, T. M., Dhillon, B., Tallentire, V. R., Patton, N. and Aspinal, P. (2004a). Development of a Forced Choice Photographic Questionnaire for Photic Phenomena and Its Testing-Repeatability, Reliability and Validity. *Ophthalmologica* **218**(6): 402-410.

Aslam, T. M., Gilmour, D., Hopkinson, S., Patton, N. and Aspinall, P. (2004b). The Development and Assessment of a Self-Perceived Quality of Vision Questionnaire to Test Pseudophakic Patients. *Ophthalmic Epidemiology* **11**(3): 241-253.

Aslam, T. M., Gupta, M., Gilmour, D., Patton, N. and Dhillon, B. (2007a). Long-Term Prevalence of Pseudophakic Photic Phenomena. *American Journal of Ophthalmology* **143**(3): 522-524.

Aslam, T. M., Haider, D. and Murray, I. J. (2007b). Principles of Disability Glare Measurement: An Ophthalmological Perspective. *Acta Ophthalmologica Scandinavica* **85**(4): 354-360.

Atchinson, D. A. and Smith, G. (2000). *Optics of the Human Eye. Oxford*. UK, Butterworth-Heinemann.

Atchison, D. A., Smith, G. and Efron, N. (1979). The Effect of Pupil Size on Visual Acuity in Uncorrected and Corrected Myopia. *American Journal of Optometry and Physiological Optics* **56**(5): 315-323.

Augusteyn, R. C. (2010). On the Growth and Internal Structure of the Human Lens. *Experimental Eye Research* **90**(6): 643-654.

Aychoua, N., Montolio, J. and Jansonius, N. M. (2013). Influence of Multifocal Intraocular Lenses on Standard Automated Perimetry Test Results. *JAMA Ophthalmology* **131**(4): 481-485.

Babizhayev, M. A., Minasyan, H. and Richer, S. P. (2009). Cataract Halos: A Driving Hazard in Aging Populations. Implication of the Halometer DG Test for Assessment of Intraocular Light Scatter. *Applied Ergonomics* **40**(3): 545-553.

Bailey, I. and Bullimore, M. (1991). A New Test for the Evaluation of Disability Glare. *American Academy of Optometry* **68**(12): 911-917.

Bailey, I. L. and Lovie, J. E. (1976). New Design Principles for Visual-Acuity Letter Charts. *American Journal of Optometry and Physiological Optics* **53**(11): 740-745.

Bailey, M. D. and Zadnik, K. (2007). Outcomes of LASIK for Myopia with FDA-Approved Lasers. *Cornea* **26**(3): 246-254.

Barisic, A., Dekaris, I., Gabric, N., Bohac, M., Romac, I., Mravicic, I. and Lazic, R. (2008). Comparison of Diffractive and Refractive Multifocal Intraocular Lenses in Presbyopia Treatment. *Collegium Antropologicum* **32**: 27-31.

Basting, D., Pippert, K. D. and Stamm, U. (2002). History and future prospects of excimer lasers. *Second International Symposium on Laser Precision Micromachining.* Singapore. SPIE Digital Library.

Bettelheim, F. A. and Ali, S. (1985). Light-Scattering of Normal Human Lens .3. Relationship between Forward and Back Scatter of Whole Excised Lenses. *Experimental Eye Research* **41**(1): 1-9.

Blaylock, J. F., Si, Z. and Vickers, C. (2006). Visual and Refractive Status at Different Focal Distances after Implantation of the Restor Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **32**(9): 1464-1473.

Bores, L. D. (1983). Historical Review and Clinical Results of Radial Keratotomy. *International Ophthalmology Clinics* **23**(3): 93-118.

Bourassa, C. M. and Wirtschafter, J. D. (1966). Mechanism of Binocular Increase of Discomfort to High Luminance. *Nature* **212**(5069): 1503-1504.

Bournas, P., Drazinos, S., Kanellas, D., Arvanitis, M. and Vaikoussis, E. (2007). Dysphotopsia after Cataract Surgery: Comparison of Four Different Intraocular Lenses. *Ophthalmologica* **221**(6): 378-383.

Boxer-Wachler, B. S., Durrie, D. S., Assil, K. K. and Krueger, R. R. (1999). Improvement of Visual Function with Glare Testing after Photorefractive Keratectomy and Radial Keratotomy. *American Journal of Ophthalmology* **128**(5): 582-587.

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., Yoo, S. and Comm, A. C. C. (2014). Multifocal Intraocular Lenses: Relative Indications and

Contraindications for Implantation. *Journal of Cataract and Refractive Surgery* **40**(2): 313-322.

Braunstein, R. E., Jain, S., McCally, R. L., Stark, W. J., Connolly, P. J. and Azar, D. T. (1996). Objective Measurement of Corneal Light Scattering after Excimer Laser Keratectomy. *Ophthalmology* **103**(3): 439-443.

Buckhurst, P. J. (2011). Evaluation of Modern Intraocular Lenses. *PhD Thesis*, Aston University.

Buckhurst, P. J., Naroo, S. A., Davies, L. N., Shah, S., Buckhurst, H., Kingsnorth, A., Drew, T. and Wolffsohn, J. S. (2015). Tablet App Halometer for the Assessment of Dysphotopsia. *Journal of Cataract and Refractive Surgery* **41**: 2424-2429.

Buckhurst, P. J., Naroo, S. A., Davies, L. N., Shah, S., Drew, T. and Wolffsohn, J. S. (2017). Assessment of Dysphotopsia in Pseudophakic Subjects with Multifocal Intraocular Lenses. *BMJ Open Ophthalmology* **1**(1).

Bullough, J. D. (2009). Spectral Sensitivity for Extrafoveal Discomfort Glare. *Journal of Modern Optics* **56**(13): 1518-1522.

Burke, T. R. and Benjamin, L. (2014). Sulcus-Fixated Intraocular Lens Implantation for the Management of Negative Dysphotopsia. *Journal of Cataract and Refractive Surgery* **40**(9): 1469-1472.

Butuner, Z., Elliott, D. B., Gimbel, H. V. and Slimmon, S. (1994). Visual Function One-Year after Excimer-Laser Photorefractive Keratectomy. *Journal of Refractive and Corneal Surgery* **10**(6): 625-630.

Buznego, C. and Trattler, W. B. (2009). Presbyopia-Correcting Intraocular Lenses. *Current Opinion in Ophthalmology* **20**(1): 13-18.

Cahane, M., Glovinsky, J. and Blumenthal, M. (1993). Glare Disability. *Journal of Cataract and Refractive Surgery* **19**(1): 112.

Calladine, D., Evans, J. R., Shah, S. and Leyland, M. (2012). Multifocal Versus Monofocal Intraocular Lenses after Cataract Extraction. *Cochrane Database Systemic Review* **9**.

Campbell, F. W. and Gubisch, R. W. (1966). Optical Quality of the Human Eye. *The Journal of Physiology* **186**(3): 558-578.

Castro, J. J., Jiménez, J. R., Ortiz, C., Alarcón, A. and Anera, R. G. (2011). New Testing Software for Quantifying Discrimination Capacity in Subjects with Ocular Pathologies. *Journal of Biomedical Optics* **16**(1): 015001.

Cervino, A., Montes-Mico, R. and Hosking, S. L. (2008). Performance of the Compensation Comparison Method for Retinal Straylight Measurement: Effect of Patient's Age on Repeatability. *British Journal of Ophthalmology* **92**(6): 788-791.

Cervino, A., Villa-Collar, C., Gonzalez-Meijome, J. M., Ferrer-Blasco, T. and Garcia-Lazaro, S. (2011). Retinal Straylight and Light Distortion Phenomena in Normal and Post-LASIK Eyes. *Graefe's Archive of Clinical Experimental Ophthalmology* **249**(10): 1561-1566.

Chan, A. and Manche, E. E. (2011). Effect of Preoperative Pupil Size on Quality of Vision after Wavefront-Guided LASIK. *Ophthalmology* **118**(4): 736-741.

Chandramani, A. and Riaz, K. M. (2017). “Management of Positive Dysphotopsia in a Patient with Prior Refractive Surgery.” *Canadian Journal of Ophthalmology / Journal Canadien d'Ophtalmologie*. ***In Press***.

Chang, J. S., Ng, J. C. and Lau, S. Y. (2012). Visual Outcomes and Patient Satisfaction after Presbyopic Lens Exchange with a Diffractive Multifocal Intraocular Lens. *Journal of Refractive Surgery* **28**(7): 468-474.

Chang, S. W., Benson, A. and Azar, D. T. (1998). Corneal Light Scattering with Stromal Reformation after Laser in Situ Keratomileusis and Photorefractive Keratectomy. *Journal of Cataract and Refractive Surgery* **24**(8): 1064-1069.

Charman, W. N. (1997). Vision and Driving - a Literature Review and Commentary. *Ophthalmic and Physiological Optics* **17**(5): 371-391.

Chehade, M. and Elder, M. (2009). Intraocular lens materials and styles: A Review. *Clinical and Experimental Ophthalmology* **25**(3): 255-263.

Cheng, J.-W., Wei, R.-L., Cai, J.-P., Xi, G.-L., Zhu, H., Li, Y. and Ma, X.-Y. (2007). Efficacy of Different Intraocular Lens Materials and Optic Edge Designs in Preventing Posterior Capsular Opacification: A Meta-Analysis. *American Journal of Ophthalmology* **143**(3): 428-436.

Chylack, L. T., 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. *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.

Cionni, R. J., Chang, D. F., Donnenfeld, E. D., Lane, S. S., McCulley, J. P. and Solomon, K. D. (2009). Clinical Outcomes and Functional Visual Performance: Comparison of the Restor Apodised Diffractive Intraocular Lens to a Monofocal Control. *British Journal of Ophthalmology* **93**(9): 1215-1219.

Cobb, P. W. (1911). The Influence of Illumination of the Eye on Visual Acuity. *American Journal of Ophthalmology* **29**: 76-99.

College of Optometrists. "Tropicamide Information Leaflet." *Patient leaflets* Retrieved 13th November 2015, from http://www.college-optometrists.org/en/utilities/document-summary.cfm/docid/4F12D11A-614C-452F-BFF1340EAC1E7A44.

Cooke, D. L., Kasko, S. and Platt, L. O. (2013). Resolution of Negative Dysphotopsia after Laser Anterior Capsulotomy. *Journal of Cataract and Refractive Surgery* **39**(7): 1107-1109.

Coppens, J. E., Franssen, L., van Rijn, L. J. and van den Berg, T. J. T. P. (2006). Reliability of the Compensation Comparison Stray-Light Measurement Method. *Journal of Biomedical Optics* **11**(3): 34027.

Corbett, M. C., Prydal, J. I., Verma, S., Oliver, K. M., Pande, M. and Marshall, J. (1996). An in Vivo Investigation of the Structures Responsible for Corneal Haze after Photorefractive Keratectomy and Their Effect on Visual Function. *Ophthalmology* **103**(9): 1366-1380.

Costello, M. J., Johnsen, S., Gilliland, K. O., Freel, C. D. and Fowler, W. C. (2007). Predicted Light Scattering from Particles Observed in Human Age-Related Nuclear Cataracts Using Mie Scattering Theory. *Investigative Ophthalmology & Visual Science* **48**(1): 303-312.

Davison, J. A. (2000). Positive and Negative Dysphotopsia in Patients with Acrylic Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **26**(9): 1346-1355.

Davison, J. A. (2002). Clinical Performance of Alcon Sa30al and Sa60at Single-Piece Acrylic Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **28**(7): 1112-1123.

Davison, J. A. and Simpson, M. J. (2006). History and Development of the Apodized Diffractive Intraocular Lens. *Journal of Cataract and Refractive Surgery* **32**(5): 849-858.

De Brouwere, D., Ginis, H., Kymionis, G., Naoumidi, I. and Pallikaris, I. (2008). Forward Scattering Properties of Corneal Haze. *Optometry and Vision Science* **85**(9): 843-848.

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.

de Vries, N. E., Webers, C. A., Montes-Mico, R., Ferrer-Blasco, T. and Nuijts, R. M. (2010). Visual Outcomes after Cataract Surgery with Implantation of a +3.00 D or +4.00 D Aspheric Diffractive Multifocal Intraocular Lens: Comparative Study. *Journal of Cataract and Refractive Surgery* **36**(8): 1316-1322.

de Vries, N. E., Webers, C. A., Touwslager, W. R., Bauer, N. J., de Brabander, J., Berendschot, T. T. and Nuijts, R. M. (2011). Dissatisfaction after Implantation of Multifocal Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **37**(5): 859-865.

de Vries, N. E., Webers, C. A. B., Montes-Mico, R., Tahzib, N. G., Cheng, Y. Y. Y., de Brabander, J., Hendrikse, F. and Nuijts, R. M. M. A. (2008). Long-Term Follow-up of a Multifocal Apodized Diffractive Intraocular Lens after Cataract Surgery. *Journal of Cataract and Refractive Surgery* **34**(9): 1476-1482.

de Wit, G. and Coppens, J. E. (2003). Straylight of Spectacle Lenses Compared with Straylight in the Eye. *Optometry and Vision Science* **80**: 395-400.

Delaye, M., Clark, J. I. and Benedek, G. B. (1982). Identification of the Scattering Elements Responsible for Lens Opacification in Cold Cataracts. *Biophysical Journal* **37**(3): 647-656.

Dewaard, P. W. T., Ijspeert, J. K., van den Berg, T. and Dejong, P. (1992). Intraocular Light-Scattering in Age-Related Cataracts. *Investigative Ophthalmology & Visual Science* **33**(3): 618-625.

Dick, H. B., Krummenauer, F., Schwenn, O., Krist, R. and Pfeiffer, N. (1999). Objective and Subjective Evaluation of Photic Phenomena after Monofocal and Multifocal Intraocular Lens Implantation. *Ophthalmology* **106**(10): 1878-1886.

Donachie, P. H., Sparrow, J. M. and Johnston, R. L. (2016). Year 1 Annual Report - Piloting of the National Ophthalmology Database Audit Methodology. National Ophthalmology Database Audit. T. R. C. o. Optometrist. London.

Donaldson, K. E., Braga-Mele, R., Cabot, F., Davidson, R., Dhaliwal, D. K., Hamilton, R., Jackson, M., Patterson, L., Stonecipher, K. and Yoo, S. H. (2013). Femtosecond Laser–Assisted Cataract Surgery. *Journal of Cataract and Refractive Surgery* **39**(11): 1753-1763.

Donnelly, W. J., Pesudovs, K., Marsack, J. D., Sarver, E. J. and Applegate, R. A. (2004). Quantifying Scatter in Shack-Hartmann Images to Evaluate Nuclear Cataract. *Journal of Refractive Surgery* **20**(5): S515-S522.

Eisenmann, D., Jacobi, F. K., Dick, B., Jacobi, K. W. and Pabst, W. (1996). Glare Sensitivity in Patients with Phakic and Pseudophakic Eyes. *Klinische Monatsblatter Fur Augenheilkunde* **208**(2): 87-92.

Elliot, R. H. (1924). A Halometer. *British Medical Journal* **1**(3301): 624.

Elliott, D. B. (1993). Evaluating Visual Function in Cataract. *Optometry and Vision Science* **70**(11): 896-902.

Elliott, D. B. and Bullimore, M. A. (1993). Assessing the Reliability, Discriminative Ability, and Validity of Disability Glare Tests. *Investigative Ophthalmology & Visual Science* **34**(1): 108-119.

Elliott, D. B., Bullimore, M. A. and Bailey, I. L. (1991). Improving the Reliability of the Pelli-Robson Contrast Sensitivity Test. *Clinical Vision Sciences* **6**(6): 471-475.

Elliott, D. B. and Hurst, M. A. (1990). Simple Clinical Techniques to Evaluate Visual Function in Patients with Early Cataract. *Optometry and Vision Science* **67**(11): 822-825.

Elliott, D. B., Hurst, M. A. and Weatherill, J. (1990). Comparing Clinical-Tests of Visual Function in Cataract with the Patients Perceived Visual Disability. *Eye* **4**: 712-717.

Ellis, M. F. (2001). Sharp-Edged Intraocular Lens Design as a Cause of Permanent Glare. *Journal of Cataract and Refractive Surgery* **27**(7): 1061-1064.

Ewbank, A. (2010). Ten Years of Trends in UK Refractive Surgery. Optician (2010) Available online at: https://www.opticianonline.net/features/ten-years-of-trends-in-uk-refractive-surgery Accessed 10th August 2017.

Fan-Paul, N. I., Li, J., Miller, J. S. and Florakis, G. J. (2002). Night Vision Disturbances after Corneal Refractive Surgery. *Survey of Ophthalmology* **47**(6): 533-546.

Fankhauser, F., 2nd (2007). Postoperative Follow up by Dynamic Light Scattering: Detection of Inflammatory Molecular Changes in the Cornea, the Vitreous and the Lens.

Technology and Health Care : Official Journal of the European Society for Engineering and Medicine **15**(4): 247-258.

Farbowitz, M. A., Zabriskie, N. A., Crandall, A. S., Olson, R. J. and Miller, K. M. (2000). Visual Complaints Associated with the Acrysof Acrylic Intraocular Lens. *Journal of Cataract and Refractive Surgery* **26**(9): 1339-1345.

Fekete, J., Sik-Lanyi, C. and Schanda, J. (2010). Spectral Discomfort Glare Sensitivity Investigations. *Ophthalmic and Physiological Optics* **30**(2): 182-187.

Ferrer-Blasco, T., Garcia-Lazaro, S., Albarran-Diego, C., Belda-Salmeron, L. and Montes-Mico, R. (2012). Refractive Lens Exchange with a Multifocal Diffractive Aspheric Intraocular Lens. *Arquivos Brasileiros De Oftalmologia* **75**(3): 192-196.

Folden, D. V. (2013). Neodymium:Yag Laser Anterior Capsulectomy: Surgical Option in the Management of Negative Dysphotopsia *Journal of Cataract and Refractive Surgery* **39** (7): 1110-1115.

Franssen, L., Coppens, J. E. and van den Berg, T. J. (2006). Compensation Comparison Method for Assessment of Retinal Straylight. *Investigative Ophtalmology & Visual Science* **47**(2): 768-776.

Franssen, L., Tabernero, J., Coppens, J. E. and van den Berg, T. J. T. P. (2007). Pupil Size and Retinal Straylight in the Normal Eye. *Investigative Ophthalmology & Visual Science* **48**(5): 2375-2382.

Fujimoto, K., Honda, K., Wada, Y. R., Tanaka, M. and Irie, T. (2010). Four-Year Experience with a Silicone Refractive Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **36**(8): 1330-1335.

Fujisawa, K. and Sasaki, K. (1995). Changes in Light-Scattering Intensity of the Transparent Lenses of Subjects Selected from Population-Based Surveys Depending on Age - Analysis through Scheimpflug Images. *Ophthalmic Research* **27**(2): 89-101.

Galor, A., Gonzalez, M., Goldman, D. and O'Brien, T. P. (2009). Intraocular Lens Exchange Surgery in Dissatisfied Patients with Refractive Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **35**(10): 1706-1710.

Gatinel, D., Pagnoulle, C., Houbrechts, Y. and Gobin, L. (2011). Design and Qualification of a Diffractive Trifocal Optical Profile for Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **37**(11): 2060-2067.

Ghaith, A. A., Daniel, J., Stulting, R. D., Thompson, K. P. and Lynn, M. (1998). Contrast Sensitivity and Glare Disability after Radial Keratotomy and Photorefractive Keratectomy. *Archives of Ophthalmology* **116**(1): 12-18.

Gil-Cazorla, R., Shah, S. and Naroo, S.A. (2016). A Review of the Surgical Options for the Correction of Presbyopia. *British Journal of Ophthalmology* **100**(1): 62-70.

Gilliland, K. O., Freel, C. D., Lane, C. W., Fowler, W. C. and Costello, M. J. (2001). Multilamellar Bodies as Potential Scattering Particles in Human Age-Related Nuclear Cataracts. *Molecular Vision* **7**(18): 120-130.

Gilliland, K. O., Johnsen, S., Metlapally, S., Costello, M. J., Ramamurthy, B., Krishna, P. V. and Balasubramanian, D. (2008). Mie Light Scattering Calculations for an Indian Age-Related Nuclear Cataract with a High Density of Multilamellar Bodies. *Molecular Vision* **14**(70-72): 572-582.

Ginsburg, A. P., Osher, R. P., Blauvelt, K. and Blosser, E. (1987). The Assessment of Contrast and Glare Sensitivity in Patients Having Cataracts. *Investigative Ophthalmology & Visual Science* **28**(3 Suppl): 397-397.

Gobbi, P. G., Fasce, F., Bozza, S., Calori, G. and Brancato, R. (2007). Far and near Visual Acuity with Multifocal Intraocular Lenses in an Optomechanical Eye Model with Imaging Capability. *Journal of Cataract and Refractive Surgery* **33**(6): 1082-1094.

Goes, F. J. (2008). Refractive Lens Exchange with the Diffractive Multifocal Tecnis Zm900 Intraocular Lens. *Journal of Refractive Surgery* **24**(3): 243-250.

Gothwal, V. K., Wright, T. A., Lamoureux, E. L. and Pesudovs, K. (2009). Using Rasch Analysis to Revisit the Validity of the Cataract Type Spec Instrument for Measuring Cataract Surgery Outcomes. *Journal of Cataract and Refractive Surgery* **35**(9): 1509-1517.

Greenwood, M., Bafna, S. and Thompson, V. (2016). Surgical correction of presbyopia: lenticular, corneal, and scleral approaches. *International Ophthalmology Clinics* **56**(3): 149-166.

Guber, I., Bachmann, L. M., Guber, J., Bochmann, F., Lange, A. P. and Thiel, M. A. (2011). Reproducibility of Straylight Measurement by C-Quant for Assessment of Retinal Straylight Using the Compensation Comparison Method. *Graefe's Archive for Clinical and Experimental Ophthalmology* **249**(9): 1367-1371.

Guillon, M., Dumbleton, K., Theodoratos, P., Gobbe, M., Wooley, C. B. and Moody, K. (2016). The Effects of Age, Refractive Status, and Luminance on Pupil Size. *Optometry and Vision Science* **93**(9): 1093-1100.

Gutierrez, R., Jimenez, J. R., Villa, C., Valverde, J. A. and Anera, R. G. (2003). Simple Device for Quantifying the Influence of Halos after LASIK Surgery. *Journal Biomedical Optics* **8**(4): 663-667.

Haag-Strait. "Bangerter Graded Occulsion Foil." Retrieved 9th January, 2014, from https://eshop.haagstreituk.com/products/orthoptic-equipment/bangerter-occlusion-foils/bangerter-graded-occlusion-foil.

Hahn, D. W. (2006). Light Scattering Theory. *Department of Mechanical and Aeorospace Engineering, University of Florida*.

Hard, A. L., Abrahamsson, M. and Sjostrand, J. (1990). A New Glare Test Based on Low Contrast Letters - Evaluation in Cataract Patients. *Acta Ophthalmologica* **68**(2): 145-150.

Haring, G., Dick, H. B., Krummenauer, F., Weissmantel, U. and Kroncke, W. (2001). Subjective Photic Phenomena with Refractive Multifocal and Monofocal Intraocular Lenses

- Results of a Multicenter Questionnaire. *Journal of Cataract and Refractive Surgery* **27**(2): 245-249.

Harman, F. E., Maling, S., Kampougeris, G., Langan, L., Khan, I., Lee, N. and Bloom, P. A. (2008). Comparing the 1cu Accommodative, Multifocal, and Monofocal Intraocular Lenses: A Randomized Trial. *Ophthalmology* **115**(6): 993-1001

Harmon, D. R. (2011). The LASIK market: yesterday's technology or poised for recovery? Cataract and Refractive Surgery Today. Available online at: https://crstoday.com/articles/2011-aug/the-lasik-market-yesterdays-technology-or-poised-for-recovery/. Accessed 20th July 2018.

Harrison, J. M., Applegate, R. A., Yates, J. T. and Ballentine, C. (1993). Contrast Sensitivity and Disability Glare in the Middle Years. *Journal of the Optical Society of America* **10**(8): 1849-1855.

Hartmann, E. and Wehmeyer, K. (1980). Investigation of Mesopic Vision and Sensitivity to Glare by Means of the New Nyktometer. *Klinische Monatsblatter Fur Augenheilkunde* **176**(5): 859-863.

Hawker, M. J., Madge, S. N., Baddeley, P. A. and Perry, S. R. (2005). Refractive Expectations of Patients Having Cataract Surgery. *Journal of Cataract and Refractive Surgery* **31**(10): 1970-1975.

Hayashi, K., Hayashi, H., Nakao, F. and Hayashi, F. (2001). Correlation between Pupillary Size and Intraocular Lens Decentration and Visual Acuity of a Zonal-Progressive Multifocal Lens and a Monofocal Lens. *Ophthalmology* **108**(11): 2011-2017.

Hayashi, K., Manabe, S. and Hayashi, H. (2009a). Visual Acuity from Far to near and Contrast Sensitivity in Eyes with a Diffractive Multifocal Intraocular Lens with a Low Addition Power. *Journal of Cataract and Refractive Surgery* **35**(12): 2070-2076.

Hayashi, K., Masumoto, M. and Hayashi, H. (2009b). All-Distance Visual Acuity in Eyes with a Nontinted or a Yellow-Tinted Diffractive Multifocal Intraocular Lens. *Japanese Journal of Ophthalmology* **53**(2): 100-106.

He, L. and Manche, E. E. (2014). Prospective Randomized Contralateral Eye Evaluation of Subjective Quality of Vision after Wavefront-Guided or Wavefront- Optimized Photorefractive Keratectomy. *Journal of Refractive Surgery* **30**(1): 6-12.

Hemenger, R. P. (1996). Dependence on Angle and Wavelength of Light Scattered by the Ocular Lens. *Ophthalmic and Physiological Optics* **16**(3): 237-238.

Hersh, P. S., Brint, S. F., Maloney, R. K., Durrie, D. S., Gordon, M., Michelson, M. A., Thompson, V. M., Berkeley, R. B., Schein, O. D. and Steinert, R. F. (1998). Photorefractive keratectomy versus laser in situ keratomileusis for moderate to high myopia – A randomized prospective study. *Ophthalmology* **105**(8): 1512-1522.

Hindman, H. B., McCally, R. L., Myrowitz, E., Terry, M. A., Stark, W. J., Weinberg, R. S. and Jun, A. S. (2007). Evaluation of Deep Lamellar Endothelial Keratoplasty Surgery Using Scatterometry and Wavefront Analyses. *Ophthalmology* **114**(11): 2006-2012.

Hirsch, R., Nadler, M. and Miller, D. (1984). Glare Measurement as a Predictor of Outdoor Vision among Cataract Patients. *Annals of Ophthalmology* **16**(10): 965-968.

Hofmann, T., Zuberbuhler, B., Cervino, A., Montés-Micó, R. and Haefliger, E. (2009). Retinal Straylight and Complaint Scores 18 Months after Implantation of the Acrysof Monofocal and Restor Diffractive Intraocular Lenses. *Journal of Refractive Surgery* **25**(6): 485-492.

Hohberger, B., Laemmer, R., Adler, W., Juenemann, A. G. M. and Horn, F. K. (2007). Measuring Contrast Sensitivity in Normal Subjects with Optec (R) 6500: Influence of Age and Glare. *Graefes Archive for Clinical and Experimental Ophthalmology* **245**(12): 1805-1814.

Holden, R., Hesler, J., Forbes, J. and Brown, N. A. P. (1993). Visual Performance and Objectively Measured Grades of Cataract - a Correlation of Methods Designed Far Use in Longitudinal Trials. *Optometry and Vision Science* **70**(11): 982-985.

Holladay, J. T., Dudeja, D. R. and Chang, J. (1999a). Functional vision and corneal changes after laser in situ keratomileusis determined by contrast sensitivity, glare testing, and corneal topography. *Journal of Cataract and Refractive Surgery* **25**(5): 663-669.

Holladay, J. T., Lang, A. and Portney, V. (1999b). Analysis of Edge Glare Phenomena in Intraocular Lens Edge Designs. *Journal of Cataract and Refractive Surgery* **25**(6): 748-752.

Holladay, J. T., Prager, T. C., Trujillo, J. and Ruiz, R. S. (1987). Brightness Acuity Test and Outdoor Visual Acuity in Cataract Patients. *Journal of Cataract and Refractive Surgery* **13**(1): 67-69.

Holladay, L. L. (1926). The Fundamentals of Glare and Visibility. *Journal of the Optical Society of America and Review of Scientific Instruments* **12**(4): 271-319.

Hollick, E. J., Spalton, D. J., Ursell, P. G., Pande, M. V., Barman, S. A., Boyce, J. F. and Tilling, K. (1999). The Effect of Polymethylmethacrylate, Silicone, and Polyacrylic Intraocular Lenses on Posterior Capsular Opacification 3 Years after Cataract Surgery. *Ophthalmology* **106**(1): 49-55.

Hood, C. T. and Sugar, A. (2015). Subjective Complaints after Cataract Surgery: Common Causes and Management Strategies. *Current Opinion in Ophthalmology* **26**(1): 45-49.

Hopkinson, R. G. (1957). Light Energy and Brightness Sensation. *Nature* **179**(4568): 1026-1027.

Hovath, K., Constantinescu, D., Vultur, F. and Mühlfay, G. (2014). Premium Intraocular Lenses: Patient Satisfaction. *Acta Medica Transilvanica* **19**(2): 228-230.

Huetz, W. W., Eckhardt, H. B., Roehrig, B. and Grolmus, R. (2006). Reading Ability with 3 Multifocal Intraocular Lens Models. *Journal of Cataract and Refractive Surgery* **32**(12): 2015-2021.

Hunkeler, J. D., Coffman, T. M., Paugh, J., Lang, A., Smith, P. and Tarantino, N. (2002). Characterization of Visual Phenomena with the Array Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **28**(7): 1195-1204.

Ijspeert, J. K., Dewaard, P. W. T., van den Berg, T. and Dejong, P. (1990). The Intraocular Straylight Function in 129 Healthy-Volunteers - Dependence on Angle, Age and Pigmentation. *Vision Research* **30**(5): 699-707.

Ijspeert, J. K. and van den Berg, T. (1992). Design of a Portable Straylight Meter. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society*.

Ivarsen, A., Fledelius, W. and Hjortdal, J. Ø. (2009). Three-Year Changes in Epithelial and Stromal Thickness after PRK or LASIK for High Myopia. *Investigative Ophthalmology & Visual Science* **50**(5): 2061-2066.

Jabbur, N. S., Sakatani, K. and O'Brien, T. P. (2004). Survey of Complications and Recommendations for Management in Dissatisfied Patients Seeking a Consultation after Refractive Surgery. *Journal of Cataract and Refractive Surgery* **30**(9): 1867-1874.

Jacobi, F. K., Kammann, J., Jacobi, K. W., Grosskopf, U. and Walden, K. (1999). Bilateral Implantation of Asymmetrical Diffractive Multifocal Intraocular Lenses. *Archives of Ophthalmology* **117**(1): 17-23.

Jacobi, P. C., Dietlein, T. S., Lueke, C. and Jacobi, F. K. (2003). Multifocal Intraocular Lens Implantation in Patients with Traumatic Cataract. *Ophthalmology* **110**(3): 531-538.

Jain, S., Khoury, J. M., Chamon, W. and Azar, D. T. (1995). Corneal Light-Scattering after Laser in-Situ Keratomileusis and Photorefractive Keratectomy. *American Journal of Ophthalmology* **120**(4): 532-534.

Javitt, J. C., Jacobson, G. and Schiffman, R. M. (2003). Validity and reliability of the Cataract TyPE Spec: an instrument for measuring outcomes of cataract extraction. *Americal Journal of Ophthalmology* **136**(2): 285-90.

Javitt, J. C. and Steinert, R. F. (2000). Cataract Extraction with Multifocal Intraocular Lens Implantation - a Multinational Clinical Trial Evaluating Clinical, Functional, and Quality-of-Life Outcomes. *Ophthalmology* **107**(11): 2040-2047.

Javitt, J. C., Wang, F., Trentacost, D. J., Rowe, M. and Tarantino, N. (1997). Outcomes of Cataract Extraction with Multifocal Intraocular Lens Implantation - Functional Status and Quality of Life. *Ophthalmology* **104**(4): 589-599.

Kadlecova, V., Peleska, M. and Vasko, A. (1958). Dependence on Age of the Diameter of the Pupil in the Dark. *Nature* **182**(4648): 1520-1521.

Kaji, Y., Obata, H., Usui, T., Soya, K., Machinami, R., Tsuru, T. and Yamashita, H. (1998). Three-dimensional organisation of collagen fibrils during corneal stromal wound healing after excimer laser keratectomy. *Journal of Cataract and Refractive Surgery* **24**(11): 1441-1446.

Kamiya, K., Hayashi, K., Shimizu, K., Negishi, K., Sato, M., Bissen-Miyajima, H., of the Japanese, S. W. G. and of Cataract, S. (2014). Multifocal Intraocular Lens Explantation: A Case Series of 50 Eyes. *American Journal of Ophthalmology* **158**(2): 215-220.

Katlun, T. and Wiegand, W. (1998). Changes in Glare and Contrast Sensitivity after PRK. *Ophthalmologe* **95**(6): 420-426.

Kaufman, P. L., Alm, A. and Adler, F. H. (2003). *Adler's Physiology of the Eye: Clinical Application - Chapter 7*. Mosby.

Kawamorita, T., Uozato, H., Aizawa, D., Kamiya, K. and Shimizu, K. (2009). Optical Performance in Rezoom and Array Multifocal Intraocular Lenses in Vitro. *Journal of Refractive Surgery* **25**(5): 467-469.

Kershner, R. M. (2011). Neuroadaptation and Premium Iols: What Does the Brain Think. *Ophthalmology Management* **15**(12): 51-54.

Kiel, A. W., Butler, T. and Alwitry, A. (2003). Visual Acuity and Legal Visual Requirement to Drive a Passenger Vehicle. *Eye* **17**(5): 579-582.

Kinard, K., Jarstad, A. and Olson, R. J. (2013). Correlation of Visual Quality with Satisfaction and Function in a Normal Cohort of Pseudophakic Patients. *Journal of Cataract and Refractive Surgery* **39**(4): 590-597.

Knorz, M. C. (1993). Vision with Bifocal Intraocular Lenses. *German Journal of Ophthalmology* **2**(1): 32-41.

Koch, D. D. (1989). Glare and Contrast Sensitivity Testing in Cataract Patients. *Journal of Cataract and Refractive Surgery* **15**(2): 158-164.

Koch, D. D., Samuelson, S. W., Haft, E. A. and Merin, L. M. (1991). Pupillary Size and Responsiveness - Implications for Selection of a Bifocal Intraocular-Lens. *Ophthalmology* **98**(7): 1030-1035.

Kohnen, T., Allen, D., Boureau, C., Dublineau, P., Hartmann, C., Mehdorn, E., Rozot, P. and Tassinari, G. (2006). European Multicenter Study of the Acrysof Restor Apodized Diffractive Intraocular Lens. *Ophthalmology* **113**(4): 578-584.e1.

Kymionis, G. D., Tsiklis, N., Pallikaris, A. I., Bouzoukis, D. I. and Pallikaris, I. G. (2007). Fifteen-Year Follow-up after LASIK: Case Report. *Journal of Refractive Surgery* **23**(9): 937-940.

Lackner, B., Pieh, S., Schmidinger, G., Hanselmayer, G., Simader, C., Reitner, A. and Skorpik, C. (2003). Glare and Halo Phenomena after Laser in Situ Keratomileusis. *Journal of Cataract and Refractive Surgery* **29**(3): 444-450.

Lahey, E., Ijspeert, J. K., van den Berg, T. and Kijlstra, A. (1993). Quantitative-Analysis of Iris Translucency in Fuchs Heterochromic Cyclitis. *Investigative Ophthalmology & Visual Science* **34**(10): 2931-2942.

Lapid-Gortzak, R., van der Linden, J. W., van der Meulen, I., Nieuwendaal, C. and van den Berg, T. (2010a). Straylight Measurements in Laser in Situ Keratomileusis and Laser-Assisted Subepithelial Keratectomy for Myopia. *Journal of Cataract and Refractive Surgery* **36**(3): 465-471.

Lapid-Gortzak, R., van der Linden, J. W., van der Meulen, I. J., Nieuwendaal, C. P., Mourits, M. P. and van den Berg, T. J. (2010b). Straylight before and after Hyperopic Laser in Situ Keratomileusis or Laser-Assisted Subepithelial Keratectomy. *Journal of Cataract and Refractive Surgery* **36**(11): 1919-1924.

Laughlin, S. B. (1992). Retinal Information Capacity and the Function of the Pupil. *Ophthalmic and Physiological Optics* **12**(2): 161-164.

Le Claire, J., Nadler, M. P., Weiss, S. and Miller, D. (1982). A New Glare Tester for Clinical-Testing - Results Comparing Normal Subjects and Variously Corrected Aphakic Patients. *Archives of Ophthalmology* **100**(1): 153-158.

Lennie, P., Pokorny, J. and Smith, V. C. (1993). Luminance. *Journal of the Optical Society of America A-Optics Image Science and Vision* **10**(6): 1283-1293.

Leyland, M. and Pringle, E. (2006). Multifocal Versus Monofocal Intraocular Lenses after Cataract Extraction. *Cochrane Database of Systematic Reviews*(4).

Leyland, M. and Zinicola, E. (2003). Multifocal Versus Monofocal Intraocular Lenses in Cataract Surgery. *Ophthalmology* **110**(9): 1789-1798.

Leysen, I., Bartholomeeusen, E., Coeckelbergh, T. and Tassignon, M.-J. B. (2009). Surgical Outcomes of Intraocular Lens Exchange: Five-Year Study. *Journal of Cataract and Refractive Surgery* **35**(6): 1013-1018.

Lichtinger, A. and Rootman, D. S. (2012). Intraocular Lenses for Presbyopia Correction: Past, Present, and Future. *Current Opinion in Ophthalmology* **23**(1): 40-46.

Lleo Perez, A., Alonso Munoz, L., Sanchis Gimeno, J. A., Marcos Jorge, M. A. and Rahhal, M. S. (2003). Comparative Clinical Study of Visual Results between Two Different Types of Bifocal Intraocular Lenses. *Archivos de la Sociedad Espanola de Oftalmologia* **78**(12): 665-673.

Loewenfeld, I. (1999). *The Pupil: Anatomy, Physiology, and Clinical Applications*, Butterworth-Heinemann.

Lohmann, C. P., Fitzke, F., Obrart, D., Muir, M. K., Timberlake, G. and Marshall, J. (1993). Corneal Light-Scattering and Visual Performance in Myopic Individuals with Spectacles, Contact-Lenses, or Excimer Laser Photorefractive Keratectomy. *American Journal of Ophthalmology* **115**(4): 444-453.

Lohmann, C. P., Gartry, D. S., Muir, M. K., Timberlake, G. T., Fitzke, F. W. and Marshall, J. (1991). Corneal Haze after Excimer Laser Refractive Surgery: Objective Measurements and Functional Implications. *European Journal of Ophthalmology* **1**(4): 173-180.

Lorente-Velazquez, A., Nieto-Bona, A., Collar, C. V. and Gutierrez Ortega, A. R. (2010). Intraocular Straylight and Contrast Sensitivity (1/2) and 6 Months after Laser in Situ Keratomileusis. *Eye and Contact Lens* **36**(3): 152-155.

MacLachlan, C. and Howland, H. C. (2002). Normal Values and Standard Deviations for Pupil Diameter and Interpupillary Distance in Subjects Aged 1 Month to 19 Years. *Ophthalmic and Physiological Optics* **22**(3): 175-182.

Magno, B. V., Datiles, M. B., Lasa, M. S. M., Fajardo, M. R. Q., Caruso, R. C. and KaiserKupfer, M. I. (1997). Evaluation of Visual Function Following Neodymium:Yag Laser Posterior Capsulotomy. *Ophthalmology* **104**(8): 1287-1293.

Mainster, M. A. and Turner, P. L. (2012). Glare's Causes, Consequences, and Clinical Challenges after a Century of Ophthalmic Study. *American Journal of Ophthalmology* **153**(4): 587-593.

Makhotkina, N. Y., Berendschot, T. T. J. M., Beckers, H. J. M. and Nuijts, R. M. M. A. (2015). Treatment of Negative Dysphotopsia with Supplementary Implantation of a Sulcus-Fixated Intraocular Lens. *Graefe's Archive for Clinical and Experimental Ophthalmology* **253**(6): 973-977.

Mamalis, N. (2000). Complications of Foldable Intraocular Lenses Requiring Explanation or Secondary Intervention--1998 Survey. *Journal of Cataract and Refractive Surgery* **26**(5): 766-772.

Mamalis, N. (2010). Negative Dysphotopsia Following Cataract Surgery. *Journal of Cataract and Refractive Surgery* **36**(3): 371-372.

Mantyjarvi, M. and Tuppurainen, K. (1999). Cataract in Traffic. *Graefes Archive for Clinical and Experimental Ophthalmology* **237**(4): 278-282.

Marcos, S. and Burns, S. A. (2000). On the Symmetry between Eyes of Wavefront Aberration and Cone Directionality. *Vision Research* **40**(18): 2437-2447.

Market Scope. (2016). "Global Demand for Refractive Surgery Growing as Economic Conditions Improve, Myopia Rises." Retrieved 31st August 2018, 2017, from https://market-scope.com/pressrelease/global-demand-for-refractive-surgery-growing-as-economic-conditions-improve-myopia-rises/.

Marshall, J., Trokel, S., Rothery, S. and Schubert, H. (1985). An Ultrastructural Study of Corneal Incisions Induced by an Excimer Laser at 193 nm. *Ophthalmology* **92**(6): 749-58.

Marshall, J., Trokel, S., Rothery, S. and Krueger, R. (1986). A comparative study of corneal incisions induced by diamond and steel knives and two ultraviolet radiations from an excimer laser. *British Journal of Ophthalmology* **70**(7): 482-501.

Masket, S. (1992). Relationship between Postoperative Pupil Size and Disability Glare. *Journal of Cataract and Refractive Surgery* **18**(5): 506-507.

Masket, S. and Fram, N. R. (2011). Pseudophakic Negative Dysphotopsia: Surgical Management and New Theory of Etiology. *Journal of Cataract and Refractive Surgery* **37**(7): 1199-1207.

Maxwell, W. A., Cionni, R. J., Lehmann, R. P. and Modi, S. S. (2009). Functional Outcomes after Bilateral Implantation of Apodized Diffractive Aspheric Acrylic Intraocular Lenses with a + 3.0 or + 4.0 Diopter Addition Power Randomized Multicenter Clinical Study. *Journal of Cataract and Refractive Surgery* **35**(12): 2054-2061.

Maxwell, W. A. and Nordan, L. T. (1991). *Current Concepts of Multifocal Intraocular Lenses*. Michigan, SLACK.

McAlinden, C., Pesudovs, K. and Moore, J. E. (2010). The Development of an Instrument to Measure Quality of Vision: The Quality of Vision (Qov) Questionnaire. *Investigative Ophthalmology & Visual Science* **51**(11): 5537-5545.

McCally, R. L. and Farrell, R. A. (1982). Structural Implications of Small-Angle Light-Scattering from Cornea. *Experimental Eye Research* **34**(1): 99-113.

McCally, R. L., Freund, D. E., Zorn, A., Bonney-Ray, J., Grebe, R., de la Cruz, Z. and Green, W. R. (2007). Light-Scattering and Ultrastructure of Healed Penetrating Corneal Wounds. *Investigative Ophthalmology & Visual Science* **48**(1): 157-165.

McDonald, J. H. (2014a). *Handbook of Biological Statistics (3rd Ed.)*. Baltimore, Maryland, Sparky House Publishing**:** 145 - 156.

Meacock, W. R., Spalton, D. J. and Khan, S. (2002). The Effect of Texturing the Intraocular Lens Edge on Postoperative Glare Symptoms - a Randomized, Prospective, Double-Masked Study. *Archives of Ophthalmology* **120**(10): 1294-1298.

Meikies, D., van der Mooren, M., Terwee, T., Guthoff, R. F. and Stachs, O. (2013). Rostock Glare Perimeter: A Distinctive Method for Quantification of Glare. *Optometry and Vision Science* **90**(10): 1143-1148.

Michael, R. and Bron, A. J. (2011). The Ageing Lens and Cataract: A Model of Normal and Pathological Ageing. *Philosophical Transactions of the Royal Society B: Biological Sciences* **366**(1568): 1278-1292.

Miller, D., Molnar, S., Wolf, E., Newman, J. and Jernigan, M. E. (1972). Laboratory Evaluation of a Clinical Glare Tester. *Archives of Ophthalmology* **87**(3): 324-332.

Montes-Mico, R., Espana, E., Bueno, I., Charman, W. N. and Menezo, J. L. (2004). Visual Performance with Multifocal Intraocular Lenses - Mesopic Contrast Sensitivity under Distance and near Conditions. *Ophthalmology* **111**(1): 85-96.

Munnerly, C. R., Koons, S. J. and Marshall, J. (1988). Photorefractive keratectomy: a technique for laser refractive surgery. *Journal of Cataract and Refractive Surgery* **14**(1): 46-52.

Munoz, G., Albarran-Diego, C., Ferrer-Blasco, T., Sakla, H. F. and Garcia-Lazaro, S. (2011). Visual Function after Bilateral Implantation of a New Zonal Refractive Aspheric Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **37**(11): 2043-2052.

Nadler, D. J., Jaffe, N. S., Clayman, H. M., Jaffe, M. S. and Luscombe, S. M. (1984). Glare Disability in Eyes with Intraocular Lenses. *American Journal of Ophthalmology* **97**(1): 43-47.

Nadler, M. P., Miller, D. and Nadler, D. J. (1990). *Glare and Contrast Sensitivity for Clinicians*. New York, Springer-Verlag.

Namiki, M. and Tagami, Y. (1993). Perimetric Glare Test and Evaluation of Intraocular Lenses. *Nippon Ganka Gakkai Zasshi* **97**(2): 210-216.

Narisada, K. and Schreuder, D. (2004). *Light Pollution Handbook*. Dordrecht, Springer.

Naroo, S. A. and Bilkhu, P. S. (2016). Clinical utility of the KAMRA corneal inlay. *Clinical Ophthalmology* **10**: 913-919.

Neumann, A. C., McCarty, G. R., Locke, J. and Cobb, B. (1988). Glare Disability Devices for Cataractous Eyes: A Consumer's Guide. *Journal of Cataract and Refractive Surgery* **14**(2): 212-216.

Niesen, U., Businger, U., Hartmann, P., Senn, P. and Schipper, I. (1997). Glare Sensitivity and Visual Acuity after Excimer Laser Photorefractive Keratectomy for Myopia. *British Journal of Ophthalmology* **81**(2): 136-140.

Obrart, D. P. S., Gartry, D. S., Lohmann, C. P., Muir, M. G. K and Marshall, J. (1994). Excimer-laser photorefractive keratectomy for myopia – comparison of 4.00-millimeter and 5.00-millimeter ablation zones. *Journal of Refractive and Corneal Surgery* **10**(2): 87-94.

O'Doherty, M., O'Keeffe, M. and Kelleher, C. (2006). Five Year Follow up of Laser in Situ Keratomileusis for All Levels of Myopia. *British Journal of Ophthalmology* **90**(1): 20-23.

Odell, N. V., Leske, D. A., Hatt, S. R., Adams, W. E. and Holmes, J. M. (2008). The Effect of Bangerter Filters on Optotype Acuity, Vernier Acuity, and Contrast Sensitivity. *Journal of AAPOS* **12**(6): 555-559.

Olsen, H. and Andersen, J. (1991). Contrast Sensitivity in Radial Keratotomy. *Acta Ophthalmologica* **69**(5): 654-658.

Olsen, T. (1982). Light-Scattering from the Human Cornea. *Investigative Ophthalmology & Visual Science* **23**(1): 81-86.

Orr, J. B., Seidel, D., Day, M. and Gray, L. S. (2015). Is Pupil Diameter Influenced by Refractive Error? *Optometry and Vision Science* **92**(7): 834-840.

Osher, R. H. (2008). Negative Dysphotopsia: Long-Term Study and Possible Explanation for Transient Symptoms. *Journal of Cataract and Refractive Surgery* **34**(10): 1699-1707.

Packer, M., Chu, Y. R., Waltz, K. L., Donnenfeld, E. D., Wallace, R. B., III, 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.

Pager, C. K. (2004). Expectations and Outcomes in Cataract Surgery. *Archives of Ophthalmology* **122**(12): 1788-1792.

Palomo-Álvarez, C. and Puell, M. C. (2015). Capacity of Straylight and Disk Halo Size to Diagnose Cataract. *Journal of Cataract and Refractive Surgery* **41**(10): 2069-2074.

Pascolini, D. and Mariotti, S. P. (2012). Global Estimates of Visual Impairment: 2010. *British Journal of Ophthalmology* **96**(5): 614-618.

Patel, S. V., McLaren, J. W., Hodge, D. O. and Bourne, W. M. (2008). The Effect of Corneal Light Scatter on Vision after Penetrating Keratoplasty. *American Journal of Ophthalmology* **146**(6): 913-919.

Patel, S. V., Winter, E. J., McLaren, J. W. and Bourne, W. M. (2007). Objective Measurement of Backscattered Light from the Anterior and Posterior Cornea in Vivo. *Investigative Ophthalmology & Visual Science* **48**(1): 166-172.

Pelli, D. G., Robson, J. G. and Wilkins, A. J. (1988). The Design of a New Letter Chart for Measuring Contrast Sensitivity. *Clinical Vision Sciences* **2**(3): 187-199.

Pepose, J. S. (2008). Maximizing Satisfaction with Presbyopia-Correcting Intraocular Lenses: The Missing Links. *American Journal of Ophthalmology* **146**(5): 641-648.

Pepose, J. S., Qazi, M. A., Davies, J., Doane, J. F., Loden, J. C., Sivalingham, V. and Mahmoud, A. M. (2007). Visual Performance of Patients with Bilateral Vs Combination Crystalens, Rezoom, and Restor Intraocular Lens Implants. *American Journal of Ophthalmology* **144**(3): 347-357.

Perez, G. M., Archer, S. M. and Artal, P. (2010). Optical Characterization of Bangerter Foils. *Investigative Ophthalmology & Visual Science* **51**(1): 609-613.

Pieh, S., Lackner, B., Hanselmayer, G., Zöhrer, R., Sticker, M., Weghaupt, H., Fercher, A. and Skorpik, C. (2001). Halo Size under Distance and near Conditions in Refractive Multifocal Intraocular Lenses. *British Journal of Ophthalmology* **85**(7): 816-821.

Pieh, S., Marvan, P., Lackner, B., Hanselmayer, G., Schmidinger, G., Leitgeb, R., Sticker, M., Hitzenberger, C. K., Fercher, A. F. and Shorpik, C. (2002). Quantitative Performance of Bifocal and Multifocal Intraocular Lenses in a Model Eye - Point Spread Function in Multifocal Intraocular Lenses. *Archives of Ophthalmology* **120**(1): 23-28.

Piñero, D. P., Alio, J. L. and Ortiz, D. (2010). Ocular Scattering. *Optometry and Vision Science* **87**(9): E682-E696.

Pipe, D. M., Rapley, L. J. and Opticians, A. o. B. D. (1997). Ocular Anatomy and Histology, Association of British Dispensing Opticians.

Plainis, S., Murray, I. J. and Carden, D. (2006). The Dazzle Reflex: Electrophysiological Signals from Ocular Muscles Reveal Strong Binocular Summation Effects. *Ophthalmic and Physiological Optics* **26**(3): 318-325.

Pop, M. and Payette, Y. (2004). Risk Factors for Night Vision Complaints after LASIK for Myopia. *Ophthalmology* **111**(1): 3-10.

Prager, T. C., Urso, R. G., Holladay, J. T. and Stewart, R. H. (1989). Glare Testing in Cataract Patients - Instrument Evaluation and Identification of Sources of Methodological Error. *Journal of Cataract and Refractive Surgery* **15**(2): 149-157.

Prager, T. C., Urso, R. G., Lewis, J. W. and Ruiz, R. S. (1988). Methodological Considerations in Glare Testing in Patients with Cataracts. *Archives of Ophthalmology* **106**(11): 1501-1502.

Puell, M. C., Perez-Carrasco, M. J., Barrio, A., Antona, B. and Palomo-Alvarez, C. (2013). Normal Values for the Size of a Halo Produces by a Glare Source. *Journal of Refractive Surgery* **29**: 618-622.

Puell, M. C., Pérez-Carrasco, M. J., Palomo-Alvarez, C., Antona, B. and Barrio, A. (2014). Relationship between Halo Size and Forward Light Scatter. *British Journal of Ophthalmology* **98**(10): 1389-1392.

Qian, W. (2000). Angular Change in Backscattering of Light from the Human Lens with Nuclear Cataract. *Eye* **14**: 56-60.

Qian, W., Soderberg, P., Lindstrom, B., Chen, E. P., Magnius, K. and Philipson, B. (1994). Spatial-Distribution of Back Scattering in the Nuclear-Area of the Non-Cataractous Human Lens. *Eye* **8**: 524-529.

Radmall, B. R., Floyd, A., Oakey, Z. and Olson, R. J. (2015). Refractive Index and Its Impact on Pseudophakic Dysphotopsia. *Clinical Ophthalmology (Auckland, N.Z.)* **9**: 1353-1358.

Ranney, T. A., Simmons, L. A. and Masalonis, A. J. (2000). The Immediate Effects of Glare and Electrochromic Glare-Reducing Mirrors in Simulated Truck Driving. *Human Factors* **42**(2): 337-347.

Rapuano, C. J., Sugar, A., Koch, D. D., Agapitos, P. J., Culbertson, W. W., de Luise, V. P., Huang, D. and Varley, G. A. (2001). Intrastromal Corneal Ring Segments for Low Myopia: A Report by the American Academy of Ophthalmology. *Ophthalmology* **108**(10): 1922-1928.

Rau, M. and Bach, C. (2003). Initial Results Obtained with the Multifocal Lens MF4. *Klinische Monatsblatter Fur Augenheilkunde* **220**(1-2): 24-28.

Rea, M. S., Radetsky, L. C. and Bullough, J. D. (2011). Toward a Model of Outdoor Lighting Scene Brightness. *Lighting Research and Technology* **43**(1): 7-30.

Reeves, B. C., Wood, J. M. and Hill, A. R. (1991). Vistech VCTS 6500 Charts - Within-Session and Between-Session Reliability. *Optometry and Vision Science* **68**(9): 728-737.

Regan, D. (1991). The Charles F. Prentice Award Lecture 1990 - Specific Tests and Specific Blindnesses - Keys, Locks, and Parallel Processing. *Optometry and Vision Science* **68**(7): 489-512.

Rossetti, L., Carraro, F., Rovati, M. and Orzalesi, N. (1994). Performance of Diffractive Multifocal Intraocular Lenses in Extracapsular Cataract-Surgery. *Journal of Cataract and Refractive Surgery* **20**(2): 124-128.

Rozema, J. J., Coeckelbergh, T., van den Berg, T. J., Trau, R., Duchateau, N. C., Lemmens, S. and Tassignon, M. J. (2010a). Straylight Before and After LASEK in Myopia: Changes in Retinal Straylight. *Investigative Ophthalmology & Visual Science* **51**(5): 2800-2804.

Rozema, J. J., van den Berg, T. J. T. P. and Tassignon, M.-J. (2010b). Retinal Straylight as a Function of Age and Ocular Biometry in Healthy Eyes. *Investigative Ophthalmology & Visual Science* **51**(5): 2795-2799.

Rubin, G. S. (1990). Contrast Sensitivity and Glare Testing in the Evaluation of Anterior Segment Disease. *Ophthalmology* **97**(9): 1233-1237.

Rubin, G. S., Adamsons, I. A. and Stark, W. J. (1993). Comparison of Acuity, Contrast Sensitivity, and Disability Glare Before and After Cataract-Surgery. *Archives of Ophthalmology* **111**(1): 56-61.

Rubin, G. S., Bandeen-Roche, K., Huang, G. H., Munoz, B., Schein, O. D., Fried, L. P., West, S. K. and Team, S. E. E. P. (2001). The Association of Multiple Visual Impairments with Self-Reported Visual Disability: See Project. *Investigative Ophthalmology & Visual Science* **42**(1): 64-72.

Ruth, A. L., Lynn, M. J., Randleman, J. B. and Stulting, R. D. (2008). Blade Source Effect on Laser in Situ Keratomileusis Flap Thickness with the Amadeus I Microkeratome. *Journal of Cataract and Refractive Surgery* **34**(3): 407-410.

Sakimoto, T., Rosenblatt, M. I. and Azar, D. T. (2006). Laser Eye Surgery for Refractive Errors. *Lancet* **367**(9520): 1432-1447.

Schaeffel, F., Wilhelm, H. and Zrenner, E. (1993). Inter-Individual Variability in the Dynamics of Natural Accommodation in Humans: Relation to Age and Refractive Errors. *The Journal of Physiology* **461**: 301-320.

Schallhorn, J. M., Schallhorn, S. C., Hettinger, K. and Hannan, S. (2017). Infectious Keratitis after Laser Vision Correction: Incidence and Risk Factors. *Journal of Cataract and Refractive Surgery* **43**(4): 473-479.

Schallhorn, S. C., Kaupp, S. E., Tanzer, D. J., Tidwell, J., Laurent, J. and Bourque, L. B. (2003). Pupil Size and Quality of Vision after LASIK. *Ophthalmology* **110**(8): 1606-1614.

Schena, L. (2005). Refractive Lens Exchange Debate. The Best of Refractive Surgery - A Digest of Recent Articles. AAO Annual Meeting Chicago October 15 - 18 2005, EyeNet Selections.

Schmidinger, G., Geitzenauer, W., Hahsle, B., Klemen, U.-M., Skorpik, C. and Pieh, S. (2006). Depth of Focus in Eyes with Diffractive Bifocal and Refractive Multifocal Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **32**(10): 1650-1656.

Schreuder, D. A. (2008). *Outdoor Lighting: Physics, Vision and Perception*. Berlin, Springer Science + Business Media.

Schwiegerling, J. (2006). Recent Developments in Pseudophakic Dysphotopsia. *Current Opinion in Ophthalmology* **17**(1): 27-30.

Sedgewick, J. H., Orillac, R. and Link, C. (2002). Array Multifocal Intraocular Lens in a Charity Hospital Training Program - a Resident's Experience. *Journal of Cataract and Refractive Surgery* **28**(7): 1205-1210.

Sekundo, W., Bonicke, K., Mattausch, P. and Wiegand, W. (2003). Six-Year Follow-up of Laser in Situ Keratomileusis for Moderate and Extreme Myopia Using a First-Generation

Excimer Laser and Microkeratome. *Journal of Cataract and Refractive Surgery* **29**(6): 1152-1158.

Sheppard, A. L. and Davies, L. N. (2010). Clinical Evaluation of the Grand Seiko Auto Ref/Keratometer Wam-5500. *Ophthalmic and Physiological Optics* **30**(2): 143-151.

Sheppard, A. L., Shah, S., Bhatt, U., Bhogal, G. and Wolffsohn, J. S. (2013). Visual Outcomes and Subjective Experience after Bilateral Implantation of a New Diffractive Trifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **39**(3): 343-349.

Shoji, N. and Shimizu, K. (1996). Clinical Evaluation of a 5.5mm Three-Zone Refractive Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **22**: 1097-1101.

Simmons, B. (2000, 19/07/17). "Mathwords: Terms and Formulas from Algebra I to Calculus." Retrieved 04/08/2017, 2017, from http://www.mathwords.com/o/outlier.htm.

Slagsvold, J. E. (2000). 3m Diffractive Multifocal Intraocular Lens: Eight Year Follow-Up. *Journal of Cataract and Refractive Surgery* **26**(3): 402-407.

Smith, G. (2002). Disability Glare and Its Clinical Significance. Optometry Today. London. **42:** 34-37.

Smith, G. T. H., Smith, R. C., Brown, N. A. P., Bron, A. J. and Harris, M. L. (1992). Changes in Light Scatter and Width Measurements from the Human Lens Cortex with Age. *Eye* **6**: 55-59.

Snell, R. S. and Lemp, M. A. (1997). *Clinical Anatomy of the Eye (2nd Ed.)*. Washington, Wiley.

Snyder, A. W. and Pask, C. (1973). Stiles-Crawford Effect - Explanation and Consequences. *Vision Research* **13**(6): 1115-1137.

Solomon, K. D., de Castro, L. E. F., Sandoval, H. P., Biber, J. M., Groat, B., Neff, K. D., Ying, M. S., French, J. W., Donnenfeld, E. D. and Lindstrom, R. L. (2009). LASIK World Literature Review: Quality of Life and Patient Satisfaction. *Ophthalmology* **116**(4): 691-701.

Souza, C. E., Muccioli, C., Soriano, E. S., Chalita, M. R., Oliveira, F., Freitas, L. L., Meire, L. P., Tamaki, C. and Belfort, R., Jr. (2006). Visual Performance of Acrysof Restor Apodized Diffractive Iol: A Prospective Comparative Trial. *American Journal of Ophthalmology* **141**(5): 827-832.

Steinert, R. F., Aker, B. L., Trentacost, D. J., Smith, P. J. and Tarantino, N. (1999). A Prospective Comparative Study of the Amo Array Zonal-Progressive Multifocal Silicone Intraocular Lens and a Monofocal Intraocular Lens. *Ophthalmology* **106**(7): 1243-1255.

Stiles, W. S. (1929). The Effect of Glare on the Brightness Difference Threshold. *Proceedings of the Royal Society of London Series B-Containing Papers of a Biological Character* **104**(731): 322-351.

Sugar, A., Rapuano, C. J., Culbertson, W. W., Huang, D., Varley, G. A., Agapitos, P. J., de Luise, V. P. and Koch, D. D. (2002). Laser in Situ Keratomileusis for Myopia and Astigmatism: Safety and Efficacy: A Report by the American Academy of Ophthalmology. *Ophthalmology* **109**(1): 175-187.

Sukhovolskiy, G. (2015) "Can't Get No Satisfaction: Post-Cataract Surgery Dysphotopsias." *Review of Optometry*.

Tan, J. C. H., Spalton, D. J. and Arden, G. B. (1998). Comparison of Methods to Assess Visual Impairment from Glare and Light Scattering with Posterior Capsule Opacification. *Journal of Cataract and Refractive Surgery* **24**(12): 1626-1631.

Tang, D. X., Borchman, D., Schwarz, A. K., Yappert, M. C., Vrensen, G., van Marle, J. and DuPre, D. B. (2003). Light Scattering of Human Lens Vesicles in Vitro. *Experimental Eye Research* **76**(5): 605-612.

Taylor, H. R. (2000). Cataract: How Much Surgery Do We Have to Do?. *British Journal of Ophthalmology* **84**(1): 1-2.

Terwee, T., Weeber, H., van der Mooren, M. and Piers, P. (2008). Visualization of the Retinal Image in an Eye Model with Spherical and Aspheric, Diffractive, and Refractive Multifocal Intraocular Lenses. *Journal of Refractive Surgery* **24**(3): 223-232.

Tester, R., Pace, N. L., Samore, M. and Olson, R. J. (2000). Dysphotopsia in Phakic and Pseudophakic Patients: Incidence and Relation to Intraocular Lens Type. *Journal of Cataract and Refractive Surgery* **26**(6): 810-816.

Thaung, J. and Sjostrand, J. (2002). Integrated Light Scattering as a Function of Wavelength in Donor Lenses. *Journal of the Optical Society of America* **19**(1): 152-157.

Theeuwes, J., Alferdinck, J. and Perel, M. (2002). Relation between Glare and Driving Performance. *Human Factors* **44**(1): 95-107.

Tobaigy, F. M., Ghanem, R. C., Sayegh, R. R., Hallak, J. A. and Azar, D. T. (2006). A Control-Matched Comparison of Laser Epithelial Keratomileusis and Laser in Situ Keratomileusis for Low to Moderate Myopia. *American Journal of Ophthalmology* **142**(6): 901-908.

Trattler, W. B., Whitsett, J. C. and Simone, P. A. (2005). Negative Dysphotopsia after Intraocular Lens Implantation Irrespective of Design and Material. *Journal of Cataract and Refractive Surgery* **31**(4): 841-845.

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.

Trokel, S. L., Srinivasan, R. and Braren, B. (1983). Excimer laser surgery of the cornea. *American Journal of Ophthalmology* **96**(6): 710-715.

Tuan, K. M. and Liang, J. (2006). Improved Contrast Sensitivity and Visual Acuity after Wavefront-Guided Laser in Situ Keratomileusis: In-Depth Statistical Analysis. *Journal of Cataract and Refractive Surgery* **32**(2): 215-220.

Valle, P. J., Oti, J. E., Canales, V. F. and Cagigal, M. P. (2005). Visual Axial PSF of Diffractive Trifocal Lenses. *Optics Express* **13**(7): 2782-2792.

Valverde, J. A. and Gonza, R. (2003). Simple Device for Quantifying the Influence of Halos after LASIK Surgery. *Journal of Biomedical Optics* **8**(4): 663-667.

van de Hulst, H. C. (2012). *Light Scattering by Small Particles*. Dover Publications.

van den Berg, T. (2017). The (Lack of) Relation between Straylight and Visual Acuity. Two Domains of the Point-Spread-Function. *Ophthalmic and Physiological Optics* **37**(3): 333-341.

van den Berg, T. J. (1986). Importance of Pathological Intraocular Light Scatter for Visual Disability. *Documenta Ophthalmologica* **61**(3-4): 327-333.

van den Berg, T. J. (1994). On the Relation between Intraocular Straylight and Visual Function Parameters. *Investigative Ophthalmology & Visual Science* **35**(6): 2659-2660.

van den Berg, T. J. (1995). Analysis of Intraocular Straylight, Especially in Relation to Age. *Optometry and Vision Science* **72**(2): 52-59.

van den Berg, T. J. (2004). "Practical Guide for Operating the Oculus C-Quant Straylight Meter [Online]." Retrieved 6th November 2013, from http://www.oculus.de/en/downloads/dyn/sonstige/sonstige/c_quant_guide.pdf.

van den Berg, T. J., Franssen, L. and Coppens, J. E. (2009). Straylight in the Human Eye: Testing Objectivity and Optical Character of the Psychophysical Measurement. *Ophthalmic and Physiological Optics* **29**(3): 345-350.

van den Berg, T. J., Hwan, B. S. and Delleman, J. W. (1993). The Intraocular Straylight Function in Some Hereditary Corneal Dystrophies. *Documenta Ophthalmologica* **85**(1): 13-19.

van den Berg, T. J. and Ijspeert, J. K. (1991). Intraocular Straylight, Studied Using the Direct Compensation Technique. *CIE Proceedings*, Vienna.

van den Berg, T. J. and IJspeert, J. K. (1992). Clinical Assessment of Intraocular Stray Light. *Applied Optics* **31**(19): 3694-3696.

van den Berg, T. J. and Ijspeert, J. K. (1995). Light-Scattering in Donor Lenses. *Vision Research* **35**(1): 169-177.

van den Berg, T. J., Ijspeert, J. K., de Waard, P. W. and Meire, F. (1990). Functional Quantification of Diaphany. *Documenta Ophthalmologica* **75**(3-4): 239-246.

van den Berg, T. J., Ijspeert, J. K. and Dewaard, P. W. T. (1991). Dependence of Intraocular Straylight on Pigmentation and Light Transmission through the Ocular Wall. *Vision Research* **31**(7-8): 1361-1367.

van den Berg, T. J., van Rijn, L. J., Franssen, L., Coppens, J. E., Kaper-Bongers, R., Vonhoff, D., Volker-Dieben, H. J., Grabner, G., Nischler, C., Emesz, M., Wilhelm, H., Gamer, D. and Schuster, A. (2003). Assessment of Visual Function of Driving Licence Holders. I-TREN E3 200/7/SI2.282826. EU Project.

van den Berg, T. J., van Rijn, L. J., Michael, R., Heine, C., Coeckelbergh, T., Nischler, C., Wilhelm, H., Grabner, G., Emesz, M., Barraquer, R. I., Coppens, J. E. and Franssen, L. (2007). Straylight Effects with Aging and Lens Extraction. *American Journal of Ophthalmology* **144**(3): 358-363.

van den Berg, T. J. T. P. (1991). On the Relation between Glare and Straylight. *Documenta Ophthalmologica* **78**(3-4): 177-182.

van den Berg, T. J. T. P., Franssen, L., Kruijt, B. and Coppens, J. E. (2013). History of Ocular Straylight Measurement: A Review. *Zeitschrift fur Medizinische Physik* **23**(1): 6-20.

van der Heijde, G. L., Weber, J. and Roukes, R. (1985). Effects of Straylight on Visual Acuity in Pseudophakia. *Documenta Ophthalmologica* **59**(1): 81-84.

van der Linden, J. W., van Velthoven, M., van der Meulen, I., Nieuwendaal, C., Mourits, M. and Lapid-Gortzak, R. (2012). Comparison of a New-Generation Sectorial Addition Multifocal Intraocular Lens and a Diffractive Apodized Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **38**(1): 68-73.

van der Meulen, I. J., Gjertsen, J., Kruijt, B., Witmer, J. P., Rulo, A., Schlingemann, R. O. and van den Berg, T. J. (2012). Straylight Measurements as an Indication for Cataract Surgery. *Journal of Cataract and Refractive Surgery* **38**(5): 840-848.

van Rijn, L. J., Nischler, C., Gamer, D., Franssen, L., de Wit, G., Kaper, R., Vonhoff, D., Grabner, G., Wilhelm, H., Volker-Dieben, H. J. and van den Berg, T. (2005). Measurement of Stray Light and Glare: Comparison of Nyktotest, Mesotest, Stray Light Meter, and Computer Implemented Stray Light Meter. *British Journal of Ophthalmology* **89**(3): 345-351.

van Rijn, L. J., Nischler, C., Michael, R., Heine, C., Coeckelbergh, T., Wilhelm, H., Grabner, G., Barraquer, R. I. and van den Berg, T. J. (2011). Prevalence of Impairment of Visual Function in European Drivers. *Acta Ophthalmologica* **89**(2): 124-131.

Varley, G. A., Huang, D., Rapuano, C. J., Schallhorn, S., Boxer-Wachler, B. S. and Sugar, A. (2004). LASIK for Hyperopia, Hyperopic Astigmatism, and Mixed Astigmatism: A Report by the American Academy of Ophthalmology. *Ophthalmology* **111**(8): 1604-1617.

Veraart, H. G., van den Berg, T. J., Hennekes, R. and Adank, A. M. (1993). Stray Light in Photorefractive Keratectomy for Myopia. *Bulletin de la Societe belge d'ophtalmologie* **249**: 57-62.

Veraart, H. G. N., van den Berg, T., Ijspeert, J. K. and Cardozo, O. L. (1992). Stray Light in Radial Keratotomy and the Influence of Pupil Size and Straylight Angle. *American Journal of Ophthalmology* **114**(4): 424-428.

Verriest, G. and Uvijls, A. (1989). Disability Glare in Normal and Diseased Eyes. *Clinical Vision Sciences* **4**(3): 253-256.

Villa, C., Gutierrez, R., Jimenez, J. R. and Gonzalez-Meijome, J. M. (2007). Night Vision Disturbances after Successful LASIK Surgery. *British Journal of Ophthalmology* **91**(8): 1031-1037.

Vingolo, E. M., Grenga, P., Iacobelli, L. and Grenga, R. (2007). Visual Acuity and Contrast Sensitivity: Acrysof Restor Apodized Diffractive Versus Acrysof Sa60at Monofocal Intraocular Lenses. *Journal of Cataract and Refractive Surgery* **33**(7): 1244-1247.

Vitale, S., Ellwein, L., Cotch, M., Ferris, F. L., Iii and Sperduto, R. (2008). Prevalence of Refractive Error in the United States, 1999-2004. *Archives of Ophthalmology* **126**(8): 1111-1119.

Vos, J. J. (1984). Disability Glare - a State of the Art Report. *CIE J* **3**: 39-53.

Vos, J. J. (2003a). On the Cause of Disability Glare and Its Dependence on Glare Angle, Age and Ocular Pigmentation. *Clinical and Experimental Optometry* **86**(6): 363-370.

Vos, J. J. (2003b). Reflections on Glare. *Lighting Research and Technology* **35**(2): 163-175.

Vos, J. J. and van den Berg, T. J. (1999). Report on Disability Glare. *CIE Collection* **135**: 1-9.

Walker, H. K., Hall, W. D. and Hurst, J. W. (1983). *Clinical Methods: The History, Physical, and Laboratory Examinations*. Elsevier Science & Technology Books.

Walkow, T., Liekfeld, A., Anders, N., Pham, D. T., Hartmann, C. and Wollensak, J. (1997). A Prospective Evaluation of a Diffractive Versus a Refractive Designed Multifocal Intraocular Lens. *Ophthalmology* **104**(9): 1380-1386.

Wang, J. H., Simpson, T. L. and Fonn, D. (2004). Objective Measurements of Corneal Light-Backscatter During Corneal Swelling, by Optical Coherence Tomography. *Investigative Ophthalmology & Visual Science* **45**(10): 3493-3498.

Wang, J. H., Thomas, J. and Cox, I. (2006). Corneal Light Backscatter Measured by Optical Coherence Tomography after LASIK. *Journal of Refractive Surgery* **22**(6): 604-610.

Waring, G. O., III, Lynn, M. J., Fielding, B., Asbell, P. A., Balyeat, H. D., Cohen, E. A., Culbertson, W., Doughman, D. J., Fecko, P. and et al. (1990). Results of the Prospective Evaluation of Radial Keratotomy Perk Study 4 Years after Surgery for Myopia. *Journal of the American Medical Association* **263**(8): 1083-1091.

Waring, G. O., Lynn, M. J., Gelender, H., Laibson, P. R., Lindstrom, R. L., Myers, W. D., Obstbaum, S. A., Rowsey, J. J., McDonald, M. B., Schanzlin, D. J., Sperduto, R. D. and Bourque, L. B. (1985). Results of the Prospective Evaluation of Radial Keratotomy (PERK) Study One Year after Surgery. *Ophthalmology* **92**(2): 177-196.

Watson, A. B. and Yellott, J. I. (2012). A Unified Formula for Light-Adapted Pupil Size. *Journal of Vision* **12**(10): 12.

Weale, R. A. (1986). Real Light Scatter in the Human Crystalline Lens. *Graefes Archive for Clinical and Experimental Ophthalmology* **224**(5): 463-466.

Wegener, A., Muller-Breitenkamp, U., Dragomirescu, V. and Hockwin, O. (1999). Light Scattering in the Human Lens in Childhood and Adolescence. *Ophthalmic Research* **31**(2): 104-109.

Weghaupt, H., Pieh, S. and Skorpik, C. (1996). Visual Properties of the Foldable Array Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **22** (Suppl 2): 1313-1317.

Weghaupt, H., Pieh, S. and Skorpik, C. (1998). Comparison of Pseudoaccommodation and Visual Quality between a Diffractive and Refractive Multifocal Intraocular Lens. *Journal of Cataract and Refractive Surgery* **24**(5): 663-665.

Weinstein, A. (2012). Surgical Experience with Pseudophakic Negative Dysphotopsia. *Journal of Cataract Refract Surg* **38**(3): 561.

Welch, N. R., Gregori, N., Zabriskie, N. and Olson, R. J. (2010). Satisfaction and Dysphotopsia in the Pseudophakic Patient. *Canadian Journal of Ophthalmology-Journal Canadien D Ophtalmologie* **45**(2): 140-143.

Westheimer, G. (1964). Pupil Size and Visual Resolution. *Vision Research* **4**(1): 39-45.

Whitaker, D., Elliott, D. B. and Steen, R. (1994). Confirmation of the Validity of the Psychophysical Light Scattering Factor. *Investigative Ophthalmology & Visual Science* **35**(1): 317-321.

Whitaker, D., Steen, R. and Elliott, D. B. (1993). Light Scatter in the Normal Young, Elderly, and Cataractous Eye Demonstrates Little Wavelength Dependency. *Optometry and Vision Science* **70**(11): 963-968.

Wickremasinghe, S. S., Smith, G. T. and Stevens, J. D. (2005). Comparison of Dynamic Digital Pupillometry and Static Measurements of Pupil Size in Determining Scotopic Pupil Size before Refractive Surgery. *Journal of Cataract and Refractive Surgery* **31**(6): 1171-1176.

Wilkins, M., McPherson, R. and Fergusson, V. (1996). Visual Recovery under Glare Conditions Following Laser Capsulotomy. *Eye* **10**(1): 117-120.

Williamson, T. H., Strong, N. P., Sparrow, J., Aggarwal, R. K. and Harrad, R. (1992). Contrast Sensitivity and Glare in Cataract Using the Pelli-Robson Chart. *British Journal of Ophthalmology* **76**(12): 719-722.

Winn, B., Whitaker, D., Elliott, D. B. and Phillips, N. J. (1994). Factors Affecting Light-Adapted Pupil Size in Normal Human Subjects. *Investigative Ophthalmology & Visual Science* **35**(3): 1132-1137.

Wirtschafter, J. D. and Bourassa, C. M. (1966). Binocular Facilitation of Discomfort with High Luminances. *Archives of Ophthalmology* **75**(5): 683-688.

Wolf, E. (1960). Glare and Age. *Archives of Ophthalmology* **64**: 502-514.

Woodhouse, J. M. and Campbell, F. W. (1975). The Role of the Pupil Light Reflex in Aiding Adaptation to the Dark. *Vision Research* **15**(6): 649-653.

Woodward, M. A., Randleman, J. B. and Stulting, R. D. (2009). Dissatisfaction after Multifocal Intraocular Lens Implantation. *Journal of Cataract and Refractive Surgery* **35**(6): 992-997.

Wooten, B. and Geri, G. (1987). Psychophysical Determination of Intraocular Light Scatter as a Function of Wavelength. *Vision Research* **27**(8): 1291-1298.

Wordenweber, B. W., J.; Boyce, P.; Hoffman, D. (2010). *Automotive Lighting and Human Vision*. Berlin, Springer-Verlag.

World Health Organisation. (2007). Global Initiative for the Elimination of Avoidable Blindness: Action Plan 2006-2011. Vision 2020. France.

Yan, Q., Perdue, N. and Sage, E. H. (2005). Differential Responses of Human Lens Epithelial Cells to Intraocular Lenses in Vitro: Hydrophobic Acrylic Versus Pmma or Silicone Discs. *Graefe's Archive for Clinical and Experimental Ophthalmology* **243**(12): 1253-1262.

Yang, Y., Thompson, K. and Burns, S. (2002). Pupil Location under Mesopic, Photopic, and Pharmacologically Dilated Conditions. *Investigative Ophthalmology & Vision Science* **43:** 2508-2512.

Yaroslavsky, I. V., Yaroslavsky, A. N., Otto, C., Puppels, G. J., Vrensen, G., Duindam, H. and Greve, J. (1994). Combined Elastic and Raman Light-Scattering of Human Eye Lenses. *Experimental Eye Research* **59**(4): 393-399.

Yu, E. Y. and Jackson, W. B. (1999). Recent advances in refractive surgery. *Canadian Medical Association Journal* **160**(9): 1329-1337.

Yuan, R. M., Yager, D., Guethlein, M., Oliver, G., Kapoor, N. and Zhong, R. L. (1993). Controlling Unwanted Sources of Threshold Change in Disability Glare Studies - a Prototype Apparatus and Procedure. *Optometry and Vision Science* **70**(11): 976-981.

Zeldovich, A. (2012). Treatment of Negative Dysphotopsia with Unique Sulcus Lens. *Clinical and Experimental Ophthalmology* **40**(8): 829-830.

Zhang, F., Sugar, A., Jacobsen, G. and Collins, M. (2011). Visual Function and Patient Satisfaction: Comparison between Bilateral Diffractive Multifocal Intraocular Lenses and Monovision Pseudophakia. *Journal of Cataract and Refractive Surgery* **37**(3): 446-453.

Zinn, K. M. (1972). *The Pupil.* Springfield, IL: Charlies C Thomas.

APPENDICES

A1. Approval for Ethics Application 595

Aston Triangle
Birmingham B4 7ET
United Kingdom
Tel +44 (0)121 204 3000
www.aston.ac.uk

Memo

Life and Health Sciences Research Ethics Committee's Decision Letter

To : Dr Amy Sheppard
Cc: Rachel Giles, administrator to the Life and Health Sciences Research Ethics Committee
From: Dr Corinne M. Spickett
Chair of the Life and Health Sciences Research Ethics Committee
Date: 19/12/2013
Subject: Project #595. Subjective and objective dysphotopsia in normal and post-refractive surgery eyes

Thank you for your resubmission. The additional information for the above proposal has been considered by the Chair of the LHS Ethics Committee.
Please see below for details of the decision and the approved documents.

Reviewer's recommendation: Approved

Please see the tabled list below of approved documents:

Documentation	Version/s	Date	Approved
Participant information sheet & Consent form	ethics_application_595_consent_form_v2_amended	8.12.13	√
Questionnaire	questionnaire_images_appl_no_595_v1.0	17.11.13	√
Risk Assessment	risk_assessment_app_595_v1.0	17/11/13	√
Response to Reviewers' queries	ethics_application_595_resubmission_v2_amended	8/12/13	√

After starting your research please notify the LHS Research Ethics Committee of any of the following:
Substantial amendments. Any amendment should be sent as a Word document, with the amendment highlighted. The amendment request must be accompanied by all amended documents, e.g. protocols, participant information sheets, consent forms etc. Please include a version number and amended date to the file name of any amended documentation (e.g. "Ethics Application #100 Protocol v2 amended 17/02/12.doc").
New Investigators
The end of the study

Please email all notifications and reports to lhs_ethics@aston.ac.uk and quote the original project reference number with all correspondence.
Ethics documents can be downloaded from: http://www.ethics.aston.ac.uk/documents-all . Please note that these documents can ONLY be opened using Mozilla Firefox or the latest Internet Explorer version (IE9).
Statement of Compliance
The Committee is constituted in accordance with the Government Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK. In accord with University Regulation REG/11/203(2), this application was considered

to
have low potential risk and was reviewed by three appropriately qualified members, including the Chair of the
Life and Health Sciences Ethics Committee.
Yours sincerely,

Dr Corinne M Spickett
Chair of the LHS Ethics Committee

A2: Amendment to Ethics Application 595

Aston Triangle
Birmingham B4 7ET
United Kingdom
Tel +44 (0)121 204 3000

www.aston.ac.uk

MEMORANDUM

DATE: 13th December 2015

TO: Dr Amy Sheppard

FROM: Dr Leon N Davies

SUBJECT: Project # 595 Subjective and objective dysphotopsia in normal and post-refractive surgery eyes

I am writing to inform you that the minor proposed changes to the above project as described in your email and attachment of 9th December 2015 have been approved.

List of Amended Items approved:

Ethics Application 595 Revised Protocol V3 08.12.15 (dated 08/12/15)
Ethics Application 595 Consent Form V3 Amended 08.12.2015 (dated 08/12/15)
Ethics Application 595 Notice of Substantial Amendment (dated 12/11/15)

The Ethics Committee's approval applies only to research conducted in accordance with the amended protocol and documentation approved by the LHS EC; any change to the protocol must be approved by the Committee prior to its implementation.

The details of the investigation will be placed on file. You should notify me of any difficulties experienced by the volunteer subjects, and any significant changes which may be planned for this project in the future.

Dr Leon N. Davies
Chair, LHS Ethics Committee

A3: NHS Ethics (LOA) Approval

Birmingham Clinical Research Office

Miss Aujla

UHB: letter of access for researchers who do not require an honorary research contract - Form RPL 2

Miss M Aujla
Vision Sciences
Aston University
Aston Triangle
Birmingham B4 7ET
R&D Office (UHB)
Education Centre (office 17), 1st Floor
Queen Elizabeth Hospital Birmingham
Mindelsohn Way,
Edgbaston
Birmingham B15 2WB
Tel. 0121 371 4185
Fax 0121 371 4204

Date: 11/05/2015

Dear Miss Aujla

Letter of access for research

This letter confirms your right of access to specified areas to conduct research through University Hospitals Birmingham NHS Foundation Trust for the purpose and on the terms and conditions set out below. This right of access commences on 01-May-2015 and ends on
06-Oct-2016 unless terminated earlier in accordance with the clauses below. Your entitlement to access to the specified area will automatically end on the date specified. It is
your responsibility to seek an extension of time for access should it become necessary.

Your right of access is granted to undertake the following activities:

Consenting and measurement of visual function
or other duties agreed with the R&D office in the Delegated Duties Log for the following study/studies:

Study Title: *Evaluating the subjective and objective performance of instrumentation used and*
intraocular devices implanted during routine ocular surgery

UHB Reference: **RRK5260**. Principal Investigator: *Dr S Kolli*

You have the right of access to conduct such research as confirmed in writing in the letter of
permission for research from this NHS organisation. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us
giving permission to conduct the project. This Letter of Access is issued on the understanding that your activities will have no direct impact on the quality of care provided to
patients of the Trust.

You are considered to be a legal visitor to UHB NHS Foundation Trust premises. You are not entitled to any form of payment or access to other benefits provided by this NHS organisation to employees and this letter does not give rise to any other relationship between you and this NHS organisation, in particular that of an employee.

While undertaking research through UHB NHS Foundation Trust you will remain accountable
to your employer **Aston University** but you are required to follow the reasonable

instructions of **Dr S Kolli** in this NHS organisation or those given on her/his behalf in relation
to the terms of this right of access.
Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any

investigation by this NHS organisation in connection with any such claim and to give all such
assistance as may reasonably be required regarding the conduct of any legal proceedings.
You must act in accordance with UHB NHS Foundation Trust policies and procedures, which
are available to you upon request, and the Research Governance Framework.
You are required to co-operate with UHB NHS Foundation Trust in discharging its duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on UHB NHS Foundation Trust premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at
all times.
You are required to ensure that all information regarding patients or staff remains secure and
strictly confidential at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice (http://www.dh.gov.uk/assetRoot/04/06/92/54/04069254.pdf) and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.
Please note that you are not regarded as a member of the healthcare team and are **not** entitled to access information about patients of the Trust without their consent.
You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that this NHS organisation accepts no responsibility for damage to or loss of personal property.
We may terminate your right to attend at any time either by giving seven days' written notice
to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of this NHS organisation or if you are convicted of any criminal offence. Your substantive employer is responsible for your conduct during this research project and may in
the circumstances described above instigate disciplinary action against you.
UHB NHS Foundation Trust will not indemnify you against any liability incurred as a result of
any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.
If your current role or involvement in research changes, or any of the information provided in

your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in this NHS organisation.
Yours sincerely
Christopher Counsell, PhD
Head of R&D (Governance)
UHB NHS Foundation Trust
11 May 2015
Birmingham Clinical Research Office
Miss Aujla
UHB: letter of access for researchers who do not require an honorary research contract - Form RPL 2
cc: Supervisor
UHB HR Department
HR Department of the substantive employer

A4: NHS Ethics (LOA) Extension

R&D Governance Office

Miss Aujla

UHB: letter of access for researchers who do not require an honorary research contract - Form RPL 2

Miss M Aujla
Vision Sciences
Aston University
Aston Triangle
Birmingham B4 7ET
UHB Research Governance Office
1st Floor, Institute of Translational Medicine
Heritage Building
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham B15 2WG
Tel. 0121 371 4185

Date: 24/04/2017

Dear Miss Aujla

Letter of access for research

This letter confirms your right of access to specified areas to conduct research through University Hospitals Birmingham NHS Foundation Trust for the purpose and on the terms and conditions set out below. This right of access commences on 01-May-2015 and ends on
06-Oct-2016 unless terminated earlier in accordance with the clauses below. Your entitlement to access to the specified area will automatically end on the date specified. It is
your responsibility to seek an extension of time for access should it become necessary.

Your right of access is granted to undertake the following activities:

Consenting and measurement of visual function
or other duties agreed with the R&D office in the Delegated Duties Log for the following study/studies:

RRK5260 Evaluating the subjective and objective performance of instrumentation used and intraocular devices implanted during routine ocular surgery
PI: Kolli,S

You have the right of access to conduct such research as confirmed in writing in the letter of
permission for research from this NHS organisation. Please note that you cannot start the research until the Principal Investigator(s) for the research project(s) has received a letter from us giving permission to conduct the project. This Letter of Access is issued on the understanding that your activities will have no direct impact on the quality of care provided to
patients of the Trust.

You are considered to be a legal visitor to UHB NHS Foundation Trust premises. You are not entitled to any form of payment or access to other benefits provided by this NHS organisation to employees and this letter does not give rise to any other relationship between you and this NHS organisation, in particular that of an employee.

While undertaking research through UHB NHS Foundation Trust you will remain accountable
to your employer **Aston University** but you are required to follow the reasonable instructions of **Mr S Kolli** in this NHS organisation or those given on her/his behalf in relation
to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising

out of or in connection with your right of access, you are required to co-operate fully with any

investigation by this NHS organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with UHB NHS Foundation Trust policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with UHB NHS Foundation Trust in discharging its duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on UHB NHS Foundation Trust premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/200146/Confidentiality_-_NHS_Code_of_Practice.pdf) and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

Please note that you are not regarded as a member of the healthcare team and are **not** entitled to access information about patients of the Trust without their consent.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that this NHS organisation accepts no responsibility for damage to or loss of personal property.

We may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of this NHS organisation or if you are convicted of any criminal offence. Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

UHB NHS Foundation Trust will not indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in
your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in this NHS organisation.
Yours sincerely
Christopher Counsell, PhD
Head of R&D (Governance)
UHB NHS Foundation Trust
cc: Supervisor
UHB HR Department
HR Department of the substantive employer

24 April 2017

SUPPORTING PUBLICATIONS

Poster presentation at ARVO 2015, Denver (Based on chapter 2 data)

Halo size and subjective complaints of dysphotopsia in a normal population

SECTION:

Purpose: Dysphotopsia including glare and haloes is the most common cause of dissatisfaction post cataract surgery with implantation of multifocal intraocular lenses (IOL). Despite good distance and near visual acuity, quality of life may be affected if activities such as night driving are compromised. There is currently no standardised method of measuring dysphotopsia. The aim of this prospective study was to investigate the relationship between objective measures and subjective complaints of dysphotopsia. The normal range of subjective/objective grade (the glare effect ratio) will be determined.

Methods: Measurements were taken both binocularly and monocularly from 100 healthy participants (mean age: 22 ± 3.21 years; range 18 to 33 years). A bespoke halometer device gave an objective measure by accurately quantifying the extent of the glare area in 8 meridians. The commercially available *C-Quant* objectively assessed the amount of straylight falling on the retina using the compensation comparison method. Subjective grading of glare was performed using simulated images found on the Photographic Images of Photic Phenomena plates.

Results: Monocular glare areas (median: 4.25 cm^2; range 1.97 to 19.61 cm^2) were found to be significantly larger than the binocular glare areas (median: 3.24 cm^2; range 1.64 to 8.26 cm^2) with the halometer ($P < 0.001$). There was no significant relationship found between halometer glare area and subjective complaints ($r_s = -0.048$, $r_s^2 = 0.002$, $P = 0.635$); *C-Quant* and subjective complaints ($r_s = 0.109$, $r_s^2 = 0.012$, $P = 0.279$); halometer and *C-Quant* ($r_s = 0.121$, $r_s^2 = 0.015$, $P = 0.231$). The normal range for the glare effect ratio was calculated for both halometry (median: 0.87; range 0 – 2.47) and for *C-Quant* (median: 3.23; range 0 – 9.41).

Conclusions: Binocular summation was evident with binocular halos being smaller than monocular halos; suggesting halometry should be performed binocularly. The lack of relationship between subjective and objective measures highlights the difficulties in being able to predict the potential subjective complaints a patient may experience from an objective measure alone. The normal range of the glare effect ratio could be used for comparison purposes pre and post refractive surgery, as individuals with the highest glare effect ratios may be less suitable for refractive surgery procedures that may induce glare.

Poster presentation at ARVO 2016, Seattle (Based on chapter 3 data)

Age-related objective and subjective dysphotopsia

SECTION:

Purpose: Dysphotopsia including glare and haloes is the most common cause of dissatisfaction post cataract surgery with implantation of multifocal intraocular lenses (MIOLs). The aim of this prospective study was to determine the relationship between objective measure and subjective complaints which could be used to identify those most likely to experience post-operative problems. The normal range of subjective/objective grade (the glare effect ratio) was determined over a wide age range.

Methods: Measurements were acquired monocularly and binocularly from 141 healthy participants (range 18 to 82 years). A bespoke halometer gave an objective measure by quantifying the extent of the glare area in 8 meridians. The *C-Quant* objectively assessed the amount of straylight falling on the retina using the compensation comparison method. Grading of subjective dysphotopsia was performed using simulated images (Photographic Images of Photic Phenomena plates).

Results: Monocular glare areas (median: 4.87 cm^2; range 1.97 to 20.87 cm^2) were larger than the binocular glare areas (median: 3.77 cm^2; range 1.64 to 12.11 cm^2) with halometry ($P < 0.001$). Binocular glare area increased with age ($r = 0.673$, $r^2 = 0.453$, $P < 0.001$). Objective findings explained only a small percentage of the variance in subjective measures; halometer glare area vs subjective complaints $r = 0.287$, $r^2 = 0.082$, $P < 0.001$; *C-Quant* vs subjective complaints ($r = 0.228$, $r^2 = 0.052$, $P = 0.007$). The normal range for the glare effect ratio was calculated for both halometry (median: 0.77; range 0 – 2.52) and for *C-Quant* (median: 3.45; range 0 – 10.62).

Conclusions: Binocular summation was evident with binocular halos being smaller than monocular halos, suggesting halometry should be performed binocularly. The lack of a strong relationship between subjective and objective measures highlights the difficulties in predicting a patient's likely subjective complaints from an objective measure alone. The normal range of the glare effect ratio could be used for screening purposes pre-refractive surgery, as individuals with the highest ratios may be the most likely to complain of subjective dysphotopsia symptoms.