ASSESSMENT OF VISUAL PERFORMANCE: COMPARISON OF NORMAL SUBJECTS AND POST-REFRACTIVE SURGERY PATIENTS

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Declaration

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Abstract

This work forms part of a study to assess the implications of excimer laser surgery for commercial aviation in light of reports of reduced visual performance and glare problems in some individuals following surgery. The literature indicates that corneal refractive surgery can increase both forward light scatter and optical aberrations, leading to a reduction in retinal image contrast. The project comprised a retrospective study of subjects that had undergone either photorefractive keratectomy (PRK) or laser assisted in situ keratomileusis (LASIK). Control subjects were also examined for comparison purposes since insufficient laser patients were available for a longitudinal study. The experimental work involved the measurement of forward light scatter using the City University Light Scatter Program and the development and utilisation of four novel tests of visual performance. An additional aim of the project was to gather information from the tests and subsequently produce a suitable technique for assessing visual performance following corneal refractive surgery that was sensitive to retinal image degradation.

Take-off, approach and landing are the most visually demanding tasks undertaken by the pilot during a flight. All three tasks require rapid scanning of a range of instrumentation panels to assimilate the relevant visual information, along with a degree of awareness of the external environment.

The novel tests of visual performance included a visual search task, selected as the principal parameter for assessment since visual search is used extensively on the flight deck for assembling information from the display systems and the outside world. The mean glimpse duration was also measured during the search task. The variability of the visual search data led to the development of a model of visual search to provide an insight into the principal factors that determine the outcome of visual search, and two further tests were developed to provide input data for the search model. These tests involved the measurement of contrast detection and orientation discrimination (i.e. a spatial acuity task) thresholds respectively. These data provided useful and relevant information on the subject's visual performance in addition to providing the data needed for the visual search model.

Fifty-two LASIK, 32 PRK and 53 control subjects were assessed during the study. Despite the long mean follow-up time of the PRK group (approximately three years), a statistically significant increase in both contrast acuity thresholds and visual search times was revealed, suggesting that the reduction in performance is permanent. This was associated with a statistically significant increase in the angular spread of straylight on the retina. The increase in total scatter as indicated by the integrated straylight parameter (k'), did not however reach statistical significance. Since surgically induced aberrations are thought to be of a similar magnitude following PRK and LASIK, these findings indicate the important role

the distribution of straylight may have in determining retinal image contrast and hence visual performance.

The LASIK group showed a small but not statistically significant increase in mean contrast acuity thresholds and mean visual search times compared to the control group. This is consistent with the findings for forward light scatter - a small, but not statistically significant increase in the scatter index (n) and the integrated straylight parameter (k'). These findings suggest that changes in scattered light as a result of LASIK do not significantly affect visual performance.

The large stimulus employed by the test meant that absolute contrast detection thresholds were relatively insensitive to retinal image degradation. Both the visual search task and contrast acuity thresholds revealed a reduction in visual performance post-PRK, but the contrast acuity threshold test appeared to be the most sensitive, identifying all symptomatic subjects as outliers and detecting the improvement in performance with follow-up time. Based on these findings we developed a Contrast Acuity Assessment (CAA) test. The parameters selected for the test were based on the results of a detailed analysis of visual tasks in the cockpit. The 'standard observer' and normal $\pm 2\sigma$ range were established, based on the assessment of 100 control subjects. The usefulness of the test is to identify those subjects with thresholds above the upper 2σ limit, as needing further investigation before the granting of a medical certificate. Preliminary data were obtained from a small group of refractive surgery subjects, many of whom produced data that clustered around the 'standard observer'. Others produced thresholds that fell outside the normal 2σ range, often showing a characteristic 'Λ-pattern' implicating increased forward scattered light and/or aberrations. All symptomatic subjects showed contrast acuity thresholds outside the 2σ range.

The Contrast Acuity Assessment (CAA) test provides a new measure of functional visual performance both for daytime and low levels of ambient illumination. Individuals can be assessed and compared to the normal range, using parameters relevant to the instrumentation found on the flight deck of a commercial aircraft. The test is sensitive to changes in retinal image contrast associated with increases in forward light scatter and/or aberrations as a result of excimer laser surgery and therefore can be used to identify those whose visual performance is inadequate for commercial aviation.

1 Introduction

1.1 Factors that influence visual performance

Visual performance depends on a number of factors including the quality of the retinal image and the integrity of the visual pathways. Neural factors consist of the size and spacing of cells within the retina, the varying degrees of spatial summation, and higher level processing within the cortex. The level of achieved visual performance is also dependent on the criterion used for assessment and the area of the retina investigated. At the fovea, the high density of cone receptors and their one-to-one relationship with midget ganglion cells is often not matched by the optics of the eye, resulting in an optically limited system. Measures such as size detection thresholds and contrast acuity can sometimes be limited by optical factors (Wang, Thibos, Lopez et al., 1996; Williams, Artal, Navarro et al., 1996). Performance in the periphery is significantly worse, largely due to changes in the receptive field organization of the retina (Hirsch and Curcio, 1989; Curcio et al., 1990). Retinal image quality also declines rapidly with eccentricity due to aberrations such as oblique astigmatism but beyond about 5° from the fovea, resolution acuity is limited by the neural factors.

Under photopic conditions, visual acuity increases approximately linearly with retinal illuminance before levelling off between two and three log trolands (Shlaer S., 1937). Because of a number of factors including disability glare, performance falls at high light levels. Under mesopic and scotopic conditions, the performance of an individual eye is less predictable because of variations in the optical quality of the eye and the state of light adaptation of the retina. A reduction in the signal-to-noise ratio of the visual stimulus due to photon noise is associated with low light levels and effectively reduces image contrast. Pupil diameter is another variable, particularly in young eyes. It has been suggested that this variation achieves a balance between retinal illuminance and ocular aberrations, hence optimising spatial resolution (Woodhouse, 1975).

The Stiles-Crawford effect of the first kind is a retinal phenomenon that can be considered as a filter that changes the spatial transmittance in the plane of the pupil, with the central region contributing most (Stiles and Crawford, 1933; Stiles, 1939).

This can be expressed mathematically as

$$T_r = e^{-\alpha 2}$$

where T_r is the transmission of the filter, α = 0.105 and r is the radial distance from the centre of the pupil (Moon and Spencer, 1944). On average, the cones are all aligned with a point close to the centre of the pupil although there is a significant variation among the normal population (Marcos and Burns, 2000), and cones have been shown to move to adapt to changes in pupil position (Applegate and Bonds, 1981). In practice, the Stiles-Crawford effect improves optical quality by reducing the luminous efficiency of any light ray that deviates from the direction of the chief ray. The effect gradually reduces over the mesopic range and is minimal under scotopic conditions (Crawford, 1937) as it is predominantly a property of the cone receptors.

1.2 Factors determining the optical quality of the retinal image

Even in an optically perfect eye free from aberrations, light from a point source fails to form a discrete point image on the retina. The best image, known as the *point spread function*, results from a combination of diffraction of light at the pupil and the scattering of light by the ocular media (Born, 1980). Aberrations and intraocular scatter both have the effect of reducing the height of the peak and increasing the spread of light within the point spread function. All three factors are dependent on pupil size.

1.2.1 Diffraction

In an eye free of intraocular light scatter and aberrations, light is diffracted at the pupil and is imaged on the retina. The point spread function for a 3mm pupil is largely diffraction limited. It takes the form of a circular, radially symmetrical diffraction pattern with approximately 84% of the light falling within the region

known as the *Airy disc*, which subtends approximately 1 min arc at the nodal point of the eye. The remaining light is imaged as a series of concentric rings with the intensity of light gradually reducing with distance from the centre of the image. The radius of the Airy disc, ρ, from its peak to the first point at which the light level drops to zero, is given approximately by:

$$\rho = 0.61\ \lambda_o / n'u'$$

where λ_o is the wavelength of light in a vacuum, n' is the refractive index in image space and u' is the maximum angle the marginal ray makes with the axis of the system (Born, 1980).

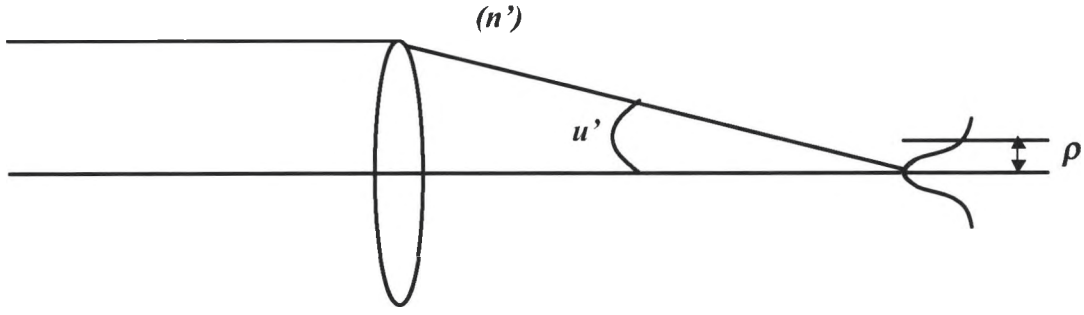


Figure 1-1: Calculation of the Airy disc diameter to the first dark ring

The angle is determined by the exit pupil and relates to the actual pupil size (i.e. the aperture stop of the eye). The exit pupil of the eye is located close to the image-side, principal plane and the distance from this plane to the retina equals the image-side focal length of the eye, f'. Hence, $u' \approx D'/2\rho'$ where D' is the diameter of the exit pupil of the eye.

Considering the effects of diffraction alone, the radius of the Airy disc decreases as the diameter of the pupil increases. In the absence of aberrations and scattered light the resolving power of the eye improves linearly with increasing pupil size.

The optical limit of resolution for two point sources occurs when the edge of one Airy disc coincides with the peak of the next so that the summed retinal illuminance includes a dip between the two peaks of about 74% of the maximum

illuminance. For a diffraction-limited system with an average pupil diameter of 3mm and light with a wavelength of 555nm, the optical limit of resolution is less than 1 min arc. The average normal eye is diffraction limited when the pupil diameter is about 2.0-2.4mm (Campbell and Gubisch, 1966; Atchison, Smith, and Efron, 1979; Charman, 1991; Rovamo, Kukkonen, and Mustonen, 1998) and smaller diameters result in a reduction in visual performance due to a larger Airy disc diameter.

1.2.2 Intraocular light scatter

Beyond a few minutes of arc from the centre of the functional point spread function, the spread of light is due to intraocular light scatter only. Scatter takes place in both forward (scattering angle less than 90°) and backward (scattering angle greater than 90°) directions with the exact proportion of light scattered in each direction dependent on the size and distribution of the scattering elements. In addition, a small proportion is absorbed by the ocular structures of the eye.

1.2.2.1 Ocular structures involved in light scatter

Some degree of light scatter occurs in every eye, with estimates ranging between 1.3% and 2% in young, healthy eyes (Wooten and Geri, 1987; Walraven, 1973).

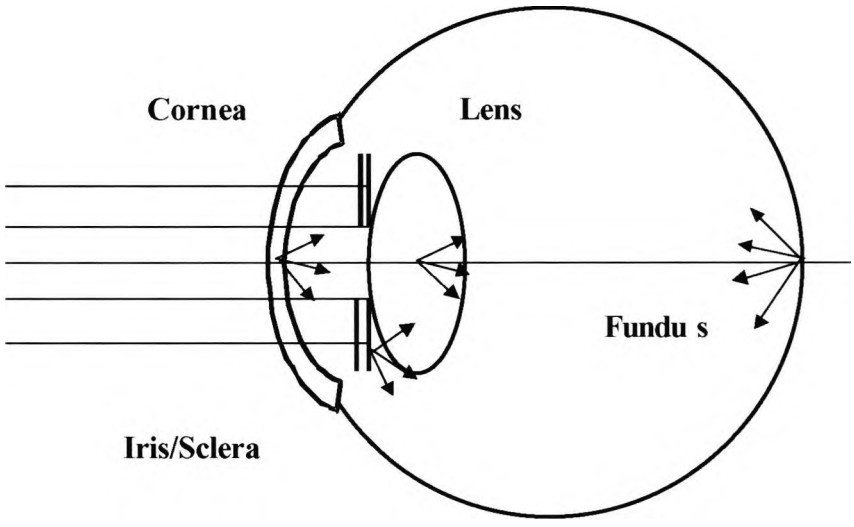


Figure 1-2: Sources of forward light scatter in the eye

Normal levels of intraocular light scatter have been attributed in the main to the cornea and crystalline lens (approximately 70%) (Demott and Boynton, 1958a; Olsen, 1982; Weale, 1986; Smith, Brown, and Shun-Shin, 1990) with an additional contribution from the retinal tissue (approximately 30%) (Demott and Boynton, 1958a; Vos and Bouman, 1964) and a small amount resulting from transillumination of the uveal tract (figure 1.2).

The variety of different scatter sources within the ocular media with a range of sizes with respect to wavelength and a range of refractive indices, combined with a relatively regular, ordered structure of the cornea and lens, produce rather complex scattering. Both the Mie and Rayleigh-Gans theories apply to some degree, as confirmed by the limited wavelength dependency across the visible spectrum (Demott and Boynton, 1958b; van den Berg, IJspeert, and de Waard, 1991; Vos and Bouman, 1964; Wooten and Geri, 1987; van den Berg et al., 1991; Whitaker, Steen, and Elliott, 1993). Mie or coherent scatter occurs in the presence of large spherical scatter sources that extend over distances that are equal to or larger than the wavelength of light, resulting in an angular distribution that follows the incident beam. The Rayleigh-Gans theory (Kerker, 1969) relates to scatter sources possessing a refractive index similar to the surrounding media and predicts that as the scatter source increases in size, forward scatter increases and backscatter decreases.

1.2.2.1.a Scatter sources within the cornea

The cornea produces 25-30% of the light scattered within the eye (Vos and Boogaard, 1963). The corneal stroma is a very regular structure composed of approximately 250 lamellae, each with a thickness of 2.0μm (Hogan, Alvarado, and Weddell, 1971). Each lamellae contains parallel collagen fibrils of regular size and shape with a refractive index of 1.47, surrounded by ground substance with a refractive index of 1.354 (Maurice, 1969). The lamellae are arranged so that the direction of the fibrils varies significantly between adjacent layers. Modern theories of corneal transparency have concluded that the corneal stroma exhibits short-range ordering of fibrils over distances of approximately one wavelength, with the fibrils displaced from the regular lattice by about 10% of the

centre-to-centre distance between fibrils (Maurice, 1957; Hart and Farrell, 1969; Feuk and McQueen, 1971; Farrell, McCally, and Tatham, 1973). This model results in the destructive interference of light in all directions apart from forwards and backwards, with approximately 1% of the incident light scattered along the incident beam. This has been confirmed by examining the wavelength dependence of scattered light for the rabbit cornea, which was found to be proportional to the cube of the wavelength as predicted by the model (McCally and Farrell, 1988). The proteoglycan molecules keratan sulphate and chondroitin/dermatan sulphate within the extracellular matrix are also implicated in transparency.

1.2.2.1.b Scatter sources within the crystalline lens

The crystalline lens is the chief source of light scatter within the eye (Boynton and Clarke, 1964; Hemenger, 1992). The main refractive volume of the crystalline lens is composed of regularly arranged lens fibres with minimal extracellular space, containing a high concentration of crystallin protein molecules with small spatial fluctuations in the number of molecules compared to the wavelength of light (Trokel, 1962; Delave and Tardieu, 1983). Scatter sources have been identified as refractive index fluctuations between the cell membranes and the surrounding cytoplasm in the lens fibre lattice due to abnormalities of the fibre cell membranes or increased separation of fibres (Kerker, 1969), and/or the clumping of protein molecules to form large aggregates (Huggert, 1946; Bettelheim, 1985; Hemenger, 1992; Whitaker et al., 1993; Yaroslavsky, Yaroslavsky, Otto et al., 1994). Aggregate molecules develop alongside age changes to the crystalline proteins resulting in an increase in straylight. The lens is also the main structure responsible for the small quantity of straylight produced by fluorescence due to the presence of fluorescent compounds such as tryptophan and others that increase with age and in the presence of cataract. Fluorescence can cause a small loss of retinal image contrast in elderly patients in the presence of significant blue or ultraviolet light (Elliott, Yang, Dumbleton et al., 1993).

1.2.2.1.c Scattered light originating from the uveal tract

For large glare angles, transillumination of the ocular wall contributes a small proportion of intraocular light scatter, the significance of which is dependent on the pigmentation level of the eye. A smaller quantity originates from transillumination of the iris. Elevated levels are found in lightly pigmented eyes with the lowest levels associated with dark brown irides and non-Caucasians (van den Berg, IJspeert, de Waard et al., 1990; van den Berg et al., 1991; IJspeert, de Waard, and de Jong, 1990; Elliott, Mitchell, and Whitaker, 1991; de Waard, IJspeert, van den Berg et al., 1992). Blue-eyed Caucasians demonstrate approximately 18% more straylight than brown-eyed Caucasians (van den Berg et al., 1991). The transmittance of these tissues falls between 0.2-1% for green and red wavelengths respectively (van den Berg et al., 1991) due to the differing absorption properties of melanin across the visible spectrum.

1.2.2.1.d Scattered light originating from the retina

Approximately one third of scattered light within the point spread function can be attributed to the backwards and sideways scatter of light by the retinal tissue (Vos, 1963; Vos, 1984), in particular the vessels within the choriocapillaris and choroidal stroma. This scatter is therefore wavelength dependent due to the transmittance/absorption characteristics of the oxyhaemoglobin and melanin (Hodgkinson, Greer, and Molteno, 1994). However, the luminous efficiency of this light is significantly reduced by the Stiles-Crawford effect (section 1.1) so the wavelength dependency is not significant for whole eye scatter (Wooten and Geri, 1987).

1.2.2.2 The distribution of forward scattered light

The distribution of intraocular light scatter is determined by the nature of the scatter sources, in particular their size, refractive index differential from the surrounding tissue, and the scale of inhomogeneities compared to the wavelength of light. The quantity of straylight at a particular point on the retina is proportional to the intensity of the source and inversely proportional to its eccentricity

(Holladay, 1926). If θ is the angle between a small glare source and the point of interest on the retina (usually considered to be the fovea), then the luminance of scattered light at the fovea, L_s (θ), can be calculated using the empirical glare formula:

$$L_s(\theta) = Ek\theta^{-n}$$

where E is the illuminance in the plane of the pupil and the parameters k and n are determined by the scattering properties of the eye (Holladay, 1926; Holladay, 1927; Stiles, 1929; Stiles and Crawford, 1937a) (figure 1.3).

The logarithm of L_s has a linear relationship with the logarithm of θ.

$$\log_{10} L_s = \log_{10}(Ek) - n\log_{10}\theta$$

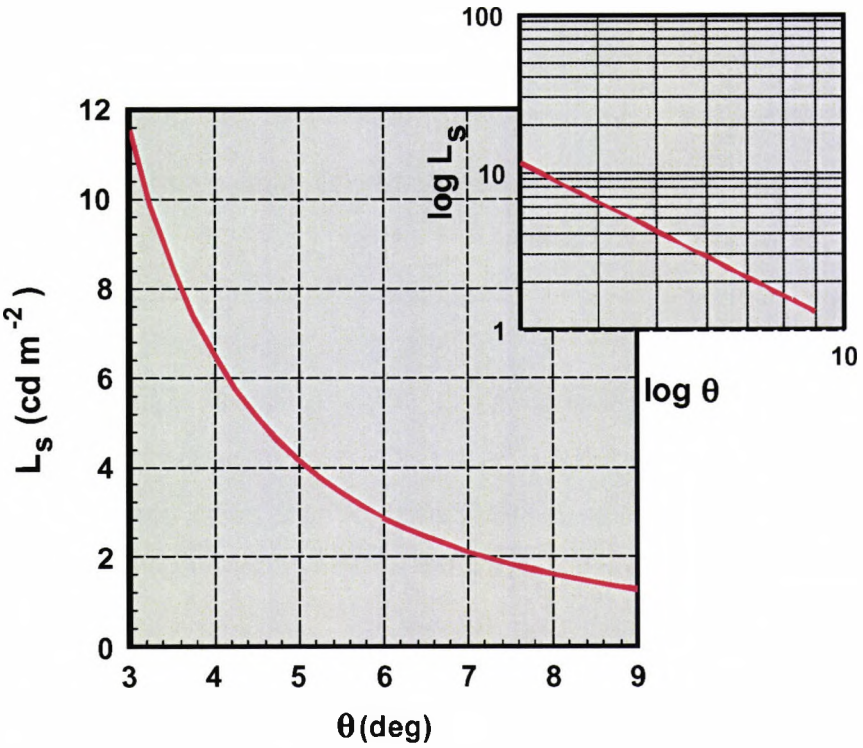


Figure 1-3: The theoretical straylight function showing how the luminance of scattered light varies with eccentricity

A knowledge of the illuminance in the plane of the pupil (E) makes it possible to compute the constants k and n by fitting the least squares line to $\log_{10} L_s$ versus $\log_{10} \theta$. The gradient of the log-log graph relates to the *scatter index* (n) and

describes the angular dependence of the scattered light. Small values of the scatter index (n) indicate a greater spread of scattered light and result from small scatter sources, whereas larger values of n indicate scattering over a narrower region relating to larger scatter sources (Barbur, de Cunha, Harlow et al., 1993). The intercept of the log-log graph gives the value of Ek and if the illuminance in the plane of the pupil (E) is known, the straylight parameter k can be calculated. For a fixed value of n, the quantity of scattered light is proportional to the straylight parameter (k) and its value relates to the density of the scattering sources. Estimates for n and k in the normal population made using a number of different measuring techniques, range from n = 2.0 - 2.8 and k = 9.3 - 29.0 over a range of glare angles between 0.75° and 25° (Vos, 1984; Stiles and Crawford, 1937b; Fry and Alpern, 1953; Vos and Boogaard, 1963; Holladay, 1926; Stiles and Crawford, 1937a). Many measurement techniques assume that n = 2.0, i.e. the quantity of straylight is proportional to θ^{-2} (the Stiles-Holladay approximation). This assumption makes it possible to measure k efficiently.

1.2.2.3 Measurement of intraocular light scatter

A number of different techniques have been developed to estimate the quantity of straylight within the eye, although small angle scatter within 1° of the glare source is impossible to measure with current techniques because the spread of light within this area of the point spread function cannot be differentiated from that resulting from diffraction or aberrations.

1.2.2.3.a Estimates of forward light scatter from measurements of backscatter

The light scattered backwards by the cornea and crystalline lens determines the clarity of the ocular media as seen by the observer and although it does not influence the contrast of the retinal image, it does have the effect of reducing the quantity of light reaching the retina. It can be assessed using slit lamp fluorophotometry in which a fibreoptic probe is employed to detect light from a minute area of the cornea or lens. The brightness of this light is then compared with a 10.6g/ml sodium fluorescein solution as the standard (Olsen, 1982). In fact,

the image of the cornea or lens seen through the slit lamp consists of both reflected (polarised) and backscattered (depolarised) light, because the lens acts partially as a diffuser, partially or wholly depolarising the light. Polarised light has been used to study the backward scatter from the crystalline lens (Weale, 1986) and scattered and reflected light can be separated by comparing the luminance of slit-lamp images through two microscope oculars, one covered by a polaroid analyser and the other with a variable neutral density filter. By viewing the image through a cross polarisor, only depolarised (backscattered) light remains visible. A detector can be used to measure the intensity and spectral composition of the radiation and has revealed backscattered light to be wavelength dependent, with greater levels of scatter for short-wavelengths, confirming the presence of Rayleigh scatter in this direction (Weale, 1986). In younger eyes, backscattered light forms a very small proportion of the light returning from the lens, the majority being reflected light. Although forward and backward scatter frequently occur together, the two are not strongly correlated (Wolf and Gardiner, 1965; Allen and Vos, 1967; Abrahamsson and Sjostrand, 1986; Feuk and McQueen, 1971; Hemenger, 1984) because light tends to be scattered more than once within the ocular media. In addition, the scatter sources present within the eye are often significantly longer than the wavelength of light, resulting in more forward scatter than backscatter (Atchison and Smith, 2000). Therefore measurements of backscatter are not suitable for estimating levels of forward light scatter.

1.2.2.3.b Indirect methods

Indirect techniques otherwise known as glare tests assess the effect that forward light scatter has on visual performance, and assume that any increase in glare is due to increased light scatter. However, the relationship between glare and scattered light is complex since glare disability may also be influenced by optical aberrations, and techniques such as contrast sensitivity measurement suffer from the uncertainties involved in threshold measurements, fluctuations in criterion and localised light adaptation factors. Only a direct assessment of forward light scatter can provide information on the distribution of straylight. Glare tests have their use in clinical practice as they are better able to predict outdoor performance than many other tests (section 2.3.1) (Holladay, Prager, and Truillo, 1987).

Direct psychophysical methods of assessment

The equivalent luminance technique

This is the conventional psychophysical method for evaluating straylight, in which the addition of a glare source to the field of view results in the superimposition of a veiling luminance across the test field. When the test object is viewed foveally, the luminance difference necessary for it to be distinguished from the background is altered by the presence of the glare source (Holladay, 1927). The effect of the glare source within the field of view is to increase the adaptive brightness of the fovea, therefore increasing the minimum perceptible brightness difference required for discrimination. The equivalent luminance (L_{eq}) is the background luminance that is needed to produce the same adaptive effect on visual sensitivity as the veil caused by a particular glare source at angle θ (Walraven, 1973). Because the method is subjective, it automatically accounts for the Stiles-Crawford effect. As predicted from the empirical glare formula, a decrease in the glare angle (θ) results in an increase in the quantity of straylight.

The equivalent luminance method assumes that the visual effects of glare are solely dependent on the straylight reaching the fovea. However, the functions describing the visual effects of glare do not correspond to those for measured illuminance, indicating that other factors must be considered (Demott and Boynton, 1958a). One such factor is likely to be the discrepancy in light distribution between the two conditions since a glare source will not produce a uniform distribution of illuminance across the retina. The equivalent background luminance generally has a different distribution and cannot completely mimic the effect of the glare source, since the retina adapts to the overall veiling luminance, not just that reaching the fovea (Fisher and Christie, 1965). Disregarding this disparity results in a very small error for small glare angles and a slightly larger error for large glare angles (Holladay, 1927) leading to the conclusion that straylight accounts for the majority of the measured psychophysical effect.

The direct compensation technique

This technique was originally developed by Le Grand (1937) and allows an accurate estimate of the equivalent veiling luminance of the glare source using the retina as a detector. Straylight originating from a flickering annulus produces a flickering veil across a central target that is in phase with the flickering of the straylight source. A compensation light of equal modulation but in counter phase to the flickering of the glare source is presented over the central test field and the amplitude of this counter phase modulation is modified until the flickering is neutralised or a minimum occurs. This provides an estimate of the amount of scattered light reaching the fovea from a particular glare angle. The main advantage of the direct compensation technique is the lack of any assessment of threshold, meaning that retinal adaptation and foveal sensitivity are not critical. Retinal function is unimportant as long as flicker can be appreciated (van den Berg and Spekreijse, 1987). Since the requirement is to null the flicker, the sensitivity of the test is unrelated to the values of straylight obtained. The direct compensation method is therefore able to avoid some of the problems encountered with the equivalent veiling glare method, such as adaptation changes and the effect of poor fixation. It is also independent of the Stiles-Crawford effect since both the light from the scatter source and that from the nulling source are scattered by the same structures over the same angle.

The van den Berg Straylightmeter

The direct compensation technique forms the basis for the van den Berg 'Straylightmeter' (van den Berg, 1986; van den Berg and IJspeert, 1991a) which consists of a viewing tube with an eyecup at one end and the stimulus at the other. The stimulus consists of a 1° central dark test target, surrounded by a bright outer circle of 2° radius with a steady luminance of 30cd/m^2 (figure 1.4). A separating annulus providing a higher luminance than the straylight is located around the central target to minimise lateral inhibitory retinal effects and hence maintain flicker sensitivity (Diamond, 1955). However, this isolating annulus scatters additional light across the retina reducing the accuracy of the straylightmeter (Beckman, Abrahamsson, Sjostrand et al., 1991).

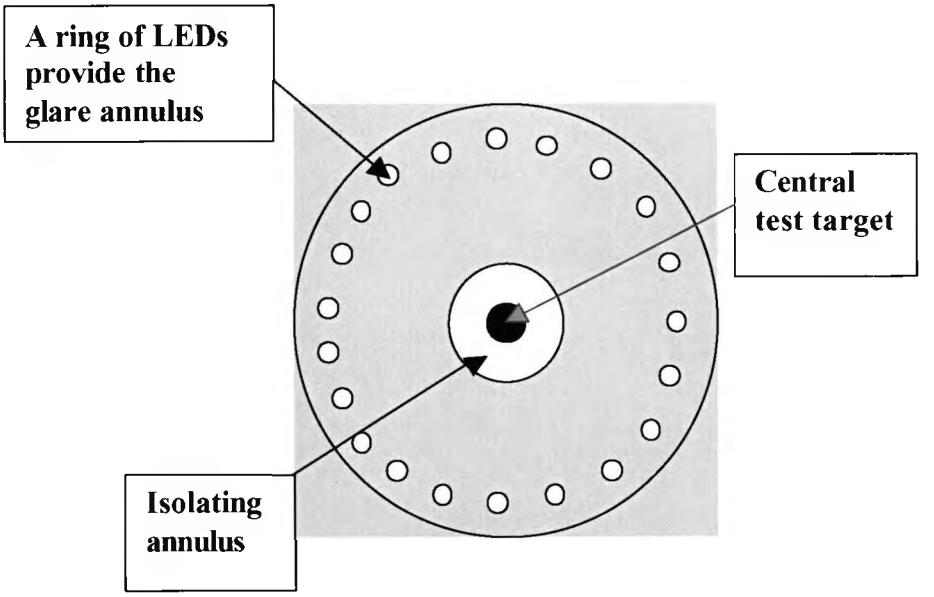


Figure 1-4: Representation of the van den Berg Straylightmeter stimulus

The glare annulus is provided by one of three concentric rings of yellow light emitting diodes (λ = 570nm) that flicker sinusoidally at 8Hz and are positioned at either 3.5°, 10° or 28° from the centre, allowing examination of the scatter function over a range of glare angles. The subject is required to fixate the central target with the eye placed firmly against the cup at the end of the viewing tube. Each ring of LEDs is flickered in turn with a light/dark ratio of one. The counter-phase modulation over the central target is adjusted to find the null point and each measurement is repeated six times. The size of the test target is a compromise, as the target must be large enough to resolve with ease and provide good flicker sensitivity but balanced against the loss of homogeneity of the scattered light with increasing target size. Overall reproducibility has been shown to be in the region of 0.06 log units (IJspeert et al., 1990) although it decreases for the 3.5° annulus due to inhomogeneity of the straylight and may also decrease for the largest angle (Elliott and Bullimore, 1993). A potential problem with the 28° annulus is that slight changes in the position of the subject's eye significantly affect the measurements at this angle (Elliott et al., 1991b).

The City University Scatter Program

Historically, the full scatter function has not been determined clinically, since the distribution of straylight (scatter index, n) was taken to be constant (n = 2) and of limited significance, leaving the straylight parameter (k) as the only important factor (section 1.2.2.2).

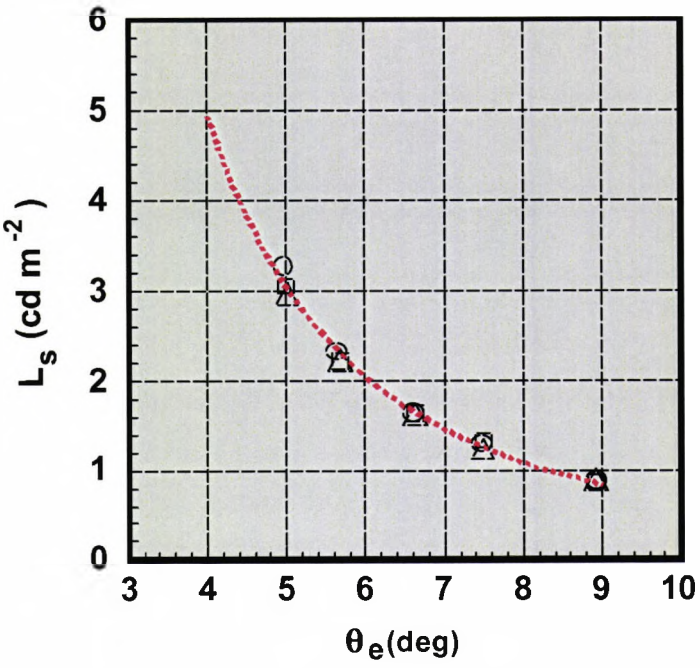


Figure 1-5: The scatter function for a single, normal subject measured using the City University Scatter Program

However, a new implementation of the flicker-nulling technique by Barbur and colleagues (1993) has allowed assessment of the full scatter function leading to the revelation that the angular distribution of scattered light does vary and can significantly affect visual performance. Both the target and glare annuli are displayed on a high-resolution colour monitor with a maximum luminance of 100cd/m^2 viewed from 70 cm (section 4.3.1). The null point is determined six times for each of five different glare angles using a staircase procedure with variable step sizes. In order to generate a sufficiently high illuminance (E) in the plane of the pupil while maintaining a low display luminance, extended scatter annuli are required with the outer eccentricity adjusted automatically to keep E constant for all five annuli. Point sources on an extended annulus have a range of eccentricities therefore the program computes the effective eccentricity (θ_e) of each annulus (Barbur et al., 1993) (figure 1.5). As is the case for the Straylightmeter, fixation errors are inconsequential since the spatial relationship of the target and surrounding glare source is not altered by changes in fixation. A

photometric calibration procedure compensates for internal scatter within the display equipment for each scatter source employed. In addition, the luminance of the yellow separation annulus is adjusted to contribute a constant level of internal display scatter regardless of its size. Its luminance of around 25 cd/m^2 and the fact that it is contiguous with the test field help to maximise flicker sensitivity.

Previous attempts to measure the quantity and angular dependence of intraocular scattered light have produced inconsistent results. This is related to the assumption that the angular distribution (n) has a constant value of 2 and that any variability between individuals is due to changes in the quantity of scatter (k) alone (section 1.2.2.2) (Fry and Alpern, 1953; Vos, 1984). Measurements of straylight using the City University Scatter Program have identified the scatter index (n) as an important variable that can affect visual performance even when the straylight parameter (k) is normal. It has been suggested that a large proportion of the variation in the straylight parameter (k) noted in normal subjects may in fact be due to fluctuations in n, even when the total amount of light scattered in the eye remains unchanged. The poor correlation between previous assessments of light scatter and contrast sensitivity may be explained by these changes in the distribution of scatter (n).

Barbur and colleagues (Barbur et al., 1993; Barbur, Edgar, and Woodward, 1995; Barbur et al., 1995) found that the integral of the scatter function, a parameter they referred to as the integrated straylight parameter (k') led to greatly reduced subject variability. This suggests that n and k are not totally independent (Hennelly, Barbur, Edgar et al., 1998). In addition, high values of k' have been shown to relate to poor visual performance. The integrated scatter parameter (k') is proportional to the total amount of light scattered and its value depends on the illuminance in the plane of the pupil. Therefore comparison with data from other instrumentation requires knowledge of the pupil diameter. Light scatter should be uniform over the whole pupil, making the integrated straylight parameter (k') independent of pupil size. However scatter appears to vary over the pupil area due to focal scatter centres and non-uniform distribution, so that dilation of the pupil can result in a significant increase in k'. This has been noted in older eyes and

some contact lens wearers (Barbur et al., 1995) (figure 1.6). This fact may prove to have particular relevance to the assessment of those who perform visual tasks under low luminance conditions, e.g. driving or flying at night.

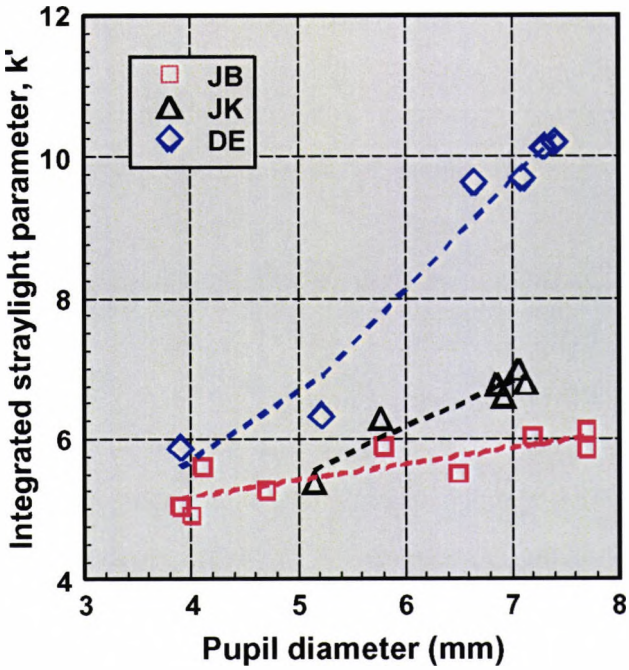


Figure 1-6: Variation in the integrated straylight parameter (k') with pupil diameter (from Barbur et al. 1995)

1.2.2.4 The effect of increased intraocular light scatter on visual performance

Intraocular scattered light can originate from an off-axis light source or bright object within the visual field. Often the straylight originates from the object of regard itself, reducing the contrast of the retinal image. Straylight from the glare source is superimposed over the retinal image resulting in an alteration of the state of adaptation of the retina and a reduction in the contrast of the retinal image (Holladay, 1926). To overcome the loss of visibility of the target, either the contrast or the size of the target must be increased. The reduction in image contrast depends on both the angular distribution and the quantity of the scattered light within the eye (Barbur et al., 1993; Barbur et al., 1995). When scattered light reduces visual performance it is said to produce disability glare (Vos, 1984). A strong correlation exists between increased forward light scatter (k) and the loss of contrast sensitivity, with the greatest effect at mid and high spatial frequencies (Wolf and Gardiner, 1965; Hess and Woo, 1978; Paulsson and Sjostrand, 1980; van den Berg, 1986; Elliott, 1987; Ginsburg, 1987; Koch and Lie, 1990; Irving and Woo, 1993). The correlation between intraocular light scatter (k) and Snellen visual acuity is significantly weaker, especially for glare angles greater than 3° (van den Berg, 1986; van den Berg and Spekreijse, 1987; Beckman et al., 1991), in agreement with the poor correlation between subjective complaints and high contrast acuity (Paulsson and Sjostrand, 1980; Abrahamsson and Sjostrand, 1986).
With reference to the empirical glare formula (Stiles, 1929):

$$L_s(\theta) = Ek\theta^{-n}$$

where $L_s(\theta)$ is the luminance of scattered light at the fovea, E is the illuminance in the plane of the pupil, visual performance is reduced when the quantity of straylight (k) increases.

Under photopic conditions, the Stiles-Crawford effect (section 1.1) reduces the impact of scattered light, defocus and aberrations on retinal image quality, although the extent of this effect on visual performance is not known (Enoch, 1972). Under low illumination, the influence of scattered light on visual

performance increases significantly, partly because of the increased brightness difference between low contrast objects and bright glare sources at night compared to during the day, but also because of the increase in straylight with increasing pupil diameter (Barbur et al., 1995). In addition, the Stiles-Crawford effect becomes less dominant as the influence of the cones is reduced (Crawford, 1937).

1.2.3 Monochromatic aberrations

For pupil diameters greater than 2.0 mm, the effect of increased aberrations dominates the point spread function and the major factors that degrade retinal image quality are defocus and on-axis astigmatism (refractive error). Both of these are correctable using conventional spectacle lenses. Optical aberrations other than defocus, on-axis regular astigmatism and tilt cannot be corrected by simple spectacle lenses. The wavefront aberration of a system represents the deviation from the ideal wavefront surface, (i.e. a spherical surface) of the actual wavefront surface. One method of describing wavefront deviations is to use Zernike polynomials with first-order terms relating to prismatic effects, and second-order terms to defocus and regular astigmatism. Higher order terms describe deviations of the wavefront that cause specific pattern distortions of the point spread image. The most important terms are coma, spherical aberration, astigmatism, distortion and field curvature.

Spherical aberration is present on-axis and is independent of object field angle. The light rays passing through the more peripheral parts of the pupil are focused in front or behind the paraxial focal point. The deviation of light rays and therefore the extent of the focusing defect increases with increasing distance from the axis of the optical system (figure 1.7). Paraxial rays are not affected and form the paraxial image point. Marginal rays passing through the edge of the pupil focus at the marginal focus. The longitudinal spherical aberration *(LSA)* is the difference between marginal and paraxial focal points specified in dioptres of blur and is proportional to the square of the pupil diameter:

$$LSA = W_{040}d^2$$

where W_{040} is a contrast depending on the level of aberration and d is the pupil diameter in millimetres. Spherical aberration can be classified as positive (under-

corrected) in which peripheral light rays converge closer to the refracting surface, or negative (over-corrected) in which peripheral light rays converge beyond the retina.

Measurements of axial monochromatic aberrations in the normal population suggest that there is significant variation between individuals (Walsh and Charman, 1985; Porter, Cox, Guirao et al., 2000). Those with a small degree of positive spherical aberration predominate (0.50D), while some individuals exhibit positive spherical aberration in the region of 1.0-2.0D and a minority exhibit negative spherical aberration (Jackson 1888). Others have reported similar findings in the adult population but a predominance of negative spherical aberration in children under six years (Jenkins, 1963; Cornsweet and Crane, 1970). Spherical aberration tends to increase with increasing myopia (Collins, Wildsoet, and Atchison, 1995; Carkeet, Luo, Tong et al., 2002). The two eyes of an individual tend to correlate well in terms of higher order aberrations (Liang and Williams, 1997).

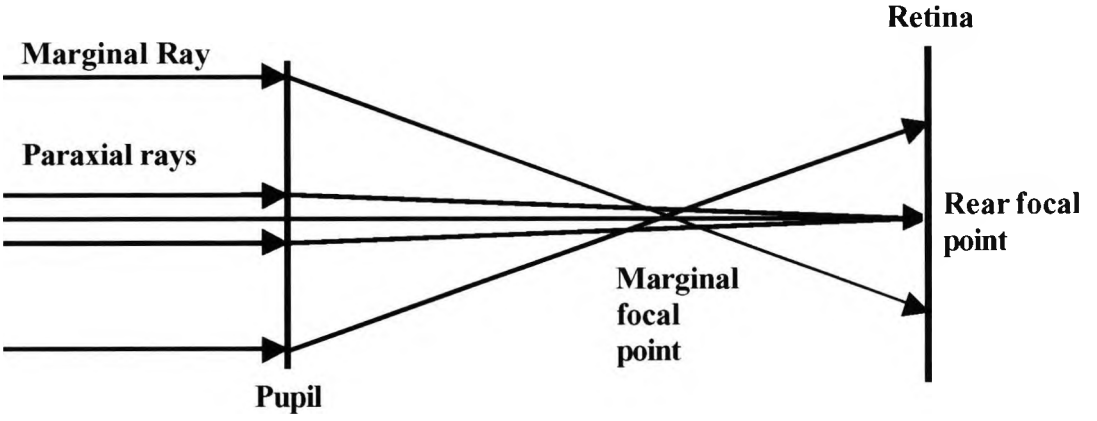


Figure 1-7: Longitudinal spherical aberration (positive) showing paraxial rays focusing on the retina and marginal rays focusing in front of the retina

The peripheral flattening of the cornea (negative asphericity) acts to minimise spherical aberration (Holladay, Lynn, Waring et al., 1991; Seiler, Reckmann, and Maloney, 1993) although both spherical aberration and coma remain significantly larger for the cornea than for the complete eye; the lens compensates for some of

the positive spherical aberration of the cornea, particularly in its accommodated state (Tomlinson, Hemenger, and Garriott, 1993; Artal and Guirao, 1998).

Like defocus, spherical aberration degrades the retinal image by increasing the width and reducing the height of the point spread function, particularly when the eye is fully corrected for defocus (Campbell and Green, 1965). This results in a loss of contrast sensitivity, particularly at mid spatial frequencies (Lyons, Mouroulis, and Cheng, 1996).

Coma is another important aberration affecting peripheral light rays that causes the retinal image of a point source to take on a teardrop shape with the greatest light intensity at the pointed end. Coma is classified as negative when the more peripheral rays are imaged closer to the axis than paraxial rays, spreading the image out towards the axis, and positive when the focus of the peripheral rays is laterally displaced away from the focal point of the paraxial rays. Because coma affects off-axis object points, its influence on central visual acuity should be limited in a normal eye, but the displacement of the fovea approximately 5° from the optical axis means that it always has some influence. The retinal image is degraded by both a reduction in the height of the point spread function and a shift of the aberration–free position.

Because both spherical aberration and coma involve peripheral rays, they are highly dependent on pupil size. These aberrations reportedly increase by a factor of between five and nine times as the pupil dilates from 3 to 7mm, with the extent of the effect increasing with age (Oshika, Klyce, Applegate et al., 1999a; Applegate, Artal, and Lakshminarayanan, 1998; Martinez, Applegate, and Klyce, 1998). As a consequence, aberrations have significantly more influence on visual performance under low illumination. Sizeable increases in spherical aberration and coma have been shown to result in a significant reduction in the modulation transfer function of the eye for large pupil diameters (Hemenger, Tomlinson, and Caroline, 1989). Not surprisingly, visual performance tends to be better when the pupil is constricted and therefore minimising the influence of aberrations, despite the reduction in retinal illuminance (Berman, Fein, Jewett et al., 1996).

Aberrations alter with the accommodative state of the eye with an increase in accommodation resulting in a reduction in positive spherical aberration that reaches a minimum for focussing distances between 0.33-0.67m from the eye (Jenkins 1963; He, Burns, and Marcos, 2000). Coma is also seen to reduce with accommodation. In addition, there is a constant micro fluctuation of aberrations, of the order of 0.1 to 0.2D with a frequency of a few Hz (Charman and Heron 1988). The measurement of aberrations is further complicated by the evaporation and thinning of the tear film (Tutt, Begley, Bradley et al., 1997; Thibos and Hong, 1999). The underlying day-to-day fluctuation is relatively small (Thibos, 2000).

Chromatic aberration is also present in the eye and prevents simultaneous focusing of all visible wavelengths at the same point. The transverse effects of chromatic aberration cause a change of magnification that varies with wavelength. Luminance contrast is mediated largely by signals from the L and M cones but chromatic aberration is greatest for short wavelengths and therefore has limited effect on the contrast sensitivity of the eye.

1.2.4 Causes of increased scatter and aberrations

1.2.4.1 Age

The transmittance of the ocular media across the visible spectrum does not change significantly between the ages of 5 and 30 years (Norren and Vos, 1974; Coren and Girgus, 1972). After this age, a 25% reduction in transmission is seen up to the age of 60 years (Said and Weale, 1959), associated with the gradual yellowing of the crystalline lens. This also results in a shift in the peak wavelength of maximum absorption during the fourth decade of life (Cooper and Robson, 1969). Other naturally occurring age changes include the loss of pigment from some ocular structures such as the iris, and a slight reduction in corneal transparency (Olsen, 1982; Smith et al., 1990). In addition, changes to the crystalline protein of lens fibres result in disorganisation of the lens fibre matrix and an increase in protein aggregate molecules, particularly in the region of the anterior cortex and nucleus (Allen and Vos, 1967). The decrease in pupil size with age (senile miosis) is well documented and results in a slight reduction in retinal illuminance and

hence a reduction in sensitivity to contrast, particularly for high spatial frequencies.

Related to the reduction in transmittance is an increase in backscatter. A four-fold increase in backscatter from the cornea and crystalline lens occurs between the ages of 10 to 80 years but because of the poor correlation with forward scatter (section 1.2.2.3.a) backscatter cannot predict the increase in contrast threshold with age (Allen and Vos, 1967; Sigelman, Trokel, and Spector, 1974). A doubling of the opacification of the lens has been detected between the ages of 10 and 40 years with a 16-fold increase between the ages of 40 and 80 years (Wolf and Gardiner, 1965).

Estimates of the mean increase in forward light scatter between the ages of 20 years and 70 years, range from 2.0 to 2.57 times (IJspeert et al., 1990; Yager, Yuan, and Mathews, 1992; Whitaker et al., 1993). The angular distribution of intraocular light scatter (n) is reportedly unrelated to age (Fisher and Christie, 1965; IJspeert et al., 1990) and on that basis Fisher and Christie determined that the straylight parameter (k) depended on age (A) as follows:

$$\mathbf{k = (0.2A + 0.4)\pi}$$

Others have noted that the increase in forward scatter only begins after the age of 40 years (Wolf, 1960; Bena-Sira, Weinberger, Bodenheimer et al., 1980; Elliott et al., 1991b; Fujisawa and Sasaki, 1995; Hennelly et al., 1998).

Ocular high-order aberrations stay relatively constant between the ages of 20 and 40 years (He et al., 2000). Over a range of pupil sizes, higher order aberrations, in particular coma, increase with age implying that the cornea becomes less symmetrical over time (Artal, Ferro, Miranda et al., 1993; Berrio, Guirao, Redondo et al., 2000; Oshika et al., 1999a). There is also some evidence to suggest an increase in positive spherical aberration with age (Jenkins, 1963; Guirao and Artal, 1999; Guirao, Redondo, and Artal, 2000; Guirao et al., 2000). On the other hand, the natural reduction in pupil size with age (senile miosis) tends to neutralise these increases (Calver, Cox, and Elliott, 1999a).

1.2.4.1.a Changes in visual performance with age

The increase in forward light scatter occurs gradually and therefore tends to go unnoticed by the individual, as they are able to adapt to the slowly reducing contrast of the retinal image up to a point (IJspeert et al., 1990). Compared to young adults, older adults over the age of about 60 years show decreased contrast sensitivity, although conclusions as to whether all spatial frequencies are affected or just mid and high, or low and mid, vary between studies (Owsley, Sekuler, and Siemsen, 1983; Derefeldt, Lennerstrand, and Lundh, 1979; Ross, Clarke, and Bron, 1985). It has been suggested that the contrast required at high and intermediate spatial frequencies is doubled in older subjects, with the difference between young and old subjects lessening with decreasing frequency until it becomes insignificant at 0.5 cycles/degree (Arundale, 1978; Derefeldt et al., 1979; Sekuler, Owsley, and Hutman, 1982; Hemenger, 1984). As with forward light scatter, little deterioration occurs before the age of 40 years (Nio, Jansonius, Fidler et al., 2000).

Assessments of glare sensitivity with age also mimic the findings of forward light scatter measurements with a gradual increase up to the age of 40 years, followed by a more rapid increase approaching a maximum at around 80 years of age (Wolf, 1960; Allen and Vos, 1967; Wolf and Gardiner, 1965; LeClaire, Nadler, and Weiss, 1982; Bailey and Bullimore, 1991; Elliott and Bullimore, 1993). The number of letters on a LogMAR chart that are lost in the presence of glare increases linearly with age (Bailey and Bullimore, 1991), but accelerates rapidly above age 65 years (Haegerstrom-Portnoy, Schneck, and Brabyn, 1999) particularly for low contrast acuity (Bailey and Bullimore, 1991). A reduction in visual acuity with age has been noted over a range of contrast levels (Martin, 1999).

The increase in intraocular light scatter with age has been attributed in the main to changes in the lens proteins and hence the structure of the lens fibre lattice (Spector, Li, and Sigelman, 1974), and the loss of contrast sensitivity with age is consistent with the increase in intraocular light scatter (Hemenger, 1984). However, one study comparing contrast sensitivity in normal age matched

patients with patients who had undergone crystalline lens removal and intraocular lens implantation, found no significant difference between the groups, suggesting that the crystalline lens is not a major contributor to the reduction in visual performance with age (Weatherill and Yap 1986). Others have also questioned the role of light scatter in the reduction in contrast sensitivity seen with increasing age, suggesting that high spatial frequency losses could be simply related to the reduction in retinal illuminance associated with senile miosis and increased lenticular light absorption (Kelly, 1972; Elliott, 1987). The reduction in the optical quality of the eye associated with increasing aberrations is unlikely to significantly affect visual function because aberrations are minimised by senile miosis (Guirao and Artal, 1999; Calver, Cox, and Elliott, 1999). Neural factors are another possible explanation for reduced contrast sensitivity with age, e.g. retinal cell degeneration associated with the build-up of waste products and a reduced vascular supply. Fifty-four percent of cells are lost between the ages of 20 and 87 in the macular projection region of the striate cortex alone (Devansy and Johnson, 1980). Comparison of the contrast sensitivity function with a measurement of retinal and neural sensitivity, bypassing the optics of the eye, has uncovered a significant decrease in contrast sensitivity at frequencies above 4 cycles/degree (medium and high frequencies) which can be primarily attributed to retinal and neural degeneration, with a much smaller contribution from the increase in light scatter with age (Elliott, 1987). Others have also confirmed the presence of a significant neural element to the reduction in visual performance seen with age (Whitaker and Elliott, 1992).

1.2.4.2 Ocular pigment disorders

van den Berg discovered that the level of pigmentation of the ocular wall and fundus plays a significant role in determining the level of intraocular light scatter. Overall pigmentation is quite well described by the colour of the iris and eyes with blue irides demonstrate higher levels of scatter than those with brown iridies (van den Berg, 1994) (section 1.2.2.1.c). Conditions such as albinism and pigment dispersion syndrome (van den Berg et al., 1990), in which the ocular pigment is reduced or absent, result in an increase in transmission through the ocular wall and iris. Pigment dispersion syndrome, whether of an idiopathic nature, related to

iritis or associated with intraocular surgery, increases scatter and can lead to debilitating glare problems (van den Berg, 1986), (figure 1.8).

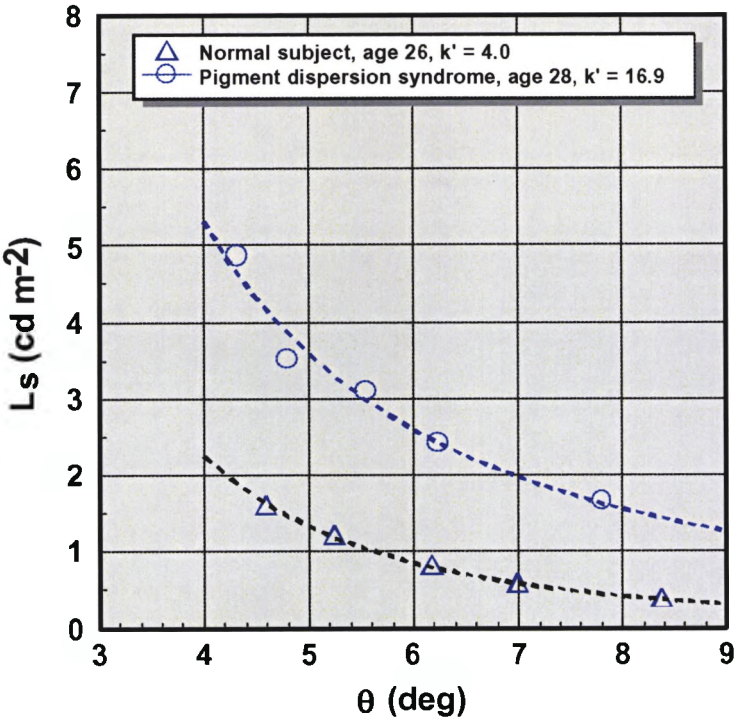


Figure 1-8: Scatter function of a subject with pigment dispersion syndrome compared to an age-matched normal

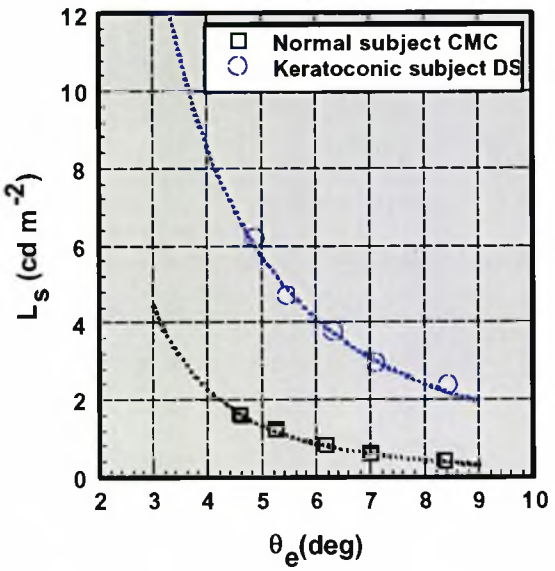
1.2.4.3 Corneal oedema, opacities and dystrophies

Oedematous corneas show reduced transparency due to an increase in backscatter (Farrell et al., 1973), and the transmission of light decreases linearly with the ratio of actual corneal thickness to normal thickness. A reduction in visual performance is also seen as the result of an increase in forward light scatter. For grossly swollen corneae, the angular distribution of straylight is modified so that its intensity varies with the inverse square of the wavelength, suggesting the presence of large inhomogeneities within the cornea. Electron micrographs of oedematous corneae have revealed large, fibril-free stromal areas known as lakes. The lakes increase in both size and number as the cornea swells, consistent with the change in angular distribution associated with wavelength.

Corneal scars result in an increase in both forward and backscatter (van den Berg, 1986) with lower density opacities resulting in greater levels of forward scatter

than dense scars. For this reason, tattooing of scars can lead to an improvement in visual performance (Woodward, 1996).

A number of corneal dystrophies such as granular dystrophy, alter the transparency of the cornea, and not surprisingly increase intraocular light scatter (van den Berg, 1986).



	Normal CMC	Keratoconic DS
Age	26	26
n	2.37	1.82
k	16.13	28.22
k'	3.99	18.18

Figure 1-9: Comparison of the scatter functions for a normal and a keratoconic subject

Keratoconus is an ectatic dystrophy that commonly causes symptoms of severe disability glare related to increased forward light scatter as the arrangement of collagen fibrils is altered and the central cornea thins (Barbur et al., 1993). Figure 1.9 compares keratoconic subject DS with an age-matched normal subject. Subject DS shows a large increase in the overall quantity of scattered light.

1.2.4.4 Contact lenses

There is overwhelming evidence that contact lenses do in some way cause increased light scatter (Bergevin and Millodot, 1967; Barbur et al., 1993; Elliott et al., 1991b; Applegate and Wolf, 1987; Lohmann, Fitzke, O'Brart et al., 1993) whether through lens deposition (Olsson, Epstein, and Philipson, 1979) or microscopic changes in the corneal structure. However, no significant correlation between deposition level and light scatter has been found (Elliott et al., 1991b). Lens wear can cause a degree of corneal oedema if the transmissibility of the lens material is poor (Woodward, 1996), they are worn for too long or the patient's cornea has a particularly high oxygen demand, although no evidence of corneal swelling was detected in eyes showing a raised light scatter parameter following contact lens wear in one study (Woodward, 1996). Elliott and colleagues detected slightly more intraocular scatter in rigid contact lens wearers than soft lens wearers, although on removal of the lenses, the trend was reversed (Elliott et al., 1991b). Immediate assessment revealed a significant difference between soft lens wearers and the control group, but not between rigid lens wearers and the controls, suggesting that the material or design of a rigid lens causes the increase in light scatter whereas soft lenses increase scatter by inducing physiological changes such as corneal oedema. Results were highly variable, indicating that increased intraocular light scatter is not significant for all lens wearers. An increase in forward light scatter as the pupil dilates, relating to the periphery of the cornea, has been reported in some long-term contact lens wearers but is not significant for young subjects (Barbur et al., 1995).

There is some evidence of a reduction in both low contrast acuity and contrast sensitivity in contact lens wearers (Hess and Carney, 1979; Woo and Hess, 1979; Lohmann et al., 1993). Some soft contact lens wearers experience glare disability while others exhibit improved visual performance in the presence of glare (Applegate and Jones, 1989), probably related to a reduction in optical aberrations with pupil constriction and variability of the lens material and corneal oxygen requirements between subjects. Verriest and Uvijls (1989) reported no reduction in visual performance under glare conditions but all assessments were undertaken

during the first few hours following lens insertion before any hypoxic changes were likely to have occurred.

1.2.4.5 Cataract

Opacification of the crystalline lens results in a condition known as cataract. Cataracts vary in their cause, location within the lens and age of onset, with senile or age-related cataract being the most prevalent. The term encompasses age-related nuclear, cortical or posterior subcapsular changes although combinations of two or three of these forms are often seen. Senile cataracts tend to appear either white or yellow (backscatter) with aggregates or the accumulation of yellow insoluble protein pigment implicated in each case respectively. Backscatter and reflected light are associated with structures significantly larger than the wavelength of light (Philipson, 1969). Increased forward light scatter has also been attributed to the aggregation of insoluble proteins of a size similar to the wavelength of light. These structures are located between the lens fibres causing disruption of the ordered array and increased inhomogeneity within the lens. The influence of cataract on the angular distribution of intraocular light scatter is uncertain, with Elliott and colleagues noting no change (Elliott, Gilchrist, and Whitaker, 1989) such that the distribution of forward light scatter could have been produced by an extreme version of aging (van den Berg, 1995). Others noted the less likely scenario of a modified distribution but no change in quantity (van den Berg, 1994). A slight increase in forward scatter at longer wavelengths is commonly seen in cataract patients, probably related to the development of a distinct yellow pigment within the lens partially masking the short wavelengths (Whitaker et al., 1993) (see section 1.2.2.1.b).

The increase in forward light scatter as a result of cataract causes a decrease in retinal image contrast (Elliott, Hurst, and Weatherill, 1991a; Adamsons, Rubin, and Vitale, 1992). The extent of the increase depends on the type of cataract since the histology of each form of cataract varies. Cortical cataracts relate to the swelling of lens fibres and the development of protein aggregates. Nuclear cataracts relate to the accumulation of high molecular weight proteins, and posterior subcapsular cataracts relate to both the swelling of lens fibres and

changes in the lens epithelium. Cortical and posterior subcapsular opacities produce very high levels of straylight (90% and 290% increase respectively), (de Waard et al., 1992). In comparison, nuclear cataracts produce less of an increase in forward scatter (approximately 80%), or perhaps no increase (Mainster, Timberlake, and Schepens, 1981; Hirsch, Nadler, and Miller, 1984; Lempert, Hopcroft, and Lempert, 1987) but the greatest level of backscatter (de Waard et al., 1992).

The variation in the quantity of scatter produced by the different types of cataract is reflected by visual performance data. All types of senile cataract produce a reduction in contrast sensitivity that is particularly significant under conditions of glare (Wolf and Gardiner, 1965; Abrahamsson and Sjostrand, 1986; Smith, Pratzer, Webster et al., 1987; Beckman et al., 1991; Superstein, Boyaner, and Overbury, 1999) or low illumination (Anderson and Holliday, 1995). Posterior subcapsular cataracts of grade two or more (LOCS III: Chylack, Wolfe, Singer et al., 1993) produce the greatest deficit and the highest prevalence of symptoms, corresponding to the most significant increase in forward light scatter (Harbin, 1973; Elliott et al., 1989; Koch, 1989; Masket, 1989; Lasa, Datiles, Caruso et al., 1993). High contrast acuity is also seen to drop significantly in the presence of a glare source such as the Brightness Acuity Tester (BAT) (Holladay et al., 1987; Elliott et al., 1989; Elliott et al., 1991a) although the correlation between high contrast acuity without glare and intraocular light scatter is poor, particularly for posterior subcapsular opacities (Paulsson and Sjostrand, 1980; van den Berg, 1986; Abrahamsson and Sjostrand, 1986).

1.2.4.6 Aphakia and pseudophakia

The surgical removal of cataract leaves the eye aphakic or more commonly pseudophakic, but some studies suggest that levels of forward light scatter are still elevated in pseudophakics with a monofocal intraocular implant (Martin, 1999) even when there is little or no posterior capsular opacification (section 1.2.4.7), (Witmer, van den Brom, Kooijman et al., 1989; IJspeert et al., 1990; Claesson, Klaren, Beckman et al., 1994). There is certainly more variability among the aphakic and pseudophakic populations. Possible reasons why the levels of

forward scatter do not always return to age-matched levels or better, include poor intraocular lens positioning or design, a large difference in refractive index between the intraocular lens and the aqueous humour, and opacification of the posterior lens capsule. Intraocular lenses with a rounded edge reduce the intensity of glare problems compared to sharp edged lenses (Holladay, Lang, and Portney, 1999).

Aphakes and psuedophakes show a deficit in contrast sensitivity compared to age-matched normals, particularly at mid and high spatial frequencies compared to age-matched normals (Hess, Woo, and White, 1985; Weatherill and Yap, 1986). Indirect measurements of intraocular light scatter in the form of glare assessments have identified some aphakes and pseudophakics with reduced glare sensitivity compared to age-matched normals (Wolf, 1960; Wolf and Gardiner, 1965; Masket, 1989), but others with greater levels of glare sensitivity corresponding to the increase in forward light scatter (Witmer et al., 1989; Miller and Lazenby, 1977). Whether patients are corrected with spectacles, contact lenses or a monofocal intraocular lens appears to make little difference to glare sensitivity (Miller and Lazenby, 1977; LeClaire et al., 1982; Nadler, Jaffe, Clayman et al., 1984; Knighton, Slomovic, and Parrish, 1985; Van der Heijde, Weber, and Boukes, 1985; Weatherill and Yap, 1986).

Not surprisingly, multifocal intraocular lenses cause a more significant reduction in contrast sensitivity, related to a greater increase in straylight and aberrations and the division of light between two focal points, but visual acuity is rarely affected (van den Berg and IJspeert, 1991b; Witmer et al., 1989) except at low contrast levels (Arens, Freudenthaler, and Quentin, 1999).

1.2.4.7 Posterior capsular opacification

Following extracapsular cataract extraction and intraocular lens implantation, it is not uncommon for the posterior surface of the capsular bag to gradually opacify as residual lens epithelial cells proliferate. In such cases, the visual benefits of surgery may be reduced or lost altogether with a significant increase in glare sensitivity related to increased forward scatter, although high contrast visual

acuity may remain unchanged (Miller and Lazenby, 1977; Knighton et al., 1985). The extent of the visual loss depends on the nature of the opacification with dense plaques causing less forward scatter and more backscatter. The Neodymium-YAG laser is used to produce a hole in the posterior capsule, causing the opacified capsule to peel back to reveal a clear optical axis. This has been shown to improve both visual acuity and glare sensitivity by a factor of two (Gardner, Straatsma, and Pettit, 1985; Slomovis and Parrish, 1985), although levels of intraocular light scatter may remain slightly elevated (Claesson et al., 1994).

1.2.4.8 Miscellaneous conditions

In addition to the conditions detailed in the preceding section, intraocular light scatter is known to increase as a result of certain pathological conditions such as anterior uveitis, due to flare and inflammatory cells in the anterior chamber, and vitreous opacities (van der Heijde et al., 1985; van den Berg, 1986). In addition, myopia greater than –6.00D (uncorrected) has been shown to cause an increase in forward light scatter (Verriest and Uvijls, 1989) although the exact cause of this effect is unknown.

1.2.4.9 Corneal refractive surgery

Surgical techniques have been developed to modify the corneal shape and hence reduce or eliminate refractive error. These include microsurgical procedures such as radial keratotomy (RK) and astigmatic keratotomy (AK) that are confined to the peripheral and mid-peripheral cornea. Excimer laser procedures involving ablation of the optic axis have also been developed and include photorefractive keratectomy (PRK) and laser assisted in-situ keratomileusis (LASIK). The three most common procedures will be discussed in terms of their effect on intraocular light scatter and resulting visual performance.

1.2.4.9.a Radial keratotomy (RK)

This was the first technique to be widely used in the treatment of myopia (Fyodorov and Durnev, 1979) and involves the use of a diamond micrometer blade to create radial incisions through 95% of the corneal thickness in the mid-peripheral and peripheral cornea, (figure 1.10) leaving a central clear zone of 3-4mm in diameter on average (Waring, Lynn, Gelender et al., 1985).

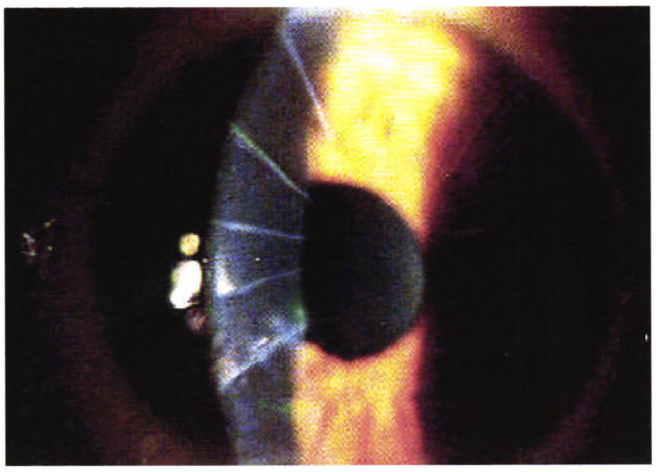


Figure 1-10: Radial scars resulting from a radial keratotomy procedure

The incisions substantially weaken the tissue, resulting in a flattening of the central cornea and hence a reduction in myopia. RK has an advantage over excimer laser procedures in that it does not involve treatment of the central cornea, potentially making it less likely to impact on visual performance.

However, some treatments require very long incisions leaving clear zones as small as 1.16mm in diameter (Grimmett and Ogawa, 1998).

Intraocular light scatter

A significant increase in the quantity of intraocular light scatter (k) has been reported during the first six months post-RK, followed by a gradual decrease over time (Veraart, van den Berg, Hennekes et al., 1995). Scatter beyond 3.5° only becomes significant for larger pupil sizes when the radial incisions are more exposed. The quantity of straylight is unrelated to the number of surgical incisions but increases by a factor of 1.4 for 4mm pupils and 2.0 for 8mm pupils, compared to a group of age-matched normals.

Aberrations

The central flattening and mid-peripheral steepening of the cornea produced by RK causes a significant increase in the optical aberrations of the eye in most cases, particularly positive spherical aberration (Hemenger et al., 1989; Holladay et al., 1991; Schwiegerling, Greivenkamp, and Miller, 1996b). One study noted that third and fourth order-like aberrations and radial corrugations were increased 11, 136 and 181-fold respectively for 7.0 mm pupils, with a strong correlation between the magnitude of the surgically induced reduction in myopia and the increase in corneal aberrations (Applegate, Hilmantel, and Howland, 1996). A significant increase in the overall corneal wavefront variance for a 3.0 mm pupil has been reported, increasing to 33 times preoperative values for a 7.0 mm pupil, with little change in the aberrations over a three year follow-up period (Applegate, Howland, Sharp et al., 1998). In addition, the size of the incision-free zone can account for 40% of the variance in the log of the wavefront error (Applegate et al., 1998). As well as causing degradation of the retinal image, large increases in spherical aberration tend to lead to a shift towards myopia with pupil dilation. Such an effect has been detected in 19% of radial keratotomy patients compared to 9% of controls, with potentially serious implications for night vision (Holladay et al., 1991).

Visual performance

The Prospective Evaluation of Radial Keratotomy (PERK) study reported a loss of two lines of corrected visual acuity (high contrast) in 13% of eyes at one year, and 3% of eyes after ten years (Waring, Lynn, and McDonnell, 1994). Others have noted no significant loss of visual acuity (Applegate et al., 1998).

Studies of contrast sensitivity post-RK are inconclusive, probably due to the variety of different methods of assessment and lighting conditions employed (section 2.2.1), and the wide range of outcomes post-RK. Some studies report no statistically significant loss of sensitivity (Waring et al., 1985; Trick and Hartstein, 1987) including under low illumination (Olsen and Andersen, 1991; Applegate, Trick, Meade et al., 1987; Applegate et al., 1987), while others show a transient loss in some patients that recovers by 10-24 months post-RK (Ginsburg, Waring, and Steinberg, 1990; Krasnov, Avetisov, Makashova et al., 1988; McDonald, Haik, and Kaufman, 1983; Ghaith, Daniel, Stulting et al., 1998). A couple of studies have reported a contrast sensitivity deficit in some patients but an increase in others (Tomlinson and Caroline, 1988; Ginsburg et al., 1990; McDonald et al., 1983). When a loss has been reported, it appears to be greatest for mid and high spatial frequencies (Tomlinson and Caroline, 1988; Hemenger et al., 1989; Ginsburg et al., 1990; Schwiegerling, Greivenkamp, and Miller, 1996a) with high spatial frequencies recovering by approximately four months but mid spatial frequencies taking longer to return to preoperative levels (Krueger, Krasinski, and Radzewicz, 1993). As with RK-induced aberrations, there seems to be a strong correlation between the loss of contrast sensitivity and the size of the clear, incision-free cornea with respect to the pupil diameter, with smaller zones leading to a greater depression of sensitivity, probably related to an increase in both aberrations and intraocular light scatter from the incisions (Ginsburg et al., 1990; Boxer-Wachler B.S., Durrie, Assil et al., 1999). The extent of the increase in corneal wavefront variance correlates with the loss of contrast sensitivity when the pupil is large (7.0 mm) (Applegate et al., 1998) but not for pupils of the order of 3.0 mm, explaining some of the variability between studies. For example, two studies failed to detect a reduction in contrast sensitivity under normal photopic conditions but detected a significant decrement both with and without glare when

pupils were artificially dilated (Atkin, Asbell, Justin et al., 1986; Bullimore, Sheedy, and Owen, 1994).

Complaints of glare, starbursts and halos at night are relatively common post-RK (Waring et al., 1985) although the PERK study group failed to detect a significant increase in glare one year after surgery despite symptoms in 52% of subjects. This was probably related to the use of the Miller-Nadler glare tester, which demonstrates poor sensitivity (section 2.3.1.a) (Waring et al., 1985). Other studies have uncovered a reduction in contrast sensitivity with glare that increases significantly in the presence of a large pupillary aperture, with a greater effect for temporally modulated targets (flicker) than spatially modulated targets (gratings) (Atkin et al., 1986; Bullimore et al., 1994). The fact that a number of studies have shown a loss of contrast sensitivity in the presence of a dilated pupil, with only a slight reduction in the presence of glare, implicates aberrations rather than scatter as the main cause of reduced visual performance post-RK (Bullimore et al., 1994).

Excimer Laser Procedures

Photorefractive keratectomy (PRK) and laser assisted in-situ keratomileusis (LASIK) involve photoablation of minute layers of corneal tissue using an Argon Fluoride excimer laser (193nm). Tissue is removed by breaking organic molecular bonds causing the photodecompensation of organic polypeptides and the ejection of debris away from the cornea at supersonic speeds. The energy is absorbed within a few microns of the ablation, minimising collateral damage. The controlling computer is programmed according to a specific algorithm to generate the diameter and depth of the ablation needed to achieve the required refractive change, based on the average amount of tissue removed per pulse (Munnerlyn, Koons, and Marshall, 1988). As with radial keratotomy, the majority of patients are treated for myopia, requiring the corneal profile to be flattened by removing more tissue centrally than peripherally.

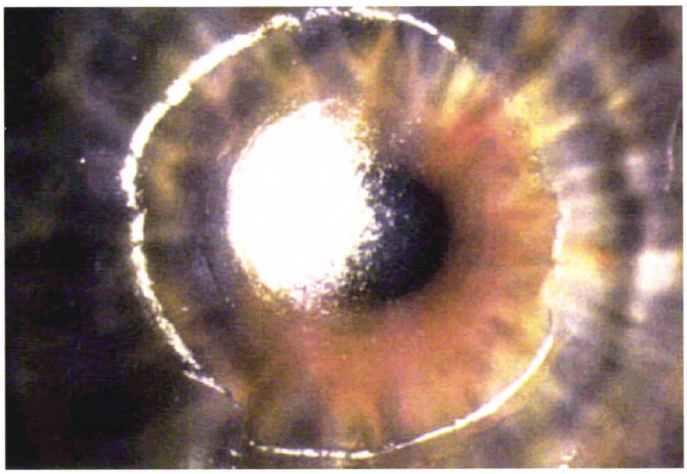


Figure 1-11: Exposed stromal bed and margin of the epithelium immediately after PRK

1.2.4.9.b Photorefractive keratectomy (PRK)

Tissue is ablated from the anterior limiting lamina and corneal stroma following manual, laser or alcohol removal of the overlying epithelium (figure 1.11). Following the procedure, epithelial cells from the margin of the wound migrate and proliferate to form a single layer of cells across the stroma within 4.6 +/- 0.2 days (McDonald, Liu, Byrd et al., 1991). Mitosis and migration gradually increase the number of layers to form stratified epithelium with normal intercellular

junctions. This process is generally complete within four weeks of PRK with areas of thickened epithelium forming over stromal defects and thinner areas found overlying protrusions, effectively smoothing the anterior corneal surface. Functional vision returns upon re-epithelialisation with 83% of low myopes (-1.00D to -5.99D) and 61.4% of high myopes (-6.00D to -19.00D) achieving an unaided vision of 6/12 at 1 week (Reich, Rosen, Unger et al., 1996). During this time period, the stroma is invaded by inflammatory cells (polymorphonucleocytes) as a result of agents released in response to the epithelial insult. These cells clean the wound and disappear on epithelial closure. Programmed cell death or apoptosis of the keratocytes within the anterior 50-200μm of the stroma is initiated by the procedure, but repopulation with irregular, activated cells occurs within a few days (Matsuda and Smelser, 1973; Fantes, Hanna, Waring et al., 1990) and signifies the beginning of stromal remodeling. These keratocytes undergo fibroblastic transformation to become involved in the synthesis of new connective tissue (collagen types I, III-VI) and proteoglycans (Corbett, Prydal, Verma et al., 1996), and release two growth factors that modulate epithelial cell growth (Wilson, 1997). Keratocyte activity returns to normal levels within about three months of PRK although a degree of hypercellularity within the new tissue can remain for many years. The new stroma gradually becomes more regular and eventually transparent but does not return to a completely regular lamellar arrangement.

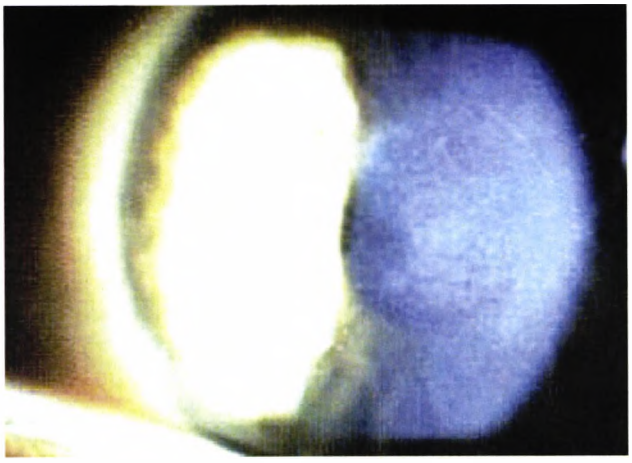


Figure 1-12: Stromal haze post-PRK visible as a result of backscattered and reflected light

The main concern following PRK is the development of a sub-epithelial opacification known as haze (figure 1.12), which first appears between two and four weeks, peaking in intensity between two and six months and gradually subsiding in most cases by 12 months (Gartry, Kerr Muir, and Marshall, 1992; Lohmann, Gartry, and Muir, 1991a; Seiler, Kahle, and Kriegerowski, 1990; McDonald, Kaufman, and Frank, 1989; McDonald, Frantz, and Klyce, 1990). Haze does not appear to follow the same time course as any of the measures of visual performance (Niesen, Businger, Hartmann et al., 1997). Initially it is homogeneous across the treated zone but as it begins to subside it becomes more heterogeneous with the development of focal patches of irregular haze. These focal areas are more likely to result in greater forward scatter than homogeneous haze (Maldonado, Arnau, Navea et al., 1995). The treatment of higher degrees of myopia is associated with more intense and more persistent haze (Gartry et al., 1992; O'Brart, Lohmann, Fitzke et al., 1994b; Maldonado et al., 1995).

Intraocular light scatter

Stromal haze is visible to the observer as a result of reflected light and to a degree, backscattered light. Levels of backscatter have been reported by a number of studies but are of limited practical use since backscatter is only weakly correlated with the quantity of forward light scatter (Allen and Vos, 1967; de Waard et al., 1992). Backscatter has been shown to correlate with logMAR visual acuity, more so than with haze (Braunstein, Jain, McCally et al., 1996). Scatterometry has revealed a strong correlation between levels of backscatter and the percentage of reformed extracellular matrix (Chang, Benson, and Azar, 1998). Lohmann and colleagues noted a biphasic increase in backscattered light with the first peak occurring two months post-PRK followed by a gradual decline (Lohmann, Gartry, Kerr Muir et al., 1991b). The second rise appeared to correspond to an increase in reflected light beginning three months post-operatively and peaking around four to six months. It was attributed to renewed cellular activity associated with the cessation of steroid treatment. Scanning laser ophthalmoscopy has revealed an increase in backscatter in the region of the transition zone, providing one explanation for the increase in scatter with pupil dilation (Tassignon, Van de Velde, and Trau, 1997).

Estimates of forward light scatter post-myopic PRK using the direct compensation technique indicate an initial increase in the quantity of straylight (k) occurring about two weeks post-PRK and lasting for 3-6 months. This is followed by a gradual reduction to levels comparable with spectacle and contact lens wearers (matched for degree of myopia) by 12 months (Veraart et al., 1995; Lohmann et al., 1993; Miller and Schoessler, 1995). The variation between PRK subjects is significantly greater than for normal or contact lens wearing subjects at three months, but the distribution returns to normal by 12 months (Lohmann et al., 1993). However, Schallhorn and colleagues detected a 5% increase in intraocular light scatter (k), one month after PRK for low myopia that returned to preoperative levels after only three months (Schallhorn, 1994). This became a 9% increase when the pupil was artificially dilated six months after PRK, suggesting greater scatter at the margins of the ablation and the potential for poor night vision. Butuner and co-workers (Butuner, Elliot, Gimbel et al., 1994) noted that 28% and 25% of PRK patients were outside the normal range of intraocular light scatter measurements (k) at glare angles of 3.5° and 10° respectively. They noted an average of 0.09 log unit increase in straylight at one year post-PRK. One study detected only a 1.5-fold increase in intraocular light scatter (k) using the Straylightmeter (section 1.2.2.3) but this was probably related to the fact that subjects were examined only one month post-PRK prior to the peak of the healing response and only for a large 10° glare angle (Harrison, Tennant, Gwin et al., 1995). No correlation has been found between forward scatter and the degree of myopic treatment (Lohmann et al., 1993). Attempts to measure forward light scatter following hyperopic PRK suggest that levels remain close to baseline, perhaps because of the limited treatment of the central cornea (O'Brart, Stephenson, Oliver et al., 1997; O'Brart, Stephenson, Baldwin et al., 2000).

Possible scatter sources in the post-PRK cornea

The initial increase in backscattered and reflected light (stromal haze) has been attributed to keratocyte activity - increased numbers, size, irregularity of shape and density of cells (Marshall, Trokel, Rothery et al., 1988; Rawe, Zabel, Tuft et al., 1992; Nuss, Puliafito, and Dehm, 1987; McDonald et al., 1989; Seiler et al.,

1990; Lohmann et al., 1991a; Lohmann et al., 1993; Corbett et al., 1996; Park and Kim, 1999).

Modification of the collagen fibril arrangement due to the presence of vacuoles and keratocytes between fibrils, has also been implicated (Lohmann et al., 1991b; Rawe et al., 1992). This is supported by the fact that the degree of stromal haze is associated with the number of adjacent collagen fibres that are transected, allowing interlamellar particles (Marshall et al., 1988). The vacuoles vary between 100nm and 4μm in size and contain proteoglycan filaments, degraded collagen or keratocytes. Epithelial hyperplasia and regenerated collagen are involved in corneal haze in rabbit eyes post-PRK (Park and Kim, 1999). New collagen tends to be less organized with a range of fibril diameters and interfibrillar spacings, also leading to a loss of the parallel lamellar structure of regions of the corneal stroma (Lohmann et al., 1991a; Corbett et al., 1996; Park and Kim, 1999). Animal studies with a much greater follow-up period than human studies have identified vacuoles between lamellae and new collagen as the major causes of long-term anatomical disturbance (Marshall, Trokel, Rothery et al., 1986). A raised level of hyaluronic acid has been show to lead to increased stromal hydration and altered lamellae spacing in rabbit eyes but this has yet to be confirmed in human subjects (Lohmann et al., 1991a).

Micro-irregularities of the stromal surface of the order of 2μm have been revealed by histopathological studies performed during the early post-operative period, and are another possible cause of increased intraocular light scatter (Lohmann et al., 1991a; Corbett and Marshall, 1996). Undulations of the basal membrane of basal epithelial cells as a result of such underlying irregularities have been shown to cause increased glare and reduced contrast sensitivity (Hersh, Schein, and Steinert, 1996a; Hersh, Shah, Geiger et al., 1996; Seiler et al., 1993; Verdon, Bullimore, and Maloney, 1996; Ludwig, Schaffer, Gross et al., 1996a; Ludwig, Schaffer, Gross et al., 1996b). The effect of these irregularities is magnified by the fact that they are located at a boundary between two different refractive indices (epithelium and stroma).

Greater numbers of keratocytes are found towards the edge of the ablation zone providing another explanation for increased forward scatter with increasing pupil diameter post-PRK (Lohmann et al., 1991a). A hypercellular zone with loss of the regular array of lamellae is present for between one and three months post-PRK (Chang et al., 1998) and cellular activity may persist for up to a year.

Aberrations

Conventional excimer laser procedures concentrate on correcting spherical and cylindrical refractive errors and are not designed to correct higher order aberrations. In fact, the modification of corneal shape required to eliminate the refractive error has been found to induce higher order aberrations in the average patient (Seiler et al., 1993; Martinez, Applegate, Howland et al., 1996), with an increase seen for most Zernike coefficients (Mierdel, Kaemmerer, Krinke et al., 1999). This is particularly true for aberrations with similar effects to spherical aberration and coma. The increase in spherical aberration following PRK for myopia relates to permanent minimisation or elimination of the natural prolate profile of the cornea (Hersh, Shah, and Holladay, 1996b; Holladay, Dudeja, and Chang, 1999), and coma can increase due to decentration of the ablation with respect to the pupil centre. Decentrations of the order of 0.42mm are commonly reported (Coorpender, Klyce, McDonald et al., 1999) and their significance increases with the degree of refractive error being corrected. The degree of induced spherical aberration is also related to the size of the attempted refractive correction (Hersh et al., 1996b) and inversely related to the diameter of the ablation zone (Oliver, Hemenger, Corbett et al., 1997a). Hyperopic PRK tends to induce an increase in negative spherical aberration (Oliver, O'Brart, Stevenson et al., 1997b).

A small percentage of patients demonstrate a reduction in higher order aberrations but an increase is far more common (Oliver et al., 1997a). Seiler, Kaemmerer, Mierdel et al., (2000) noted that the overall mean wavefront error (rms) could increase by as much as a factor of 18 times in some patients at three months post-PRK. Spherical aberration appears to increase by a factor of between 3.0-5.1 while coma-like aberrations increase by a factor of between 2.0-4.0 (Oliver et al.

1997; Mrochen, Kaemmerer, Mierdel et al., 2001). Factors that play a part in these differing results include the range of preoperative refractive error, the type of laser-control device, ablation algorithms, eye-tracker systems and importantly, the size of the pupil for aberration measurement (Schwiegerling and Snyder, 2000). For a 3.0 mm pupil, these aberrations return to preoperative levels by three months but they remain permanently elevated in the presence of 5.5 and 7.0 mm pupils (Oliver et al., 1997b), stabilising after two to three months. In normal subjects, the natural increase in aberrations associated with pupil dilation (3.0 to 7.0 mm) is of the order of five to nine times. Following excimer laser refractive surgery, this has been shown to increase 25-32 fold in one study (Oshika, Klyce, Applegate et al., 1999b), with a second study reporting a 100-fold increase at one month reducing to 70-fold thereafter (Martinez et al., 1998).

In addition to changes in the profile of the anterior corneal surface, an increase in the curvature of the posterior cornea post-PRK has been demonstrated by a number of authors using the Orbscan system (Naroo and Charman, 2000; Kamiya, Oshika, Amano et al., 2000). Such changes alter the whole-eye aberrations and therefore influence visual performance, but do not affect corneal aberrations estimated from topography data, the method used by most of the studies discussed above.

Visual performance

A reduction in visual performance is seen in some patients post-PRK, particularly under conditions of low illumination. This is likely to be related to a combination of increased intraocular light scatter from elevated cellular activity, structural changes within the cornea, low-grade irregularities (Vetrugno, Quaranta, Maino et al., 2000), and an increase in higher order aberrations.

By one year post-PRK, the percentage of eyes exhibiting a loss of two or more lines of best-corrected acuity has been reported as between zero and 1.8% (Seiler and Wollensak, 1991; Sher, Chen, Bowers et al., 1991; McDonald, Deitz, Frantz et al., 1999; Pallikaris, Koufala, Siganos et al., 1999) with an average loss of half a line (Verdon et al., 1996). These figures are for the treatment of low myopia

(less than –6.00D) but the loss tends to be greater and more widespread for higher degrees of myopia (Seiler and McDonnell, 1995). High contrast visual acuity has proved to be a poor indicator of patient satisfaction (section 2.2.3) with numerous studies reporting a poor correlation between acuity results and glare tests or patient satisfaction (Bourque, Cosand, and Drews, 1986; Maguire, 1994). Visual acuity using a 20% contrast letter chart shows an initial reduction but recovers quickly within six weeks of PRK. Low contrast acuity measurements (5%) demonstrate the greatest disparity from normal values at three months post-PRK during the period of maximum wound healing and tissue remodeling, with full recovery by four to five months post-surgery (Lohmann et al., 1991a; Lohmann et al., 1991b; Lohmann et al., 1993; Olson, Bullimore, and Maloney, 1997). A persistent deficiency of approximately 1.5 lines has been reported by other studies, particularly under low illumination (natural pupil dilation) (Strolenberg, Jackson, Mintsioulis et al., 1996; Verdon et al., 1996; Gauthier, Holden, Epstein et al., 1998). The variability between PRK subjects for 5% contrast acuity is significantly greater than for the normal population (Lohmann et al., 1993). Under conditions of natural pupil dilation, the loss of low contrast acuity correlates with the ablation zone size. There is also a degree of correlation with backscatter and forward light scatter but not with the degree of haze, since this is partly composed of reflected light (Lohmann et al., 1991b).

As with radial keratotomy, opinions regarding the effect of PRK on contrast sensitivity vary significantly between studies, with the outcome highly dependent on the testing methods and light level employed. There are studies that show either no reduction or an increase in spatial contrast sensitivity in some patients (Sher et al., 1991; Sher, Barak, Daya et al., 1992; Eiferman, O'Neill, Forgey et al., 1991; Inoue, Ishikawa, Nakayasu et al., 1996; Piebenga, Matta, Deitz et al., 1995). Many others have reported a reduction in contrast sensitivity that takes between three and 12 months to recover, depending on the degree of initial myopia. Intermediate spatial frequencies most commonly affected (Esente, Passarelli, Falco et al., 1993; Piebenga et al., 1995; Ficker, Bates, Steele et al., 1993; Ambrosio, Cennamo, De Marco et al., 1994; O'Brart et al., 1994b; Beade and Haight, 1996; Pallikaris, McDonald, Siganos et al., 1996; Boxer-Wachler,

Frankel, Krueger et al., 1996; Hodkin, Lemos, McDonald et al., 1997; Niesen et al., 1997; Shafik, Ragai, Mohamed et al., 1997; Ghaith et al., 1998; Vetrugno, Quaranta, et al. 2000). Oliver and colleagues calculated theoretical modulation transfer functions based on corneal aberration measurements alone and predicted a similar result to clinical findings - a significant deterioration in contrast sensitivity, particularly for spatial frequencies between two and 15 cycles per degree when the pupil diameter was 5.0 mm or greater (Oliver et al., 1997b). However, the nature of the study meant that neither intraocular scatter nor whole eye aberrations were considered. One study reported both contrast sensitivity results and electrodiagnostic assessment of the visual system's response to contrast using VEP's (Visually Evoked Potentials). Both methods revealed a significant loss of sensitivity across the range of spatial frequencies at three months, which began to recover by six months but still showed some loss at 12 months post-PRK, particularly at low and medium spatial frequencies (Vetrugno et al., 2000). The loss of sensitivity was greater in those treated for myopia greater than –6.00D. Another study detected a strong correlation between the size of the ablation zone and sensitivity at six and 12 cycles per degree, suggesting that induced aberrations play a significant role, but this finding could only be produced when one particular contrast sensitivity test was used (Boxer-Wachler, Durrie, Assil et al., 1999).

A comprehensive study undertaken by Butuner and colleagues (Butuner et al., 1994) one year post-PRK, discovered that 56% of PRK patients fell outside the 95% confidence limits for normal data in at least one test of visual performance. Twenty-two percent fell outside these limits for three out of five tests, suggesting that a relatively high proportion of patients suffer from a persistent degradation of the retinal image as a result of PRK. The assessments included high and low contrast logMAR acuity, contrast sensitivity using the Pelli-Robson chart and intraocular light scatter using the Straylightmeter with glare angles of 3.5° and 10°. A loss of dynamic contrast sensitivity has been reported in the presence of normal visual acuity and static contrast sensitivity (Ambrosio et al., 1994).

As with contrast sensitivity, the effect of glare on visual performance post-PRK varies significantly between studies. One study reported a reduction in high contrast acuity with glare that correlated with the induced spherical aberration (Seiler et al., 1993). The general trend, however, appears to be that acuity under daylight conditions is relatively unaffected by glare (Ambrosio et al., 1994; Dutt, Steinert, Raizman et al., 1994; Dajud, Ocmand, Doubrava et al., 1997) but is degraded under dim illumination when the pupil dilates (Verdon et al., 1996). Low contrast acuity is more sensitive to reduced visual performance and shows a greater deficit than high contrast acuity, particularly in the presence of a glare source or with pupil dilation due to low illumination or the use of a mydriatic. Schallhorn (1994) reported a reduction in contrast acuity at one month both with and without glare, associated with a significant increase in intraocular light scatter. Contrast acuity recovered by three months. A number of studies have reported a persistent visual deficit more than one year post-PRK (Seiler and Wollensak, 1991; Kriegerowski, Schlote, Thiel et al., 1996; Strolenberg et al., 1996; Verdon et al., 1996; Niesen et al., 1997; Bullimore, Olson, and Maloney, 1999). One study reported that 55% of PRK patients failed the German night driving standard requiring recognition of a Mesoptometer target of 1:5 (20%) contrast, compared to only 2.5% of spectacle wearers and no soft contact lens wearers. Under glare conditions, 67% of PRK patients compared to 18% of spectacle wearers and 2.5% of soft contact lens wearers failed the standard (Schlote, Kriegerowski, Bende et al., 1997). The primary reason for such a high number of failures in the PRK group was probably the small diameter of the ablation zone (4.0 or 5.0 mm) compared to the pupil diameter under mesopic conditions. Most treatment zones are now 6.0 mm in diameter or more but the area over which full correction of the refractive error is attempted (optical zone) is generally smaller than this. In addition, some young patients have pupils that dilate to 7.0 mm or more at night (Koch, Samuelson, Haft et al., 1991), leading to the formation of a blurred annulus around each retinal image. This is particularly noticeable when observing light sources against a dark background and can be very distracting.

A prolonged or persistent reduction in vision in the presence of a glare source is more common in eyes that have undergone a greater change in refractive error or exhibit a degree of decentration of the ablation zone (Seiler and Wollensak, 1991; Seiler, Holschbach, Derse et al., 1994; Verdon et al., 1996) implicating coma-like aberrations (Oliver et al., 1997b; Seiler et al., 2000). Seiler (2000) reported a correlation between the increase in total wavefront error and a reduction in low contrast visual acuity or glare disability. The recovery time for a particular measure of visual performance depends on the pupil diameter (Strolenberg et al., 1996; Verdon et al., 1996); normal levels of low contrast acuity appear to return by three months when pupils were undilated and 12 months with dilated pupils (Schallhorn, 1994), implicating both scatter and aberrations in the reduction in visual performance.

Complaints of night halos under low illumination were commonplace during the early years of PRK (Seiler et al., 1990; Seiler and Wollensak, 1991; Kim, Hahn, Lee et al., 1993; Kim, Sah, and Hahn, 1994; Gimbel, Van Westenbrugge, and Johnson, 1993; Quah, Wong, Tseng et al., 1996; BenSira, Loewenstein, Lipshitz et al., 1997) with 78% of subjects reporting halos in one of the earliest studies (Gartry et al., 1992). Halos result from the refraction of light by the untreated paracentral cornea; the entrance pupil can become larger than the ablation zone when the pupil dilates. Myopic blur circles are superimposed over the retinal image and the magnitude of the effect is dependent on the difference in refractive power between the central and paracentral cornea, making it proportional to the induced change in refractive error (O'Brart, Lohmann, Fitzke et al., 1994a; O'Brart, Lohmann, Fitzke et al., 1994c). The increase in ablation zone diameters to an average of 6.0 mm (Vetrugno et al., 2000), and a reduction in the upper limit of myopia treated by PRK, has significantly reduced the prevalence of halos (Dello Russo, 1993; David, Mayer, Assouline et al., 1996; O'Brart, Corbett, Verma et al., 1996; Hadden, Ring, Morris et al., 1999). However, attempts to predict the likelihood of symptoms from the preoperative scotopic pupil diameter have proved only partially successful. The degree of refractive error, ablation zone diameter and the initial corneal aberrations are also factors to consider in calculating the risk of night vision problems (Haw and Manche, 2001).

1.2.4.9.c Laser assisted in-situ keratomileusis (LASIK)

LASIK was developed from automated lamellar keratoplasty (ALK) in an attempt to overcome the problems of post-operative haze and scar formation following PRK (Pallikaris, Papatzanaki, Stathi et al., 1990; Pallikaris, Papatzanaki, Siganos et al., 1991; Barraquer, 1996). The procedure involves cutting a thin flap of corneal tissue (approximately 160μm) using a microkeratome. The underlying stromal bed is then ablated using an excimer laser and the flap repositioned (figure 1-13). Minimal epithelial interference and preservation of Bowman's membrane lead to very little new collagen or extracellular matrix formation. There is also less stimulation of the inflammatory cascades, minimising the activation of abnormal wound healing compared to PRK (Chang et al., 1998). As a consequence there is less pain, a quicker visual recovery and a more rapid refractive stability than is seen post-PRK.

Imaging of the human cornea after LASIK using confocal microscopy reveals normal surface and basal epithelium at three days post-surgery (Vesaluoma, Petroll, Perez-Santonja et al., 2000b). Keratocyte apoptosis and subsequent cellular activity is restricted to the tissue immediately either side of the lamellar interface (Wilson, 1997). Keratocyte activity is greatest on the third day post-LASIK, lasting for up to two months before gradually declining to preoperative levels between 2.5 and six months post-surgery (Perez-Santonja, Linna, Tervo et al., 1998a). Increased anterior chamber activity (flare and cells) has been reported during the first post-operative week (El-Harazi, Chuang, and Yee, 2001). Epithelial hyperplasia and the formation of irregularly arranged collagen fibres take place around the wound site but unlike the post-PRK cornea, the lamellar structure of the stroma is maintained centrally within both the flap and stromal bed. Development of a small number of regularly arranged collagen fibres has been detected between the flap and stromal bed in rabbit eyes.

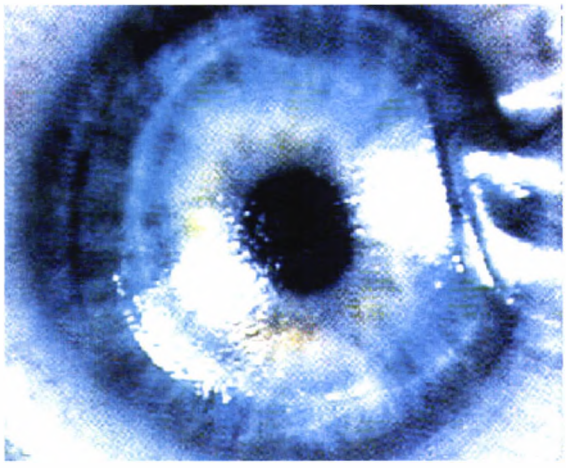


Figure 1-13: LASIK – the corneal flap is lifted to exposure the stromal bed, which is then ablated before the flap is repositioned

Due to the limited deposition of irregular, regenerated collagen, fewer scatter sources are created by LASIK compared to PRK. Minimal tissue proliferation results in a transparent interface, although *in vivo* confocal microscopy has revealed corneal flap interface particles in all LASIK patients, with microfolds in Bowman's layer in 96.8% of patients (Vesaluoma et al., 2000a). The interface debris has been attributed to meibomian gland secretions, metallic flakes from the keratome and dust and debris from the environment, sponges etc. The number of activated keratocytes increases around the margins of the flap, associated with the disruption of the epithelium but these cells remain stable in size and shape and are arranged parallel to the stromal structure (Park and Kim, 1999; Vesaluoma, Petroll, Perez-Santonja et al., 2000b). They do not disrupt the lamellar structure of the central stroma, resulting in a clear cornea (Perez-Santonja et al., 1998a; Wachtlin, Langenbeck, Schrunder et al., 1999). Wound constriction appears to be complete within six months of surgery in the majority of cases (Vesaluoma et al., 2000a) although the presence of disorganised collagen fibrils at the lamellar interface, suggesting continued healing, has been reported nine months after LASIK (Kato, Nakayasu, Hosoda et al., 1999).

Intraocular light scatter

There are no published studies on the effect of LASIK on forward light scatter, probably as a result of the incorrect assumption that no central haze means no forward light scatter. An assessment of backscatter over a period of 12 weeks post-LASIK suggests that it remains close to preoperative levels and is consistently lower than that seen post-PRK (Jain, Khoury, Chamon et al., 1995; Chang et al., 1998).

Aberrations

For 3.0 mm pupils, the amplification of higher-order aberrations occurs to the same magnitude following LASIK as it does following PRK. Using root mean square (rms) as a measure of mean wavefront error, third and higher-order aberrations increase by a factor of about two post-LASIK (Moreno-Barriuso, 2000; Marcos, 2001a; Marcos, 2001b) with most of the increase related to spherical aberration. The increase is greatest immediately after surgery and regresses slightly over a period of about two months (Hong and Thibos, 2000). Calculation of the effect on retinal image quality suggests no significant difference from the preoperative image quality for small and medium pupils but a significant decrease in quality for pupils greater than 4.0 mm in diameter (Hong and Thibos, 2000). For 7.0 mm pupils, significantly greater spherical aberration has been reported following LASIK compared to PRK. This has been attributed to the smaller transition zone around the optical zone commonly used in LASIK (Oshika et al., 1999b). The natural increase in aberrations associated with pupil dilation is increased from approximately five-fold to 28-46 fold after LASIK.

As with PRK, there is mounting evidence to suggest that the posterior corneal surface shifts forwards and increases in oblate asphericity during the early post-LASIK period, as the cornea readjusts to its reduced thickness (Baek, Lee, Kagaya et al., 2001; Seitz, Torres, Langenbucher et al., 2001). This undoubtedly influences the aberrations of the eye and could provide one explanation for the change in aberrations seen over time in some post-LASIK eyes.

Initial studies into wavefront-guided LASIK look promising, with some eyes achieving high contrast acuities in the region of 6/3 (Snellen fraction). The root mean square (rms) wavefront error is still increased compared to preoperative values (by a factor of 1.44 for a 5.0 mm pupil), but this is significantly lower than the results of conventional laser surgery (Seiler, Mrochen, and Kaemmerer, 2000; Mrochen, Kaemmerer, and Seiler, 2000). On average, the correction of spherical aberration is inadequate but coma and other higher-order aberrations are well corrected. The rms wavefront error for all higher-order aberrations shows a decrease between one month and three months, probably due to biomechanical factors and changes in the corneal flap.

Visual performance

The percentage of eyes exhibiting a loss of two or more lines of best-corrected acuity at one year post-LASIK is between zero and 1% for low and medium levels of preoperative myopia (Wang, Chen, and Yang, 1997; Pop and Payette, 2000). An average of 0.9% has been calculated for a large collection of LASIK studies published between 1991 and 1997 (Farah, Azar, Gurdal et al., 1998). As with PRK, the percentage increases for high levels of preoperative myopia (Knorz, Wiesinger, Liermann et al., 1998).

Contrast sensitivity assessments vary with the method of assessment employed but the general trend is a reduction in sensitivity, particularly for mid spatial frequencies (3 and 6 cycles per degree). Contrast sensitivity recovers by three months post-LASIK (Perez-Santonja, Sakla, and Alio, 1998b; Mutyala, McDonald, Scheinblum et al., 2000).

An assessment of contrast acuity under photopic conditions revealed no loss of high contrast acuity, a significant loss for intermediate contrast acuity (15%) at one week that recovered by one month, and a significant loss of low contrast acuity (2.5%) that recovered by three months. A persistent loss for both the low and intermediate contrast levels was noted for a group that underwent LASIK for more than –6.00D of myopia (Nakamura, Bissen-Miyajima, Toda et al., 2001). Holladay et al. (1999) detected a significant reduction in visual performance for

acuity at high, medium and low contrast levels for up to one week following LASIK. After this point in time, the visual deficit was only present for medium contrast (13%) acuity and contrast thresholds measured in the dark (natural pupil dilation). Both measures of visual performance were reduced six months after surgery. A few patients, however, demonstrated a persistent reduction in contrast sensitivity at distinct spatial frequencies - three cycles per degree being most commonly affected. Another study reported reduced sensitivity at three months at both mid and high spatial frequencies (Alanis, Ramirez, Suarez et al., 1996). These differences are likely to be associated with the errors and approximations inherent in the various testing methods and stimulus conditions employed by different studies.

2 Methods of assessing visual performance

There are numerous tests available to assess different aspects of visual performance, many designed to be quick and easy to use in a clinical setting and others more suited to research work. A selection of the most commonly used tests will be discussed in terms of the information they provide about the visual system and their drawbacks.

2.1 High contrast letter charts

Unaided vision and best-corrected visual acuity are measurements of visual performance that are normally carried out under optimal conditions of high contrast and high luminance. Very few 'real-world' targets share these characteristics but, in spite of this, acuity for high contrast optotypes is used by the majority of clinicians, often to the exclusion of other techniques. It is a simple task for subjects to determine the smallest high contrast letter that can be resolved, and the effects of blur are easy to distinguish at high spatial frequencies. This makes high contrast charts particularly useful for determining the subjective refractive error of the eye. A number of different high contrast charts are available varying in their choice of optotype (letters, Landolt rings etc.), design (size scaling between lines, characters per line etc.), and scoring technique.

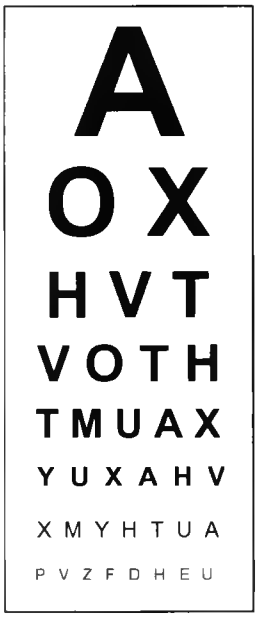


Figure 2-1: A typical Snellen letter chart

2.1.1 Snellen letter chart

The Snellen letter chart (Figure 2-1) was introduced by Snellen in 1862 (Bennett, 1965) and is composed of high contrast optotypes, (contrast approximately 94%), most commonly lit from behind to achieve a background luminance of approximately 120 cd/m^2. It is the most widely available test for assessing high contrast vision

and the Snellen fraction has become the standard recording technique.

Despite its widespread use, the Snellen chart possesses a number of significant drawbacks:

- The size scaling between lines of letters does not follow a geometrical progression. A reduction in vision from 6/4 to 6/6 does not equate to a reduction from 6/6 to 6/12, yet both would be recorded as a loss of two lines of acuity, (a frequently used criterion for judging the impact of a refractive surgery procedure on visual performance). In addition, some letter charts also incorporate an additional line of letters corresponding to 6/7.5.
- Some Snellen charts are designed such that the smallest line of letters is composed of 6 metre letters (each limb relates to one minute of arc) rather than 5 metre or 4 metre letters. Consequently, patients capable of resolving letters on the 6/5 or 6/4 line will have their acuity recorded as 6/6, making the test insensitive to any small changes in visual performance that may occur in the future. One study of subjects who had undergone photorefractive keratectomy found that 47% of eyes lost one line of acuity using a letter chart that ranged from 6/60 to 6/4 (Halliday, 1995) - a substantially larger proportion than that quoted by other studies that used a chart terminating at 6/6.
- The letters employed vary considerably in their legibility, despite the fact that they are generally restricted to the British Standard letter series (BS 4274 1968) (Raasch, Bailey, and Bullimore, 1998). There is, however, little difference between acuities obtained with letters and Landolt rings (Bailey, Bullimore, Raasch et al., 1991; Raasch et al., 1998) provided that the letters chosen span the range of legibilities. Even with Landolt rings, perfectly equal legibility cannot be achieved because meridional differences may favour certain orientations (Mitchell, Freeman, Millodot et al., 1973).
- The scoring system is inadequate, particularly when the observer is unable to identify all the letters on a line.

- High contrast optotypes are relatively insensitive to the effects of scattered light and aberrations (section 1.2.2.4)

2.1.2 LogMAR Charts

Some of the problems of the Snellen chart can be overcome by using a high contrast logMAR chart ($\log_{10}$ Minimum Angle of Resolution) such as the Bailey-Lovie chart (Bailey and Lovie, 1976; Bailey and Lovie, 1980), (Figure 2-2). This uses an equal number of letters per row and a logarithmic size progression of 0.1 log units (1.26x) between lines.

The choice of letters is restricted to Sloan letters but some variability in the legibility of these letters has been identified (Elliott, Whitaker, and Bonette, 1990). Each letter that can be resolved is individually scored (one letter = 0.02 log units, one line = 0.1 log units), greatly improving test-retest reliability (Arditi and Cagenello, 1993). The logMAR chart has been shown to be twice as repeatable as the Snellen chart (Lovie-Kitchin, 1988), but like the Snellen chart, it is composed of high contrast optotypes.

Figure 2-2: High contrast LogMAR chart

2.1.3 Disadvantages of high contrast acuity

It is not uncommon for patients to exhibit good high contrast acuity and yet complain of poor quality vision (Hess and Woo, 1978). High contrast acuity has been shown to provide an inadequate indication of the extent of visual handicap experienced by patients with various pathological conditions (van den Berg, 1986). It fails to predict accurately visual performance for 'real-world' tasks such as reading a car number plate (Owsley and Sloane, 1987; Currie, Bhan, and Pepper, 2000).

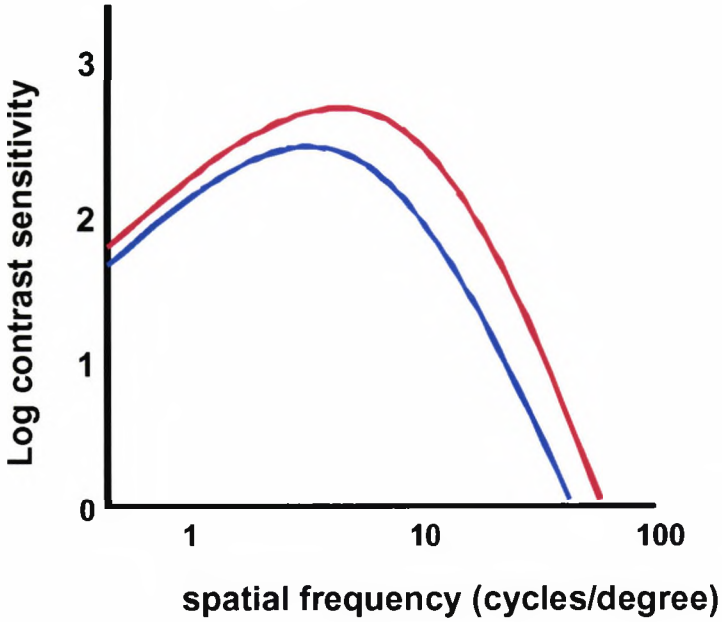


Figure 2-3: The contrast sensitivity function for a normal eye (red) and an eye suffering from an increase in intraocular light scatter (blue)

High contrast acuity correlates poorly with intraocular light scatter, especially for light scatter originating from more than 3° away from the fovea (van den Berg and Spekreijse, 1987; Beckman et al., 1991; Elliott and Bullimore, 1993), (section 1.2.2.4). The reduction in retinal image contrast resulting from an increase in forward light scatter will not reduce the retinal image contrast of a high contrast letter below the discrimination threshold unless the amount of scattered light is very large (Miller, Jernigan, Molnar et al., 1972).

2.2 Contrast Sensitivity

The ability to resolve spatial information is visually extremely important and this is usually described by the contrast sensitivity function. This function is dependent on the optical transfer function of the eye and is further modified by neural factors during the processing of spatial information. Both of these factors are influenced by age and certain pathological conditions (section 1.2.4). Contrast sensitivity is defined as the reciprocal of the contrast threshold, i.e. the lowest contrast at which a sine-wave grating can be detected as a function of spatial frequency. Sensitivity varies with spatial frequency with a peak around 3-5 cycles per degree, (Figure 2-3). The most sensitive spatial frequency (i.e. the peak of the contrast sensitivity function) varies with the light adaptation level and stimulus size (Barlow and Molton, 1982; Rovamo, Mustonen, and Nasanen, 1994).

Assessment of the contrast sensitivity function was first described by Young in 1918 (Young, 1918) and has been shown to provide significantly more information with regard to loss of visual function than high contrast acuity measurements (Paulsson and Sjostrand, 1980; van den Berg, 1986). The ability to see 'real-world' targets such as faces is better predicted by the measurement of performance at low and middle spatial frequencies (Owsley and Sloane, 1987; Ginsburg, Evans, Sekule et al., 1982). A strong correlation has been detected between intraocular light scatter and contrast sensitivity attenuation across the range of spatial frequencies (Irving and Woo, 1993), with the most significant effect occurring at mid and high spatial frequencies (Wolf and Gardiner, 1965). High contrast letter acuity tends to remain relatively unaffected by increased light scatter (Arden, 1978). This can be explained by examining the high frequency cut-off point at which the contrast sensitivity function meets the x-axis (around 50-60 cycles per degree), and comparing it with the principal spatial frequency of a six-metre letter (figure 2-3). A letter of this size equates to a principal spatial frequency of around 12 cycles per degree and therefore resolution is only affected when very large increases in intraocular light scatter result in a massive depression of the contrast sensitivity function. This also partly explains the lack of any strong association between contrast sensitivity and high contrast acuity (Martin, 1999; Hard, Abrahamsson, and Sjostrand, 1990; Ginsburg, 1980; Owsley et al., 1983).

2.2.1 Contrast sensitivity tests

A wide variety of techniques are available for assessing the contrast sensitivity function of the eye. The 'Gold Standard' involves determining the contrast threshold over a range of spatial frequencies using computer generated sine-wave gratings (Campbell and Robson, 1968; Ginsburg, Evans, Cannon et al., 1984; Ginsburg and Cannon, 1983; Ginsburg et al., 1984; Long and Penn, 1987). The threshold contrast needed to just see the gratings bars can be established using a number of different psychophysical techniques. A significant practice effect has often been reported and differences between study outcomes remain unexplained (Ginsburg et al., 1984; Long and Penn, 1987). In designing simple tests for clinical use the number of spatial frequencies examined is often small to save

time. The most useful spatial frequencies to use when considering conditions that affect scatter and aberrations such as refractive surgery should in theory be the high frequencies in the range of 12 to 18 cycles per degree. However, the steepness of the function for high spatial frequencies results in increased variability and poor sensitivity to high frequency attenuation (Rabin, 1994b; Rabin, 1994a; Boxer-Wachler and Krueger, 1998), leaving mid spatial frequencies as a reasonable option.

Some techniques employ sine-wave gratings (Vistech Consultants Inc., 2001) but others are based on letters, such as the Pelli-Robson chart that aims to sample the peak of the contrast sensitivity function (Pelli, Robson, and Wilkins, 1988). Like square-wave gratings, letters are composed of a range of different spatial frequencies (Parish and Sperling, 1991; Alexander, Xie, and Derlacki, 1994) but provide a valid stimulus for the measurement of contrast sensitivity providing they are large and therefore contain the fundamental spatial frequencies of the corresponding curve. They have the advantage of being more familiar to subjects than gratings (Hard et al., 1990), making the task easier to perform. However, contrast thresholds are very dependent on the nature of the stimulus – a 6/6 letter should correspond to a grating of 12-24 cycles per degree but a grating only requires simple resolution rather than identification; thresholds using different stimuli cannot be directly compared. Big differences have been identified between the detection of gratings (grating acuity) and the recognition of letters, with letter recognition being more sensitive to neural changes that affect sampling density (Thibos and Bradley, 1993).

2.2.1.1 Charts based on sine-wave gratings

2.2.1.1.a Vision Contrast Test System 6500 (VCTS 6500)

The Vistech chart (Vistech Consultants) is a photographic-based, front lit chart displaying sine-wave grating patches, orientated either vertically or 15° to the right or left of vertical. Contrast decreases across the chart (nine steps of approximately 0.23 log units) while spatial frequency increases down the chart (five spatial frequencies from 1.5 to 18 cycles per degree). Contrast sensitivity is

measured at 3 metres with 'best levels of luminance', (68-240 cd/m^2). For each spatial frequency the subject must report the lowest contrast at which the grating can be correctly identified. This chart has been shown to suffer from repeatability problems (Reeves, Wood, and Hill, 1991). In addition, it shows poor sensitivity to changes in visual performance occurring post surgery (Niesen et al., 1997), largely as a result of the large contrast steps between lines.

2.2.1.1.b VectorVision CVS 1000E chart

This follows a very similar design to the Vistech chart with four spatial frequencies (3, 6, 12, 18 cycles/degree) and nine contrast levels. The chart is designed for use in a darkened room, resulting in a larger pupil size than other tests and consequently greater sensitivity to retinal image degradation post-refractive surgery (Boxer-Wachler et al., 1999).

2.2.1.1.c Stereo Optical Functional Acuity Contrast Test (FACT)

The FACT chart is similar to the two previous charts, employing five spatial frequencies and nine contrast levels but with 0.15 log unit contrast steps. The chart is front-lit to achieve a luminance of 85 cd/m^2.

2.2.1.1.d Arden Gratings

The sine-wave gratings are arranged in a booklet containing one spatial frequency per plate (six in total). Contrast varies down the page and the 'score' for each plate is the highest number on the scale exposed before the pattern is detected. The total score is obtained by summing the score from all six plates (Arden, 1988).

2.2.1.1.e Cambridge Low Contrast Gratings

The test consists of a booklet of square-wave gratings with a fundamental spatial frequency of four cycles per degree when viewed at six metres (Wilkins, Della Sala, Somazzi et al., 1988). A forced-choice paradigm is employed - the subject must differentiate between a blank page and the grating. The contrast of the grating reduces with each page from 13% to 0.11%. The chart should be lit to achieve a luminance of 100 cd/m^2.

2.2.1.2 Letter charts

2.2.1.2.a Pelli-Robson chart

This test employs large letters arranged in 16 triplets of decreasing contrast (figure 2-4), (Pelli et al., 1988). The chart is front-lit to achieve a luminance of 45-250 cd/m^2. The lowest contrast level at which two out of a triplet of letters can be identified correctly is taken as the contrast sensitivity score. However, reliability is improved by scoring each letter as 0.05 log units (Elliott, Bullimore, and Bailey, 1991) leading to a test/retest score of 0.12 log units (~one triplet) (Alexander, Xie, and Derlacki, 1997). Each letter limb subtends 34 mins of arc at a distance of one metre, corresponding to a fundamental spatial frequency of approximately 1 cycle per degree (Pelli et al., 1988). Alternatively, the chart can be used at three metres in which case the fundamental spatial frequency increases to 3.6 cycles per degree (Haegerstrom-Portnoy et al., 1999), examining visual function close to the peak of the contrast sensitivity curve. Due to the range of spatial frequencies incorporated in the letters, the test is relatively insensitive to changes in working distance. High spatial frequency components are rendered sub-threshold by the low contrast of the letters and therefore do not contribute to letter identification. Thresholds with the Pelli-Robson test have been shown to correlate with the fundamental frequency of the component letters (Woods, 1993) and are relatively insensitive to defocus due to the low fundamental spatial frequency (Jansonius and Kooijman, 1997). As with acuity thresholds the legibility of the letters varies (Elliott et al., 1990) but the range is limited by the use of such large letters (Alexander et al., 1997; Robson, Pelli, and Zhang, 1990).

Figure 2-4: Pelli-Robson letter chart

2.2.1.2.b Rabin Small Letter Contrast Test (SLCT)

This chart is very similar to the Pelli-Robson chart except that it employs small letters of 20/25 size and is viewed from four metres (equivalent to 6/11 letter). The original format consisted of a front-lit printed chart (Rabin, 1995) but fading of the chart has led to the design of a new back-lit version (Rabin, 2001). The chart possesses 14 lines with ten letters per line. Contrast decreases down the chart by 0.1 log units per line (scored as 0.01 log units per letter) and the contrast threshold relates to the line of lowest contrast that can be identified. The illumination is specified as 'normal room illumination'. The small letter size employed leads to potential problems with variable letter legibility and the test/retest variability has be reported as between one and three lines (Rabin, 1994a; Rabin and Wicks, 1996; Alexander et al., 1997). The similarities in spatial frequency composition between 25 foot letters and 20 foot letters mean that the Rabin chart adds little information beyond that gained from the measurement of high contrast acuity (Elliott and Situ, 1998). It also means that the SLCT is very sensitive to optical defocus (Rabin, 1994b).

2.2.1.2.c Low contrast letter charts

Although not strictly classed as contrast sensitivity charts, low contrast letter charts can provide some information about the shape of the contrast sensitivity function. There is a relatively small difference between high and low contrast acuity in normal subjects due to the steepness of the contrast sensitivity function at that point (approximately 13 letters for the Bailey-Lovie charts - Haegerstrom-Portnoy et al., 1999), but the difference increases with age. Changes to the shape of the contrast sensitivity function increase the difference between the two measures of acuity (Regan, 1988). Charts available include a 10% version of the Bailey-Lovie chart (Bailey and Lovie, 1976; Bailey, 1993) and a 11% Regan chart (Regan and Neima, 1983; Regan, 1988) as well as a range of low contrast ETDRS logMAR charts.

Despite the advantages of measuring contrast sensitivity, data collection is fraught with difficulties (Legge and Rubin, 1986; Wilkins et al., 1988; Moseley and Hill, 1994):

- A full assessment is time consuming and therefore clinical tests have to restrict the number of spatial frequencies that are examined.
- There is no single score by which to judge normality/abnormality, further complicated by the fact that normal values change significantly with age.
- Viewing and illumination conditions vary between tests. One study reported a reduction in contrast sensitivity both with and without a glare source for artificially dilated pupils but not for natural pupils (Bullimore et al., 1994). Since light levels can vary considerably between tests, leading to different pupil sizes, this provides one possible explanation for the inconsistency of contrast sensitivity data.
- A wide range of psychophysical techniques are used (e.g. criterion dependent, staircase procedure etc.) (Millodot, 1973) which can significantly influence contrast thresholds (Ginsburg and Cannon, 1983; Woods, 1996).
- Many of the tests demonstrate poor repeatability (Jones, Moseley, and Thompson, 1994; Reeves et al., 1991).

These factors make it very difficult to compare results from different tests (McFadden, 1994).

2.3 Disability glare

The levels of scattered light found in a normal eye under average lighting conditions do not tend to affect vision. They increase in the presence of an intense glare source, which can lead to a reduction in visual performance, (disability glare) (Vos, 1959; Vos, 1984). The effect is much more dramatic in those suffering from an increase in baseline intraocular light scatter. Glare sensitivity can be determined by assessing how a particular measure of visual performance, such as acuity, is affected by scattered light both with and without a glare source. Glare testing is more specific than contrast sensitivity measurements alone for anterior segment disorders as most glare tests employ a large bright glare source capable of raising wide-angle scatter to a clinically significant level. For example, corneal oedema has been shown to cause only a slight reduction in contrast sensitivity, but a threefold reduction in contrast sensitivity in the presence of glare

(Carney and Jacobs, 1984). Subjective complaints of glare correlate with glare test results but not visual acuity measurements (Paulsson and Sjostrand, 1980; Abrahamsson and Sjostrand, 1986; Beckman et al., 1991).

2.3.1 Glare tests

Clinical glare tests do not measure the scatter function of the eye - a direct assessment of stray light requires complicated techniques similar to those described in chapter 1 (section 1.2.2.3). The relationship between glare and scattered light is complex and it is possible that neural factors may also be involved in glare measurements (Vos, 1984; van den Berg, 1991; van den Berg, 1994). Lateral retinal effects may exist, particularly for large annular sources contiguous with the test field (Guth, 1973) although significant alterations to light scatter values have been discounted (Wooten and Geri, 1987).

Unfortunately, no standards for the background illumination, target configuration etc. have been established, (Cataract Management Guideline Panel, 1993) and the optimal glare source for reliable, reproducible testing has yet to be identified. Point glare sources provide a good simulation of real-life glare sources, such as car headlights, but they have the disadvantage of requiring a high luminous intensity in order to produce the desired effect, resulting in pupil constriction and in some cases an associated improvement in visual performance due to a reduction in aberrations and scatter (Boxer-Wachler et al., 1999). They also tend to attract the attention of the observer, resulting in the bleaching of macular receptors during accidental glances (Abrahamsson and Sjostrand, 1986). Extended, circular glare sources cause fewer after-images due to the lower retinal illuminance involved and in addition, their format aids fixation of the central target (Miller et al., 1972). Low intensity glare sources under mesopic conditions have also been suggested as a more suitable method for assessing night driving performance, a situation in which glare sensitivity can cause serious visual disability (Applegate et al., 1987). The effect of glare on visual function is undoubtedly increased if the pupils are dilated by the careful choice of a glare source or viewing conditions, or the use of mydriatic drugs. The American Academy of Ophthalmology (1990)

recommended that any glare test should be criterion-free (forced choice) and employ a test chart of equal logarithmic steps.

2.3.1.a The Miller-Nadler Glare Test (MNGT)

This consists of a projector and test slides, providing a series of randomly orientated Landolt rings each subtending 1.7° at 36cm on a variable contrast background (Miller et al., 1972; LeClaire et al., 1982). The subject is required to identify the gap in each Landolt ring (four alternative forced choice) against the circular background (diameter 40 mm). The contrast of the ring decreases with each slide from 80% to 2.5%, in 5% and 2.5% steps until the patient can no longer identify the orientation of the gap. It is viewed firstly without the glare source to determine baseline values, and then with the glare source, which is provided by the surround, and subtends 30° by 30° with a luminance of approximately 5000 cd/m^2. The results are expressed as the percentage contrast between the ring and background at the end point and can be converted to a visual acuity value. The ratio between the contrast levels reached with and without the glare source gives the disability glare score. The test suffers from poor repeatability related to the large step size between contrast levels and the limited number of useful contrast levels for the 'without glare' situation. It also suffers from a significant reduction in glare intensity if the subject moves off axis (Van der Heijde et al., 1985). Pupillary constriction is unavoidable when using the bright glare source (Miller et al., 1972).

2.3.1.b The Vistech MCT8000

This test presents sine-wave gratings over a range of spatial frequencies between 1.5 and 18 cycles/degree, as employed by the VCTS 6500 (section 2.2.1.1.a). Each presentation consists of seven discs containing gratings of a particular spatial frequency with either a vertical orientation or tilted 15° to the right or left of vertical. The contrast of the gratings decreases in 0.25 log steps between discs and the subject is required to identify the orientation of the grating until a disc is reached where no grating can be seen. Measurements are taken under 'night-time' ($3cd/m^2$) then 'daytime' ($125\ cd/m^2$) luminance conditions with and without a central and peripheral glare source ($130\ cd/m^2$). The fact that the Vistech test is criterion-dependent makes it less reliable than tests that use a forced choice method (Vaegan and Halliday, 1982). It fails to meet any of the criteria suggested by the American Academy of Ophthalmology (American Academy of Ophthalmology, 1990). Like the Miller Nadler Glare Test, the Vistech has a limited number of contrast levels and large step sizes, reducing test reliability (Bailey et al., 1991). Along with other automated glare testers such as the InnoMed True Vision Analyser and the EyeCon 5, this test is rarely used.

2.3.1.c The Berkeley Glare Test

This test consists of a reduced low contrast Bailey-Lovie letter chart (18% contrast) on an opaque panel, mounted in the centre of an opal plexiglass sheet (Bailey and Bullimore, 1991). The chart is front illuminated to achieve a luminance of $80\ cd/m^2$ and the glare source is provided by transillumination of the plexiglass (luminance of $3000\ cd/m^2$ or $800cd/m^2$). Low contrast visual acuity is measured at one metre both with and without a glare source. Each letter is scored as 0.02 log units (ten alternative forced choice method) and the disability glare index is calculated by comparing the acuity with and without glare.

2.3.1.d The Brightness Acuity Tester (BAT)

This piece of apparatus consists of an internally illuminated, 60 mm diameter hemispherical bowl, with a central aperture of 12mm (Holladay et al., 1987). When held up to the patient's eye or spectacles, the BAT provides a glare source covering a concentric annulus between 8-90°. The patient views the chosen test chart through the central aperture in a darkened room using one of three brightness settings: low, medium or high, simulating overhead commercial lighting, a partly cloudy day, and direct overhead sun respectively. The glare sensitivity score is recorded in terms of the number of lines of acuity or contrast sensitivity lost with glare compared to the baseline value with no glare. Studies suggest that the results correlate well with outdoor visual performance, particularly when the medium glare setting (345 cd/m^2) is used (Neumann, McCarty, Locke et al., 1988; Holladay et al., 1987; Elliott and Bullimore, 1993). The highest setting has the tendency to overestimate the effects of glare (Holladay et al., 1987). Any test chart can be used within reason, although low contrast logMAR or contrast sensitivity charts such as the Pelli-Robson provide the best discriminative ability (Elliott and Bullimore, 1993).

2.3.2 Comparison of tests

A number of studies have attempted to compare glare tests including the work of Elliott and Bullimore (1993), who rigorously assessed the Miller Nadler Glare Test (MNGT), the Vistech MCT8000, the Berkeley Glare Test, and the BAT, in conjunction with the Pelli-Robson and Regan charts. A measurement of forward light scatter using the van den Berg Straylightmeter (section 1.2.2.3) (van den Berg and IJspeert, 1991a), was taken as the Gold Standard. Three groups of subjects were evaluated: young normals, older normals and cataract patients. The tests were evaluated for repeatability (comparing test scores on two different occasions), discriminative ability (the ability to differentiate between young and old subjects and between old normals and cataract patients), and validity (comparing the test results with the van den Berg Straylightmeter). All visual acuity based tests demonstrated good repeatability, particularly the Berkeley and Regan tests used with the BAT. The 11% contrast Regan chart with the BAT gave

the highest discriminative ability, the Berkeley glare test and 25% Regan chart producing similar results. This is not surprising considering the findings of Regan and colleagues in cataract patients - acuity in the presence of glare for the 25% Regan chart was reduced by a factor of three when the contrast of the chart was reduced to 11% (Regan, Giaschi, and Fresco, 1993). Of the contrast tests, the Pelli-Robson with BAT demonstrated the highest validity and excellent discriminative ability, and the results demonstrated a high correlation with light scatter. The MNGT and Vistech chart test performed poorly in terms of discrimination due to large contrast increments between lines/slides.

The outcome of glare testing is often reported in terms of a glare score – the ratio between the performance with and without glare (Paulsson and Sjostrand, 1980). Variation within each measurement, however, was found to give an even greater variation in glare score, resulting in poor discriminative ability (Elliott and Bullimore, 1993). Multiple regression analysis was used to consider which tests provided information in addition to that obtained from standard visual acuity measurement. The Pelli-Robson chart with glare was found to provide virtually all the additional information required. They concluded that the Pelli-Robson or a low contrast letter chart with glare provided the best reliability, repeatability and discriminative ability for visual assessment in the presence of increased intraocular light scatter (Elliott and Bullimore, 1993).

Smith and colleagues (Smith et al., 1987) compared the Miller-Nadler Glare Tester (MNGT) and the Brightness Acuity Tester (BAT) used with a high contrast Snellen letter chart, for a group of normals and a group of patients with crystalline lens opacities. In the presence of posterior subcapsular opacities, a greater glare disability was found with the BAT compared to the MNGT. This was probably related to the poor repeatability and limited contrast range of the MNGT. The brightness of the BAT produced a smaller pupil diameter than the MNGT but pinhole effects were found to be negligible, perhaps due to the poor sensitivity of the Snellen chart to an increase in glare disability.

Neumann and co-workers (Neumann et al., 1988) evaluated five different glare testers to determine which technique most accurately predicted the patient's outdoor Snellen acuity. The glare test results achieved within one Snellen line of outdoor vision in 73% of cases for the Brightness Acuity Tester, 69% of cases for the InnoMed True Vision Analyser, 56% of cases for the Vistech VCT 8000, 47% of cases for the Miller-Nadler glare test and only 15% of cases for the EyeCon 5, demonstrating the wide disparity between tests.

2.4 Summary

A wide range of clinical tests is available for the assessment of visual performance but all tests possess drawbacks, such as poor repeatability, poor scoring methods or insensitivity to increases in intraocular light scatter. In addition, it is difficult to extrapolate the findings from such tests to 'real-world' tasks, although a number of studies have attempted to do so (Evans and Ginsburg, 1985; Ginsburg et al., 1982; Owsley and Sloane, 1987). Taking into account the lessons learnt from the development and use of previous tests, it is clear that more specific tests of functional visual performance are needed to examine the ability of certain groups to perform specific visual tasks, such as those investigated in this study.

3 Experimental Methods

3.1 Equipment and Set-up

All computer-based tests were run on the P_SCAN 100 system (Barbur, Thomson, and Forsyth, 1987; Alexandridis, Leendertz, and Barbur, 1991). This allows presentation of either positive or negative contrast stimuli on a 21″ high resolution Sony Trinitron monitor (model 500PS, 1280 x 1024 pixels, 60Hz, maximum luminance of 100 cd/m^2), driven by an ELSA Gloria XL 10 bit graphics card. The LUMCAL program developed by Barbur and colleagues was used in conjunction with a LMT 1000 luminance meter to calibrate the luminance characteristics of the monitor every month throughout the study. This involved determining the luminance versus applied voltage relationship for each gun. The spectral output of each phosphor was measured using a Gamma Scientific Telespectroradiometer (model 2030-31) and this provided the chromaticity coordinates of each phosphor. In addition, the internal scatter of the display was measured following each monitor calibration as required by the City University Scatter Program (see chapter 4). The monitor was allowed to warm up for a minimum of 20 minutes before use on each occasion to allow the luminance output to stabilise (Dr P Forsyth – personnel communication).

All tests were completed in a darkened room where the only light came from a current-regulated halogen spotlight (11.5 Volts) directed towards a white diffuser on the ceiling above the visual display. This arrangement contributes negligible light to the actual display but prevents dark adaptation. The surrounding walls were painted matt black and all other surfaces visible to the subject were coated with a non-reflecting black felt material. This included the inside of the housing for the patient, consisting of a head and chinrest of adjustable height positioned behind the infrared transmitting mirror of the P_SCAN 100 system (figure 3-1). This dichroic mirror is set at 45° to the line of sight and transmits 95% of visible light while reflecting infrared light. The calibration was always undertaken through the mirror to simulate the normal viewing condition. The two infrared cameras were located below the line of sight as were the pulsed infrared sources. A matt black cloth was used to cover all but the lens of each camera during testing

to eliminate their reflection in the mirror. Details of the set-up for pupil measurement are given in chapter 6.

Figure 3-1: Experimental set-up employed throughout the study, showing the subject viewing the monitor through the P_SCAN 100 system with the left eye occluded

All subjects who met the selection criteria as detailed in section 3.4 underwent a subjective refraction to determine the appropriate refractive correction for the testing distance of 70 cm, (used for all tests except the CAA test which was conducted at 150 cm with a suitable correction in place). If the subjects' own glasses were not suitable, a trial lens(es) was placed in a specially adapted spectacle frame. Although small degrees of defocus have no significant effect on the measurement of the scatter function of the eye (Barbur, 1997), the appropriate correction was used throughout since defocus is known to significantly alter contrast thresholds and is likely to impair visual search performance, particularly for low contrast targets (Ho and Bilton, 1986; Lohmann et al., 1991a). In all cases, the correcting lens was cleaned before use to ensure that it scattered as little light as possible. In control and refractive surgery subjects for whom both eyes were suitable for testing, only the dominant eye was examined. The other eye was occluded throughout the experimental procedure (figure 3-1). All subjects

underwent a brief trial run of each experiment before the actual measurements were made.

3.2 Choice of target

The four tests of visual performance developed for this study employed a Landolt ring stimulus. This stimulus format was chosen, rather than a sine-wave grating, largely because the Landolt ring stimulus is similar to the alpha-numerics utilised on the flight deck displays. In addition, the Landolt ring provides a simple stimulus for use in a four alternative forced choice procedure that can be easily understood by inexperienced subjects. The single Landolt ring stimulus for the threshold tests (chapter 5) and the target for the visual search task (chapter 6) had an orientation of 45° to the vertical and a gap size that comprised 20° of the ring, (visual angle: diameter 72 mins of arc, gap 12.5 mins of arc at 700 mm – figure 3.2). Contrast was always defined as $\delta L/L_b$ where δL was the difference in luminance between the target and background and L_b denotes background luminance. This is equivalent to the Michelson contrast corresponding to periodic stimuli but is suitable for specifying higher contrasts when dealing with positive increments and aperiodic stimuli, as were used in this study.

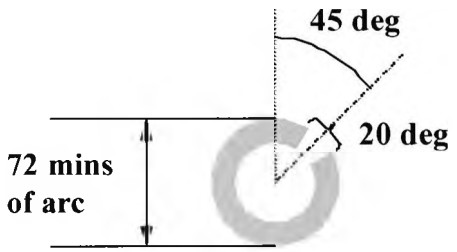


Figure 3-2: Dimensions of Landolt ring target

Both contrast threshold and visual search performance involved measurements at discrete locations over a circular field of approximately 20°. The contrast threshold tests required accurate and steady fixation throughout. The P_SCAN 100 system allowed fixation to be monitored, with verbal instruction if the subject's eye wandered. The stimulus presentation times were generally short (e.g.

250ms) in order to minimise the influence of eye movements on visual performance.

Following preliminary visual search experiments with an annular glare source surrounding the test field, the glare source was discarded (see chapter 6). Some subjects demonstrated an increase in visual search performance in the presence of the glare source associated with pupil constriction. A similar finding has been reported by Boxer and colleagues (Boxer-Wachler et al., 1999).

3.3 Psychophysical techniques

Both absolute contrast detection and contrast acuity thresholds (chapter 5) were measured using a staircase procedure driven by the subject's responses. An adaptive staircase method was used in which the contrast of the stimulus was increased following a 'no' or incorrect response, but a decrease in contrast required the target to be seen or identified correctly on two consecutive occasions (1-up, 2-down). The up and down steps were of equal size. The same technique was used to determine size scaling (stimulus size altered in response to subject answers) and contrast acuity thresholds in chapter 7. Such a strategy gives a performance at threshold of 70.7% correct (Lee, Koch, and Braun, 1997).

3.4 Patient selection and characteristics

The majority of subjects were recruited from two private refractive surgery clinics. These will be referred to as clinics A and B in this thesis. A large proportion of the control subjects were recruited from among a group of pre-surgical patients at clinic A. This arrangement had the potential advantage of providing data on the same subjects pre and post-surgery. Consequently these subjects tended to be myopic with many giving a history of recent contact lens wear. The control group was supplemented with subjects recruited from within City University.

Most of the LASIK subjects were also recruited from clinic A. Since many of the patients had to travel a long distance for their appointment, they were asked on arrival if they would be willing to participate and were tested either before or after

their consultation with the surgeon, to minimise disruption to staff and patients. This arrangement was not ideal and often resulted in incomplete data sets when patients ran out of time. Very few patients were available for examination both before and after surgery and therefore longitudinal data is not included in this thesis. Most LASIK subjects were examined within one year of their procedure since they were discharged from the clinic after this period of time.

Most of the PRK patients came from clinic B and had agreed at the time of surgery to participate in future research. The majority of PRK subjects had a follow-up time of one year or more.

The research followed the tenets of the Declaration of Helsinki and informed consent was obtained from all subjects prior to testing. This followed a detailed explanation of the nature of the study along with any possible consequences (Appendix A). The study was approved in advance by both the University and Departmental Research and Ethics Committees.

A detailed history was taken for each potential subject to allow identification and exclusion of pregnant women and subjects with systemic disease such as diabetes, or medication that might influence visual function. A subjective refraction was undertaken to ensure that all subjects were fully corrected prior to testing and achieved a minimum visual acuity of 6/9. Ocular health was examined to exclude eyes with any pathology, including lens opacities classified using the LOCS III system (Chylack et al., 1993). All subjects were examined by the primary investigator, *CMC*. All refractive surgery subjects had been treated with the aim of correcting their full preoperative refractive error. All refractive surgery patients were considered by the surgeon to have had a successful outcome with a corrected visual acuity of 6/9 or better. All those with intraoperative or post-surgical complications were excluded.

A total of 53 control subjects were examined, consisting of 25 females and 28 males.

Control Group	Mean	Standard Deviation	Range
Age (years)	37.4	+/- 10.2	22 to 69
Age distribution	39 subjects < 45 years, 14 subjects > 45 years		
Mean Spherical Error (MSE)	-3.20D	+/- 2.74	+2.75D to –9.00D
Astigmatism	0.82DC	+/- 0.83	0.00 to 4.25DC
MSE distribution	5 emmetropes, 4 hyperopes, 16 astigmats, 19 low myopes, 8 medium myopes and 1 high myope		

Table 3-1 Control group profile

A total of 52 LASIK patients were examined, consisting of 25 females and 27 males.

LASIK Group	Mean	Standard Deviation	Range
Age (years)	39.0	+/- 9.31	20 to 57
Age distribution	34 subjects < 45 years, 18 subjects > 45 years		
Preoperative MSE	-4.66D	+/- 2.73	+3.25D to –8.75D
Preoperative Astigmatism	1.05DC	+/- 1.12	0.00 to 5.50DC
MSE distribution	4 hyperopes, 12 astigmats, 19 low myopes, 12 medium myopes and 5 high myopes		
Follow-up period (weeks)	16.25	+/- 28.21	1 to 160
Follow-up time distribution	< 5w: 20, 6-10w: 11, 11-20w: 9, 21-40w: 7, >41w: 4		
Manifest MSE	0.00D	+/ 0.53	+1.25 to –1.50D

Table 3-2 LASIK group profile

A total of 32 PRK patients were examined, consisting of 19 females and 13 males.

PRK Group	Mean	Standard Deviation	Range
Age (years)	36.9	+/- 8.3	24 to 55
Age distribution	25 subjects < 45 years, 7 subjects > 45 years		
Preoperative MSE	-4.31D	+/- 2.27	+3.00D to –8.50D
Preoperative Astigmatism	0.64DC	+/- 0.49	0.00 to 2.00DC
MSE distribution	1 hyperope, 3 astigmats, 18 low myopes, 9 medium myopes and 1 high myope		
Follow-up period (weeks)	135.6	+/- 108.8	1 to 339
Follow-up time distribution	<5w: 2, 6-10w: 3, 11-20w: 3, 21-40w: 2, >41w: 22		
Manifest MSE	+0.03D	+/- 0.64	+1.50D to –1.00D

Table 3-3 PRK group profile

3.5 Statistical techniques

The retrospective nature of the study and the considerable time involved in obtaining a full data set for each subject had a number of consequences. When subjects were categorised for analysis, the distribution of subject numbers in the various age, preoperative refractive error and follow-up time categories was very uneven, as none of these factors could be controlled for in the selection of subjects. This meant that the influence of these variables on the data was difficult to assess. Secondly, it was impossible to obtain complete data sets for all subjects and therefore the group characteristics vary slightly between tests.

As for many psychophysical measures of human performance, much of the data demonstrated a skewed distribution (Appendix B). Transformation of most of these skewed data sets ($\log_{10}$), resulted in a normal distribution. Outliers were defined as those whose data fell outside the upper 2σ limit. They were removed prior to the statistical analysis and are described in Appendix D.

For each set of test data, the means were corrected for the effects of age, refractive error and follow-up time, to overcome any differences between groups, most notably follow-up time. A three sample, three-way analysis of variance (ANOVA) was used to compare the corrected means for each experiment (Altman 1991). The hypothesis in each case was that the corrected means were the same for all three data sets. The level of significance was set at 5% for all tests ($p=0.05$ or less). In some cases, the three corrected means were evenly spaced, and a further two sample analysis was required.

A one-way ANOVA was used to examine the effects of age, preoperative refractive error and follow-up time on the data. A two-way ANOVA was used to look for any interactions between the three variables, since features of corneal healing such as stromal haze and regression have been shown to vary with age (Hersh et al., 1996a; Corbett, O'Brart, Warburton et al., 1996).

The analyses reported in chapters 4-6 reveal that the manifest refractive error of the control group does not significantly influence the measures of visual performance considered in this study. Therefore, the small, post-operative refractive errors exhibited by the PRK and LASIK groups were disregarded.
It was not possible to examine interactions between preoperative refractive error and follow-up time for any of the data sets due to the uneven distribution of subjects between analysis categories.

3.5.1 Age, refractive error and follow-up time categories

Subjects were divided in to two groups according to age: 44 years and younger and 45 years and over. Although greater than the mean for all subject groups, the age of 45 years was chosen as the dividing line for the age classification because of the reported increase in forward light scatter around this age (Wolf, 1960; Elliott et al., 1991b; Hennelly et al., 1998).

Subjects were placed in to one of five categories for preoperative refractive error (or manifest error for the control group): emmetropia (+0.75 D to –0.50D), low myopia (-0.75D to –5.00D), medium myopia (-5.25D to –8.00D), high myopia (>

-8.25D) and hypermetropia (>+1.00D). The classification of refractive errors was based partly on the entry criterion of <-5.00D of myopia applied to commercial pilots by the UK Civil Aviation Authority, and also the classification used by two prominent studies into the effects of preoperative refractive error on the accuracy and predictability of refractive surgery (Gartry et al., 1992; Tuunanen and Tervo, 1998). Since all refractive surgery patients were treated for their full refractive error, their preoperative refraction is closely related to the degree of treatment applied to the cornea.

Refractive surgery subjects were also classified according to the length of time that had elapsed since surgery (follow-up time): 1-5 weeks, 6-10 weeks, 11-20 weeks, 21-40 weeks and 41-1000 weeks. The categories for the time period between surgery and assessment were based on the typical healing response post-PRK: stromal haze tends to develop within the first four-five weeks, followed by a gradual reduction in haze between 10-20 weeks (Fantes et al., 1990; Lohmann et al., 1991a; Wilson, 1997). Occasionally haze may persist for up to one year post-surgery with regression continuing for 18-24 months following PRK for higher refractive errors (Gartry et al., 1992). The same classification was applied to the LASIK group.

4 Forward Light Scatter

4.1 Chapter Summary

Forward light scatter was assessed using the City University Scatter Program. The subject was required to fixate a central black disc throughout the measurement and respond to the presence or absence of flicker over this disc, created by the sinusoidal modulation of one of five extended scatter annuli. By modulating the target luminance in counter phase to the scatter source, a null point was found, giving an estimate of the retinal luminance of the scattered light originating from a glare source at a particular eccentricity. The scatter index, n, and the straylight parameter, k were calculated along with the integral of the scatter function, k'.

An analysis of variance was used to compare the corrected means of the LASIK, PRK and control groups. Considering the overall quantity of straylight (k'), there was no statistically significant difference between the corrected means of the three subject groups. The mean scatter index (n) was significantly lower in the PRK group than either the control or LASIK group, indicating a change in the distribution of straylight as a result of PRK surgery. The mean straylight parameter (k) was significantly higher in the LASIK group than either the control or PRK group. No statistically significant relationships were identified between forward light scatter and either age or follow-up time. The straylight parameter, k, showed a statistically significant increase with increasing preoperative refractive error for the PRK group, but not the LASIK or control groups.

4.2 Introduction

As discussed in section 1.2.4.9.b, both forward and back scattered light are known to increase as a result of PRK (Butuner et al., 1994). Observation suggests that levels of back-scattered and reflected light remain close to baseline following routine LASIK procedures (Jain et al., 1995) but there is no published data on forward scatter post-LASIK.

The increase in forward light scatter with age is well documented (Yager et al., 1992; Whitaker et al., 1993; Hennelly et al., 1998) (section 1.2.4.1). The relationship between the degree of preoperative refractive error and forward scatter post-surgery is less clear; back-scatter in the form of stromal haze is associated with PRK treatments for higher degrees of myopia (Gartry et al., 1992) and therefore one might expect a relationship between preoperative refractive error and forward scatter. Forward light scatter is known to reduce over time post-PRK (Lohmann et al., 1993), with preoperative levels returning by around 12 months.

One of the aims of this study was to measure forward light scatter following both PRK and LASIK and attempt to relate the findings to measures of visual performance. In addition, the effects of age, preoperative refractive error and follow-up time on forward light scatter were investigated.

4.3 Methods and Subjects

4.3.1 Instrumentation

To assess forward light scatter, the full scatter function of the eye was measured using the City University Scatter Program at a working distance of 70 cm. This test was implemented on the P_SCAN 100 system (Barbur et al., 1987; Alexandridis et al., 1991) making use of the visual display system described in section 3.1. The program employs a direct compensation technique similar to that described by van den Berg and colleagues (van den Berg, 1986; van den Berg and Spekreijse, 1987). The implementation makes use of extended annuli to generate increased scatter and a new algorithm to reduce an extended annulus to an 'equivalent' narrow ring (Barbur et al., 1993), as needed to extract the scatter function of the eye. The program has been described in detail elsewhere (Barbur et al., 1993; Barbur et al., 1995) (section 1.2.2.3.c) but since it was used extensively in the study, a brief description follows. The stimulus consists of a 1° black fixation disc surrounded by a dark yellow isolating annulus to help disconnect flicker over the central target from that over the glare annulus, and a dark blue background to maintain a steady state of adaptation (figure 4-1). In order to generate a sufficiently high illuminance, E, in the plane of the pupil while maintaining display stability, the program employs extended scatter annuli with the outer eccentricity adjusted automatically to keep the illuminance in the pupil plane constant for all annuli. Point sources on each extended annulus have a range of eccentricities and the program computes the 'effective eccentricity' of each annulus (Barbur et al., 1993). The program generates sinusoidal modulation of the scatter annulus luminance at a frequency of 8.6 Hz and duration of 0.35s, resulting in the appearance of flicker over the central target due to the fluctuation of retinal illuminance. The target luminance is modulated in counter-phase to the scatter source and the amplitude altered until the null point is found, giving an estimate of the retinal luminance scattered from a glare source at a particular eccentricity (figure 4-2).

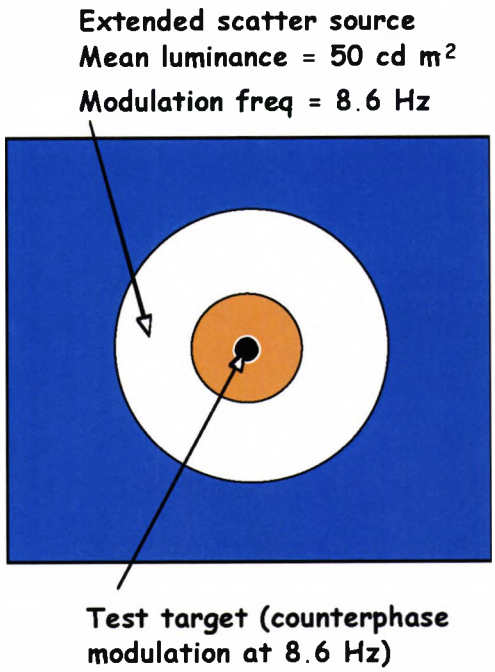


Figure 4-1: Test target and sample glare annulus, City University Scatter Program

A set of response buttons is used to decrease or increase the target modulation in a modified staircase procedure until the flicker is minimised. The initial step size is 0.15cd/m^2, reducing with each change of direction. Error-weighted, linear regression analysis is used to compute the scatter index, n, and the straylight parameter, k. A new parameter, k', is also calculated by integrating the scatter function of the eye from approximately 2° to ∞ (Barbur et al., 1993), (section 1.2.2.3.c).

Prior to testing, the screen is calibrated to allow the luminance of the separation annulus to be adjusted. This ensures that it contributes a constant level of scatter, regardless of its size and the size of the glare annulus in use, allowing compensation for internal scatter (Barbur et al., 1993; Barbur et al., 1995).

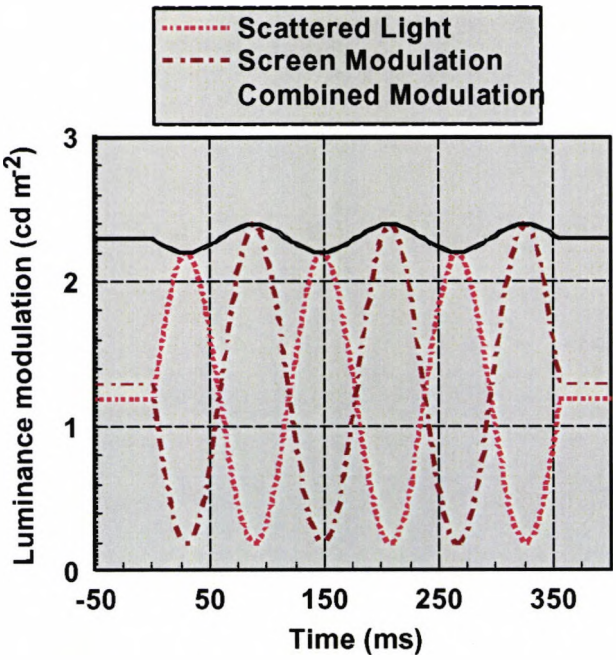


Figure 4-2: Nulling of the scattered light by modulation of the screen luminance

Although small refractive errors do not affect the measurement of intraocular light scatter (Barbur, 1997) each subject wore their full spectacle correction for 70cm during the measurement in order to be consistent with the other assessment methods employed in the study, all of which require full correction of any refractive error. The other eye remained patched throughout the procedure. The mean luminance required to produce nulling of the flicker was found by averaging six estimates at each of five glare angles, allowing the scatter function of the eye to be estimated.

4.3.2 Subjects

Table 4-1 describes the characteristics of all subjects who completed the City University Scatter Program. Those tested were a subgroup of the full subject groups described in section 3.4.

Subject group (eyes)	Age (years)	Follow-up time (weeks)	Pre-op MSE (D)	Pre-op astigmatism (DC)	Post-op MSE (D)
Controls (40)	37.31 +/- 10.91	N/A	-3.10 +/- 2.71	0.76 +/- 0.90	N/A
LASIK (31)	38.23 +/- 7.63	20.94 +/- 34.53	-5.21 +/- 2.48	0.95 +/- 0.89	-0.08 +/- 0.43
PRK (25)	37.92 +/- 8.32	147.20 +/- 112.32	-4.06 +/- 2.39	0.64 +/- 0.53	0.01 +/- 0.64

Table 4-1: Characteristics of subjects who completed the City University Scatter Program (mean +/- 1SD). MSE: mean spherical error

4.4 Results

Following the removal of outliers using the technique described in section 3.5, the scatter index (n), straylight parameter (k) and integrated straylight parameter (k') data were normally distributed (appendix B). The exception was the scatter index (n) data for the LASIK group, which demonstrated a left-skewed distribution that remained skewed following logarithmic transformation of the data. Two control, one LASIK and two PRK subjects were identified as outliers for one or more of the scatter parameters (n, k, k'). These outliers are detailed in appendix D. Table 4-2 shows the group characteristics following the removal of outliers, which did not differ significantly from the distributions stated in table 4-1.

Subject group (eyes)	Age (years)	Follow-up time (weeks)	Pre-op MSE (D)	Pre-op astigmatism (DC)	Post-op MSE (D)
Controls (38)	37.39 +/- 11.19	N/A	-3.17 +/- 2.54	0.77 +/- 0.92	N/A
LASIK (30)	38.47 +/- 7.64	21.27 +/- 35.07	-5.28 +/- 2.48	0.95 +/- 0.91	-0.07 +/- 0.43
PRK (23)	37.27 +/- 8.61	153.95 +/- 107.91	-4.08 +/- 2.49	0.61 +/- 0.46	-0.05 +/- 0.58

Table 4-2: Group characteristics following the removal of outliers (mean +/- 1SD). MSE: mean spherical error

4.4.1 Analysis

Figures 4-3 and 4-4 illustrate the scatter functions for the three subject groups and tables 4-3 and 4-4 list the mean measured scatter parameters. The means for each subject group were adjusted for the effects of age, preoperative refractive error and follow-up time. A three sample, three-way ANOVA was used to compare the corrected means for each parameter (table 4-5). Graphs showing the full data sets are shown in Appendix C.

There was no overall difference between the corrected mean integrated straylight parameters (k') of the three groups. This is in agreement with the scatter functions

plotted in figures 4-3 and 4-4. The mean scatter index (n) was significantly lower for the PRK group than either the LASIK or control group. This was associated with a small but not statistically significant decrease in the mean straylight parameter (k). This is possible, despite the lack of any significant difference between the mean k' values because n and k are not always independent (Barbur et al., 1995). Conversely, the mean straylight parameter (k) for the LASIK group was significantly higher than for either the PRK or control group, associated with a small, but not statistically significant increase in the mean scatter index (n), but no change in the overall quantity of forward scatter (k').

	Corrected Means (Scatter function)			**Three sample test**		**Post-hoc analysis**	
	Controls	**LASIK**	**PRK**	**p value Significant?**		**Samples compared**	**p value Significant?**
n	2.28	2.33	**2.15**	**0.000**	**Yes**	Controls and LASIK	p=0.352 No
k	36.51	**42.01**	34.14	**0.031**	**Yes**	Controls and PRK	p=0.535 No
k'	10.29	10.58	11.71	0.128	No	Controls and PRK	p=0.061 No

Table 4-3: ANOVA applied to scatter data (corrected means and statistical significance). Statistically significant p values are in bold

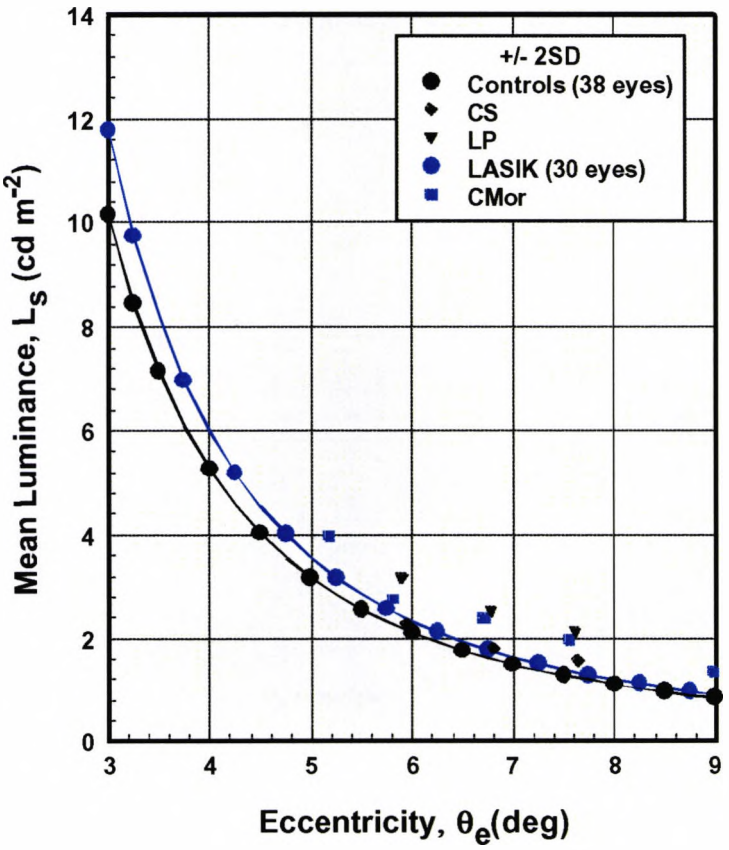


Figure 4-3: Scatter functions for LASIK and control groups

	n	k	k'
Controls	2.29 +/- 0.21	36.58 +/- 14.23	10.20 +/- 3.32
CS	**1.55**	9.28	10.99
LP	**1.67**	15.86	14.12
LASIK	2.33 +/- 0.20	43.09 +/- 18.69	10.81 +/- 3.05
CMor	**1.67**	14.53	12.85

Table 4-4: Measured scatter parameters (mean +/- 1SD)

The parameter(s) for which subjects were outliers are in bold

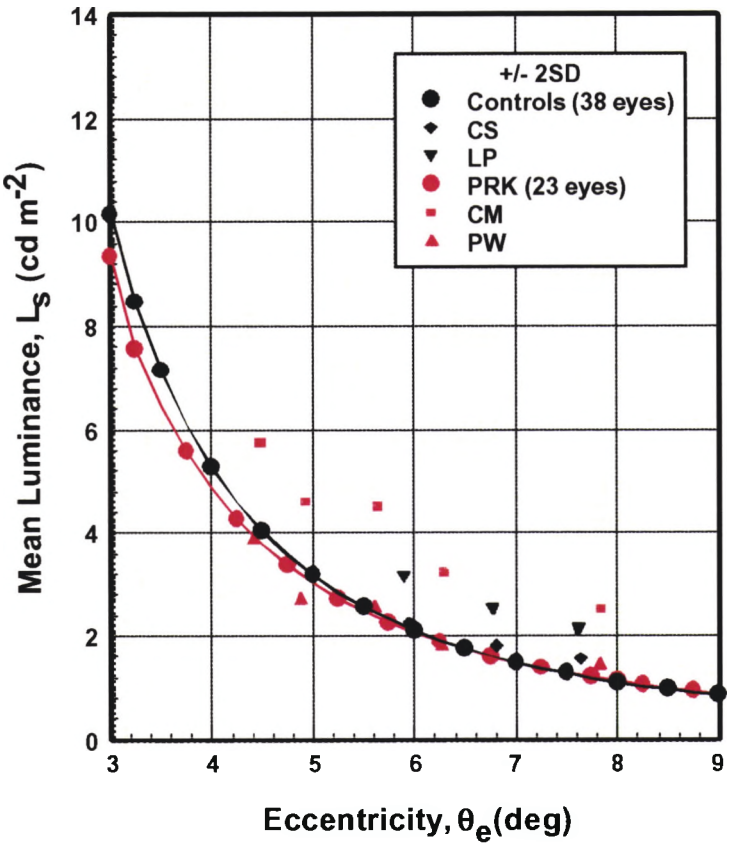


Figure 4-4: Scatter functions for PRK and control groups

	n	k	k'
Controls	2.29 +/- 0.21	36.58 +/- 14.23	10.20 +/- 3.32
CS	**1.55**	9.28	10.99
LP	**1.67**	15.86	14.12
PRK	2.12 +/- 0.18	32.01 +/- 11.56	11.52 +/- 2.35
CM	**1.42**	18.45	**31.55**
PW	**1.57**	13.99	15.74

Table 4-5: Measured scatter parameters (mean +/- 1SD)

The parameter(s) for which subjects were outliers are in bold

4.4.1.1 Influence of other factors

A one-way ANOVA was used to examine the influence of age on forward scatter in each group. In addition, the influence of manifest refractive error for the control group and preoperative refractive error and follow-up time were examined for the two refractive surgery groups. Interactions were also considered.

4.4.1.1.a Age

	n	k	k'
Control	p=0.531	p=0.507	p=0.921
LASIK	p=0.403	p=0.701	p=0.255
PRK	p=0.359	p=0.173	p=0.234

Table 4-6: Effect of age on scatter parameters

Although there was a trend towards increasing k and k' values (quantity) and a reduction in n (increased spread) with age, these trends did not reach statistical significance for any of the three subject groups (table 4-6). However, there were only two age categories with the majority of subjects falling into the lower age category.

4.4.1.1.b Refractive Error

	n	k	k'
Control (manifest Rx)	p=0.693	p=0.538	p=0.149
LASIK (Pre-op Rx)	p=0.640	p=0.590	p=0.916
PRK (Pre-op Rx)	p=0.621	**p=0.037**	p=0.085

Table 4-7: Effect of refractive error on scatter parameters. Statistically significant p values are in bold.

Considering forward light scatter for the control group, there was no trend with increasing refractive error (whether myopia or hyperopia). Similarly, no trends with preoperative refractive error were noted for the LASIK data (table 4-7). For the PRK group, an increase in all parameters with increasing preoperative error was noted but the effect only reached statistical significance for the straylight parameter (p=0.037. Scatter index n: p=0.621, integrated straylight parameter k': p=0.085).

A two-way ANOVA tested for interactions between refractive error and age, (i.e. differences in the effect of refractive error on the scatter parameters between the two age groups). The small number of subjects over the age of 45 years limited the power of this analysis. No statistically significant effects were seen for any of the three subject groups (table 4-8) and no trends were noted.

	n	k	k'
Control (manifest Rx)	p=0.661	p=0.146	p=0.312
LASIK (Pre-op Rx)	p=0.844	p=0.802	p=0.830
PRK (Pre-op Rx)	p=0.900	p=0.181	p=0.228

Table 4-8: Interactions between refractive error and age for the scatter parameters

4.4.1.1.c Follow-up Time

	n	k	k'
LASIK	p=0.905	p=0.650	p=0.189
PRK	p=0.565	p=0.348	p=0.074

Table 4-9: Effect of follow-up time on scatter parameters

Follow-up time was not seen to significantly effect scatter for either the PRK or LASIK groups and no trends were noted (table 4-9). The distribution of PRK subjects between the various subcategories was very uneven.

	n	k	k'
LASIK	p=0.680	p=0.464	p=0.094
PRK	p=0.604	p=0.308	p=0.061

Table 4-10: Interactions between follow-up time and age for the scatter parameters

When a two-way ANOVA was used to test for interactions between follow-up time and age, (i.e. differences in the effect of follow-up time on the scatter parameters with age), no statistically significant effect was seen for either of the two refractive surgery groups and no trends were noted (table 4-10). The power of this analysis was greatly reduced by the limited number of subjects in the upper age groups, particular for the PRK data.

A two-way ANOVA was used to test for interactions between preoperative refractive error and follow-up time, but the large number of categories and limited number of subjects in each category greatly restricted the power of this analysis. No statistically significant relationships or trends were identified (table 4-11).

	n	k	k'
LASIK	p=0.579	p=0.554	p=0.122
PRK	p=0.602	p=0.174	p=0.135

Table 4-11: Interactions between refractive error and follow-up time for the scatter parameters

4.5 Chapter Conclusion

Comparison of the mean scatter functions of each of the three subject groups assessed using the City University Scatter Program indicate that on average, there is a small but not statistically significant increase in the quantity of intraocular light scatter following both LASIK and especially PRK. However, PRK surgery appears to significantly modify the distribution of straylight across the retina resulting in a wider spread of scattered light (lower n value). Conversely, LASIK

surgery appears to increase the quantity of straylight while slightly narrowing the distribution (larger n value). The quantity of straylight, k, shows a statistically significant increase with the degree of preoperative refractive error post-PRK. No such effect was seen for either the control or LASIK groups. Age and follow-up time did not appear to significantly influence forward light scatter for any of the three subject groups assessed in this study.

These results cannot rule out an increase in small angle scatter (within 3°), since it is not possible to measure scatter so close to the object of regard. Unfortunately, it is the small angle scatter (i.e. light scatter originating from the image of interest) that is more likely to degrade retinal image quality rather than large angle scatter (Beckman et al., 1991; van den Berg and Spekreijse, 1987).

5 Contrast Thresholds

5.1 Chapter Summary

Absolute contrast detection thresholds and contrast acuity (gap orientation discrimination) thresholds were assessed to examine the extent to which such measurements can be used to detect the effects of excimer laser refractive surgery on retinal image quality. Thresholds were assessed over a circular field of 10° radius for a background luminance of 12 cd/m^2. The target consisted of a Landolt ring that was presented at one of seven randomly interleaved eccentricities. The subject was required to indicate either the presence of (detection) or the gap orientation (contrast acuity) of the Landolt ring by pressing the relevant response button. The target contrast was modified using a staircase procedure that generated six interleaved averages in response to the subject's answers (section 3.4).

An analysis of variance (ANOVA) was used to compare the corrected means of the LASIK, PRK and control groups. An increase in absolute contrast detection thresholds was seen for the PRK and LASIK groups compared to the control group but the increase did not reach statistical significance except at the highest eccentricity (9.4°). An increase in absolute contrast detection thresholds was noted with age, which was statistically significant at various eccentricities for each subject group. An increase in absolute contrast detection thresholds with refractive error was also demonstrated but not found to be statistically significant. No trends with follow-up time were identified.

Contrast acuity thresholds (gap orientation discrimination) were significantly higher in the PRK group than the control group at all but the highest eccentricity (9.4°), and there was some evidence to suggest a similar but weaker effect in the LASIK group that only reached statistical significance at one eccentricity (3.8°). All subject groups demonstrated an increase in thresholds with age but the effect was only statistically significant at the three lowest eccentricities for the control group data. Increasing refractive error was associated with a small but not statistically significant increase in contrast acuity thresholds, which tended to be

greater in the older age group (>45 years). This interaction reached statistical significance at various eccentricities across the three groups. There was a trend towards decreasing thresholds with increasing follow-up time post-LASIK, and this also tended to be greater for the older age group (>45 years), but this was only statistically significant at 9.4° eccentricity. Combined with the knowledge that optical degradation will result in a greater impairment of contrast discrimination thresholds than absolute contrast detection thresholds, these findings suggest that contrast acuity thresholds are the more sensitive measure of a reduction in visual performance resulting from optical factors such as increased small angle intraocular light scatter and/or aberrations induced by excimer laser refractive surgery.

5.2 Introduction

Two tests were designed to examine contrast thresholds as a function of eccentricity in both control and refractive surgery subjects, in an attempt to assess the sensitivity of such tests as a measure of reduced retinal image quality. These tests were originally intended to provide input data for the visual search model, (section 6.6), but it was felt that they could also contribute valuable information regarding visual performance in their own right. They involve the rapid detection of a target over the visual field and therefore have some similarities to visual tasks involved in piloting an aircraft, such as the detection of novel information on instrument displays. The bulk of the visual information displayed in the cockpit is located in small, localised areas of the visual field. At any one time, the pilot attends to only one of these areas for the purpose of processing and interpreting high acuity information (see section 7.3.1).

Both absolute contrast detection and acuity thresholds would be expected to increase with eccentricity due to the reduction in sampling density with eccentricity, both at a retinal level (cones and retinal ganglion cells), and in the cortex (Hirsch and Curcio, 1989). In addition, the modulation transfer function (MTF) of the eye is reduced with increasing eccentricity, although it reduces only gradually compared to the reduction in resolving power associated with neural

structures (Navarro et al., 1998). The change in the MTF is associated with an approximately linear increase in the root mean square wave-front error with eccentricity (Navarro et al., 1998). The shape of the MTF changes little with eccentricity but the range of resolvable spatial frequencies is shifted towards lower frequencies with increasing eccentricity (Jennings and Charman, 1997).

One might expect that both absolute contrast detection and acuity thresholds would be elevated in the two refractive surgery groups compared to the control group, related to surgically induced scattered light and/or increased aberrations (section 1.2.4.9). A greater increase would be expected for acuity thresholds because the task requires resolution of a small gap in the ring composed of relatively high spatial frequency information - a task more likely to be masked by scatter and aberrations than the complete target. In addition, both absolute detection and acuity thresholds might be expected to increase with age (Kline, 1987) as a result of an increase in intraocular scattered light (Allen and Vos, 1967; Whitaker et al., 1993; Hennelly et al., 1998) and aberrations (Oshika et al., 1999a), the reduction in retinal ganglion cell population with age (Anderson and McDowell, 1997) and other neural factors (Elliott, 1987).

The degree of preoperative refractive error is known to influence the visual outcome of refractive surgery in terms of high contrast acuity (Rao, Mukesh, Bakshi et al., 1996; Seiler and McDonnell, 1995; Seiler and McDonnell, 1995). An increase in absolute contrast detection and acuity thresholds might be expected in those treated for higher preoperative refractive errors, related to the greater incidence of stromal haze post-PRK (Gartry et al., 1992) and the more profound change in corneal profile post-PRK and LASIK (Hersh et al., 1996b) (section 1.2.4.9).

Finally, an inverse relationship between absolute contrast detection and acuity thresholds, and follow-up time would be expected, based on reports that both high contrast acuity (Maguen, Salz, Nesburn et al., 1994) and contrast sensitivity (Holladay et al., 1999; Perez-Santonja et al., 1998b; Perez-Santonja et al., 1998b) improve with time following surgery. These changes may be attributable to the

reported peak in intraocular light scatter between four and six weeks post-PRK that gradually returns to preoperative levels by 12 months (Lohmann et al., 1993).

5.3 Methods and Subjects

The two tests were designed to measure the contrast required to either detect or discriminate a target over a range of eccentricities within a circular field of 10° radius, (figure 5-1 and 5-2). The programs were implemented on the P_SCAN 100 system (Barbur et al., 1987; Alexandridis et al., 1991) (section 3.2). The subject's head was positioned on the chin rest to maintain a constant working distance of 70 cm. The eye under test was fully corrected for this distance while the other eye remained patched throughout. In each case, the stimulus consisted of a single Landolt ring (section 3.2) with an orientation of 45° and gap size comprising 20° of the overall ring. Contrast thresholds were measured at seven eccentricities within the 10° field, with each eccentricity allocated a small annulus in which the target could be presented, (as required by the design of the visual search program on which the tests were based). The mean eccentricity for each of the seven positions was calculated at the end of each run along with the standard deviation, E.g. 1.41 +/- 0.11°. Contrast was defined as $\delta L/L_b$ (i.e. the increment in luminance δL, divided by the background luminance, L_b). The background luminance L_b was 12 cd/m^2 with chromaticity coordinates of (0.3, 0.334), consistent with the visual search program (chapter 6). Initially, subjects were assessed at all seven eccentricities but this proved to be very time consuming and so threshold measurements were restricted to the first, third, fifth and seventh eccentricities for the majority of the subjects. Subjects underwent a ten minute training run prior to each assessment, the time limited by the logistics of testing patients within a working clinic. Limited learning has been demonstrated for similar peripheral tasks (Beard, Levi, and Reich, 1995).

5.3.1 Absolute Contrast Detection Threshold Program

The average contrast required to detect the presence of the target was measured at between four and seven interleaved eccentricities (0-10°) (figure 5-1). The subject was required to fixate the central red target throughout. The stimulus was presented for 250ms and the subject pressed a response button to indicate whether or not the target was detected (two-way forced choice paradigm - yes/no). A 'yes' resulted in a reduction in contrast when the target was next presented at that eccentricity. A 'no' resulted in an increase in contrast. Target contrast was modified using a random interleaved staircase with an initial step size of 3% contrast for two averages reducing to 0.5% for a further four averages (section 3.4).

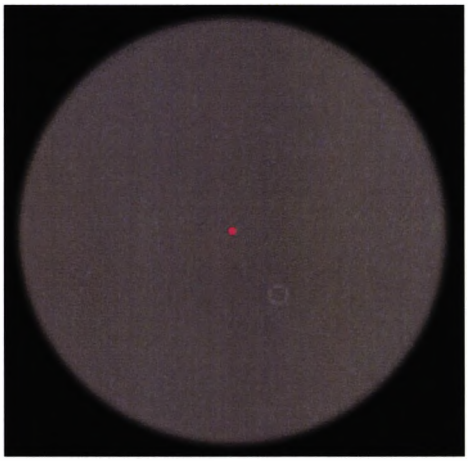


Figure 5-1: Absolute contrast detection threshold program – example stimulus 3.6° from fixation

5.3.1.1 Subjects

Subject group (eyes)	Age (years)	Follow-up time (weeks)	Pre-op MSE (D)	Pre-op astigmatism (DC)	Post-op MSE (D)
Controls (50)	37.61 +/- 10.25	N/A	-3.31 +/- 2.68	0.85 +/- 0.84	N/A
LASIK (48)	39.73 +/- 8.79	17.29 +/- 29.13	-4.72 +/- 2.76	1.03 +/- 1.14	0.01 +/- 0.55
PRK (33)	36.91 +/- 8.33	135.61 +/- 108.84	-4.31 +/- 2.27	0.64 +/- 0.49	0.03 +/- 0.64

Table 5-1: Characteristics of subjects who completed the contrast detection test (mean +/- 1SD). MSE: mean spherical error.

Table 5-1 describes the characteristics of all subjects who completed the contrast detection test. Those tested were a subgroup of the full subject groups described in section 3.4.

5.3.2 Contrast Acuity Program

The average contrast required to discriminate the orientation of the gap in the Landolt ring target was measured for each eccentricity. The subject was required to fixate the central red target throughout. The stimulus was presented for 250ms at one of up to seven randomly interleaved eccentricities (0-10°) (figure 5-2). The subject was required to press one of four response buttons to indicate the orientation of the gap in the ring (four-choice response paradigm - up-right, up-left, down-right, down-left) (figure 5-3). If the position of the gap could not be identified, the subject was forced to guess. At each eccentricity,

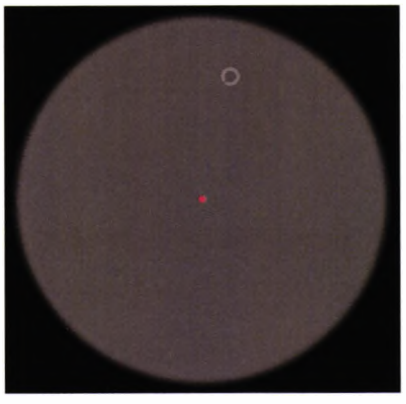


Figure 5-2: Contrast acuity threshold program - example stimulus 6.7° from fixation

two consecutive correct answers were required to reduce the target contrast. A single incorrect answer resulted in an increase in contrast at the next presentation. This ensured that the chance of a reduction in contrast resulting from a correct guess was reduced to one in 16. Target contrast was modified using a random interleaved staircase with an initial step size of 3% contrast (two averages) gradually reducing to 0.5% for a further four averages (section 3.4).

Figure 5-3: Response button box for the contrast acuity test

5.3.2.1 Subjects

Table 5-2 describes the characteristics of all subjects who completed the contrast acuity test. Those tested were a subgroup of the full subject groups described in section 3.4.

Subject group (eyes)	Age (years)	Follow-up time (weeks)	Pre-op MSE (D)	Pre-op astigmatism (DC)	Post-op MSE (D)
Controls (45)	36.87 +/- 9.92	N/A	-3.48 +/- 2.37	0.89 +/- 0.88	N/A
LASIK (47)	38.94 +/- 9.11	17.60 +/- 29.36	-4.79 +/- 2.50	1.05 +/- 1.14	-0.03 +/- 0.53
PRK (33)	36.91 +/- 8.33	135.61 +/- 108.83	-4.31 +/- 2.27	0.64 +/- 0.49	0.03 +/- 0.64

Table 5-2: Characteristics of subjects who completed the contrast acuity threshold test (mean +/- 1SD). MSE: mean spherical error.

5.4 Results

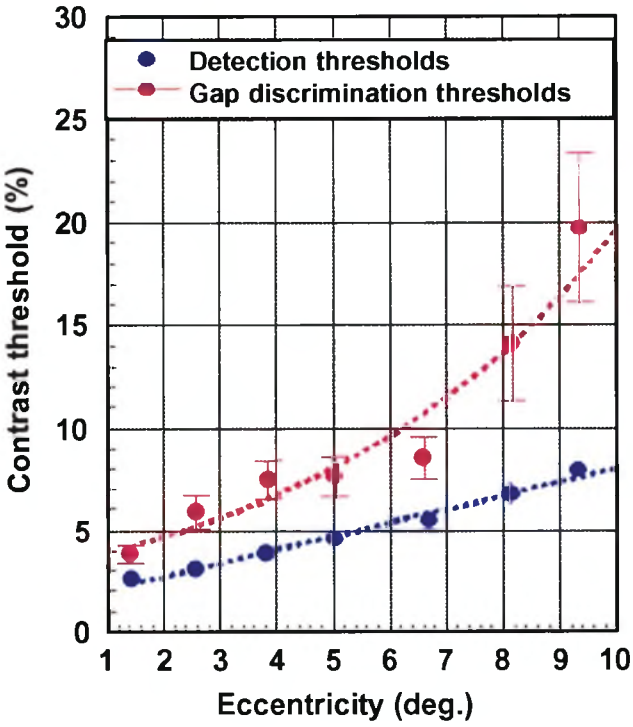


Figure 5-4:

Contrast thresholds for absolute detection and discrimination of a target for a single subject (average of five runs +/- SE)

Contrast thresholds for both target detection and gap orientation discrimination (acuity) increase with increasing target eccentricity. Figure 5-4 illustrates the data for a single subject showing the gradual rise in absolute detection thresholds compared to the rapid increase in gap discrimination thresholds with target eccentricity. This reflects a reduction in sampling density with eccentricity (Curcio et al., 1990) and the reduced optical performance of the eye away from the visual axis (Artal and Guirao, 1998; Navarro et al., 1998). The results suggest that these visual functions involve different populations of ganglion cells that largely differ in their sampling densities with eccentricity. The variance of the gap discrimination data increases sharply with eccentricity.

5.4.1 Absolute contrast detection thresholds

Table 5-3 describes the group characteristics following the removal of outliers, which did not differ significantly from those stated in table 5-1.

Subject group (eyes)	Age (years)	Follow-up time (weeks)	Pre-op MSE (D)	Pre-op astigmatism (DC)	Post-op MSE (D)
Controls (50)	37.61 +/- 10.25	N/A	-3.31 +/- 2.68	0.85 +/- 0.84	N/A
LASIK (47)	39.68 +/- 8.87	14.26 +/- 20.37	-4.65 +/- 2.73	1.03 +/- 1.15	0.02 +/- 0.55
PRK (32)	36.91 +/- 8.33	135.61 +/- 108.84	-4.32 +/- 2.27	0.64 +/- 0.49	-0.03 +/- 0.64

Table 5-3: Group characteristics following the removal of outliers (mean +/- 1SD). MSE: mean spherical error

The average contrast required to detect the presence of the target was plotted against mean target position as shown in figures 5-5 and 5-6. Graphs showing the full data sets are shown in Appendix C. Two subjects (one subject from each refractive surgery group) were identified as outliers using the technique described in section 3.5. These outliers (PL and ND) are discussed further in Appendix D.

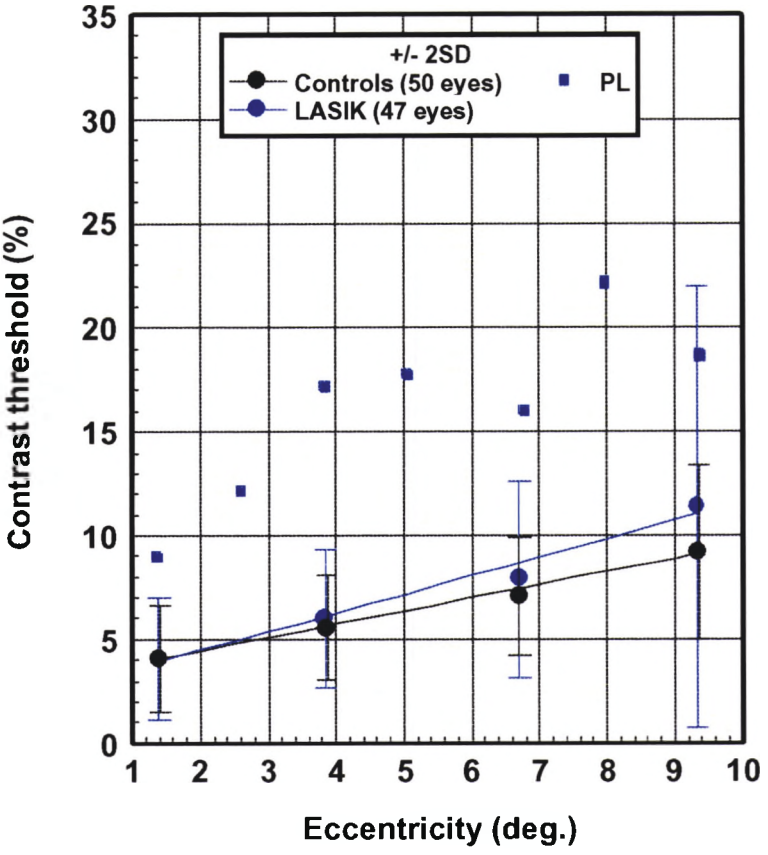


Figure 5-5: Mean absolute contrast detection thresholds for control and LASIK groups

Ave Ecc.	1.4°	3.8°	6.7°	9.4°
Controls	4.08 +/- 1.27	5.53 +/- 1.26	7.05 +/- 1.44	9.18 +/- 2.09
LASIK	4.04 +/- 1.47	6.02 +/- 1.68	7.90 +/- 2.36	11.37 +/- 5.31
PL	8.92	17.16	15.98	18.62

Table 5-4: Measured absolute contrast detection threshold data (mean +/- 1SD)

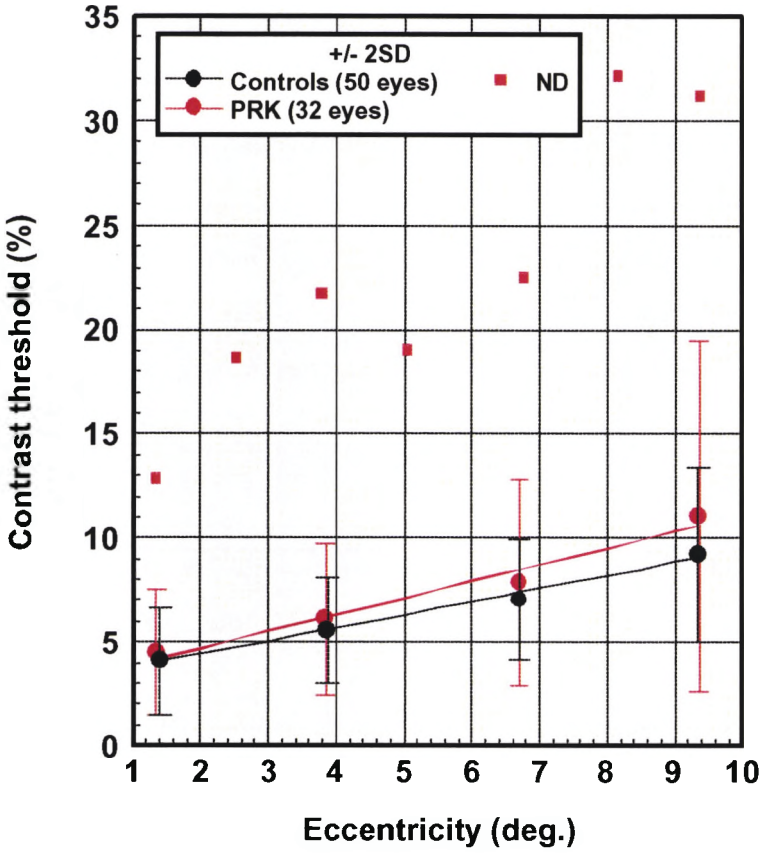


Figure 5-6: Mean absolute contrast detection thresholds for control and PRK groups

Ave Ecc.	1.4°	3.8°	6.7°	9.4°
Controls	4.08 +/- 1.27	5.53 +/- 1.26	7.05 +/- 1.44	9.18 +/- 2.09
PRK	4.46 +/- 1.53	6.10 +/- 1.82	7.84 +/- 2.50	11.06 +/- 4.23
ND	12.84	29.75	22.47	31.34

Table 5-5: Measured absolute contrast detection threshold data (mean +/- 1SD)

5.4.1.1 Analysis

Following the removal of outliers, the absolute contrast detection data tended to demonstrate a skewed distribution for all three subject groups (Appendix B). The distribution remained skewed at all but the highest eccentricity (9.4°) following logarithmic transformation. Following correction of the means for the effects of age, preoperative refractive error and follow-up time, a three sample three-way ANOVA was used to compare the corrected means (transformed data), at each eccentricity (table 5-6). Further two sample testing was undertaken where required.

	Corrected means (log contrast detection thresholds)			**Three sample test**		**Post-hoc analysis**	
Ecc.	**Control**	**LASIK**	**PRK**	**p value**	**Significant?**	**Samples compared**	**p value Significant?**
1.4°	0.578	0.559	0.630	0.370	No	LASIK vs PRK	p=0.076 No
3.8°	0.731	0.751	0.774	0.218	No	Control vs PRK	p=0.101 No
6.7°	0.842	0.879	0.873	0.106	No	Control vs LASIK	p=0.068 No
9.4°	**0.954**	1.016	1.023	**0.019**	**Yes**	LASIK vs PRK	p=0.694 No

Table 5-6: ANOVA applied to transformed absolute contrast detection threshold data (corrected means and statistical significance)

For the stimulus parameters employed in this test, there tended to be a small but not statistically significant increase in the corrected mean absolute contrast detection thresholds of the two refractive surgery groups compared to the control group (table 5-6). However, at the highest eccentricity (9.4°), the control group exhibited significantly lower absolute contrast detection thresholds than either of the two refractive surgery groups ($p = 0.019$). A number of subjects from all three

groups reported difficulty in responding to the most peripheral targets, possibly reducing the validity of the data at 9.4°.

5.4.1.2 Influence of other factors

A one-way ANOVA used to examine the influence of age on absolute contrast detection thresholds in each group. In addition, the influence of refractive error for the control group, and preoperative refractive error and follow-up time were examined for the two refractive surgery groups. Interactions were also considered.

5.4.1.2.a Age

The control data demonstrated an increase in absolute contrast thresholds for detection with age that reached statistical significance at all but the highest eccentricity (see table 5-7). An increase in absolute contrast detection thresholds with age was also seen for the LASIK and PRK data but the relationship did not reach statistical significance at the two lowest eccentricities for the LASIK data (1.4° and 3.8°), and at the lowest eccentricity for the PRK data (1.4°).

	1.4°	3.8°	6.7°	9.4°
Control	**p=0.022**	**p=0.019**	**p=0.003**	p=0.095
LASIK	p=0.212	p=0.388	**p=0.006**	**p=0.019**
PRK	p=0.207	**p=0.036**	**p=0.018**	**p=0.019**

Table 5-7: Effect of age on absolute contrast detection thresholds (transformed data) Statistically significant p values are in bold.

5.4.1.2.b Refractive error

The control group showed a trend towards increasing absolute contrast detection thresholds with increasing refractive error, but the relationship did not reach statistical significance. Consequently, the much smaller mean manifest refractive error (refractive error on the day of assessment) of the refractive surgery patients was assumed to be insignificant. Absolute contrast detection thresholds also showed a tendency to increase with the degree of preoperative refractive error but the effect did not reach statistical significance for either the LASIK or PRK groups (table 5-8).

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
Control (manifest Rx)	p=0.947	p=0.873	p=0.927	p=0.910
LASIK (pre-op Rx)	p=0.185	p=0.232	p=0.137	p=0.064
PRK (pre-op Rx)	p=0.073	p=0.177	p=0.291	p=0.064

Table 5-8: Effect of refractive error on absolute contrast detection thresholds (transformed data)

A two-way ANOVA was used to test for interactions between refractive error and age, i.e. differences in the effect of refractive error on absolute contrast detection thresholds between the two age groups. For the control group, no trend was found with increasing manifest refractive error for either age group. Therefore interactions between manifest refraction and age were assumed to be insignificant for the two refractive surgery groups. Similarly, no trend was found between the two factors for the LASIK group. Although the interaction was supposedly highly statistically significant at an eccentricity of 9.4° (p=0.000), there were too few subjects in the older age subgroups (>45 years) for this to be anything other than a random statistical error rather than a real effect. Considering the PRK group, a definite trend was noted with the younger age group demonstrating a smaller increase in absolute contrast detection thresholds with increasing preoperative

refractive error than the older age group, with the interaction reaching statistical significance at all but the lowest eccentricity (p=0.084), (table 5-9).

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
Control (manifest Rx)	p=0.670	p=0.696	p=0.359	p=0.714
LASIK (pre-op Rx)	p=0.285	p=0.517	p=0.109	**p=0.000**
PRK (pre-op Rx)	p=0.084	**p=0.013**	**p=0.011**	**p=0.000**

Table 5-9: Interactions between refractive error and age for the absolute contrast detection thresholds (transformed data) Statistically significant p values are in bold.

5.4.1.2.c Follow-up time

No trend could be identified when the relationship between absolute contrast detection thresholds and follow-up time was examined for the LASIK group (table 5-10). The PRK group showed a small but not statistically significant reduction in thresholds between those examined within five weeks of surgery and those with a follow-up time greater than five weeks.

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
LASIK	p=0.624	p=0.720	p=0.832	p=0.150
PRK	p=0.149	p=0.975	p=0.092	p=0.150

Table 5-10: Effect of follow-up time on absolute contrast detection thresholds (transformed data)

A two-way ANOVA was used to look for interactions between follow-up time and age, i.e. a difference in the effect of follow-up time (speed of healing process) on absolute contrast detection thresholds between the two age groups. There were

too few subjects in the older age subgroups to identify any trends in either the LASIK or PRK data, despite the supposedly statistically significant finding at 9.4° for the LASIK group, and 6.7° and 9.4° for the PRK group (table 5-11).

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
LASIK	P=0.401	p=0.836	p=0.245	**p=0.025**
PRK	P=0.064	p=0.329	**p=0.017**	**p=0.025**

Table 5-11: Interactions between follow-up time and age for the absolute contrast detection thresholds (transformed data)
Statistically significant p values are in bold.

A two-way ANOVA was used to look for interactions between preoperative refractive error and follow-up time, i.e. a difference in the effect of follow-up time on absolute contrast detection thresholds between different refractive error categories. No trends were identified despite the statistically significant finding for the PRK group at 1.4° (table 5-12).

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
LASIK	p=0.620	p=0.305	p=0.067	p=0.129
PRK	**p=0.021**	p=0.758	p=0.072	p=0.136

Table 5-12: Interactions between preoperative refractive error and follow-up time for absolute contrast detection thresholds (transformed data)
Statistically significant p values are in bold.

5.4.2 Contrast acuity thresholds (gap orientation discrimination)

Table 5-13 describes the group characteristics following the removal of outliers, which did not differ significantly from those stated in table 5-2.

Subject group (eyes)	Age (years)	Follow-up time (weeks)	Pre-op MSE (D)	Pre-op astigmatism (DC)	Post-op MSE (D)
Controls (45)	36.87 +/- 9.92	N/A	-3.48 +/- 2.37	0.89 +/- 0.88	N/A
LASIK (44)	38.57 +/- 8.96	15.11 +/- 20.77	-4.88 +/- 2.23	1.07 +/- 1.18	0.00 +/- 0.48
PRK (32)	36.91 +/- 8.33	135.61 +/- 108.84	-4.31 +/- 2.27	0.64 +/- 0.49	0.03 +/- 0.64

Table 5-13: Group characteristics following the removal of outliers (mean +/- 1SD). MSE: mean spherical error.

The average contrast required to discriminate the gap in the Landolt ring target was plotted against mean target position as shown in figures 5-7 and 5-8. Graphs showing the full data sets are shown in Appendix C. Three LASIK subjects and one PRK subject were identified as outliers using the technique described in section 3.5. These outliers (HJR, MS, PL and ND) are discussed further in Appendix D.

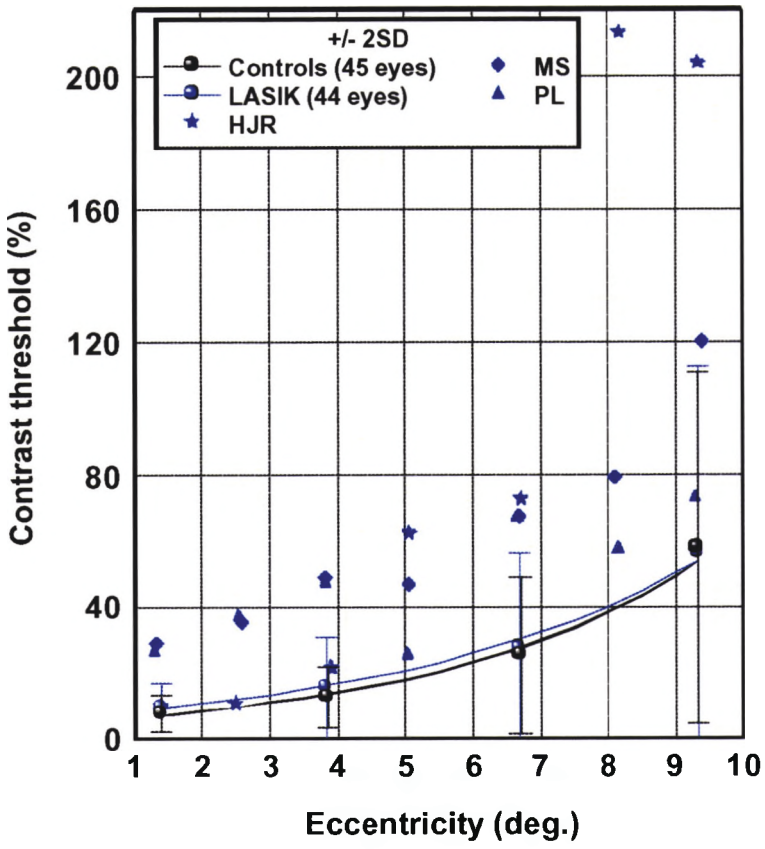


Figure 5-7: Mean contrast acuity thresholds for control and LASIK groups

Ave Ecc.	1.4°	3.8°	6.7°	9.4°
Controls	7.66 +/- 2.76	12.50 +/- 4.54	25.17 +/- 11.88	57.65 +/- 26.62
LASIK	9.28 +/- 3.70	15.45 +/- 7.46	27.18 +/- 14.36	56.40 +/- 27.99
HJR	9.66	28.71	72.45	203.77
MS	28.71	48.73	67.00	119.88
PL	26.62	47.58	67.36	73.27

Table 5-14: Measured contrast acuity threshold data (mean +/- 1SD)

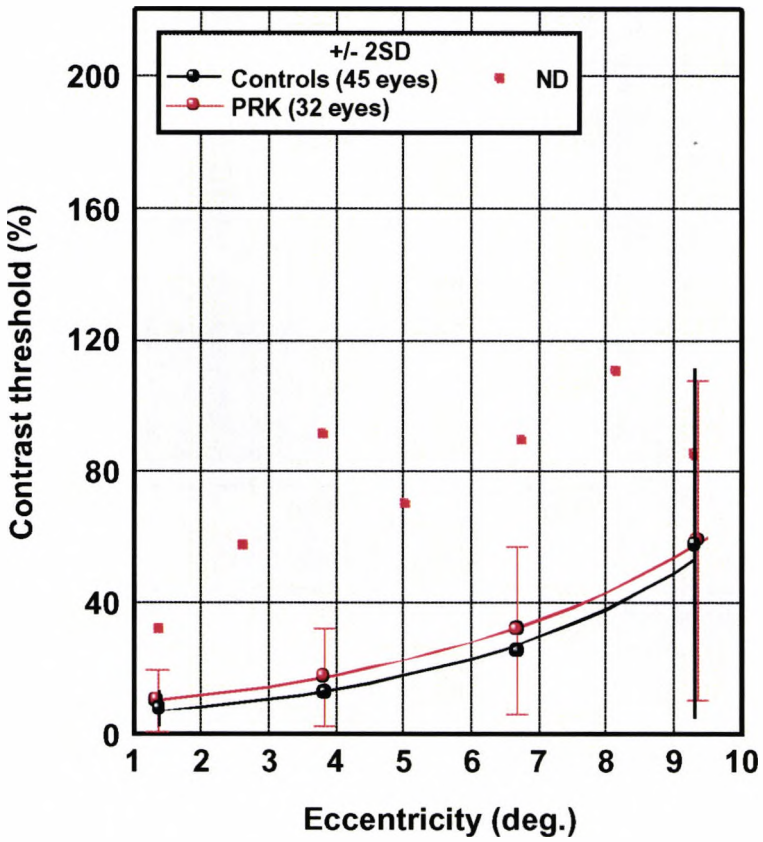


Figure 5-8: Mean contrast acuity thresholds for control and PRK groups

Ave Ecc.	1.4°	3.8°	6.7°	9.4°
Controls	7.66 +/- 2.76	12.50 +/- 4.54	25.17 +/- 11.88	57.65 +/- 26.62
PRK	10.27 +/- 4.69	17.42 +/- 7.43	31.80 +/- 12.79	58.93 +/- 24.29
ND	32.32	91.49	89.54	85.21

Table 5-15: Measured contrast acuity threshold data (mean +/- 1SD)

5.4.2.1 Analysis

The contrast acuity data exhibited either a normal or skewed distribution depending on the subject group and target eccentricity (Appendix B). Logarithmic transformation of the data resulted in a normal distribution at all eccentricities for all three groups. Following correction of the means for the effects of age, preoperative refractive error and follow-up time, a three sample, three-way ANOVA was used to compare the corrected means (transformed data) at each eccentricity (see table 5-16). Further two sample testing was undertaken where required.

	Corrected Means (log Contrast Acuity Thresholds)			**Three sample test**		**Post-hoc analysis**	
Ecc.	**Control**	**LASIK**	**PRK**	**p value**	**Significant?**	**Samples compared**	**p value Significant?**
1.4°	0.856	0.913	**1.003**	**0.003**	**Yes**	Controls vs LASIK	p=0.074 No
3.8°	1.069	1.133	**1.219**	**0.000**	**Yes**	Controls vs **LASIK**	**p=0.041 Yes**
6.7°	1.360	1.371	**1.463**	**0.045**	**Yes**	Controls vs LASIK	p=0.787 No
9.4°	1.717	1.706	1.723	0.764	No	LASIK vs PRK	p=0.713 No

Table 5-16: ANOVA applied to transformed contrast acuity threshold data (corrected means and statistical significance)

For the stimulus parameters employed in the test, there was a statistically significant difference between the corrected means of the transformed contrast acuity data at all eccentricities except 9.4°. Examination of the transformed corrected means reveals that the contrast acuity thresholds for the PRK group are higher than the corresponding means for the control or LASIK groups, except at an eccentricity of 9.4°, where the difference between the means does not reach statistical significance. In addition, at an eccentricity of 3.8°, the corrected mean for the LASIK group is significantly higher than the control mean (p=0.041). This

indicates that PRK causes a significant increase in contrast acuity thresholds that may have been masked at the highest eccentricity by the increased variability of the data. There is also the suggestion of a small, less pronounced effect following LASIK.

5.4.2.2 Influence of other factors

A one-way ANOVA was used to examine the influence of age on contrast acuity thresholds for each group. In addition, the influence of preoperative refractive error and follow-up time were examined for the two refractive surgery groups. Interactions were also considered.

5.4.2.2.a Age

A trend towards increasing contrast acuity thresholds with increasing age was demonstrated by all three subject groups. The trend only reached statistical significance for the control group data at eccentricities of 1.4°, 3.8° and 6.7° (see table 5-17).

	1.4°	3.8°	6.7°	9.4°
Control	**p=0.002**	**p=0.000**	**p=0.003**	p=0.169
LASIK	p=0.143	p=0.192	p=0.150	p=0.921
PRK	p=0.088	p=0.227	p=0.186	p=1.000

Table 5-17: Effect of age on contrast acuity thresholds (transformed data) Statistically significant p values are in bold.

5.4.2.2.b Refractive error

The control group data showed a trend towards increasing contrast acuity thresholds with increasing manifest refractive error but the effect did not reach statistical significance at any eccentricity (table 5-18). Both refractive surgery groups but particularly the PRK group, showed a trend towards increasing contrast acuity thresholds with increasing preoperative myopia but these trends were not statistically significant at any eccentricity.

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
Control (manifest Rx)	p=0.892	p=0.269	p=0.102	p=0.832
LASIK (pre-op Rx)	p=0.185	p=0.232	p=0.137	p=0.064
PRK (pre-op Rx)	p=0.073	p=0.177	p=0.291	p=0.064

Table 5-18: Effect of refractive error on contrast acuity thresholds (transformed data)

A two-way ANOVA was used to look for interactions between manifest refractive error and age, i.e. a difference in the effect of refractive error on contrast acuity thresholds between different age groups. No valid analysis was possible for the control group due to the lack of subjects in most of the older age categories, despite the supposedly statistically significant interaction at 3.8° (table 5-19). Both refractive surgery groups showed a trend towards a greater increase in contrast acuity thresholds with preoperative refractive error in the older age group (>45 years). The interaction reached statistical significance all eccentricities for the LASIK group but only at a single eccentricity (3.8°) for the PRK group.

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
Control (manifest Rx)	p=0.202	**p=0.012**	p=0.064	p=0.656
LASIK (pre-op Rx)	**p=0.022**	**p=0.008**	**p=0.008**	**p=0.008**
PRK (pre-op Rx)	p=0.297	**p=0.000**	p=0.275	p=0.989

Table 5-19: Interactions between refractive error and age for the contrast acuity thresholds (transformed data)

Statistically significant p values are in bold.

5.4.2.2.c Follow-up time

The LASIK group data showed a trend towards decreasing contrast acuity thresholds with follow-up time but the effect only reached statistical significance at the highest eccentricity (9.4°), (table 5-20). No such trend was demonstrated by the PRK group data but this is not surprising since the majority of PRK subjects had a follow-up time greater than 40 weeks (see section 3.5).

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
LASIK	p=0.181	p=0.141	p=0.740	**p=0.021**
PRK	p=0.654	p=0.314	p=0.825	p=0.805

Table 5-20: Effect of follow-up time on contrast acuity thresholds (transformed data). Statistically significant p values are in bold.

A two-way ANOVA was used to look for interactions between follow-up time and age, i.e. differences in the effect of follow-up time on contrast acuity thresholds between the two age groups. No trends could be identified for either refractive surgery group, in fact the analysis for the PRK group was invalidated by

the uneven distribution of subjects between the 12 different analysis categories, due to the long average follow-up time and limited number of subjects over the age of 45 years (see section 3.5).

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
LASIK	p=0.192	p=0.146	p=0.428	p=0.093
PRK	p=0.320	p=0.379	p=0.852	p=0.810

Table 5-21: Interactions between follow-up time and age for the contrast acuity thresholds (transformed data)

A two-way ANOVA was used to look for interactions between preoperative refractive error and follow-up time, i.e. a difference in the effect of follow-up time on contrast acuity thresholds between different refractive error categories. For the LASIK group, the increase in contrast acuity thresholds with increasing preoperative refractive error was found to decrease with follow-up time. The effect only reached statistical significance at an eccentricity of 9.4° (table 5-22). Despite the significant p value at 3.8°, it was not possible to identify a trend in the PRK group data since the subjects were not adequately distributed between the 30 different refractive error and follow-up time categories.

Ave. Ecc.	1.4°	3.8°	6.7°	9.4°
LASIK	p=0.168	p=0.174	p=0.128	**p=0.012**
PRK	p=0.549	**p=0.009**	p=0.791	p=0.110

Table 5-22: Interactions between preoperative refractive error and follow-up time for contrast acuity thresholds (transformed data). Statistically significant p values are in bold.

5.5 Chapter Conclusion

Absolute contrast detection thresholds

For the stimulus parameters employed, there was no statistically significant difference between the absolute contrast detection thresholds of the three subject groups at the three lowest eccentricities. At the highest eccentricity (9.4°), the thresholds for the LASIK and PRK groups were significantly higher than those of the control group, but did not differ significantly from each other. All subject groups demonstrated an increase in thresholds with age, which reached significance at various eccentricities depending on the subject group. Increasing refractive error, whether manifest (control) or preoperative (LASIK and PRK), also tended to lead to an increase in contrast detection thresholds, although the effect did not reach statistical significance at any eccentricity. The PRK group showed a smaller increase with increasing refractive error for the younger age group (<45 years) than the older group (>45 years), with the interaction reaching statistical significance at the three highest eccentricities. No trends with follow-up time could be identified.

Contrast acuity thresholds

For the stimulus parameters employed, there was a statistically significant increase in contrast acuity thresholds at all but the highest eccentricity (9.4°) in the PRK group compared to both the LASIK and control groups. Contrast acuity thresholds were also generally higher for the LASIK group than the control group but the difference was only statistically significant at an eccentricity of 3.8°. These findings indicate that PRK causes a reduction in visual performance as assessed by contrast acuity thresholds.

All subject groups demonstrated an increase in thresholds with age but the effect was only statistically significant for the control group at the three lowest eccentricities. Increasing refractive error, whether manifest (control) or preoperative (LASIK or PRK), also led to an increase in contrast acuity thresholds, although the effect did not reach statistical significance at any eccentricity. As with absolute contrast detection thresholds, a greater increase in

contrast acuity thresholds with increasing refractive error was seen for the older age group (>45 years) with the interaction reaching statistical significance at various eccentricities across the two refractive surgery groups. There was a trend towards decreasing thresholds with increasing follow-up time post-LASIK, but the effect was only statistically significant at 9.4° eccentricity.

6 Visual Search

6.1 Chapter Summary

A visual search task was used to assess visual performance in relation to target contrast. Mean glimpse duration was also measured. An analysis of variance (ANOVA) was used to compare the corrected means of the control, LASIK and PRK groups. Visual search data showed considerable inter-subject variability in all three groups. The mean visual search times for the LASIK group did not differ significantly from the control group. The PRK group showed a statistically significant increase in mean search times compared to the control and LASIK groups, indicating a reduction in visual search performance. There was no statistically significant difference in mean glimpse duration between the three groups. Few outliers were identified and neither age, preoperative refractive error, nor follow-up time were found to significantly influence either visual search performance or mean glimpse duration. These findings suggest that visual search performance, and in particular, glimpse duration, are relatively insensitive to retinal image degradation. In addition to retinal image quality, other factors appear to make a significant contribution to the outcome of visual search. A model of visual search was produced to aid understanding of the factors that influence visual search performance.

6.2 Introduction

Visual search is an important strategy for the extraction of information from natural scenes. It is particularly important in tasks such as driving (Fairclough and Maternaghan, 1993). Segregation of some objects in relative isolation or objects possessing certain unique characteristics (feature differences) involves pre-attentive mechanisms – i.e. the object 'pops out' (Bravo and Nakayama, 1992). More realistic scenes generally contain numerous objects requiring segregation from each other and the background. They require the rapid identification of the objects of interest by the deployment of attention from one item in a cluttered scene to the next and hence utilise the attentive mechanism. Successful search strategies require a stored representation of the object and a means of selecting

that object from others in the scene. Searching for a specific object within a cluttered scene involves high-level visual processing and co-operation between memory and attention. There is evidence to suggest that neurons in the inferior temporal cortex are involved in selecting the objects to which we attend and foveate (Chelazzi, Miller, Duncan et al., 1993), and that attention is associated with enhancement of neuronal responses as early as area V1 (Roelfsema, Lamme, and Spekreijse, 1998; Watanabe, Sasaki, Miyauchi et al., 1998; Watanabe et al., 1998). The direction of attention away from the fixation point to the target of interest has been shown to enhance spatial resolution and therefore significantly improve performance, particularly in the peripheral field where spatial resolution is low (Yeshurun and Carrasco, 1998).

Visual search experiments have been used to study different aspects of visual performance including orientation discrimination, the effects of crowding, texture segmentation and colour coding (Barbur, Forsyth, and Wooding, 1991; Backs and Walrath, 1992). Performance is most commonly graded in terms of average search time or percentage accuracy in detecting and discriminating the target.

Human factors studies have attempted to establish a link between simple measures of visual performance such as acuity and contrast sensitivity, and performance in 'real-world' tasks such as driving a car or piloting an aircraft (Kruk and Regan, 1983). Although a correlation has been demonstrated in some cases (Ginsburg et al., 1982), there are factors that limit the ability of simple visual tests to predict 'real-world' visual performance (Currie et al., 2000). This is not surprising considering the high levels of processing involved in such visual tasks. The work presented in this thesis forms part of a study designed to examine the implications of surgically-degraded visual performance for commercial airline pilots. It is hoped that the similarities between this laboratory study and many of the visual tasks undertaken on an aircraft flight deck will allow some insight into the advantages and disadvantages of using a more realistic technique to assess visual performance.

6.3 Methods and Subjects

6.3.1 Visual Search Program

The visual search program was designed as a dynamic test of suprathreshold performance, averaged over a circular field subtending 20° (diameter), at a fixation distance of 70 cm. All subjects were fully corrected for this working distance. The luminance of the background was set to 12cd/m^2 with chromaticity co-ordinates of (0.3,0.334), consistent with the two contrast threshold tests (chapter 5). The target was a Landolt ring of 72 mins of arc diameter and a gap size comprising 20° of the overall ring (section 3.2). The stimulus was presented at one of five pre-selected contrast levels: 6, 10, 16, 32, 64%. The distractors also took the form of a Landolt ring with a range of diameters between 60 and 84 mins of arc, gap sizes between 10° and 25° and contrast levels between 5 and 70%. The subject was required to search the field containing an array of 15 randomly positioned, vertically orientated distractor elements, and a single, obliquely orientated target (figure 6-1). A central fixation target appeared for a period of 1.6 seconds prior to each presentation to ensure that each search pattern was initiated from the same point. The subject was instructed to press a response button immediately on identification of the target to allow a measure of search time, since the manual response time is known to closely relate to the actual time taken to fixate and recognise a target (Binello, Mannan, and Ruddock, 1995). A four-choice response box was then used to confirm correct identification of the orientation of the target gap. The random positioning of the test target with respect to initial fixation resulted in considerable variability in search time between successive trials, requiring a large number of trials to be undertaken. The five different targets were randomly interleaved and the mean search time for each target was based on the average of 36 measurements. Patterns were presented for a maximum duration of 10 seconds or until the target was identified. If a target was missed on three consecutive occasions, that particular contrast level was omitted from the remainder of the test.

Each subject underwent a ten minute training session to familiarise themselves with the task. Due to the considerable time taken to complete the assessment for

A relatively complex visual search task requiring an attentive mechanism was chosen to study the relationship between target contrast and search time, since the luminance contrast of a target has been identified as one of the major factors in determining search time (Barbur et al., 1991). Subjects who have undergone excimer laser surgery can suffer from a reduction in visual performance, attributable to a surgically induced increase in intraocular light scatter (Lohmann et al., 1993; Miller and Schoessler, 1995; Veraart et al., 1995) and/or aberrations (Martinez et al., 1996; Martinez et al., 1998; Seiler et al., 2000). The hypothesis was that this degradation of the retinal image would be revealed as an increase in visual search times particularly for the lower contrast targets closest to the discrimination threshold.

Eye movements were monitored using the P_SCAN 100 system (section 3.1) and the average glimpse duration was calculated (average time taken by the visual system to process the information gained during a single fixation, before moving on to the next location). The hypothesis was that average glimpse duration would increase if the quality of the retinal image decreased, as indicated by preliminary tests in which targets were low-pass filtered to emulate the effects of scattered light (Barbur, 1998). The fixation duration is, however, influenced by other factors such as the spatial context of the scene, the contrast of peripheral targets around fixation and hence the size of the visual lobe (Cornelissen and Kooijman, 1999).

Pupil diameter was measured where possible during the visual search task to allow a comparison of pupil data between the three subject groups. Intraocular scattered light is known to increase with pupil dilation (Barbur et al., 1995), and aberrations generally result from peripheral light rays and therefore their influence on retinal image quality is strongly associated with pupil diameter (Campbell and Green, 1965).

all five targets, visual search could not be assessed at all contrasts for all patients. The majority were assessed for targets of 6%, 16%, 32% and 64% contrast only and the mean search time was plotted against the target contrast to obtain the visual search function.

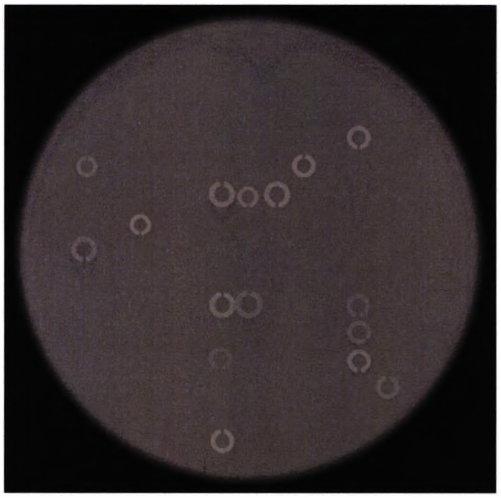


Figure 6-1: Example of the visual search screen with a high contrast oblique target and 15 vertically orientated distractor elements

6.3.1.1 Test Design

The gap size for the Landolt ring target was chosen to be 20°. This was a compromise between a small gap leading to a long mean search time, and a large, very easily resolvable gap that was associated with a short mean search time (figure 6-2).

1.2.4.9). The findings in this study with regard to forward light scatter (section 4.4.1) also seem to support this. Absolute contrast detection thresholds however, did not differ significantly from those of the control group, except at the highest eccentricity (9.4°), where both the PRK and LASIK groups demonstrated significantly higher contrast detection thresholds than the control group. This may be associated with differences in the degree of myopia and hence retinal resolution, rather than a reduction in retinal image quality, since contrast thresholds for the detection of a large target such as those used in this study, are not optically limited. Although an increase in mean visual search times was detected for both the PRK and LASIK groups compared to the control group, the difference only reached statistically significance for the PRK group and visual search performance varied significantly within all subject groups. Modeling of the visual search process revealed that factors such as attention and fatigue (amplified by the significant duration of the test), along with learning, search strategy, glimpse duration during fixations, and memory length for storing previously visited locations in the visual field contributed to visual search performance in addition to target contrast. Therefore an increase in intraocular scatter and/or aberrations does not necessarily result in poor search performance. Glimpse duration data showed significant variability and appeared to be unaffected by excimer laser surgery.

These findings suggest that of all the techniques considered in this study, contrast acuity thresholds are the most suitable measure of reduced visual performance associated with degraded retinal image quality. Although the increase in contrast acuity thresholds post-PRK is statistically significant, it is not known how applicable this loss of visual performance actually is to 'real-world' tasks, in particular the safe piloting of an aircraft. Consequently, a final measure of functional visual performance was designed, based on contrast acuity thresholds. The parameters for this test were selected after a detailed assessment of the primary visual tasks involved in piloting a modern commercial aircraft.

7.3 Consideration of test requirements

The Scientific Peer Advisory and Review Services of the American Institute of Biological Sciences, in their report on PRK, strongly recommended that any test to evaluate visual function following refractive surgery should include parameters other than high contrast acuity alone, ideally using measures tailored to the visual tasks involved. They recommended that the targets used should include luminance, contrast and spatial frequency elements, in order to reveal conditions showing increased sensitivity to the presence of light scatter and irregular aberrations. They also suggested that pupil size and the effects of glare could be considered. It may seem sensible to incorporate a glare source in to the test to mimic the effect produced by glare sources such as runway approach lights. However, a point source within the field chosen to simulate the luminance of car headlights at 30 metres can improve contrast sensitivity relative to the no-glare situation, as a result of pupil constriction (Boxer-Wachler B.S. et al., 1999). This effect may relate to non-uniform scatter over the pupil with the periphery contributing the most (Edgar, Barbur, and Woodward, 1995). Such an effect was noted in preliminary visual search experiments with an annular glare source (section 6.3.1.1). Excimer laser surgery tends to increase forward light scatter and irregular aberrations (section 1.2.4.9), particularly under dilated pupil conditions making a 'pupil-sparing' test essential.

The effects of scattered light can manifest themselves even in the absence of a bright glare source. Scatter originating from the object of interest itself and scatter within the image, contribute significantly to local image degradation, particularly when the target demonstrates positive polarity such as the Landolt ring targets employed in this study. An isolated glare source is not essential to detect an increase in forward light scatter as long as suitable testing conditions are employed.

7.3.1 Visual task analysis

A detailed visual task analysis within a modern flight deck was undertaken to establish the relevant test parameters, such as minimum target size, light level, effective visual field, range of stimulus contrasts, etc. Target size measurements

Figure 7-1: Modern instrumentation arrangement (Airbus A320)

indicated that the smallest alphanumeric characters that are considered important subtend between 12 and 18 mins of arc at the eye (for an average working distance of 80 cm). Assuming a standard character format in which each limb is one fifth of the overall target size (as for a Landolt ring, section 3.2), the minimum angle of resolution required to discriminate the alphanumeric characters, ranges between 2.5 and 3.6 mins of arc – approximately three times the maximum nominal, high contrast visual acuity of the eye. These target sizes, combined with the very high contrast levels generated on flight deck displays ($\delta L/L_b > 200\%$) under both photopic and mesopic light levels (figure 7-1), mean that resolution of the alphanumerics is one of the easiest tasks involved in piloting an aircraft. Careful design has ensured that all targets within a single screen are at least resolvable although not necessarily interpretable, when the pilot fixates the

centre of the screen. However, analogue instruments in older aircraft employ much lower contrasts, and other targets within the visual scene tend to be of significantly lower contrast. Additional tasks such as scanning for air traffic, searching for the runway, and reading airport maps, tend to involve lower contrast targets. Consideration of only high contrast display information is therefore unjustified.

Since the information on adjacent screens on the flight deck cannot be resolved because of the large drop in resolution with eccentricity (Millodot 1966; Millodot 1972), the functional visual field of interest corresponds to the angular subtense of a single screen covering an area of 5° either side of the visual axis when the displays are viewed from approximately 80 cm. In order to examine information from another display screen, the eye is forced to saccade to a different region of the visual field. There are advantages to restricting assessment to the central +/-5° of the visual field. The meridional differences in visual performance are minimal over the central field and the demand on attention is minimised (Millodot, 1972; Yeshurun and Carrasco, 1999).

A background light level of 12 cd/m^2 was selected for photopic test measurements. This figure falls within the photopic range, but because it is a lot lower than the average daylight luminance on the flight deck instrumentation displays, less pupil constriction occurs making the test more sensitive to aberrations and forward light scatter. At night, the measured background light levels within the flight deck were approximately 0.05 cd/m^2, although the high contrast instrumentation graphics ensure that the fovea remains photopic and hence good colour discrimination is retained. This luminance value falls within the mesopic range in which both rod and cone receptors contribute to visual function. Testing under mesopic conditions can provide valuable information since the low retinal illuminance results in pupil dilation and exacerbation of the effects of forward light scatter and aberrations. Although the loss of the Stiles-Crawford effect at such low light levels results in more scattered light reaching the receptors, the predominance of rod vision yields only poor spatial resolution, making it more tolerant to scattered light and aberrations.

7.4 General Test Parameters

The Contrast Acuity Assessment (CAA) test was designed to assess orientation discrimination based on contrast acuity over a field of ±5°, corresponding to the functional visual field. The stimulus was presented randomly at the following eccentricities in the visual field: -5°, -2.5°, -1.25°, 0°, +1.25°, +2.5°, +5° along the

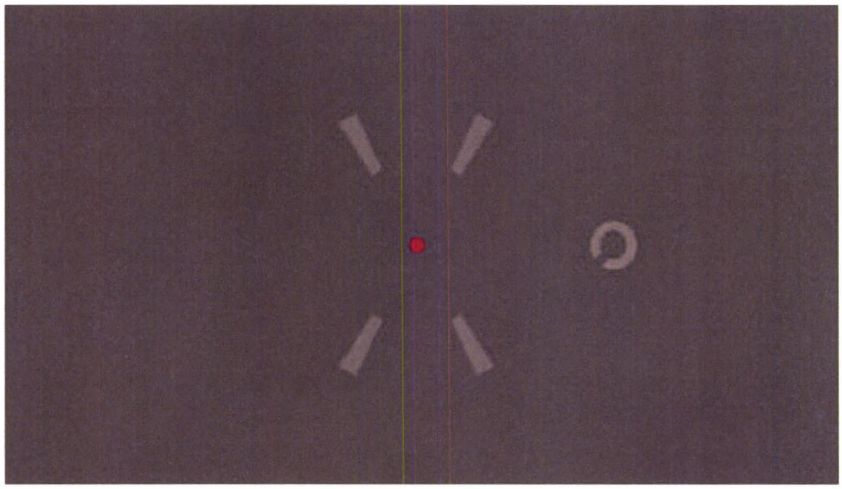


Figure 7-2: Stimulus configuration employed by the CAA test. The picture shows the stimulus at +2.5° eccentricity together with the central fixation target and fixation guides

horizontal meridian (figure 7-2). Four oblique guides surrounded the fixation target to aid central fixation. The stimulus duration was 120 ms to ensure that the stimulus would not trigger a saccadic eye movement that could precede the offset of the stimulus (Barbur, Forsyth, and Findlay, 1988). The screen was viewed from a distance of 150 cm in order to ensure that the resolution of the screen did not affect the definition of the smallest target generated. In each of the experiments detailed below, the target was presented at the seven different stimulus locations in a random order. A four-alternative, forced-choice procedure was used to determine the threshold for the variable in question, (i.e. upper left, upper right, lower left, lower right), as described in section 3.3. The subject was required to press one of four response buttons to indicate the position of the gap in the ring. Two sequential correct answers resulted in a reduction of either stimulus size

(variable for size scaling experiments) or contrast (variable for contrast acuity assessment test). If the gap could not be resolved, a guess was made and a button pressed, with a single incorrect guess resulting in an increase in target size or contrast. This technique yields the target size or contrast needed for approximately 70% probability of correct discrimination.

The display preparation and experimental set-up are identical to previous chapters and are detailed in section 3.1. In preparation for mesopic testing, the subject was required to wear a light-proof patch over the selected eye while sitting in a darkened room for a minimum of 15 minutes to ensure a state of adaptation appropriate for the mesopic background luminance employed. Mesopic light levels were achieved by viewing the display through a spectrally calibrated neutral density filter (nominal optical density of 2). The display was viewed through the P_Scan 100 chin rest set-up to ensure that only light that had passed through the filter could reach the subject's eye. The spectral absorption of the filter was taken into account to ensure that the luminance chromaticity specified remained unaffected by the non-uniform spectral transmittance of the filter.

7.5 Size scaling experiments

It was decided that the target size for the contrast acuity assessment test should be scaled with eccentricity, since contrast acuity thresholds increase rapidly with eccentricity (section 5.4.1) and the flight deck displays are composed of a range of target sizes. For a given contrast, different target sizes are needed to resolve the target due to the reduction in sampling density with eccentricity. The relationship between target size and eccentricity is highly contrast dependent with low contrasts resulting in a steeper decline in acuity than high contrast targets. If a high contrast target were chosen for the size scaling experiment, it would have the advantage of mimicking more closely the high contrast flight deck instrumentation. However, this would yield a much smaller angle of resolution (i.e., the high contrast acuity limit) than that encountered on the flight deck, and such measures of visual performance are therefore unlikely to be representative of other important tasks undertaken on the flight deck. More critically, the resolution

of high contrast targets is largely insensitive to the presence of scattered light (Elliott and Bullimore, 1993; van den Berg and Spekreijse, 1987). If a target of very low contrast were chosen, it would be more sensitive to image degradation but the target size required under such conditions would be significantly greater than the minimum critical target size employed for displaying alphanumeric information in the cockpit. Such large stimuli sizes would also reduce sensitivity to image degradation.

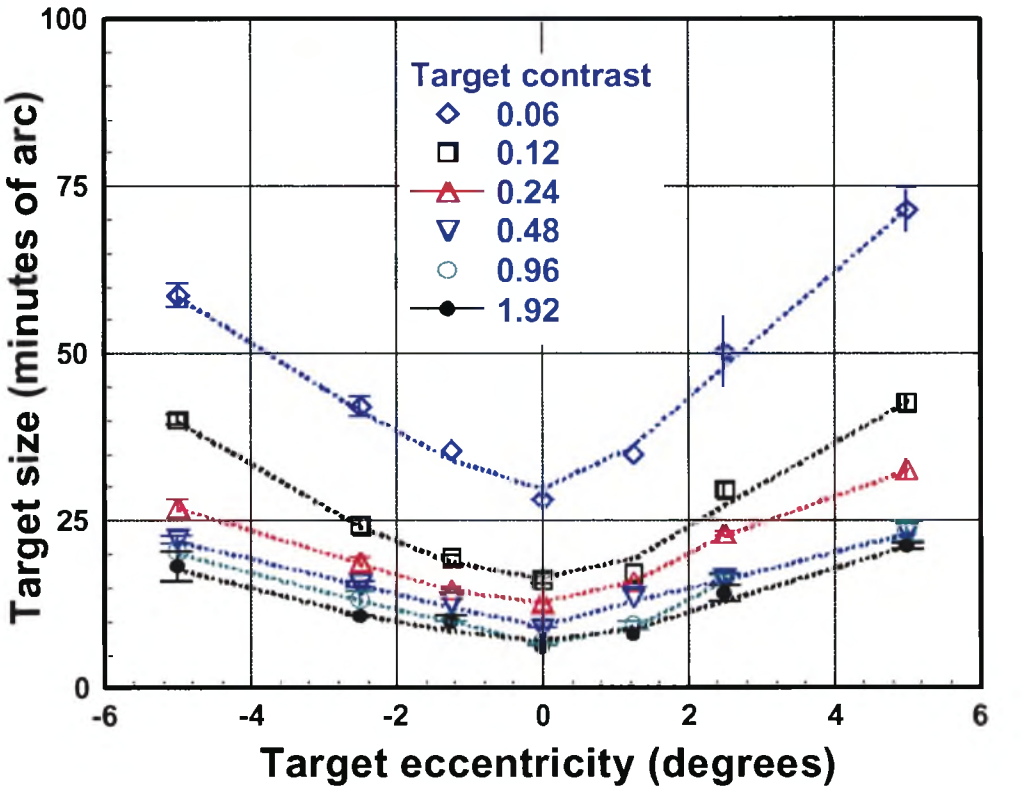


Figure 7-3: Photopic gap acuity measurements averaged for three normal subjects at each of six contrast levels

To aid selection of the most suitable target size for use in such experiments, three experienced normal observers completed a gap discrimination test in which the size of the target was varied systematically for a number of different contrast levels. As described above, thresholds were measured at seven locations within the ±5° field using a four-alternative, forced-choice procedure. The size threshold was measured by averaging four out of six reversals (first two discarded). Under

photopic conditions, the step change in stimulus size decreased exponentially with each reversal from a step size of 2 mins of arc down to 0.5 mins of arc. Under mesopic conditions, the step size varied from 5 mins of arc down to 1 minute of arc. The measurement of size threshold was repeated three times for each of a series of different target contrasts ($\delta L/L_b$: 6, 12, 24, 48, 96, 192%), under both photopic and mesopic light levels. For each condition, the smallest resolvable gap size was determined at each chosen eccentricity within the visual field.

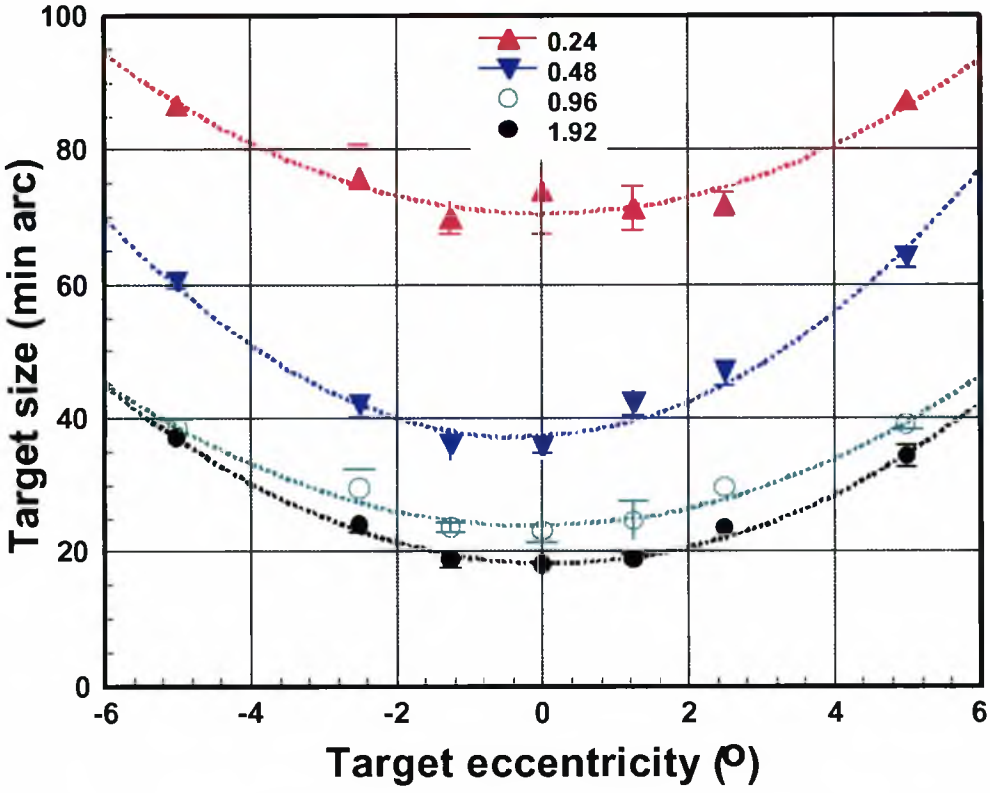


Figure 7-4: Mesopic gap acuity measurements for three subjects at each of four contrast levels

The data illustrated in figure 7-3 show that the minimum resolvable target size is highly dependent on target contrast, particular for the low contrast range. Size thresholds increase with eccentricity, related to the increase in spatial summation and reduction in sampling density with eccentricity (Levi and Waugh, 1994; Millodot, 1972).

The smallest alphanumeric characters that are considered important on the flight deck display subtend a visual angle in the range 12 to 18 mins of arc. At a contrast

of 24%, the size threshold test yields a foveal measurement that closely matches the minimum target size required by a pilot to resolve and interpret the alphanumeric information presented on flight deck displays without ambiguity. Higher contrast levels do not yield significantly lower size thresholds, but are known to be less affected by increased scatter in the eye (van den Berg and Spekreijse, 1987). All three subjects found the 6% and 12% contrast runs very difficult and this resulted in increased variability. In view of these arguments, the target sizes obtained for the 24% contrast were selected for use in the photopic test of contrast acuity.

The mesopic data illustrated in figure 7-4 show a similar pattern to the photopic data in that the minimum resolvable target size increases significantly with eccentricity. Completing the test at 6% and 12% proved impossible for all three subjects and the 24% contrast run was very difficult. The data demonstrate the massive loss of visual acuity when rod vision is involved. Targets in the low contrast range are virtually unresolvable due to the lower sampling density of rod receptors. The 48% contrast was selected to establish the size scaling in the mesopic range since this was the lowest contrast level at which the task could be easily performed. In addition, this contrast would be more sensitive to image degradation than targets of 96% or 192% contrast.

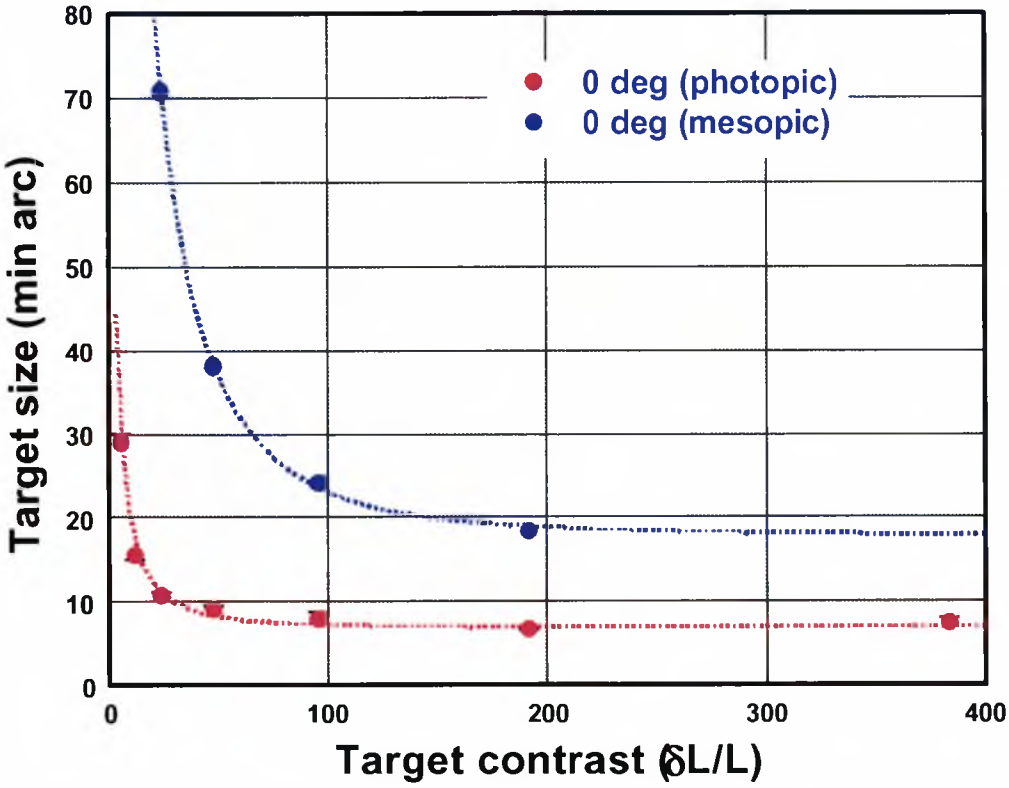


Figure 7-5: Foveal data showing the relationship between target size and target contrast, under both photopic and mesopic conditions. Mean data for three normal subjects

Figure 7-5 shows the relationship between target size and contrast for the fovea alone, taken from the photopic and mesopic measurements of size scaling at different contrast levels. The data provide further justification for the choice of 24% (photopic) and 48% (mesopic) contrast levels for the size scaling of the CAA test. For the high contrast targets, a reduction in retinal image contrast causes little change in target size. In order to remain sensitive to the reduction in image contrast produced by the presence of scattered light and irregular aberrations, the target contrast must be located on the steep portion of the curve, where any reduction in image contrast will translate into a large change in target size (i.e., visual acuity), as is the case for the 24% contrast photopic data and the 48% contrast mesopic data. Figure 7-6 depicts the size-scaling data averaged for three subjects under the two selected conditions.

7.5.1 Size scaling data collection

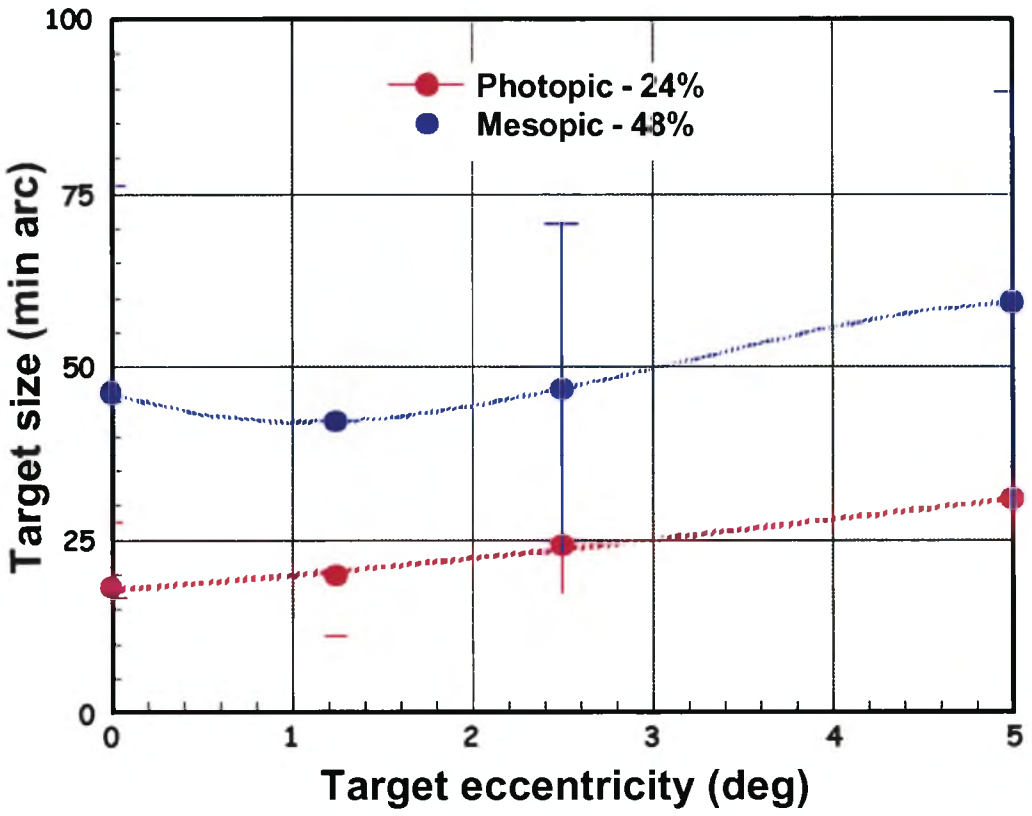


Figure 7-6: Mean size-scaling data for three normal subjects at photopic and mesopic light levels, at contrasts of 24% and 48% respectively

Having selected 24% and 48% contrast levels for the photopic and mesopic conditions respectively, and determined the size-scaling data for three subjects, it was important to obtain similar data for a much larger population of normal subjects, to establish the performance of the 'standard normal observer' for size scaling with eccentricity.

7.5.1.1 Subjects

A group of 62 normal subjects completed the gap discrimination task with size as the variable under both photopic (24% contrast, 12 cd/m^2 background) and mesopic (48% contrast, 0.05 cd/m^2 background) conditions. The majority of

subjects were naive observers although one quarter of the subjects had been involved in the initial studies of contrast acuity, visual search, etc. The selection criteria were the same as for all previous tests (section 3.4) with all subjects undergoing an examination of their ocular health to exclude those with any abnormality. In addition, a subjective refraction was undertaken to ensure that the eye under test was fully corrected for a working distance of 150 cm, and only those that could be corrected to a minimum of 6/9 acuity were included. The subjects wore their own glasses or contact lenses where possible but if their current prescription was unsuitable, full aperture trial lenses were placed in a frame before the eye under test. The average age of the normal subjects was 30.9 +/- 11.0 years.

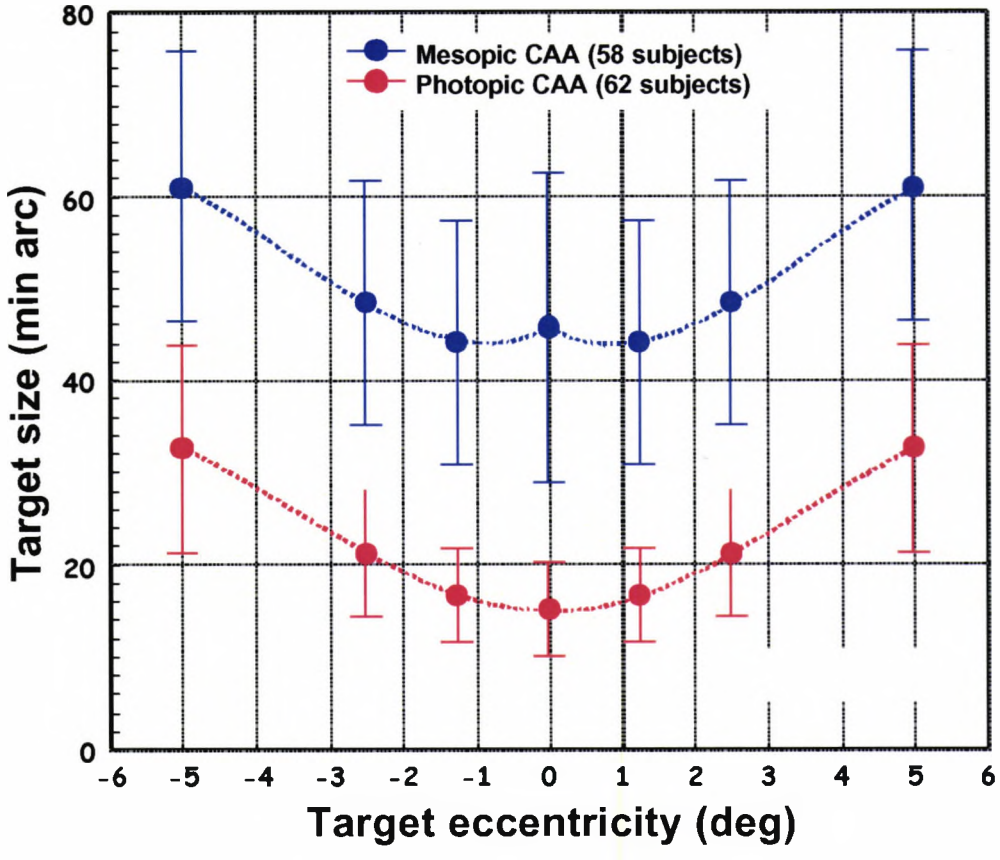


Figure 7-7: Target size thresholds for gap acuity with eccentricity measured under photopic (24% contrast) and mesopic (48% contrast) conditions. Average of 62 normal subjects showing the expected change in resolution acuity for the 'standard normal observer'

All subjects performed three repeats under each condition and the mean was calculated. Figure 7-7 shows the mean size-scaling data for each condition with an increase in target size with eccentricity. The data show significant inter-subject variability, particularly in the mesopic range, which increases with increasing target eccentricity. On examination of the data there was no significant difference between the size thresholds in the temporal and nasal fields over the 10° field, therefore the results were combined. A small increase in minimum resolvable target size is seen at the fovea for the mesopic data, indicating the predominance of rod receptor function under low illumination and the absence of rods in the foveal region.

7.6 The Contrast Acuity Assessment Test (CAA Test)

Contrast acuity thresholds were measured with size scaling for 24% contrast (photopic) and 48% contrast (mesopic) as illustrated in figure 7-7. A group of 102 normal subjects (age range 18-58) that included 36 class 1 medical certificate holders (both commercial pilots and licence holders about to commence training) completed three runs of the contrast acuity assessment test at each light level to derive the normal range. Thirty-nine percent of normals had also participated in the size scaling experiment. The remaining subjects were naive recruits who met the control criteria specified in section 3.4.

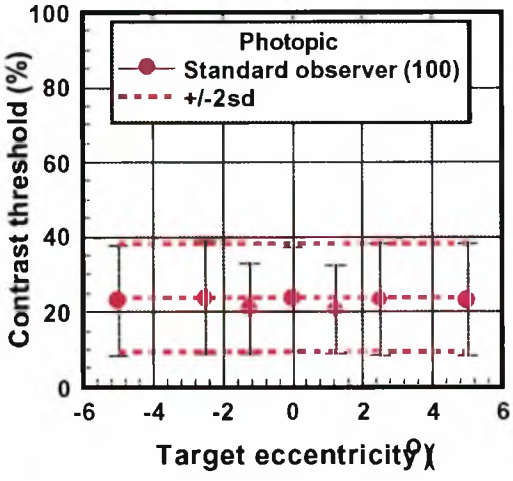


Figure 7-8: Mean photopic contrast acuity thresholds for a group of 100 normals (+/-2sd) (the 'standard observer')

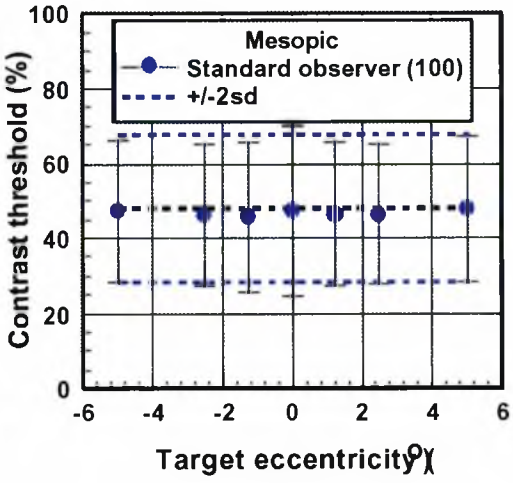


Figure 7-9: Mean mesopic contrast acuity thresholds for a group of 100 normals (+/-2sd) (the 'standard observer')

Scaling the overall target size and hence the gap size with eccentricity compensates for the loss of retinal visual acuity with eccentricity. When contrast acuity thresholds are measured with this size scaling in place, a simple zero gradient, straight-line relationship is expected for both photopic and mesopic measurements, i.e. the 'standard observer' is expected to require precisely 24%

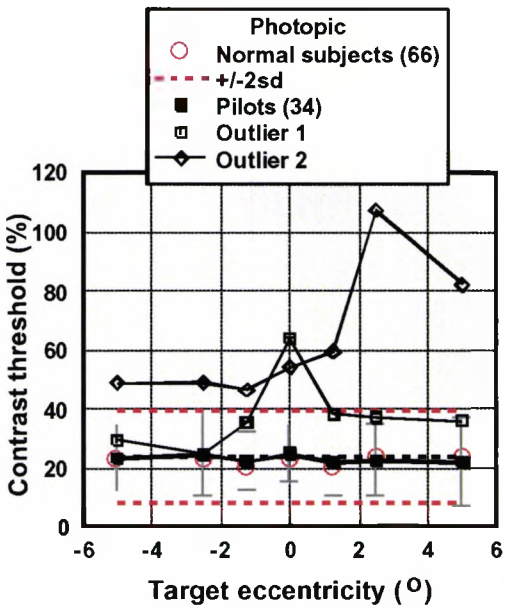


Figure 7-10: Mean photopic contrast acuity thresholds for a group of 34 pilots (+/-2sd) compared to 66 normal subjects

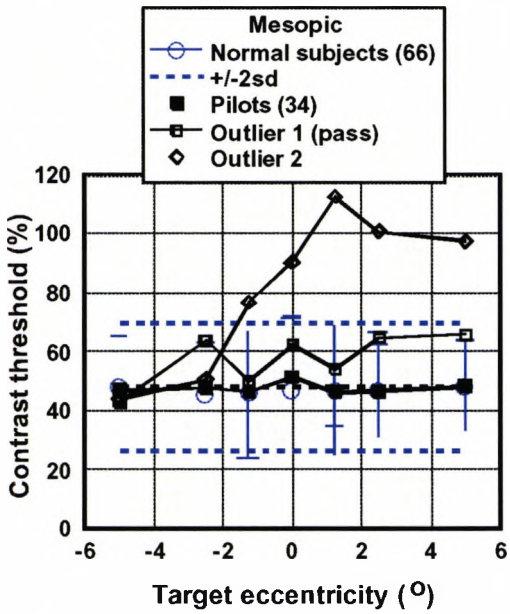


Figure 7-11: Mean mesopic contrast acuity thresholds for a group of 34 pilots (+/-2sd) compared to 66 normal subjects

(photopic) and 48% mesopic contrast to resolve the gap in the Landolt ring target, independent of target eccentricity. This ensures that the results are easy to interpret. Normal subjects will resolve the targets at contrasts close to these values as shown in figures 7-8 and 7-9.

Data below or above the expected 'normal' line indicate better or worse performance than the 'standard observer' respectively. Examination of the data revealed an approximately normal distribution for both the 66 normal subjects, 34 pilots and the full 100 normal group, allowing the use of standard parametric statistical tests. The 95% (±2sd) range was determined by calculating the variance

of the difference between the contrast value measured for each observer and the 'expected value' as predicted by the 'standard observer'. Two outliers were identified and excluded from the normal group and the mean contrast acuity thresholds for the remaining 100 normal subjects were used to define the 'standard observer'.

7.7 Contrast acuity thresholds in class 1 medical certificate holders

Thirty-four class 1 medical certificate holders (to be known as the 'pilot' group), showed contrast acuity thresholds within the normal range under both photopic and mesopic conditions (figure 7-10 and 7-11). Following the removal of two outliers, a Welsh test revealed that there was no statistically significant difference between the mean contrast acuity thresholds of the 'pilot' group and the remainder of the normal group, under either photopic ($p=0.41$) or mesopic ($p=0.24$) conditions. The 'pilot' group data showed less variability than the normal group data. The two data sets were added together, increasing the number of normal subjects on which the 'standard observer' was based to 100. Outlier 1 (age 34) showed a characteristic increase in contrast acuity thresholds at the fovea only, indicative of optical degradation due to an increase in forward light scatter and/or aberrations. His mesopic data fell within the normal ±2sd range. The data for outlier 2 (age 23) fell outside the normal ±2sd range under both photopic and mesopic conditions with a large increase in thresholds in the temporal field (right eye only).

7.8 Contrast acuity thresholds post-refractive surgery

A small group of 27 corneal refractive surgery patients (17 PRK and 10 LASIK) were examined to validate the test. All had been classified by their surgeon as having a successful outcome in terms of high contrast visual acuity (6/9 or better) and no intra-operative or post-surgical complications. Thirty-seven percent of subjects ($n=10$) reported visual symptoms with the majority ($n=7$) reporting problems such as 'faint' or 'washed-out' vision under all lighting conditions, and

a further three subjects reporting symptoms at night only. All other subjects were asymptomatic. An overall increase in contrast acuity thresholds was expected because of the increase in contrast acuity thresholds after refractive surgery reported in chapter 5, particularly for the PRK subjects. The CAA Test, however, was designed to measure contrast acuity in relation to the functional visual performance expected of pilots in commercial aviation. The test does not therefore necessarily employ the stimulus parameters that are most affected by scattered light and aberrations.

	Refractive Surgery Subjects	
	PRK	**LASIK**
Number of subjects	17	10
Average age	38.3 years	35.6 years
Average preoperative Rx	-3.58D	-5.58D
Average photopic pupil diameter (mm)	5.43mm	5.37mm
Average mesopic pupil diameter (mm)	7.06mm	7.10 mm
Average ablation zone diameter (mm)	5.83mm	5.83mm
% reporting symptoms (day and night)	24% (n=4)	30% (n=3)
% reporting symptoms (night only)	12% (n=2)	10% (n=1)

Table 7-1: Characteristics of refractive surgery subjects who completed the Contrast Acuity Assessment test

7.8.1 Preliminary results

Eight of the 17 PRK subjects (47%) and five of the ten LASIK subjects (50%) demonstrated contrast acuity thresholds within the normal range (+/-2sd) under photopic conditions. Under mesopic conditions, ten of the 17 PRK subjects (59%) and four of the ten LASIK subjects (40%) demonstrated contrast acuity thresholds within the normal range (+/-2sd). All subjects who reported symptoms during the day and/or at night, fell outside the normal range at the corresponding light level. In addition, four PRK subjects and two LASIK subjects demonstrated photopic contrast thresholds outside the normal range despite reporting no symptoms. One PRK subject and two LASIK subjects demonstrated mesopic contrast thresholds

outside the normal range despite reporting no symptoms, although the PRK subject did not drive a motor vehicle, (subject SR, figures 7-20 and 7-21). For these data, there was no significant relationship between mean contrast acuity thresholds and the degree of preoperative refractive error (R^2=0.20 photopic, R^2=0.29 mesopic) or high contrast visual acuity (R^2=0.23 photopic, R^2=0.19 mesopic). There was no relationship between mean contrast acuity thresholds and pupil diameter (R^2=0.06 photopic, R^2=0.38 mesopic) or between mean contrast acuity thresholds and the difference between pupil and zone diameter (R^2=0.06 photopic, R^2=0.01 mesopic).

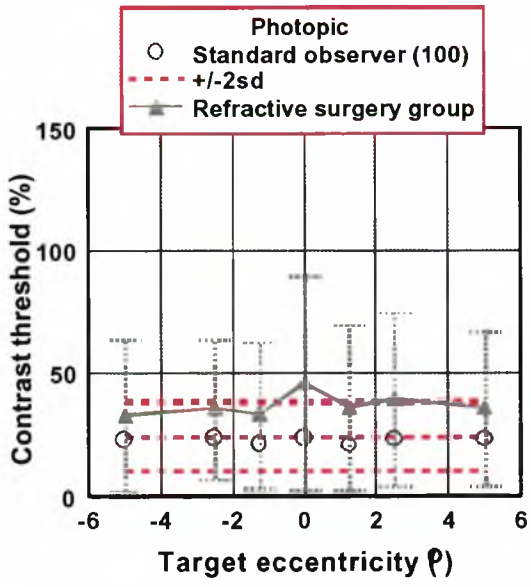


Figure 7-12: Mean photopic contrast acuity thresholds for the full refractive surgery group

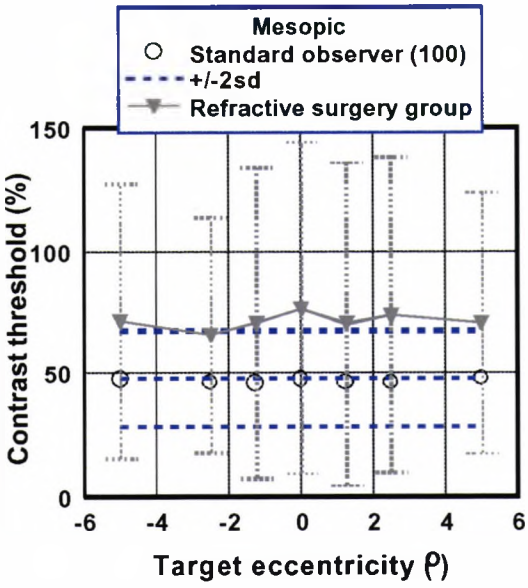


Figure 7-13: Mean mesopic contrast acuity thresholds for the full refractive surgery group

In examining the data from the CAA test it should be remembered that the PRK and LASIK subgroups were small and contained a larger than average proportion of symptomatic subjects. This was done in order to assess the sensitivity of the test. Any conclusions based on estimates of the percentage of subjects whose

visual performance fell outside the normal range, are unlikely to be representative of refractive surgery patients in general.

Following the removal of LASIK subject PL (figure 7-23 and 7-23), who was identified as an extreme outlier using the technique described in section 3.5, a Mann-Whitney test was used to compare the mean contrast acuity thresholds for the refractive surgery group (right skewed distribution) with the 'standard observer' (100 normal subjects showing an approximately normal distribution). Under photopic conditions, the mean contrast acuity thresholds of the whole refractive surgery group were significantly higher than those of the normal group, ($p=0.000$, table 7-2). The data for the refractive surgery group are located around the upper limit of the normal range with a small peak at the fovea (figure 7-12). When those refractive surgery subjects who failed the photopic CAA test (data points fall outside the normal ± 2sd range) were excluded, the data became normally distributed, allowing a two-sample Student's t-test (unequal variance) to be used. However, the mean contrast acuity thresholds of this subgroup remained significantly higher than those of the normal group ($p=0.000$, table 7-2). This also applied when the 'passes' from the PRK and LASIK groups were compared with the 'standard observer' individually, ($p=0.012$ and $p=0.007$ respectively).

Under mesopic conditions, the mean contrast acuity thresholds of the whole refractive surgery group were significantly higher than those of the normal group (Mann-Whitney test $p=0.000$, table 7-2). When those refractive surgery subjects who failed the mesopic CAA test (data fell outside the normal 95% range) were excluded from the analysis, the refractive surgery data showed a normal distribution allowing a two-sample Student's t-test to be used. The mean contrast acuity thresholds for the remaining refractive surgery subjects were still significantly higher than those of the normal group ($p=0.024$, table 7-2). When the mesopic 'passes' from the PRK and LASIK groups were compared with the 'standard observer' individually, the PRK 'passes' group data did not differ significantly from the 'standard observer' ($p=0.710$) although the LASIK 'passes' group data did ($p=0.000$).

Photopic conditions	**p value**
Normals vs. all refractive surgery patients (Mann-Whitney)	p = 0.000
Normals vs. refractive surgery patients within normal range (passes) (Student's t-test)	p = 0.000
Normals vs. PRK subjects within the normal range (passes) (Student's t-test)	p = 0.012
Normals vs. LASIK subjects within the normal range (passes) (Student's t-test)	p = 0.007
Mesopic conditions	
Normals vs. all refractive surgery patients (Mann-Whitney)	p = 0.000
Normals vs. refractive surgery patients within normal range (passes) (Student's t-test)	p = 0.024
Normals vs. PRK subjects within the normal range (passes) (Student's t-test)	**p = 0.710 Same**
Normals vs. LASIK subjects within the normal range (passes) (Student's t-test)	p = 0.000

Table 7-2: Results of statistical tests comparing various refractive surgery groups with the group of 100 normal subjects under photopic and mesopic conditions

The contrast thresholds for those refractive surgery patients who 'failed' the CAA test showed a distinct peak around the foveal region, particularly under photopic conditions. The data for the refractive surgery group who 'passed' the CAA test form an approximate straight line.

Examination of the individual data from the refractive surgery subjects revealed a number of distinct trends that are illustrated in the following section by a few representative examples.

7.8.1.1 Visual performance within the normal range

Overall, 13 out of 27 refractive surgery subjects showed photopic contrast acuity thresholds within the normal range (±2sd). Under mesopic conditions, 14 out of 27 subjects showed mesopic contrast acuity thresholds within the normal ±2sd range. The data points tended to form an approximate straight line, similar to the 'standard observer' although in some cases, a peak in the data occurred around the foveal region, indicative of some increase in intraocular light scatter and/or aberrations.

7.8.1.1.a Better than average visual performance

Better than average visual performance (data points below those of the 'standard observer') was exhibited by four subjects under both photopic and mesopic conditions, e.g. subject KC (figures 7-14 and 7-15).

Subject KC, age 37. PRK six years previously, preoperative refraction: -2.00/-0.25x180. Ablation zone diameter: 6.0 mm. No corneal haze. Mean photopic pupil diameter: 6.2 mm. Mesopic pupil diameter not available. Refraction on day of testing: +0.50/-0.25x180, visual acuity 6/4. Asymptomatic.

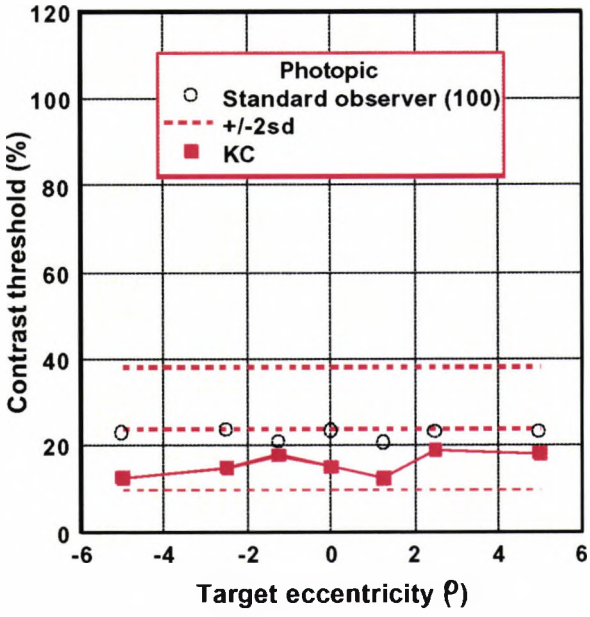


Figure 7-14: Photopic contrast acuity thresholds for subject KC. Data points below the standard observer indicate better than average visual performance.

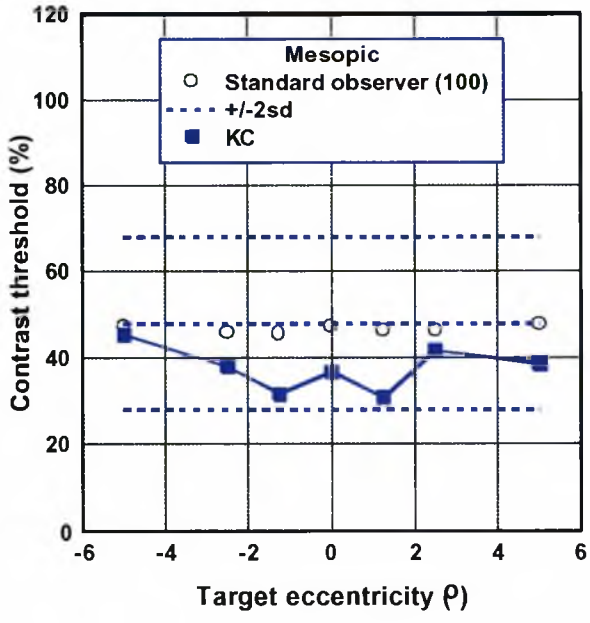


Figure 7-15: Mesopic contrast acuity thresholds for subject KC. Data points below the standard observer indicate better than average visual performance.

7.8.1.1.b Average visual performance

Average visual performance (data points clustered around the 'standard observer') was exhibited by two subjects and one subject under photopic and mesopic conditions respectively, e.g. subject IC (figures 7-16 and 7-17).

Subject IC, age 25, PRK 2 years previously, preoperative refraction: -2.00DS. Ablation zone diameter: 6.5 mm. Trace (grade 0.5) corneal haze. Mean photopic pupil diameter: 5.6 mm. Mean mesopic pupil diameter: 7.06 mm. Refraction on day of testing: plano, visual acuity 6/5. Asymptomatic.

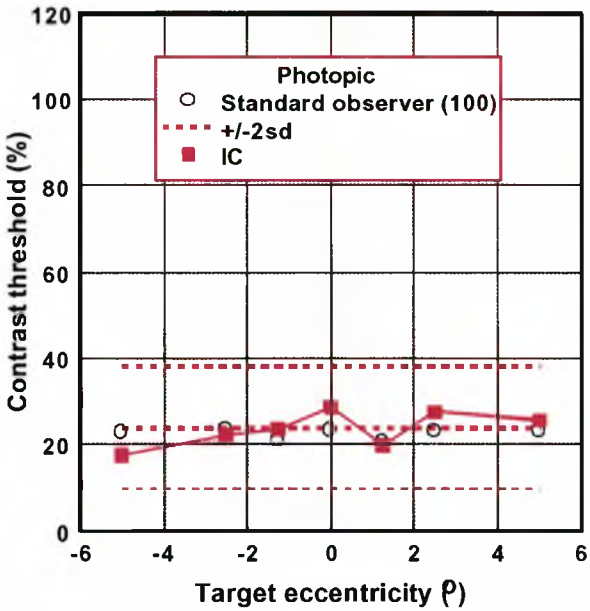


Figure 7-16: Photopic contrast acuity thresholds for subject IC. Data points clustered around the standard observer indicate average visual performance.

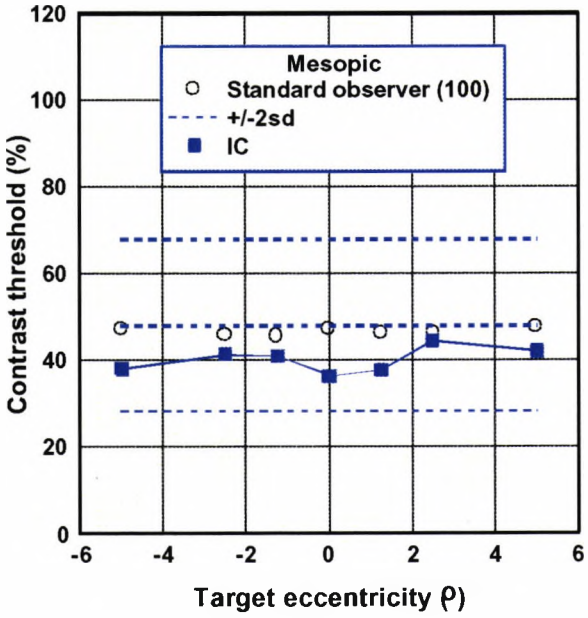


Figure 7-17: Mesopic contrast acuity thresholds for subject IC. The data points fall slightly below the 'standard observer', indicating better than average mesopic visual performance.

7.8.1.1.c Worse than average visual performance within the normal range

Seven and nine subjects exhibited worse than average visual performance (data points above those of the 'standard observer') under photopic and mesopic conditions respectively. In some cases, the data points formed an approximate straight line, while in others a peak in the data was seen around the foveal region.

Subject JQ, age 36. LASIK 9 months previously, preoperative refraction: -5.25/-0.75x10. Ablation zone diameter: 6.5 mm. No corneal haze. Mean photopic pupil diameter: 6.6 mm. Mean mesopic pupil diameter: 7.0 mm. Refraction on day of testing: +0.25DS, visual acuity 6/5. Asymptomatic.

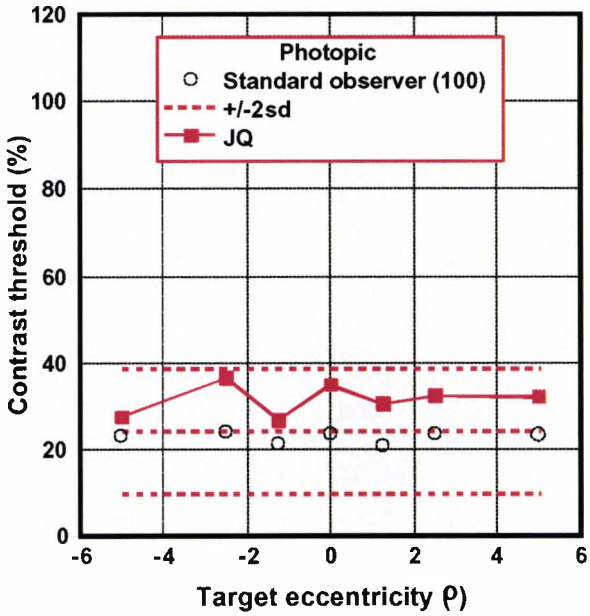


Figure 7-18: Photopic contrast acuity thresholds for subject JQ. Data points above the 'standard observer' indicate worse than average visual performance.

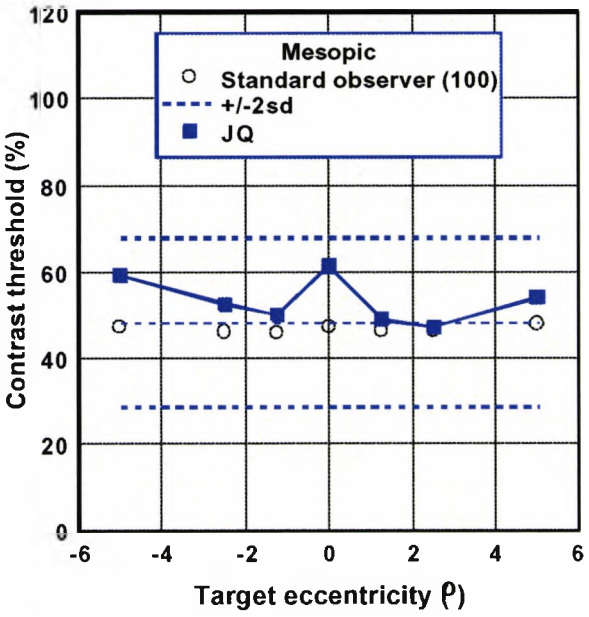


Figure 7-19: Mesopic contrast acuity thresholds for subject JQ. Data points above the 'standard observer' indicate worse than average visual performance. There is the suggestion of a peak in the data around the foveal region.

7.8.1.2 Visual performance outside the normal range

Fourteen and 13 subjects showed contrast acuity thresholds outside the normal ±2sd range, under photopic and mesopic conditions respectively, with the majority 'failing' under both photopic and mesopic conditions. The disparity between the thresholds and the +2sd limit of the normal range tended to be greatest in the foveal region such that the thresholds produced a 'Λ-pattern', e.g. subject SR, (figures 7-20 and 7-21).

Subject SR, age 28. PRK 5 years previously, preoperative refraction -1.75/-1.00x20. Ablation zone diameter: 5.52 mm. No corneal haze. Mean photopic pupil diameter: 5.9 mm. Mean mesopic pupil diameter: 6.6 mm. Refraction on day of testing: +0.50/-0.25x165, visual acuity 6/6. Asymptomatic but non-driver.

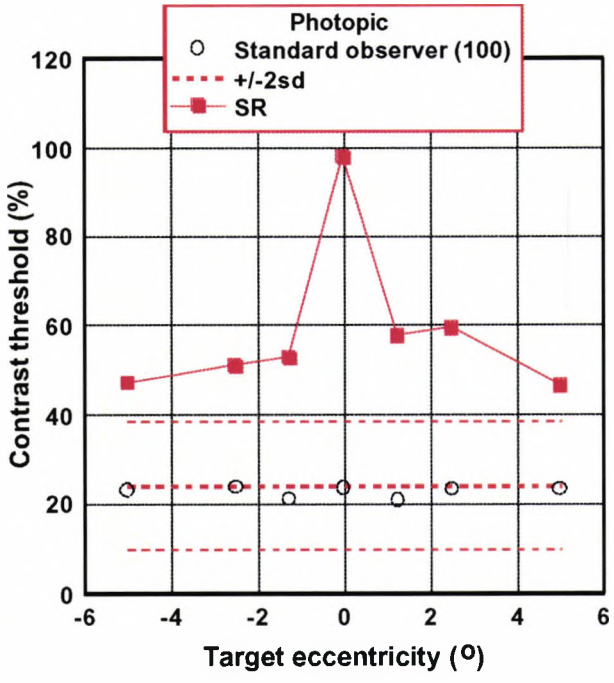


Figure 7-20: Photopic contrast acuity thresholds for subject SR. All data points lie outside the normal range with a large peak around the foveal region.

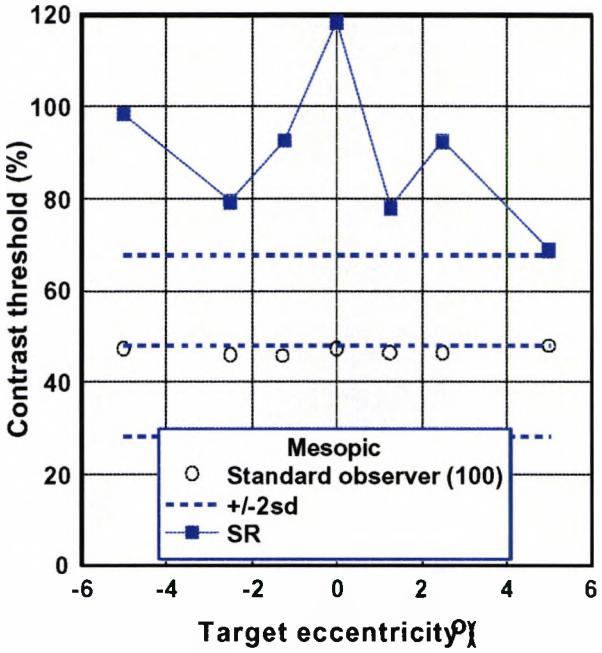


Figure 7-21: Mesopic contrast acuity thresholds for subject SR. All data points lie outside the normal range with a large peak around the foveal region.

Subject PL, age 43. LASIK four years previously, preoperative refraction: -8.00/-1.25x70. Ablation zone diameter: 4.8 mm. No corneal haze. Mean photopic pupil diameter: 4.1 mm. Mean mesopic pupil diameter was not available. Refraction on day of testing: -0.25DS, visual acuity of $6/6^{-4}$. Retinoscopy suggested a degree of central corneal irregularity. Symptoms of poor quality, 'faded' vision at all times, starbursts and glare at night, relieved to some degree by wearing a rigid contact lens to provide a smooth refracting surface. Subject PL was identified as an extreme outlier with irregular contrast acuity thresholds falling more than ±3sd away from the mean thresholds for the refractive surgery group under both lighting conditions, consistent with his symptoms, (figures 7-22 and 7-23).

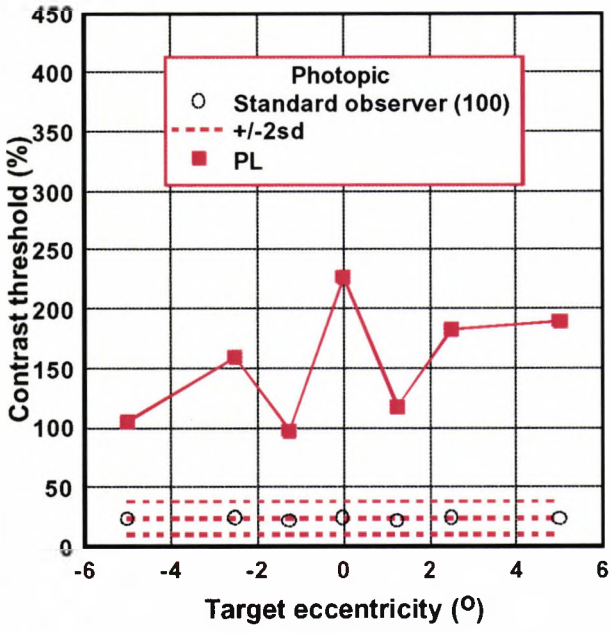


Figure 7-22: Photopic contrast acuity thresholds for subject PL. All data points fall a long way outside the normal ±2sd range, consistent with his symptoms. There is the suggestion of a central peak.

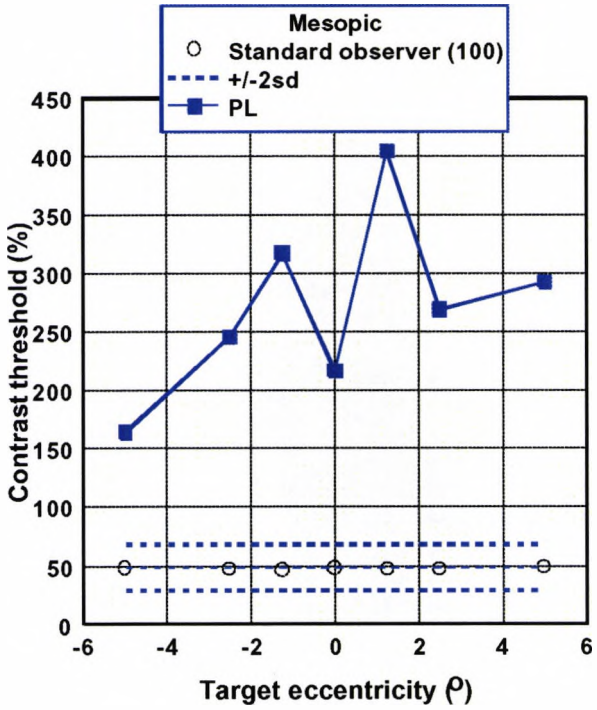


Figure 7-23: Mesopic contrast acuity thresholds for subject PL. All data points fall a long way outside the normal ±2sd range, consistent with his symptoms.

Two subjects (1 LASIK, 1 PRK) exhibited photopic contrast acuity thresholds within the normal range but mesopic contrast acuity thresholds outside the normal range, (e.g. subject LS, figures 7-24 and 7-25).

Subject LS, age 35. PRK seven years previously, preoperative refraction: -3.75DS. Ablation zone diameter: 6.5 mm. No corneal haze. Mean photopic pupil diameter: 5.8 mm. Mean mesopic pupil diameter was not available. Refraction on day of testing: -1.00DS, visual acuity 6/5. Night vision slightly reduced since surgery.

Figures 7-24 and 7-25 suggest that subject LS experiences a significant increase in scattered light and/or aberrations associated with dilation of the pupil under mesopic conditions.

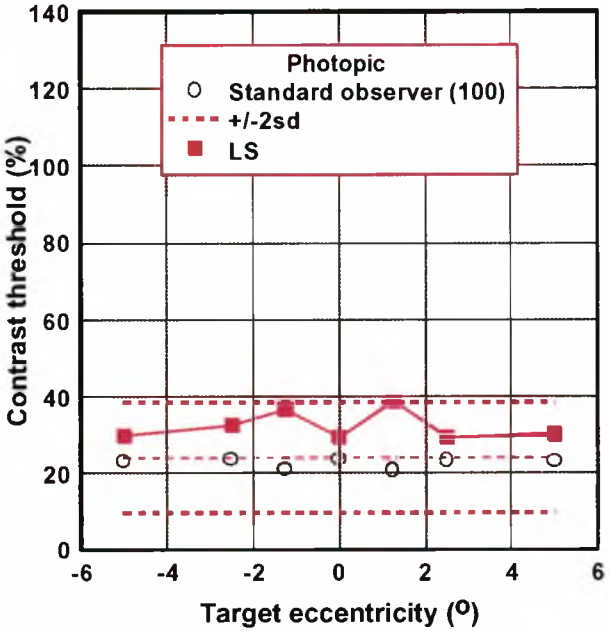


Figure 7-24: Photopic contrast acuity thresholds for subject LS. Worse than average visual performance within the normal range.

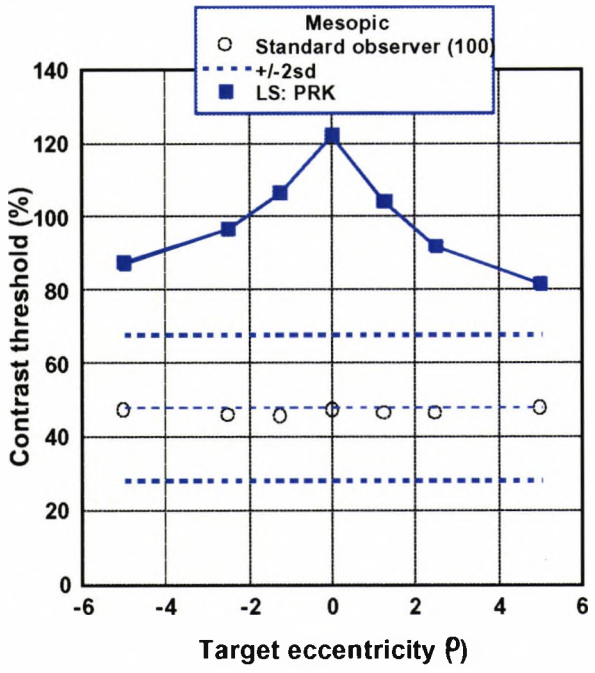


Figure 7-25: Mesopic contrast acuity thresholds for subject LS. All data points fall outside the normal ±2 range.

Three PRK subjects showed contrast acuity thresholds outside the normal photopic range but normal mesopic thresholds, (e.g. subject GI, figures 7-26 and 7-27). In all three cases, the photopic data points only just fell outside the upper +2sd limit.

Subject GI, age 53. PRK 3 years previously, preoperative refraction: -2.50/-1.25x170. Ablation zone diameter: 6.0 mm. No corneal haze. Mean photopic pupil diameter: 6.2 mm. Mean mesopic pupil diameter: 8.0 mm. Refraction on day of testing: -0.25/-0.50x35, visual acuity 6/5. Asymptomatic.

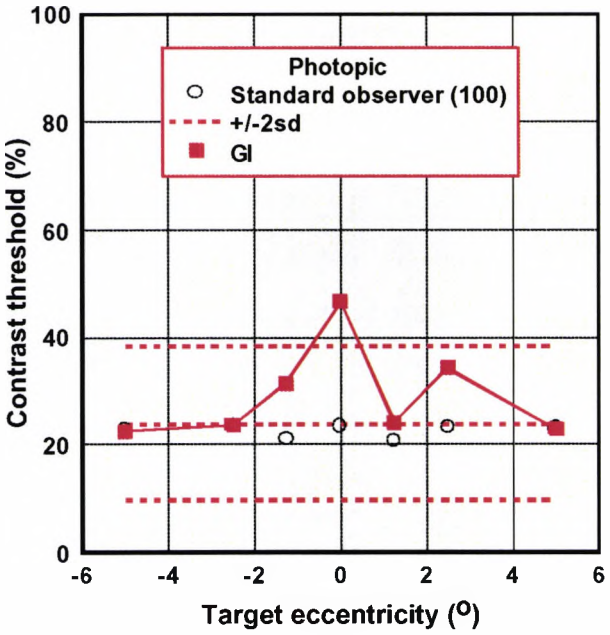


Figure 7-26: Photopic contrast acuity thresholds for subject GI. The majority of data points fall within the normal ±2sd range, the foveal thresholds are elevated, constituting a 'fail' under photopic conditions.

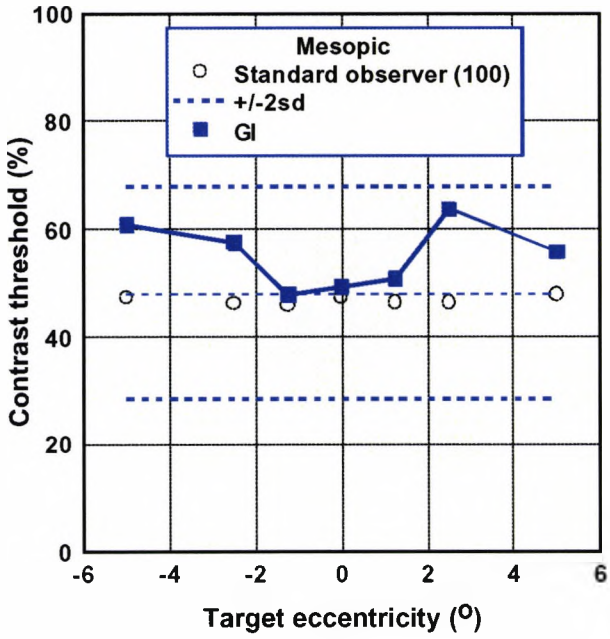


Figure 7-27: Mesopic contrast acuity thresholds for subject GI. All data points fall within the normal range, including the foveal data.

7.9 Chapter conclusion

The Contrast Acuity Assessment (CAA) test has been developed to assess functional visual performance under both daytime and low levels of ambient illumination (Chisholm et al. 2003). The normal ±2sd range has been established based on 100 normal observers. The outcome of the CAA test is simple to interpret by comparing the results obtained for any subject against the limits of the normal range. Examination of a small group of refractive surgery subjects revealed a range of outcomes. Approximately half of these subjects showed contrast acuity thresholds within the normal range following an approximately straight line. Contrast acuity thresholds for some of these subjects suggest better than average visual performance. All symptomatic subjects exhibited data points outside the normal range under the corresponding lighting condition. Subjects with increased forward light scatter and/or aberrations tend to show a characteristic ? -shaped distribution of contrast thresholds.

8 Discussion

Chapters 4-6 consider the design and validation of novel tests developed to investigate the effect of excimer laser refractive surgery on intraocular light scatter and visual performance. In this chapter, the results of the two contrast threshold tests (chapter 5) are discussed in relation to measurements of forward light scatter (chapter 4) and the known increase in optical aberrations as a result of excimer laser surgery. Visual search performance (chapter 6) is considered in relation to visual lobe sizes, derived from the absolute contrast detection and contrast acuity threshold measurements (chapter 5). A comparison of the different methods of assessing visual performance was undertaken in an attempt to determine which technique would be most sensitive to a reduction in retinal image contrast as a result of optical degradation, using the refractive surgery subjects as an example. As a consequence of this, the Contrast Acuity Assessment test was developed (chapter 7).

8.1 Forward light scatter

8.1.1 Effect of excimer laser refractive surgery

In this study, forward light scatter is described in terms of the scatter index, n, the straylight parameter, k, and the integrated straylight parameter, k'. As discussed in section 1.2.2.3.c, the integrated straylight parameter is thought to be the most useful measure of forward light scatter, since it exhibits the smallest within subject variability (Barbur et al., 1993). Analysis of the data obtained with the City University Scatter Program revealed no statistically significant difference between the mean integrated straylight parameter (k') values of the three groups ($p=0.13$). However, the PRK group, and to some degree the LASIK group showed an increase in k' compared to the control group. The greatest disparity occurred between the control and the PRK groups, but this did not reach statistical significance ($p=0.06$).

The LASIK data did exhibit a statistically significant increase in the mean straylight parameter (k) ($p=0.03$), associated with a small, but not statistically significant increase in the mean scatter index (n) ($p=0.35$) compared to the control group. This represents an increase in the quantity of forward scatter but spread over a narrower area. The slight increase in the mean LASIK scatter index value may be associated with the skewed distribution of n (Appendix B, figure B-2.1). It is possible that some patients respond to LASIK surgery differently from others and subjects whose corneae heal in a particular way might experience a narrowing of the distribution of straylight (higher n value) post-surgery that does not occur in all LASIK patients. Significant differences in the healing response have been reported in PRK patients (Durrie, Lesher, and Cavanaugh, 1995) but this has not been considered post-LASIK.

Previous studies of forward light scatter post-refractive surgery have considered PRK but not LASIK. The study by Harrison and colleagues (1995) is the only one to report no statistically significant increase in the straylight parameter at one month post-PRK but most other studies report an increase during the early post-operative period that reduces over time (Butuner et al., 1994; Lohmann et al., 1993; Miller and Schoessler, 1995; Veraart et al., 1995). However, the PRK group in this study displayed a small but not significant reduction in the mean k value ($p = 0.54$) compared to the control group. This is not surprising considering the long average follow-up time of the PRK group in this study (approximately three years). The healing process should be complete for the average PRK subject (Corbett et al., 1996; Marshall et al., 1988). Levels of scattered light measured using a Straylightmeter (van den Berg and Spekreijse, 1987) (see section 1.2.2.3.c) have been shown to return to preoperative levels by 12 months post-PRK (Butuner et al., 1994; Lohmann et al., 1993; Miller and Schoessler, 1995; Veraart et al., 1995). Most of these studies examined eyes that had undergone PRK using a small ablation zone diameter (4.0–5.0 mm), which therefore tended to exhibit a particularly vigorous healing response, associated with the presence of moderate stromal haze. Treatment zones have since been expanded to an average diameter of 6.0 mm, reducing the likelihood of stromal haze and night vision problems. Most refractive surgery subjects examined in our study underwent

treatment over an area of 6.0 mm or larger. Comparison with our results is complicated by the fact that previous studies assumed that straylight had a fixed distribution on the retina (n=2), a fact that influences the value of k.

In this study, the small reduction in the straylight parameter (k) post-PRK was associated with a statistically significant reduction in the mean scatter index value (p=0.00). This indicates a more gradual decrease in scattered light with eccentricity, which can be associated with significant visual degradation (Barbur et al., 1993) (section 1.2.2.2). The parameters n and k are not independent (Barbur et al., 1995) and therefore these variations are consistent with the lack of a significant difference between the mean k' values of the three groups (Pearson correlation coefficient between n and k: LASIK =0.76, R^2=0.58, PRK =0.80, R^2=0.64, Control =0.69, R^2=0.47).

The differences in the distribution and height of the scatter functions for the PRK and LASIK groups, may relate to differences in healing between the two procedures (Wang et al., 1997) (see section 1.2.4.9). The vigorous healing response seen post-PRK is characterised by numerous keratocytes, the presence of small vacuoles and inclusions, and the deposition of atypical collagen (Lohmann et al., 1991a). An increase in keratocyte density (hypercellularity) may also be implicated (Fantes et al., 1990). Fewer activated keratocytes are detected post-LASIK and wound healing tends to be limited to the deposition of new collagen fibres around the flap interface (Kato et al., 1999). An additional explanation for the difference between the two surgical techniques may be provided by the presence of stromal micro-irregularities post-PRK (Lohmann et al., 1991a). The effect of these irregularities is magnified by their location at a boundary between two corneal layers of differing refractive index - the stroma and the epithelium. With the exception of a very small proportion of LASIK patients who suffer from flap striae, the standard micro-irregularities created by the excimer laser ablation during LASIK are located in the mid-stroma at the level of the corneal flap, rather than at a refractive index boundary. The variation in healing response between the two types of surgery is not sufficient to cause a statistically significant difference in the overall quantity of forward light scatter after PRK and LASIK for the

subjects examined in this study, almost certainly because of the long mean follow-up time exhibited by the PRK group, allowing some of these irregularities to even out over time.

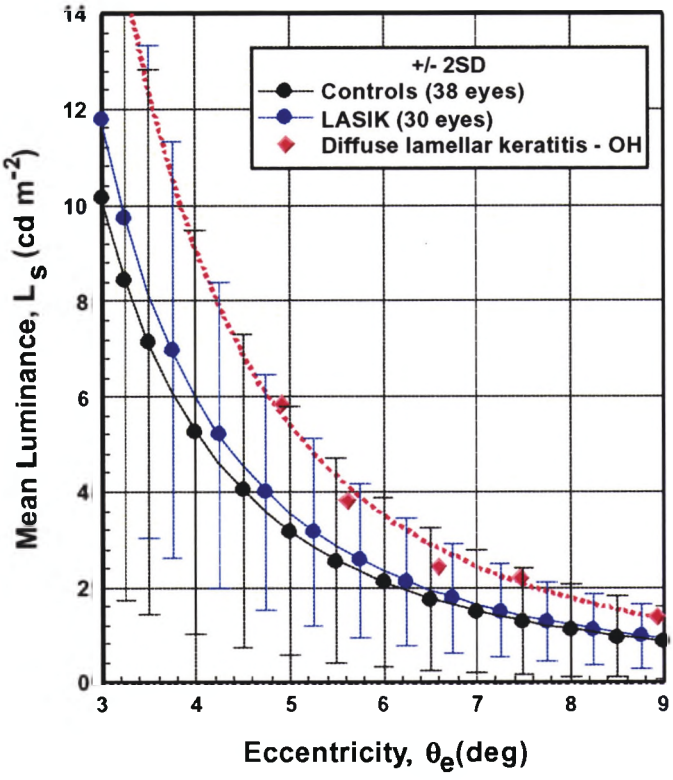


Figure 8-1: Best-fit scatter function data for LASIK subject OH (suffering from Diffuse Lamellar Keratitis) compared to control and LASIK groups

The healing process post-LASIK is significantly less intense than that seen post-PRK and lasts for around nine months post-surgery (Kato et al., 1999; Latvala, Barraquer Coll, Tervo et al., 1996). There have been no published studies to date that directly assessed forward light scatter following LASIK. There is evidence to suggest that LASIK has little or no significant effect on corneal back-scatter (Goble, Lohmann, Fitzke et al., 1994), but the relationship between forward and backward scatter is not straightforward (Allen and Vos, 1967). In this study, the average follow-up time post-LASIK was relatively short (21 weeks), and yet no statistically significant increase in the mean integrated straylight parameter (k') was detected. Since the healing process should still be active at this time in the average LASIK subject (Kato et al., 1999), this strongly supports the theory that LASIK does not significantly impact on intraocular light scatter. Three LASIK

subjects were examined but excluded from the study due to complications that were revealed shortly after the surgical procedure (two cases of visible interface debris and one case of diffuse lamellar keratitis). All three subjects demonstrated elevated k' values ranging between 17 and 21, indicating that LASIK can lead to an increase in the overall quantity of forward light scatter in the presence of certain complications. The best-fit scatter function data for the subject with diffuse lamellar keratitis are illustrated in figure 8-1.

An alternative explanation for the lack of a statistically significant increase in the integrated straylight parameter (k') could be that any effect was masked by the variability of the data. The scatter data for the control group showed large variability, although a similar degree of variability was exhibited by both the PRK and LASIK scatter data. The control group was not representative of the normal population as reported by Hennelly et al. (1998) since many of the subjects were recruited while attending the laser clinic for a preoperative consultation and were primarily myopic. Both contrast sensitivity and low contrast acuity tend to be lower in myopes (Fiorentini and Maffei, 1976; Niesen et al., 1997; Lim, Hoh, Aung et al., 2000), but this reduction in visual performance cannot necessarily be attributed to forward light scatter, and there is no published evidence to suggest that straylight is increased in myopes. More likely explanations include neural factors (reduced sampling density with increasing axial myopia (Strang, Winn, and Bradley, 1998)) and greater levels of higher order aberrations in myopes compared to near emmetropes (Applegate et al., 1998). A large proportion of the control subjects wore spectacles or contact lenses, or gave a history of recent contact lens wear. There is evidence to suggest that spectacle lenses cause a small increase in forward light scatter, particularly if no anti-reflection coating is present (Coupland and Kirkham, 1981). Any scratches or dirt on the lens would exacerbate this effect although the lenses worn by patients during the study were always cleaned before testing. Contact lenses (section 1.2.4.4) have been shown to increase the quantity and distribution of intraocular light scatter due to the presence of raised levels of corneal oedema associated with hypoxia in some wearers (Elliott et al., 1991b). This effect occurs in addition to the increase in scattered light noted in wearers without significant corneal swelling (Lohmann et

al., 1993; Woodward, 1996). This has been attributed to chronic microscopic tissue changes and sub-clinical oedema.

Despite the fact that the increase in the overall quantity of forward light scatter (k') post-surgery did not reach statistical significance, an increase in small angle scatter (within 2°) cannot be ruled out. It is not possible to measure scatter so close to the centre of the scattering source with current techniques. Unfortunately, under most viewing conditions, small angle scatter is more likely to degrade retinal image quality than large angle scatter (van den Berg and Spekreijse, 1987; Beckman et al., 1991).

8.1.2 Influence of other factors

8.1.2.1 Age

An increase in forward light scatter (k) with age associated with changes to the ocular media, has frequently been reported in the literature (Fisher and Christie, 1965; McGrath and Morrison, 1981; Owsley et al., 1983; Yager et al., 1992; Whitaker et al., 1993) (section 1.2.4.1), but only becomes significant after the age of 45 years (Elliott et al., 1991b; Hennelly et al., 1998). In this study, there was a trend towards increasing k and k' values (increase in quantity) and a reduction in n (increased spread) with age, but the effect did not reach statistical significance for any of the three subject groups (section 4.4.1.1.a). This is not surprising since the power to detect an age effect was limited by the relatively small number of subjects in the older age category, the vast majority of which were under 50 years of age.

8.1.2.2 Preoperative refractive error

The PRK group showed a statistically significant increase in the straylight parameter (k) with increasing preoperative myopia, but the trends towards increasing scatter index (n) and integrated straylight parameter (k') values did not reach statistical significance. Although forward scatter and backscatter are not strongly related (Allen and Vos, 1967), this finding is consistent with the increase

in stromal haze (backscatter) with increasing preoperative refractive error reported in the literature (Gartry et al., 1992; O'Brart et al., 1994b; Seiler and Wollensak, 1991). Individuals who undergo PRK for higher degrees of myopia are more likely to experience persistent stromal haze.

No trends in forward light scatter with preoperative refractive error were noted for the LASIK group, reflecting the less vigorous healing response seen after LASIK compared to PRK (Kato et al., 1999) and the minimal influence of refractive error on the post-LASIK healing response. Likewise, the control group did not exhibit a statistically significant relationship between forward light scatter and refractive error. There is no reason why manifest refractive error should cause increased forward light scatter other than the small contribution associated with the presence of a spectacle or contact lens, irrespective of its power (Coupland and Kirkham, 1981).

The intensity of the healing response is known to relate to the degree of myopia treated but the link between age at the time of surgery and the healing response is unclear. One study ruled out age as a factor in the degree of corneal haze and regression post-PRK (Hefetz, Domnitz, Haviv et al., 1997). Others have reported a reduction in the predictability of the refractive outcome for patients undergoing PRK over the age of 50 years (Hersh et al., 1996a; Rao, Chuck, Chang et al., 2000) suggesting that age does influence the wound healing response of the cornea. The effective ablation rate increases with age due to changes in collagen structure (Daxer, Misof, Grabner et al., 1998), leading to greater tissue ablation for the same number of laser pulses, and an associated increase in the post-surgical healing response (Ferincz, Ratkay-Traub, and Bor, 2000). In our study, it was not possible to examine the interactions between age and preoperative refractive error for the scatter data due to the uneven distribution of subjects between categories.

8.1.2.3 Follow-up time

An inverse relationship between follow-up time and both haze (backscatter) and forward light scatter has been reported in the literature (Lohmann et al., 1991a; Lohmann et al., 1993; Veraart et al., 1995). An uneven distribution of subjects between different follow-up time categories prevented examination of the effect of follow-up time on forward light scatter post-PRK. There were sufficient LASIK subjects in each follow-up time sub-category but no trends with follow-up time were noted. This is not surprising since corneal structural changes would be coming to an end by 21 weeks post-LASIK (mean follow-up time), (Perez-Santonja et al., 1998a; Vesaluoma, Perez-Santonja, Petroll et al., 2000a).

Interactions between age and follow-up time, and preoperative refractive error and follow-up time could not be examined due to the uneven distribution of subjects amongst analysis categories. An effect might have been expected since the removal of more corneal tissue (when treating higher refractive errors) is known to initiate a more vigorous and longer lasting healing response following PRK (Tuunanen and Tervo, 1998). Intense and more persistent stromal haze can be seen following PRK for myopia greater than –6.00D compared to less than –6.00D (Gartry et al., 1992; Maldonado, Bas, Onnis et al., 1995; O'Brart et al., 1994b; Maldonado et al., 1995), and contrast sensitivity takes longer to recover after the treatment of myopia greater than –6.00D (Vetrugno et al., 2000).

8.1.3 Outliers

There were relatively few outliers for forward light scatter (two control, one LASIK and two PRK subjects - figures 4-3 and 4-4). All were outliers due to a low scatter index (n) value (more than 2σ below the mean), indicating a wider distribution of straylight on the retina. One PRK subject was also an outlier on the basis of a high, integrated straylight parameter (k') value, associated with grade 2.5 stromal haze. These outliers are considered further in Appendix D.

8.2 Absolute contrast detection thresholds

Absolute contrast thresholds for detection were seen to increase linearly with eccentricity, primarily relating to a reduction in sampling density. This occurs in the retina due to an increase in centre-to-centre cone spacing (Curcio et al., 1990a; Hirsch and Curcio, 1989; Curcio et al., 1990b) and increased spatial pooling by retinal ganglion cells with eccentricity (Levi and Waugh, 1994). Sampling density is also reduced at the level of the visual cortex. There is an increase in optical aberrations with increasing eccentricity, resulting in a loss of retinal image quality (Navarro et al., 1998; Strasburger, Harvey, and Rentschler, 1991), which may make some contribution to the increase in absolute detection threshold with eccentricity. However, it is thought that optical factors have a minimal effect on absolute detection thresholds when the stimulus size is large.

8.2.1 Effect of excimer laser surgery

For the stimulus parameters employed in the contrast detection threshold test, there was a small but not statistically significant increase in the mean absolute contrast detection thresholds of both the PRK and LASIK groups compared to the control group. This difference only reached statistical significance at the highest eccentricity, 9.4° ($p=0.019$). The significant increase in absolute contrast detection thresholds at the highest eccentricity may have occurred by chance, as random errors can occur when the level of statistically significance is taken as $p=0.05$, particularly considering the statistical approach taken in this study (section 3.5). However, the fact that both refractive surgery groups showed a significant increase in absolute contrast detection thresholds compared to the control group may suggest that this is a real effect.

The lack of a statistically significant increase in mean absolute contrast detection thresholds in the PRK and LASIK groups compared to the control group at the three lower eccentricities, is not surprising given the relatively large target size employed in this study. An increase in forward scatter and aberrations would result in a reduction in mid and high spatial frequency information (Williams et al., 1996). However, absolute detection thresholds for such a large target (72 mins

of arc) are relatively insensitive to optical degradation because both scatter originating from the target itself and aberrations are unlikely to decrease significantly the retinal illuminance of the target. In addition, the optical degradation for the average refractive surgery subject caused by scattered light, is likely to be minimal, since the increase in the integrated straylight parameter does not reach statistical significance for either the PRK ($p=0.06$) nor the LASIK ($p=0.68$) groups (section 4.4.1). The effects of increased small angle scatter and aberrations cannot however be excluded. There is strong evidence that higher-order aberrations such as coma and spherical aberration remain persistently elevated following both PRK and LASIK, particularly for eyes with a pupil diameter greater than 4.0 mm (Hong and Thibos, 2000; Martinez et al., 1998; Moreno-Barriuso, Lloves, Marcos et al., 2001; Oshika et al., 1999b; Schwiegerling and Snyder, 2000). The photopic testing conditions had been expected to produce a degree of pupil constriction, possibly masking the effect of increased ocular aberrations, however, the photopic background luminance of 12 cd/m^2 led to a relatively large mean pupil diameter (e.g. 5.72 ±1.01mm LASIK group, section 6.4.2). It is also possible that the effects of surgically induced retinal image degradation are masked by the large variability of the data. The ability to spread and maintain attention over a 10° field, and the effect of fatigue would have increased the variability of the data for all three subject groups. The ability to focus attention is known to play a significant role in peripheral thresholds (Millodot 1966; Yeshurun and Carrasco 1999) and some subjects in this study did report difficulty in attending to the more peripheral targets. This is reflected in the increased variability of the data at higher eccentricities (section 5.4.1).

At an eccentricity of 9.4°, both the PRK and LASIK groups demonstrated a statistically significant increase in mean absolute contrast detection thresholds. Such a finding at a single eccentricity may be due to random statistical fluctuations, particularly in view of the greater variability of the absolute contrast detection data at 9.4° for the two refractive surgery groups compared to the control group. This variability may relate to the slightly wider range of myopic refractive errors (Strang, Winn, and Bradley, 1998) in the refractive surgery

groups compared to the control group, and/or the large differences in the optical quality of the cornea observed between subjects following surgery (Guirao and Artal, 1999). Our findings do however show a systematic increase in contrast detection thresholds for the LASIK group when compared to the control group with increasing eccentricity, suggesting a gradual worsening of image quality with eccentricity that reaches a statistically significant value at 9.4°. The modulation transfer function (MTF) of the dioptrics of the normal eye decreases with eccentricity (Navarro, Artal, and Williams, 1993). The known increase in on-axis aberrations following refractive surgery (Moreno-Barriuso et al., 2001; Marcos, 2001a) is likely to be even greater for off-axis image points. In principle, large retinal image degradation with increasing eccentricity caused by a rapid increase in off-axis aberrations following surgery, could explain the statistically significant increase in absolute contrast thresholds at 9.4°.

It is likely that the loss of retinal image quality with eccentricity (Strasburger et al., 1991) does influence absolute contrast detection thresholds for a Landolt ring target, but only when the degradation is severe enough, i.e. as may be the case at large eccentricities in subjects with large, surgically induced aberrations. Subjects ND and PL (figures 5-5 and 5-6 and Appendix D) were identified as outliers for the contrast detection thresholds and were also outliers in all other tests of visual performance, suggesting a severe reduction in retinal image quality.

8.2.2 Influence of other factors

8.2.2.1 Age

Age is known to cause a reduction in visual performance and an increase in the variability between individuals (Haegerstrom-Portnoy et al., 1999; Johnson and Choy, 1987) (section 1.2.4.1.a). In this study, the control group demonstrated an increase in absolute contrast detection thresholds with age that reached statistical significance at all but the highest eccentricity (9.4°, p=0.095), where the effect may have been masked by the variability of the data, (see table 5-7). An increase in absolute contrast detection thresholds with age was also detected for the two refractive surgery groups, although the effect did not reach statistical significance

at all eccentricities. Variability introduced by differences in the post-surgical healing process between individuals may provide an explanation for the inconsistent effect in these two groups. Age is known to influence the outcome of refractive surgery; predictability decreases with age due to changes in the healing response of the eye (Rao et al., 2000; Ferincz et al., 2000). In addition, the power to detect the effect of age on absolute contrast detection thresholds was reduced by the limited number of subjects over 45 years of age, particularly in the two refractive surgery groups.

The increase in absolute contrast detection thresholds with age could reflect the reduction in retinal image contrast as a result of an increase in scattered light and/or aberrations with age. As discussed previously (section 1.2.4.1), levels of both forward light scatter and aberrations are known to increase with age with the effect becoming significant after the age of 45 years. The increase in forward scatter with age in this study, however, did not reach statistical significance for any of the subject groups (table 4-6), perhaps due to the age distribution of the subjects. Since absolute contrast detection thresholds for such a large Landolt ring target are relatively insensitive to optical degradation, a more likely explanation is the reduction in the sampling density of the visual system due to a decrease in both the retinal ganglion cell population with age and the loss of other neurons within the visual pathway (Anderson and McDowell, 1997).

8.2.2.2 Preoperative refractive error

For the two refractive surgery groups examined in this study, there was a trend towards increasing absolute contrast detection thresholds with increasing preoperative refractive error but the effect did not reach statistical significance for either group, (lowest p value was $p=0.064$, at 9.4° eccentricity for both the PRK and LASIK groups, table 5-8). There was also a trend towards increasing absolute contrast detection thresholds with increasing manifest refractive error for the control group, but again the trend did not reach statistical significance.

Studies have reported a reduction in visual performance following both PRK and LASIK that increases with the level of myopia treated (Jimenez, Anera, and del Barco, 2001). The percentage of eyes that lose two or more lines of Snellen acuity has been shown to increase with increasing preoperative myopia (Seiler and McDonnell, 1995; Rao et al., 1996). The PRK group in this study did show a statistically significant increase in the straylight parameter (k) with increasing preoperative refractive error (section 4.4.1.1.b). The extent of surgically induced aberrations is also known to relate to the degree of treatment (Marcos, 2001a). However, absolute contrast detection thresholds for such a large target are relatively insensitive to optical degradation unless it is severe. The small but not statistically significant trend with increasing manifest refractive error seen in the control group suggests that a reduction in retinal sampling density associated with increased axial length in myopic subjects (Strang, Winn, and Bradley, 1998), may have a role to play.

No examination of the interactions between age and refractive error was possible for the control and LASIK groups due to the inadequate distribution of individuals amongst the analysis categories; some of the older age categories only contained one subject. A trend towards a larger increase in absolute contrast detection thresholds with increasing preoperative refractive error was noted for the older PRK group (>45 years), compared to the younger PRK group. The interaction reached statistical significance at all but the lowest eccentricity ($p=0.084$ at 1.4° eccentricity, table 5-9). Following PRK, both preoperative refractive error and age are thought to be linked to the intensity of the healing process (Rao et al., 2000), which in turn influences the refractive outcome, speed of recovery and the likelihood of an increase in backward light scatter (stromal haze). A reduction in the predictability of the refractive outcome for PRK patients over the age of 50 years has been reported (Hersh et al., 1996a; Rao et al., 2000). There is evidence to suggest that the effective laser ablation rate (amount of tissue removed per pulse) increases with age due to changes in corneal hydration (Ferincz et al., 2000). This would be worse in those undergoing a deeper ablation for the correction of higher refractive errors. Deeper ablations are known to result in higher surgically induced aberrations (Hersh et al., 1996b; Marcos, 2001a;

Marcos, Barbero, Llorente et al., 2001; Marcos et al., 2001). It is possible that older refractive surgery patients who have undergone PRK for higher degrees of preoperative myopia are more likely to suffer levels of optical degradation severe enough to cause a statistically significant increase in absolute contrast detection thresholds.

8.2.2.3 Follow-up time

Follow-up time relates to the speed of the healing process post-surgery but this varies significantly between individuals (Durrie et al., 1995; Ehlers and Hjortdal, 1992). Contrast sensitivity and low contrast acuity take longer to recover following excimer laser treatment for the correction of higher degrees of myopia (Pallikaris et al., 1996; Vetrugno et al., 2000; Montes-Mico and Charman, 2001). In this study, the effect of follow-up time could not be examined for the PRK group due to the uneven distribution of subjects between analysis categories. It was not found to influence significantly the absolute contrast detection thresholds for the LASIK group and no trends could be identified. The lack of a statistically significant follow-up effect is not surprising since absolute contrast detection thresholds for the Landolt ring target are relatively insensitive to optical degradation.

No examination of interactions between age and follow-up time, or preoperative refractive error and follow-up time were possible due to the uneven distribution of both PRK and LASIK subjects amongst the analysis categories.

8.2.3 Outliers

One LASIK (PL) and one PRK subject (ND) were identified as outliers for the contrast detection threshold test (figures 5-5 and 5-6). Both outliers were symptomatic but a number of other subjects reporting visual symptoms were not identified as outliers. This suggests that absolute contrast detection thresholds are rather insensitive to a reduction in visual performance.

8.3 Contrast acuity thresholds

Contrast acuity thresholds for gap orientation discrimination were seen to increase rapidly with eccentricity, relating to a reduction in sampling density with eccentricity (Curcio et al., 1990a; Hirsch and Curcio, 1989; Levi and Waugh, 1994) (see section 8.2). The increase in thresholds is more rapid for discrimination tasks than detection tasks (Johnson, Keltner, and Balestrery, 1981) since the peripheral retina is designed for detection rather than discrimination (Harris and Fahle, 1996). The increase in optical aberrations with eccentricity (Navarro et al., 1998) and the subsequent reduction in mid and high spatial frequency information (Williams et al., 1996), is expected to have a greater influence on acuity tasks than detection tasks, since resolution of small detail is required. For some tasks, differences in visual performance between the fovea and the periphery, can be removed by scaling the target for size using the cortical magnification factor (Virsu and Rovamo, 1979). However, contrast acuity thresholds for Landolt rings do not follow the cortical magnification factor, since they are strongly influenced by the loss of retinal image quality with eccentricity (Strasburger et al., 1991), in addition to retinal under-sampling (Virsu, Nasanen, and Osmoviita, 1987).

8.3.1 Effect of excimer laser surgery

The PRK group showed an increase in mean contrast acuity thresholds compared to the control and LASIK groups, reaching statistical significance at all but the highest eccentricity (9.4°) (table 5-16). The mean contrast acuity thresholds for the LASIK group were also greater than those of the control group but the difference only reached statistical significance at an eccentricity of 3.8° ($p=0.041$, but $p=0.074$ at 1.4°). Since the average follow-up time exhibited by the PRK group was relatively long (33 months), this suggests that PRK may permanently impair visual performance. LASIK may reduce visual performance to some degree under the conditions considered in this study, (mean follow-up time: 15 weeks).

The increase in mean contrast acuity thresholds relates to surgically induced degradation of the retinal image. Considering forward light scatter, both refractive surgery groups demonstrated a small but not statistically significant increase in the integrated straylight parameter (k'). The PRK group, however, demonstrated a statistically significant reduction in the mean scatter index (n) compared to the control group, associated with a small but not statistically significant decrease in the mean straylight parameter (k), (section 4.4.1). A low n value indicates a more gradual decrease in scattered light with eccentricity, which can be associated with significant visual degradation (Barbur et al., 1993) (section 1.2.2.2). Straylight from a point source, such as the edge of the Landolt ring gap, is spread over a wider area, reducing the contrast of the gap. In contrast, the LASIK group demonstrated a statistically significant increase in the mean straylight parameter (k) associated with a small but not significant increase in the mean scatter index (n).

The increase in higher-order aberrations that follows excimer laser surgery is known to cause a reduction in the modulation transfer function of the eye (Marcos, 2001a; Oliver et al., 1997b), which would be expected to influence contrast acuity thresholds. It was not possible to measure the aberrations of the subjects examined during this study. There is some suggestion that LASIK is associated with a greater increase in aberrations than PRK (Oshika et al., 1999b), due to the use of smaller treatment zones for corresponding degrees of refractive correction. This suggests that the statistically significant increase in mean contrast acuity thresholds demonstrated by the PRK group compared to the LASIK and control groups, must be primarily related to the change in the distribution of straylight (reduced n value), rather than aberrations.

8.3.2 Influence of other factors

8.3.2.1 Age

For the control group, age resulted in a statistically significant increase in contrast acuity thresholds (table 5-17) at all but the highest eccentricity (9.4° p=0.169). A trend towards increasing contrast acuity thresholds with age was also seen for

both the PRK and LASIK groups but the effect did not reach statistical significance for either group. The effect of age may have been masked in these two groups by variations in the post-surgery corneal healing response between individuals. This increase in mean contrast acuity thresholds is likely to be caused by both an increase in forward scatter and/or aberrations, and neural factors. In this study, an increase in the integrated straylight parameter (k') with age was noted for all subject groups, but the effect did not reach statistical significance (see section 4.4.1.1.a). In addition, small angle scatter cannot be excluded. Higher order aberrations are known to stay relatively constant between the ages of 20 and 40 years (He et al., 2000). After this age, coma and spherical aberration in particular, are seen to increase (Guirao et al., 2000; Artal et al., 1993; Berrio et al., 2000; Jenkins, 1963; Oshika et al., 1999a) (section 1.2.4.1), although aberration levels vary significantly between individuals (Walsh and Charman, 1985; Porter et al., 2000). This increase is generally thought to have little impact on retinal image quality since the magnitude of the aberrations is limited by the natural reduction in average pupil size with age (Calver et al., 1999a; Winn, Whitaker, Elliot et al., 1994). Pupil size is unlikely to significantly limit aberrations in this study - taking the control group as an example where the age effect was most marked, the mean pupil size with a photopic background luminance of 12 cd/m^2 was 5.54mm (range of 3.70 to 7.20 mm). Pupil size did show a slight decrease with age but the relationship was weak (R^2=0.27). It was not possible to measure the aberrations of the subjects involved in this study, but the relatively large mean pupil diameter suggests that aberrations are likely to have increased significantly with age.

With respect to the two refractive surgery groups, there is evidence to suggest that the effective laser ablation rate (amount of tissue removed per pulse) increases with age, due to changes in corneal hydration (Ferincz et al., 2000). The depth of the ablation is closely linked to the level of surgically induced aberrations (Hersh et al., 1996b), suggesting that older refractive surgery patients made be more likely to suffer a reduction in the optical quality of the cornea as a result of refractive surgery.

Contrast sensitivity thresholds for gratings (an acuity task more akin to contrast acuity thresholds than absolute detection thresholds), show a decline with age (section 1.2.4.a). The reported reduction in contrast sensitivity appears to be consistent with the increase in intraocular light scatter (Hemenger, 1984) but neural factors have also been implicated (Devansy and Johnson, 1980; Elliott, 1987; Whitaker and Elliott, 1992). Little deterioration in contrast sensitivity occurs before the age of 40 years (Nio et al., 2000), although some studies suggest that the decline does not begin until the age of 50 (Derefeldt et al., 1979; Owsley et al., 1983; Ross et al., 1985), or even 65 years (Haegerstrom-Portnoy et al., 1999). Our study only included one subject over the age of 60 years, reducing the ability to detect the influence of age on contrast acuity thresholds. It is likely that neural factors, such as the decrease in ganglion cell population with age, play a role in the increase in absolute contrast detection thresholds with age. Such factors are known to influence peripheral resolution tasks more than detection tasks (Kline, 1987; Anderson and McDowell, 1997). The decrease in the attentional field size with age is also likely to be an important factor in peripheral contrast acuity thresholds as measured in this study (Haegerstrom-Portnoy et al., 1999).

8.3.2.2 Preoperative refractive error

In this study, there was a trend towards increasing mean contrast acuity thresholds with increasing preoperative refractive error but the effect did not reach statistical significance for either refractive surgery group (table 5-18). The manifest refractive error of the control group did not influence the contrast acuity thresholds. All subjects were fully corrected throughout the experiments.

Some relationship between contrast acuity thresholds and preoperative refractive error had been expected since a number of studies have reported a link between the degree of myopia treated and visual performance (Jimenez et al., 2001); the percentage of eyes that lose two or more lines of Snellen acuity increases with increasing preoperative myopia (Seiler and McDonnell, 1995; Rao et al., 1996). The relationship between surgically induced aberrations and the degree of preoperative myopia (Marcos et al., 2001) would also be expected to influence the

retinal image contrast and hence contrast acuity thresholds. Larger degrees of myopia require the removal of more stromal tissue and are often associated with smaller ablation zones in an attempt to minimise tissue removal (section 1.2.4.9) (Jimenez, Anera, del Barco et al., 2000). The degree of induced spherical aberration is related to the size of the attempted refractive correction (Hersh et al., 1996b) and inversely related to the diameter of the ablation zone (Oliver et al., 1997a). One study noted that eyes with small ablation zones and steep edges tend to exhibit the greatest loss of low contrast visual acuity (Gauthier et al., 1998), strongly implicating aberrations as the principal cause of the reduction in visual performance. Decentrations of the treatment zone are more significant for the treatment of larger refractive errors and lead to an increase in coma (Coorpender et al. 1999; Mrochen et al. 2001). Myopic treatments over –6.00D may be further complicated by the increase in effective ablation rate when removing deeper stromal tissue (Ferincz et al., 2000), and this may lead to greater increases in aberrations.

The degree of preoperative myopia is also known to influence the quantity of backward light scatter. Stromal haze (backscatter) is known to be greater in those PRK patients undergoing surgical correction of larger refractive errors (Gartry et al., 1992; O'Brart et al., 1994a; Seiler and Wollensak, 1991). One might therefore expect a similar relationship with forward light scatter, although there have been no publications on this matter to date. The results of chapter 4 indicate a statistically significant increase in the straylight parameter (k) ($p=0.037$) with preoperative refractive error, and small but not statistically significant increases in both the scatter index (n) and the integrated straylight parameter (k') for the PRK group (section 4.4.1.1.b). The fact that the significant increase in k with increasing preoperative myopia, does not translate in to a statistically significant increase in contrast acuity thresholds, may be because k does not relate as closely to visual performance as k', and k is also more variable than k' (Barbur et al., 1995).

Considering interactions between age and preoperative refractive error, no valid analysis was possible for the control group, due to the limited number of individuals in the older age/refractive error analysis categories. When the PRK

and LASIK group data were examined, a greater increase in contrast acuity thresholds with increasing preoperative refractive error was seen for the older age group compared to the younger group. This interaction reached statistical significance at all eccentricities for the LASIK group and at 3.8° for the PRK group, (table 5-19). These interactions mimic that seen for absolute contrast detection thresholds for the PRK group (section 5.4.1.2.b), and are probably related to a reduction in retinal image quality associated with larger surgically induced aberrations; greater levels of aberrations are induced by the surgical correction of increasing degrees of preoperative refractive error, perhaps augmented by age-related changes in the laser ablation rate due to differences in stromal hydration (Ferincz et al., 2000) and collagen fibril characteristics (Daxer et al., 1998). The influence of preoperative refractive error and age on the intensity of the healing process (Gartry et al., 1992; Hefetz et al., 1997) may also be a factor.

8.3.2.2 Follow-up time

Some association between contrast acuity thresholds and follow-up time was expected since both forward light scatter (PRK) and induced aberrations (PRK and LASIK) are known to decrease with increasing follow-up time (section 1.2.4.9) (Lohmann et al., 1993; Martinez et al., 1998; Oliver et al., 1997b; Miller and Schoessler, 1995). No examination of the effect of follow-up time on contrast acuity thresholds post-PRK was possible in this study, due to the limited number of subjects in many of follow-up time categories. The distribution of follow-up times for the LASIK group was more uniform and a trend towards a reduction in contrast acuity thresholds with increasing follow-up was noted, although the effect only reached statistical significance at the highest eccentricity (9.4°) (table 5-20). This trend may relate to a gradual reduction in surgically induced off-axis aberrations but this hypothesis remains to be investigated. The lack of a significant effect at all eccentricities may be due to the mean follow-up time post-LASIK (14.8 weeks for the contrast acuity data), since the rapid and relatively passive healing response seen post-LASIK tends to be nearing completion by this time (Perez-Santonja et al., 1998a; Vesaluoma et al., 2000b). Following PRK with

its more vigorous healing response, high contrast acuity recovers within four months and contrast sensitivity within 6-12 months of the procedure (Ambrosio et al., 1994; Wang et al., 1997). The recovery of contrast sensitivity post-LASIK is even quicker (4-6 months) (Wang et al., 1997; Perez-Santonja et al., 1998b; Chan, Edwards, Woo et al., 2002).

No statistically significant interactions between follow-up time and age were revealed for the contrast acuity data of the LASIK group (table 5-21). There was a similar reduction in contrast acuity thresholds over time for each of the two age groups. No examination of interactions between either follow-up time and age, or follow-up time and preoperative refractive error was possible for the PRK group due to the uneven distribution of subjects between analysis categories. Some effect had been expected due to the link between rate of healing post-excimer laser surgery and age (Loewenstein, Lipshitz, Levanon et al., 1997; Rao et al., 2000).

Interactions between preoperative refractive error and follow-up time were examined due to the link between the degree of tissue removal and speed of healing following PRK (Durrie et al., 1995). Low contrast acuity and contrast sensitivity are reduced for approximately three months following PRK treatments for less than –6.00D, and for around six months for treatments greater than -6.00D (Esente et al., 1993; Ambrosio et al., 1994; Pallikaris et al., 1996; Montes-Mico and Charman, 2001; Vetrugno et al., 2000). The distribution of LASIK subjects between analysis categories was relatively uniform and indicated that an increase in follow-up time reduces the effect of different degrees of preoperative refractive error; there was a smaller increase in contrast acuity thresholds between the low and medium myopic groups with increasing follow-up time. The effect only reached statistical significance at the largest eccentricity investigated (9.4°).

8.3.3 Outliers

One PRK and three LASIK subjects were identified as outliers in the contrast acuity threshold test (figures 5-7 and 5-8). Three of the four outliers were

symptomatic despite being told they had a good surgical outcome. These outliers are considered further in Appendix D.

8.4 Visual Search Performance

The relationship between stimulus contrast and mean search time followed theoretical predictions - a reduction in search time with increasing target conspicuity. This relationship can be explained by the fact that for a fixed point of regard, the higher the contrast of the stimulus, the larger the area surrounding fixation in which the stimulus attribute can be discriminated. Fewer fixations are therefore needed to scan the visual field, leading to a shortened mean search time. Low contrast stimuli are much closer to the discrimination threshold, resulting in a small discrimination lobe. Centrally located stimuli may be detected quickly, while more peripheral targets are associated with a much longer search time, increasing the variability of the data when search performance is averaged over a large area such as in this study (±10°).

8.4.1 Effect of excimer laser surgery

For the stimulus parameters employed in this visual search task, the PRK group showed an increase in mean search times compared to the control and LASIK groups that reached statistical significance at all contrast levels (other than 6% contrast). In comparison, there was no statistically significant difference between the mean search times of the LASIK group and the control group for any of the four target contrast levels. In fact, the mean search times were very similar for the two groups.

The increase in mean visual search times in the PRK group compared to the control and LASIK groups, can be linked to the findings of chapter 5 – a small increase in absolute contrast detection thresholds (only statistically significant at 9.4°), and the statistically significant increase in contrast acuity thresholds post-PRK, signalling contraction of the detection and discrimination lobes respectively. The detection lobe is defined as the region over which a particular target can be detected relative to fixation and the discrimination lobe is the area over which a particular target can be discriminated relative to fixation. This would increase the number of fixations required to detect and resolve the target during the visual search task, leading to an increase in the mean visual search time. Extending the

same reasoning to the LASIK data, the lack of a significant increase in mean visual search times reflects the insignificant increase in contrast acuity thresholds compared to the control group (table 5-16). These findings suggest that the size of the discrimination lobe (based on contrast acuity thresholds) has more impact on visual search performance than the size of the detection lobe (based on absolute contrast detection thresholds).

The statistically significant increase in both contrast acuity thresholds and visual search times for the PRK group compared to the control and LASIK groups, indicate that on average, PRK causes some degradation of the retinal image, whereas LASIK has a more limited effect on visual performance. This is so, despite the long mean follow-up time for the PRK group (33 months compared to 16 weeks post-LASIK for visual search data) and may indicate a permanent reduction in visual performance post-PRK. As discussed in section 8.3.1, the increase in mean contrast acuity thresholds and therefore the reduction in visual search performance can be attributed to degradation of the retinal image due to forward light scatter and/or aberrations. The findings of chapter 4 suggest that changes in the angular distribution of straylight within the eye as a result of PRK, have an important role in determining visual performance. Surgically induced aberrations and small-angle scatter are also likely to have played a part.

Considering the 6% contrast target in isolation, the PRK group demonstrated a significantly higher mean visual search time than the LASIK group but not the control group. This is despite the expectation that the stimulus of lowest contrast would be most sensitive to retinal image degradation. The data for the 6% contrast stimulus showed greater variability compared to other stimuli, (coefficient of variation was approximately 25% for the 6% contrast target compared to 15-16% for other stimuli). This would have reduced the significance of any differences between subject groups. There were four PRK and five LASIK subjects who were unable to resolve the 6% contrast target but were not classified as outliers since they showed search times within the normal range for all other target contrasts. Hence the data for the 6% contrast target are somewhat distorted, but removal of these individuals does not alter the outcome for any of the contrast levels.

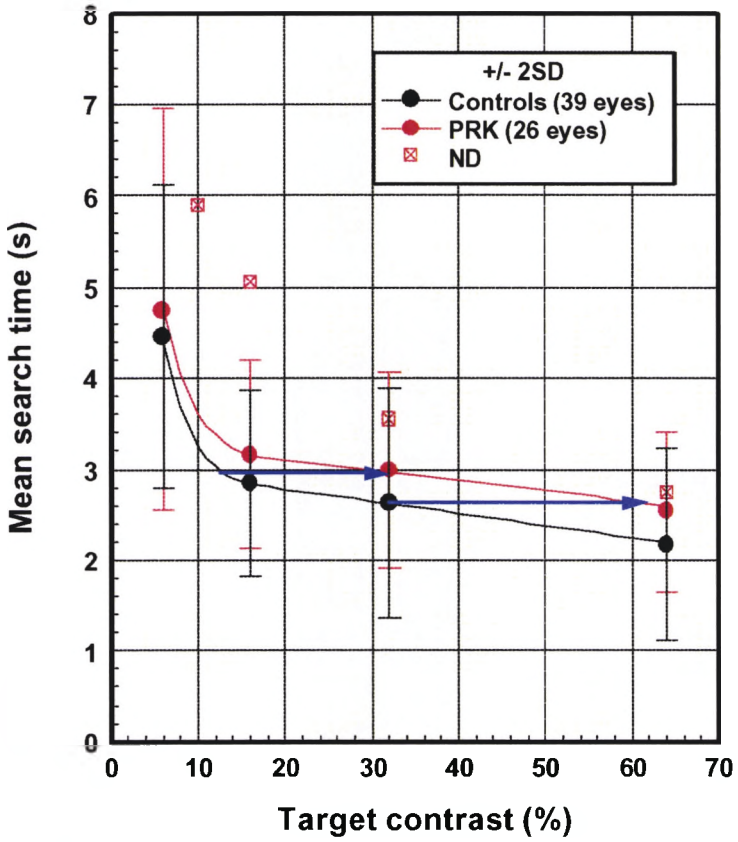


Figure 8-2: Visual search time as a calibration for retinal image contrast for the PRK data

An increase in forward light scatter and aberrations would be expected to influence lower contrast targets more than high contrast targets, since their proximity to threshold makes them more susceptible to retinal image degradation. The superior conspicuity of high contrast stimuli should make them relatively resistant to optical degradation. This does not appear to be the case in this study when considering the PRK group as a whole; the increase in the mean search time for the PRK group compared to the control group is similar across the range of contrast levels tested. The PRK outlier ND does however show a larger increase in mean search times with reducing stimulus contrast (figure 8-2). Barbur and Forsyth (1988) reported that the use of luminance contrast to predict search performance could only accurately be applied to targets of low luminance contrast and that additional factors were probably involved in the processing of high contrast stimuli. Psychological factors may play a role, such as the tendency for some subjects to concentrate on searching for stimuli of lowest contrast, ignoring the more obvious stimuli. Figure 8-2 shows that the average PRK subject requires the stimulus contrast to increase from 32% to approximately 64% in order to show

the same mean visual search time as the average control subject. A contrast of 32% for the PRK group equates to approximately 15% for the control group, illustrating the non-linear nature of the relationship. This is an interesting finding, consistent with a reduction in visual lobe size for target discrimination and hence less efficient visual search performance. The size of the visual lobe over which stimulus discrimination can be carried out would be expected to extend significantly as the effective image contrast of visual stimuli on the retina is increased. This effect is of great interest and remains to be investigated further.

8.4.2 Influence of other factors

8.4.2.1 Age

There was a trend towards increasing mean visual search times with age but the effect did not reach statistical significance for any of the three subject groups (table 6-7). This may relate to the large inter-subject variability and the limited number of subjects over the age of 45 years (e.g., three out of 22 PRK subjects). An increase had been expected since both absolute contrast detection thresholds and mean contrast acuity thresholds showed an increase with age. Increased thresholds lead to constriction of the visual lobes over which the stimulus can be detected and resolved, resulting in a need for more fixations and longer search times.

The reduction in the size and sensitivity of the peripheral field with age in the presence of an attentional load (Haegerstrom-Portnoy et al., 1999), is also likely to decrease visual search performance in older subjects. In addition, an age-related reduction in sampling efficiency (Madden and Allen, 1995) can cause increased variability (Haegerstrom-Portnoy et al., 1999; Johnson and Choy, 1987) and a reduction in visual search performance.

8.4.2.2 Preoperative refractive error

A trend towards increasing mean visual search times with increasing myopia was revealed but it did not reach statistical significance for any of the three subjects

groups. The trend is consistent with the small, but not statistically significant increase in both absolute detection and contrast acuity thresholds with increasing myopia. This would result in constriction of the detection and discrimination lobes, leading to more fixations and longer search times. Possible causes have been discussed previously (sections 8.2.2.2 and 8.3.2.2) and include an increase in induced aberrations and forward light scatter in those treated for higher preoperative refractive error (Hersh et al., 1996b). The fact that a trend is also seen for the control group suggests the involvement of other factors such as the increase in aberrations with increasing myopia in normal eyes (Carkeet et al., 2002; Collins et al., 1995), and perhaps the reduction in retinal sampling density with increasing axial myopia (Strang, Winn, and Bradley, 1998).

It was not possible to examine interactions between refractive error and age for the visual search data due to the uneven distribution of subjects between the different analysis categories, with too few in the older age groups. Some interaction might be expected since a greater increase in both absolute contrast detection thresholds (PRK group only – table 5-9), and contrast acuity thresholds (PRK and LASIK groups – table 5-19), with increasing preoperative refractive error was seen for the older subjects compared to the younger subjects.

8.4.2.3 Follow-up

A trend towards decreasing mean visual search times with increasing follow-up time was identified for the LASIK group but it did not reach statistical significance. This finding is consistent with the decrease in contrast acuity thresholds with time following LASIK, which was attributed primarily to a reduction in aberrations over time (Oliver et al., 1997b; Martinez et al., 1998). No valid analysis was possible for the PRK group due to the poor distribution of individuals between different follow-up time categories.

When interactions between follow-up time and age were examined, no trends were identified for the LASIK group. The visual search performance of the younger age group might have been expected to recover more quickly due to changes in healing with age (Loewenstein et al., 1997; Rao et al., 2000). This

would be consistent with the findings for absolute contrast detection and contrast acuity thresholds for the LASIK group (tables 5-11 and 5-21). No valid analysis was possible for the PRK group due to the uneven distribution of subjects between analysis categories.

8.4.3 Outliers

The outliers for visual search comprised one LASIK and one PRK subject (figures 6-8 and 6-9). Both outliers were known to have significant surgically induced corneal irregularities (ND and PL) and were extreme outliers in the other measures of visual performance (absolute contrast detection and acuity thresholds), although not for forward light scatter. They were both symptomatic despite having been classified as having a good outcome (good visual acuity) by their operating surgeon. These two individuals are considered further in Appendix D.

8.5 Glimpse duration

8.5.1 Effect of excimer laser surgery

There was no statistically significant difference between the mean glimpse duration data of the three subject groups (table 6-14). The mean glimpse duration values were similar to previously reported values for normals of around 0.3s (Kraiss and Knaeuper, 1982; Barbur et al., 1991). In this study, the measure of glimpse duration does not reflect the degradation of the retinal image indicated by the increase in mean contrast acuity thresholds and mean visual search times post-PRK. This is not surprising since glimpse duration was measured during a relatively complex visual task. Only a portion of each glimpse is involved in the processing of visual information with the remainder involved in planning the next saccade.

8.5.2 Influence of other factors

8.5.2.1 Age

No statistically significant relationship between age and mean glimpse duration could be identified for any of the three subject groups (table 6-15). One would expect glimpse duration to increase with age due to the reduction in retinal image quality associated with an increase in intraocular light scatter and aberrations, and the reduction in sampling efficiency (Madden and Allen, 1995), leading to an increase in processing time. The lack of an age effect may relate to the complexity of the visual task; glimpse duration depends on much more than simply the conspicuity of the target and the quality of the retinal image (Cornelissen and Kooijman, 1999). The limited age range of the subjects examined in this study may also play a role.

8.5.2.2 Preoperative refractive error

There was a trend towards increasing mean glimpse duration with increasing preoperative myopia for the PRK and LASIK groups, but this trend was not statistically significant. No trends were noted for the control group. These

findings suggest that retinal image quality does have an important role to play in determining glimpse duration. An alternative explanation is reduced retinal sampling associated with an increase in axial myopia (Strang, Winn, and Bradley, 1998).

Interactions between preoperative refractive error and age could not be examined for any of the subject groups due to the poor distribution of subjects between analysis categories. Another difficulty was the reduced size of the data sets for glimpse duration compared to other measures of visual performance, resulting from the introduction of the glimpse duration instrumentation partway through the study.

8.5.2.3 Follow-up time

A trend towards a reduction in mean glimpse duration with increasing follow-up time was seen for both refractive surgery groups although the effect did not reach statistical significance for either group. The validity of the analysis for the PRK is questionable due to the poor distribution of subjects between analysis categories. Along with the trend seen for preoperative refractive error, these findings indicate that retinal image quality does play a role in determining glimpse duration as it is the only factor that could vary with follow-up time. Retinal image contrast increases over time following both PRK and LASIK surgery due to the gradual reduction in forward light scatter and aberrations (Lohmann et al., 1993; Martinez et al., 1998).

No trend was identified when interactions between follow-up time and age were examined for the LASIK glimpse duration data (table 6-20). The corresponding analysis for the PRK group was not carried out because of the uneven distribution of subjects between analysis categories.

These findings suggest that retinal image quality does influence mean glimpse duration but that other factors are also involved. Many of the stimuli used in the visual search task were significantly above threshold. Despite this, the PRK group

did show a statistically significant increase in mean visual search times for the high contrast stimuli. It may be that any reduction in retinal image contrast only significantly affects glimpse duration when the contrast of the stimulus is close to the discrimination threshold. Glimpse duration was measured during a visual search task employing a wide range of stimulus and distractor contrast levels. This could reduce the sensitivity of the glimpse duration measurements to reduced retinal image quality if 'normal' glimpse durations were associated with the majority of the targets presented.

8.5.3 Outliers

One control and one PRK subject were identified as outliers for glimpse duration. At the time of assessment, the control subject was 69 years of age and therefore the result is not surprising. A relatively large age-related increase in both forward light scatter and aberrations, and reduction in neural sampling density would be expected for a 69 year old individual. This would lead to a marked increase in target processing speed. The outlier from the PRK group (subject ND) was an outlier in all other measurements of visual performance undertaken in this study, suggesting a severe reduction in retinal image quality. Interestingly, LASIK subject, PL, demonstrated a mean glimpse duration within the normal range despite being an outlier for all other assessments of visual performance. These outliers are discussed further in Appendix D.

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8.6 Contrast Acuity Assessment (CAA) Test

The 'standard normal' $\pm 2\sigma$ range under both photopic and mesopic conditions, was determined by assessing a group of 100 normal subjects using the Contrast Acuity Assessment (CAA) test. Scaling the target size with eccentricity to compensate for the loss of retinal visual acuity ensured that the 'standard observer' displayed contrast acuity thresholds of approximately 24% (photopic) and 48% (mesopic). These values were contrast independent of target eccentricity, making the results easy to interpret. Data below or above the expected 'normal' line indicate better or worse performance than the 'standard observer' respectively. The normal group showed a relatively wide range of contrast acuity thresholds, illustrating the variation in optical quality in the normal population with age (Allen and Vos, 1967; Oshika et al., 1999a), refractive error and race (Carkeet et al., 2002). The normal $\pm 2\sigma$ range was larger still under mesopic conditions due to the added variation in the level of retinal adaptation between individuals at $0.05cd/m^2$.

The normal group included 36 holders of a class 1 medical certificate (both commercial pilots and licence holders about to commence training). Two outliers were identified and excluded from the normal group. There was no statistically significant difference between the mean contrast acuity thresholds of this group and the remaining 66 normal subjects, although the standard deviation was slightly smaller for the 'pilot' group. Although pilots might be expected to have better than average visual performance, they are only required to have a corrected high contrast visual acuity of 6/9 or better, a level comparable with the normal population. There is currently no specification for visual performance in the contrast domain for the class 1 medical certificate. Outlier 1 showed $\wedge$-shaped contrast acuity thresholds under photopic conditions, indicative of optical degradation due to an increase in forward light scatter and/or aberrations. His mesopic data fell within the normal $\pm 2\sigma$ range. Both forward light scatter and aberrations are known to increase under mesopic conditions as the pupil dilates (Charman, 1991; Edgar et al., 1995). There is also a reduction in the Stiles-Crawford effect (Stiles and Crawford, 1933), increasing the susceptibility to

forward scattered light. Despite this, the CAA test appears to be less sensitive to optical degradation under mesopic than photopic conditions, as demonstrated by this subject. The larger target size and higher contrast level required for the target to be resolved at low light levels make the mesopic task less susceptible to the effects of optical degradation. In addition, the greater inter-subject variability exhibited by the normal group under mesopic conditions is likely to have masked some of the effect. Outlier 2, also from the 'pilot' group, demonstrated contrast acuity thresholds outside the normal $\pm 2\sigma$ range with a large increase in thresholds in the temporal field under both photopic and mesopic conditions, (figures 7-10 and 7-11. N.B. right eye only examined). Such a pattern is strongly suggestive of a retinal or neurological defect and a similar outcome was noted for a patient with sub-clinical retinal degeneration associated with sickle cell anaemia. Although the test has been designed for use in pilots or initial class 1 medical certificate applicants who have undergone refractive surgery, it is equally appropriate for use in other tasks that require assessment of adequate functional vision rather than the limits of visual performance.

The study was designed to give an insight into the possible effects of refractive surgery on visual performance measured using the Contrast Acuity Assessment (CAA) test. The study is however unlikely to produce data representative of the general refractive surgery population, since the subject group was small and was not selected at random. Out of interest, the refractive surgery group data were compared with the normal range and a statistically significant increase in mean contrast acuity thresholds was noted for the refractive surgery group under both photopic and mesopic conditions ($p = 0.000$). Even when those subjects whose contrast acuity thresholds fell outside the normal $\pm 2\sigma$ range were excluded (fails), the remaining refractive surgery group (passes) still showed a statistically significant increase in both photopic ($p = 0.000$) and mesopic ($p = 0.024$) mean contrast acuity thresholds compared to the normal group. This indicates that, on average, for this particular group of subjects, excimer laser refractive surgery causes a small reduction in visual performance. This is so despite the fact that the mean thresholds for this subgroup fell within the normal range, indicating that their functional visual performance remained within normal limits.

The increase in photopic contrast acuity thresholds compared to the normal group can be attributed to a rise in both forward light scatter and aberrations. None of the 27 refractive surgery subjects exhibited significant corneal haze (back scatter) but forward light scatter was not assessed for the subjects in this sub-study and therefore an increase in scatter cannot be excluded. However, the data presented in chapter 4 suggest that although a small increase in forward light scatter can occur as a result of both PRK and LASIK, the increase is not statistically significant. The significant increase in the spread of straylight (reduced n value) post-PRK may be more relevant. Small-angle scatter is likely to be a factor but cannot be easily quantified using currently available techniques. Aberrations probably play the primary role since although both aberrations and forward scatter increase as the pupil dilates, scatter is less dependent on pupil size than aberrations. A number of studies have shown that post-surgical visual problems are at a maximum when the pupil is dilated (Holladay et al., 1999; Strolenberg et al., 1996; Schallhorn, 1994).

When the refractive surgery subjects who 'passed' the CAA test (data within $\pm 2\sigma$ normal range) were further divided into those who had undergone PRK and those who had been treated with LASIK, the mean contrast acuity thresholds for the PRK 'passes' under mesopic conditions did not differ significantly from the normal group ($p=0.710$). The mean contrast acuity thresholds for the LASIK under both photopic ($p=0.007$) and mesopic ($p=0.000$) conditions and PRK group under photopic conditions ($p=0.012$), remained significantly higher than the normal group data. This suggests that for this particular group of subjects, successful PRK surgery leads to a better visual outcome than successful LASIK surgery. This differs from the findings of chapters 5 and 6, where the PRK group showed a reduction in visual performance, whereas the LASIK group did not. The original group of PRK subjects had generally been treated at least five years previously, prior to improvements in laser technology. The small group of PRK subjects who were examined using the CAA test, had been treated more recently. There is evidence to suggest that LASIK surgery induces greater ocular aberrations than PRK (Oshika et al., 1999b) but for this small group of subjects, the difference between the contrast acuity thresholds for the PRK and LASIK

'passes' is more likely to be associated with the large disparity in mean preoperative refractive error (PRK –1.82D, LASIK –6.10D) and perhaps the mean zone size (PRK 6.3mm, LASIK 5.9mm). In addition, the number of subjects examined was small (PRK passes: eight photopic, ten mesopic, LASIK passes: five photopic, four mesopic), and therefore direct comparisons between the PRK and LASIK groups cannot be generalised.

8.6.1 Characteristic outcomes

The examples in section 7.7.1 illustrate the two most commonly encountered outcomes of the CAA test for the group of refractive surgery subjects considered in this study. Approximately half the subjects exhibited contrast acuity thresholds within the normal $\pm 2\sigma$ range ('pass') with the data points clustered around the straight-line data of the 'standard observer', (e.g., subjects KC, IC and JQ, figures 7-14 to 7-19). This tended to be the case under both photopic and mesopic conditions. The remaining subjects exhibited contrast acuity thresholds above the upper $\pm 2\sigma$ limit of the normal range ('fail'), with the greatest disparity occurring around the central $\pm 2.5^{\circ}$ of the field, (e.g., subject SR, figures 7-20 and 7-21). This $\wedge$-pattern is characteristic of an increase in forward light scatter and/or aberrations following surgery, since the resulting reduction in image contrast would be of greater significance for the smaller, central targets, due to the loss of critical image contours. A few of the subjects who 'passed' the CAA test also showed a small central peak despite their contrast acuity thresholds falling within the normal $\pm 2\sigma$ range. Small-angle scatter can be particularly degrading for small, centrally located retinal images. A number of studies have reported an increase in irregular aberrations following corneal refractive surgery, particularly for pupils greater than 4.0 mm (Hong and Thibos, 2000; Martinez et al., 1996; Martinez et al., 1998; Oshika et al., 1999b; Schwiegerling and Snyder, 2000; Seiler et al., 2000). Aberrations are likely to play a major role in the elevation of contrast acuity thresholds of this group, particularly since the photopic pupil diameter was known to exceed the diameter of the ablated zone for seven eyes (photopic pupil data only available for 22 eyes). Under mesopic conditions, 20 out of 22 eyes with mesopic pupil data exhibited a pupil diameter larger than the ablation zone. When

the pupil dilates to become larger than the ablated zone, higher-order aberrations similar to spherical aberration increase significantly. Peripheral rays are able to pass through untreated regions of the cornea, forming myopic blur circles around the retinal image. Some subjects report halos around lights at night. However, the relationship between pupil diameter, ablation zone and visual performance is unclear. Of those whose pupil diameter exceeded the ablation zone diameter, approximately half of the subjects showed contrast acuity thresholds within the normal $\pm 2\sigma$ range (pass) and half outside the normal $\pm 2\sigma$ range (fail). This was the case under both photopic and mesopic conditions. The role of the pupil in visual performance post-refractive surgery is not easy to predict (Gomerperalta, Tan, and Epstein, 2001), and this is supported by our findings.

The majority of subjects showed an identical outcome for the photopic and mesopic CAA tests, with 11 'passes' and 11 'fails'. Two subjects 'passed' under photopic conditions but 'failed' under mesopic conditions (figures 7-24 and 7-25). This suggests that the optical quality of the central cornea is relatively good in such individuals, with significant optical degradation only occurring as the pupil dilates, leading to an increase in both forward scatter and aberrations (Edgar et al., 1995; Martinez et al., 1998). One such subject specifically reported poor quality night vision but no visual problems during the day.

A further three eyes 'failed' under photopic conditions but 'passed' under mesopic conditions (figures 7-26 and 7-27). In all three cases, the photopic data points only just fell outside the upper $+2\sigma$ limit. As was the case for outlier 1 from the 'pilot' group, such a result can be attributed to the reduced sensitivity of the mesopic CAA test to increased light scatter or aberrations, associated with the need for a target that is both larger and of higher contrast than that used by the photopic CAA test. This highlights the need to assess refractive surgery patients under both photopic and mesopic conditions.

8.6.2 Sensitivity of the CAA test to visual symptoms

Unlike the previously discussed measures of visual performance (chapters 5 and 6), all symptomatic subjects were identified by the CAA test as having degraded visual performance with contrast acuity thresholds outside the normal $\pm 2\sigma$ range at the corresponding light level. The proportion of subjects reporting symptoms was much higher than average in order to assess the sensitivity of the test (37% versus 15% - Schein, Vitale, Cassard et al., 2001). Seven of the 27 refractive surgery subjects reported symptoms under both photopic and mesopic conditions and a further three reported symptoms under low illumination only. It is more common for symptoms to be noticed under low illumination, not only because of the increase in pupil diameter and therefore reduction in optical quality, but also because visual tasks tend to be closer to threshold and noise levels increase under such conditions.

The CAA test also identified four subjects who exhibited contrast acuity thresholds outside the normal $\pm 2\sigma$ range, despite claiming to be asymptomatic at that light level. Two subjects reported night vision problems but normal daytime vision despite 'failing' the test at both light levels. A further two subjects reported no visual symptoms at all, despite 'failing' the test at both light levels. One such subject (SR) did not drive since she lived in a large city and was able to use public transport. Since driving is one of the most demanding visual tasks that we undertake at night, it may be that this individual failed to appreciate her significant visual degradation because she was never required to complete visually difficult tasks under low illumination. An alternative explanation may be the psychological effect noted in some individuals following refractive surgery; even some of those whose visual performance is made worse by the surgery report high levels of satisfaction associated with no longer requiring an optical correction (McGhee, Craig, Sachdev et al., 2000; Schein et al., 2001).

In summary, the CAA test allows functional visual performance to be compared to the established normal range, under both for daytime and night-time illumination. It is sensitive to a reduction in retinal image contrast caused by

increases in forward light scatter and/or aberrations as a result of corneal refractive surgery.

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9 Conclusions

The work carried out in this project falls naturally in to two categories:

- **The design and validation of novel tests** - four novel tests of visual performance were developed and assessed to determine which technique would be most sensitive in detecting a reduction in retinal image quality caused by forward light scatter and/or aberrations.

- **The assessment of visual performance in normal subjects and in patients with corneal refractive surgery, using the four novel tests.** Forward light scatter in the eye was measured using the City University Light Scatter Program and parameters describing light scatter in the eye were examined in relation to the results of the four tests. A control group was also assessed for comparison with the two refractive surgery groups, in an effort to quantify the effect of PRK and LASIK on intraocular light scatter and visual performance.

9.1 Major findings

9.1.1 Photorefractive Keratectomy

- A statistically significant reduction in the scatter index (n) was noted following PRK, indicating an increase in the angular distribution of straylight in the eye. The quantity of forward light scatter did not show a statistically significant increase following PRK.

- Both mean contrast acuity thresholds and mean visual search times showed a statistically significant increase in the PRK group compared to the control group.

- These findings suggest that the distribution of forward light scatter on the retina has considerable implications for visual performance. Previous studies have only considered the quantity of straylight. The decrease in the

scatter index suggests changes to the properties of the scatter sources within the post-PRK cornea. The microirregularities created at the interface between the epithelium and anterior stroma may provide a possible explanation.

- An increase in the spread of straylight and an associated reduction in visual performance were evident despite the long mean follow-up time of the PRK group (approximately three years). Previous studies have reported that the quantity of forward light scatter returns to normal levels within 12 months of PRK surgery but these findings suggest that PRK can cause permanent changes to the light scattering properties of the eye with possible effects on visual performance.

9.1.2 Laser assisted in-situ keratomileusis

- Results in LASIK patients show a statistically significant increase in the straylight parameter (k), associated with a small but not statistically significant increase in the scatter index (n) and the integrated straylight parameter (k'). This suggests a small increase in the quantity of scattered light, but a narrowing of the distribution on the retina. Such small changes may have only minimal or insignificant effects on visual performance.

- In agreement with the findings for forward light scatter, the LASIK group showed a small but not statistically significant increase in mean contrast acuity thresholds and mean visual search times compared to the control group.

- The mean follow-up time for the LASIK group was significantly shorter than that of the PRK group (four months compared to three years), although this time period is still towards the end of the healing process for the typical eye treated with LASIK. These findings suggest that on average, LASIK does not significantly degrade visual performance and

that a small increase in the straylight parameter alone does not lead to a significant reduction in visual performance.

9.1.3 General findings

- It was not possible to assess optical aberrations during this study but existing findings in the literature suggest that surgically induced aberrations are likely to be a major factor in the decrease in visual performance noted for the PRK group. There is no evidence to suggest that PRK causes greater aberrations than LASIK and therefore the change in the distribution of straylight (scatter index, n) is strongly implicated in the decrease in visual performance seen for the PRK group.

- The findings of this study highlight the importance of assessing both the quantity and distribution of forward light scatter. They also show that the light scatter index (n) cannot be assumed to have a fixed value of 2.0 in all individuals.

- There were outliers from both refractive surgery groups who suffered a significant reduction in visual performance despite a 'good surgical outcome' according to their high contrast visual acuity. In particular, two refractive surgery subjects were classified as outliers for all measures of visual performance. This reduction in visual performance is likely to have been caused by large increases in irregular aberrations associated with corneal shape changes, rather than an increase in forward light scatter.

9.1.4 Comparison of tests

- Absolute contrast detection thresholds proved to be relatively insensitive to retinal image degradation. This is not surprising given the large stimulus size employed. The two refractive surgery groups showed an increase in detection thresholds compared to the control group. The difference increased with eccentricity to reach statistical significance at the highest eccentricity (9.4°). A possible explanation could be a worsening of off-

axis image quality due to an increase in surgically induced off-axis aberrations.

- Glimpse duration measurements proved particularly insensitive to retinal image degradation, with almost identical values for all three groups. This reflects the numerous factors that influence glimpse duration in addition to retinal image contrast.

- The visual search program did reveal a statistically significant increase in mean search times for the PRK group compared to the control and LASIK groups.

- Contrast acuity thresholds appeared to be the most sensitive of the four measures of visual performance with an increase in mean thresholds revealed for both the PRK (statistically significant) and the LASIK groups (not statistically significant at every eccentricity). In addition, more outliers were identified for the contrast acuity test than other tests and all of them reported visual symptoms of some form. The relative sensitivity of contrast acuity thresholds to retinal image degradation is also supported by the findings for the effect of age, refractive error and follow-up. A statistically significant improvement in contrast acuity thresholds with increasing follow-up time was noted for the LASIK goup and interactions between age and refractive error, and refractive error and follow-up time were also revealed for the contrast acuity test alone. Age was found to have a statistically significant influence on both contrast detection and contrast acuity thresholds, suggesting that neural factors are the primary cause.

Our aim was to apply these findings to the field of commercial aviation and to develop a relevant measure of visual performance, sensitive to the visual degradation that can occur post-refractive surgery. The current methods for determining the suitability of an individual's eyesight for commercial aviation are based on the assessment of visual acuity, the measurement of refractive error and

examination of the health of the eyes. The only assessment of visual performance is the measurement of high contrast acuity, which is relatively insensitive to effects of forward scattered light and aberrations. The visual acuity pass/fail criterion of 6/9 or better cannot be related to specific tasks involved in aviation and measurement conditions are not in any way similar to those found on the flight deck. Attempts were made in this study to develop a test that resembled more closely the visual tasks involved in piloting an aircraft. As shown in this thesis, the influence of image contrast on more realistic tasks such as visual search and glimpse duration is difficult to identify, due to the large number of additional factors that influence search performance. The visual search model identified these parameters, which include the pipe memory length, the search pattern strategy employed and the ability to spread attention over the test field. The visual search data also showed significant variability, failed to identify all of the symptomatic outliers and data collection was very time consuming. The assessment of contrast acuity thresholds appears to be the most sensitive measure of retinal image degradation.

Consequently the Contrast Acuity Assessment (CAA) test was developed from the contrast acuity threshold program, with modifications to further increase its sensitivity to intraocular light scatter, and make the test appropriate and relevant to commercial aviation. The CAA test has the distinct advantage that it is based on a thorough analysis of the cockpit, incorporating target sizes, critical field diameter and lighting conditions into the test, and is relatively quick and simple to complete. Examination of a large group of control subjects allowed the normal range ($\pm 2\sigma$) to be established. The upper limit of the normal range is taken as the 'pass/fail' criteria for determining whether an individual possessed the visual performance necessary to safely pilot an aircraft or whether they required further investigation. Individuals whose contrast acuity thresholds fall outside the normal range, whether due to refractive surgery induced visual degradation or any other ocular condition influencing visual performance, should be referred for further investigation. Preliminary data were obtained from a small group of refractive surgery subjects who completed the test at both photopic and mesopic light levels. Many subjects produced data that clustered around the 'standard observer'. Others

produced data that fell outside the normal 95% range, often showing a characteristic '∧-pattern' implicating forward scattered light and aberrations. On average the refractive surgery group showed a statistically significant increase in contrast acuity thresholds under both photopic and mesopic conditions compared to the control group, but the preliminary data sets were small and therefore this finding should be interpreted with caution. The study highlights the need to examine applicants under both photopic and mesopic conditions in order to detect all those with reduced visual performance. The test is capable of detecting those with visual symptoms on the basis of their contrast acuity thresholds, but is also able to identify those with reduced visual performance who claim to be asymptomatic, a problem that is encountered by regulatory authorities.

9.2 Shortcomings of the current study

- A retrospective investigation was all that was possible in this study. A longitudinal study would have been better, with subjects assessed both before and after surgery, providing a more complete portrayal of the changes in visual performance produced by PRK and LASIK over time. However, practical difficulties in recruiting suitable refractive surgery subjects from private clinics made this impossible.

- The effects of age, preoperative refractive error and follow-up time were difficult to assess. These characteristics varied widely within the refractive surgery groups and it was not possible to achieve an even distribution of subjects between the chosen analysis categories within the time available. Frequently, interactions between the different factors could not be examined due to the uneven distribution of subjects between categories. The PRK subjects were mostly recruited from clinic B, that only allowed us to contact individuals who had undergone surgery some years previously (long average follow-up time). This meant that the effect of follow-up time on visual performance and forward light scatter could not be adequately examined, but the results do shed some light on the long-term effects of PRK.

- Although the boundaries chosen for the different analysis categories can be justified based on the current literature, different limits may have provided a better distribution of individuals between categories, improving the analysis of the effects of age, refractive error and follow-up time.

- Statistical testing of the differences between the three subject groups was undertaken at each eccentricity (contrast thresholds) and each stimulus contrast (visual search) rather than by comparing the curves for each group. This led to a large number of computations, greatly increasing the chances of detecting statistically significant differences that were in fact due to chance. The advantage of this approach is that it did allow some insight into the change in visual performance with eccentricity/contrast.

- Apparatus was not available for the assessment of aberrations during this study therefore it was difficult to differentiate between the effects of forward light scatter and aberrations on visual performance. It was also not possible to measure small angle scatter at the time.

- The strength of the conclusions reached following the initial assessment of the CAA test using refractive surgery subjects, is somewhat limited by the small number of subjects examined in chapter 7.

9.3 Further work

Work currently in progress employs the CAA test to assess visual performance in a larger group of patients who have undergone conventional LASIK surgery in one eye and a customised LASIK ablation (minimising surgically induced aberrations) in the other. Initial studies into the benefits of customised ablations for visual performance have shown limited benefit for the average myope (Nuijts, Nabar, Hament et al., 2002), but they have relied on high contrast visual acuity assessment rather than measures of visual performance that are sensitive to the effects of scattered light and aberrations such as the CAA test.

Appendix A: Consent form and subject information sheet

All subjects read the information sheet prior to completing and signing the consent form, examples of which are shown below.

Study name: Refractive surgery and visual performance

Information sheet

This research study has been set up to examine the effects of Photorefractive Keratectomy (PRK) and Laser in situ Keratomileusis (LASIK) on vision. The aim is to determine whether or not PRK and LASIK refractive surgery are suitable for treating refractive errors, usually corrected by spectacles or contact lenses, in commercial pilots. A group of control subjects, who have not undergone any surgery on their eyes, will be examined for comparison.

Initially you will be asked a series of questions regarding your general and ocular health. Those with certain conditions such as diabetes, or taking certain medications will be excluded from the rest of the research. In addition, pregnant women will also excluded. You will undergo a standard eye examination to determine your refractive correction, if any, and to check the health of your eyes. Your vision will be assessed using computer-based tests. In these tests you respond to targets presented on the screen by pressing a button. All techniques are non-invasive (there is no contact with the eyes) and they will not result in any discomfort or blurring of your vision. You will be asked if you are sensitive to flickering lights and if this is the case, you will be excluded from the research, since one of the tests involves looking at a flashing light.

If you are a contact lens wearer, you will be asked not to wear your lenses on the day of the assessment. Your spectacles can be worn unless the prescription is out of date, in which case corrective lenses will be supplied for the tests.

The full set of tests may take up to 90 minutes to complete. Please inform the investigator at the start of the session if this likely to be a problem. All tests require the subject to concentrate on the computer screen and you are likely to feel

tired after the session. If at anytime you feel that tiredness is preventing you from concentrating on the task, please inform the investigator.

Risks of involvement in the research study: none

Benefits: All subjects will receive an eye examination but apart from this there are no benefits associated with this study.

The data from this study will be published as a Civil Aviation Authority report at some time in the future but none of your personal details will be included. You will only be identified in the report by your initials, if at all. You are free to withdraw from this research study at any time without giving a reason.

Consent form

Study: Refractive surgery and visual performance

Name of subject:.....

Address:.....

.....

Daytime telephone number:.....

Email address: .....

Date of birth: .....

I .....(name) **confirm that I have read and understood the information sheet provided. I have been given the opportunity to ask questions regarding the project and these have been answered to my satisfaction. I consent to taking part in the research project and for the data to be published in the future.**

Signed.....**Date**:.....

Appendix B: Data Distribution

B.1 Control Group

Anderson-Darling Test of Normality

A p value greater than 0.05 indicates a normal distribution. A p value less than 0.05 indicates a skewed distribution.

Table B-1 Data distribution for control group (p values)

Parameter examined	Untransformed data – p values		Transformed data (log_{10}) – p values	
	Full data set	Without Outliers	Full data set	Without Outliers
Scatter index, n	0.366 normal	0.445 normal	0.114 normal	0.722 normal
Straylight parameter, k	0.266 normal	0.201 normal	0.111 normal	0.136 normal
Integrated Straylight parameter, k'	0.917 normal	0.882 normal	0.180 normal	0.281 normal
Detection thresholds 1.4°	0.000	No outliers	0.000	No outliers
Detection thresholds 3.8°	0.001	No outliers	0.000	No outliers
Detection thresholds 6.7°	0.002	No outliers	0.012	No outliers
Detection thresholds 9.4°	0.053 normal	No outliers	0.097 normal	No outliers
Contrast Acuity 1.4°	0.002	No outliers	0.582 normal	No outliers
Contrast Acuity 3.8°	0.007	No outliers	0.587 normal	No outliers
Contrast Acuity 6.7°	0.001	No outliers	0.761 normal	No outliers
Contrast Acuity 9.4°	0.027	No outliers	0.805 normal	No outliers

Parameter examined	Untransformed data – p values		Transformed data (log_{10}) – p values	
	Full data set	**Without Outliers**	**Full data set**	**Without Outliers**
Visual Search 16% Contrast	0.152 normal	No outliers	0.487 normal	No outliers
Visual Search 32% Contrast	0.339 normal	No outliers	0.444 normal	No outliers
Visual Search 64% Contrast	0.355 normal	No outliers	0.050 normal	No outliers
Glimpse Duration	0.001	0.900 normal	0.097 normal	0.797 normal

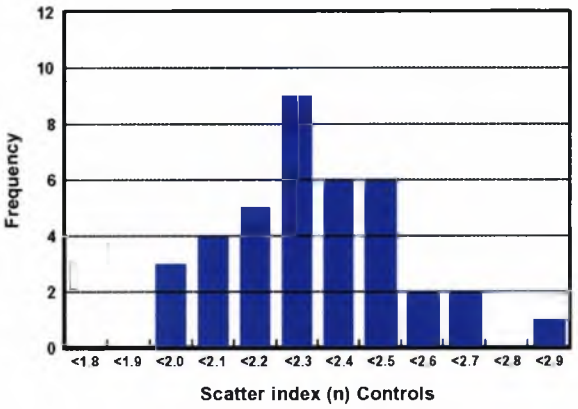

Figure B1.1: Distribution of scatter index (control group without outliers)

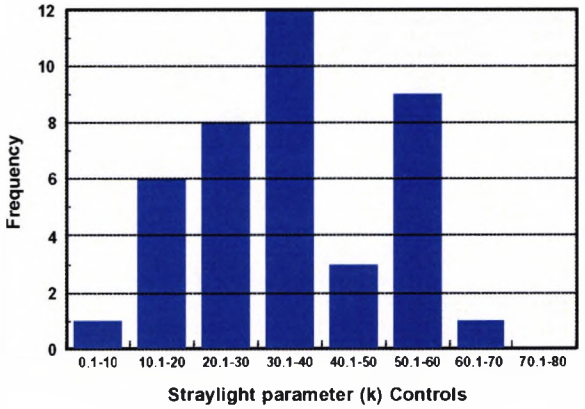

Figure B1.2: Distribution of straylight parameter (control group without outliers)

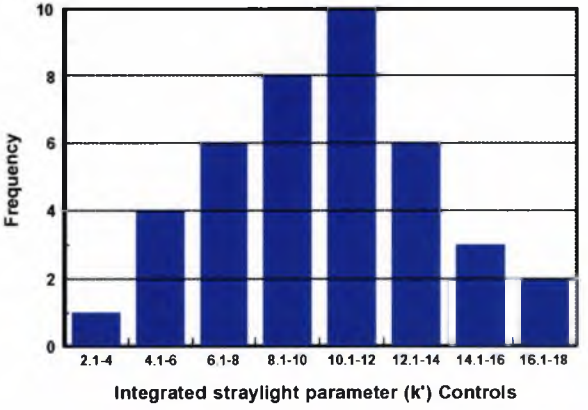

Figure B1.3: Distribution of integrated straylight parameter (control group without outliers)

B.2 LASIK Group

Anderson-Darling Test of Normality

A p value greater than 0.05 indicates a normal distribution. A p value less than 0.05 indicates a skewed distribution.

Table B-2 Data distribution for LASIK group (p values)

Parameter examined	Untransformed data – p values		Transformed data (log_{10}) – p values	
	Full data set	Without Outliers	Full data set	Without Outliers
Scatter index, n	0.001	0.001	0.000	0.000 (see figure B-1)
Straylight parameter, k	0.207 normal	0.131 normal	0.350 normal	0.351 normal
Integrated Straylight parameter, k'	0.445 normal	0.330 normal	0.523 normal	0.548 normal
Detection thresholds 1.4°	0.000	0.000	0.000	0.000
Detection thresholds 3.8°	0.001	0.001	0.004	0.003
Detection thresholds 6.7°	0.000	0.000	0.000	0.000
Detection thresholds 9.4°	0.000	0.000	0.000	0.000
Contrast Acuity 1.4°	0.000	0.032	0.245 normal	0.280 normal
Contrast Acuity 3.8°	0.000	0.000	0.194 normal	0.381 normal
Contrast Acuity 6.7°	0.003	0.066 normal	0.880 normal	0.706 normal
Contrast Acuity 9.4°	0.000	0.017	0.834 normal	0.767 normal

Distribution of measured data Appendix B

Parameter examined	Untransformed data – p values		Transformed data (log_{10}) – p values	
	Full data set	**Without Outliers**	**Full data set**	**Without Outliers**
Visual Search 16% Contrast	0.023	0.154 normal	0.186 normal	0.412 normal
Visual Search 32% Contrast	0.031	0.035	0.137 normal	0.133 normal
Visual Search 64% Contrast	0.027	0.041	0.355 normal	0.408 normal
Glimpse Duration	0.005	No outliers	0.077 normal	No outliers

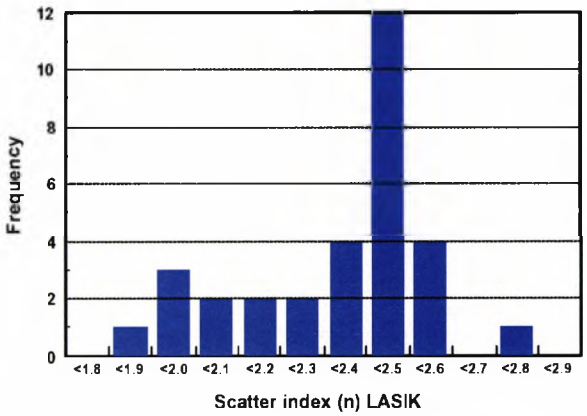

Figure B2.1: Distribution of scatter index (LASIK group without outliers)

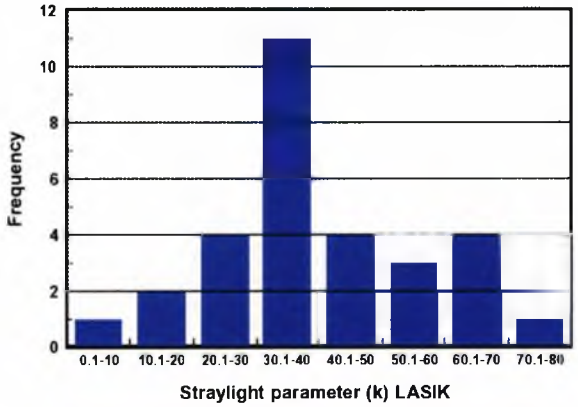

Figure B2.2: Distribution of straylight parameter (LASIK group without outliers)

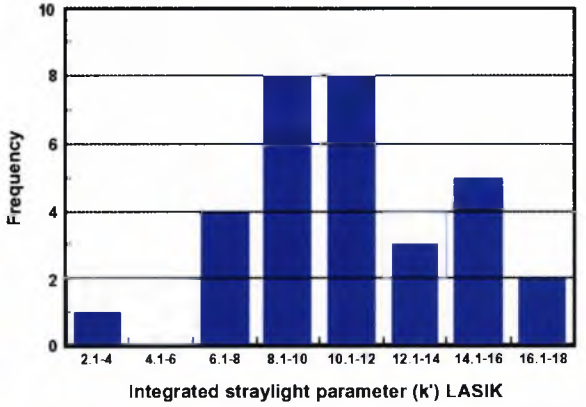

Figure B2.3: Distribution of integrated straylight parameter (LASIK group without outliers)

B.3 PRK Group

Anderson-Darling Test of Normality

A p value greater than 0.05 indicates a normal distribution. A p value less than 0.05 indicates a skewed distribution.

Table B-3 Data distribution for PRK group (p values)

Parameter examined	Untransformed data – p values		Transformed data (log_{10}) – p values	
	Full data set	**Without Outliers**	**Full data set**	**Without Outliers**
Scatter index, n	0.213 normal	0.964 normal	0.035 normal	0.941 normal
Straylight parameter, k	0.360 normal	0.530 normal	0.175 normal	0.233 normal
Integrated Straylight parameter, k'	0.000	0.910 normal	0.147 normal	0.459 normal
Detection thresholds 1.4°	0.000	0.029	0.010	0.005
Detection thresholds 3.8°	0.000	0.000	0.000	0.007
Detection thresholds 6.7°	0.000	0.000	0.002	0.007
Detection thresholds 9.4°	0.001	0.006	0.235 normal	0.319 normal
Contrast Acuity 1.4°	0.000	0.000	0.111 normal	0.325 normal
Contrast Acuity 3.8°	0.000	0.003	0.066 normal	0.636 normal
Contrast Acuity 6.7°	0.151 normal	0.553 normal	0.574 normal	0.257 normal
Contrast Acuity 9.4°	0.111 normal	0.325 normal	0.390 normal	0.511 normal

Distribution of measured data Appendix B

Parameter examined	Untransformed data – p values		Transformed data (log_{10}) – p values	
	Full data set	**Without Outliers**	**Full data set**	**Without Outliers**
Visual Search 16% Contrast	0.725 normal	0.961 normal	0.743 normal	0.758 normal
Visual Search 32% Contrast	0.102 normal	0.060 normal	0.196 normal	0.314 normal
Visual Search 64% Contrast	0.507 normal	0.524 normal	0.238 normal	0.390 normal
Glimpse Duration	0.024	0.182 normal	0.224 normal	0.459 normal

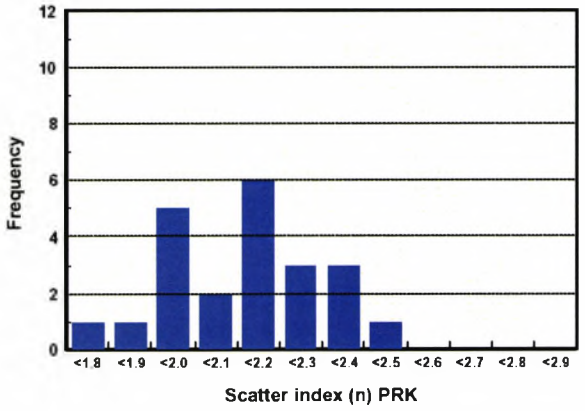

Figure B3.1: Distribution of scatter index (PRK group without outliers)

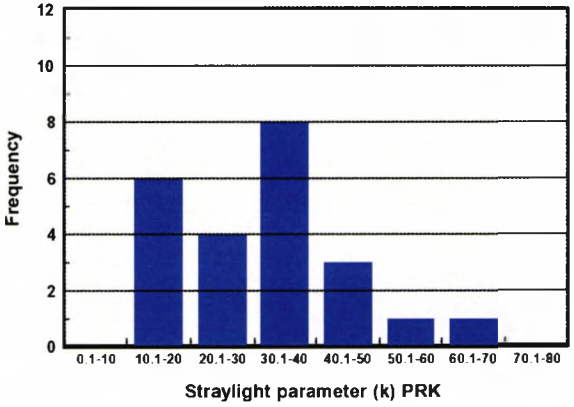

Figure B3.2: Distribution of straylight parameter (PRK group without outliers)

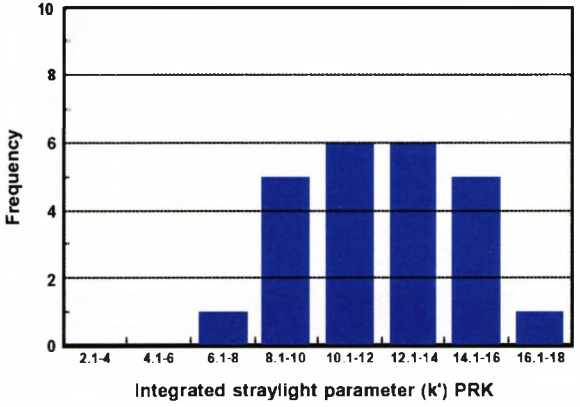

Figure B3.3: Distribution of integrated straylight parameter (PRK group without outliers)

Appendix C: Complete data sets

C.1 Scatter

The method used to assess forward light scatter in the control, LASIK and PRK groups is described in chapter 4.

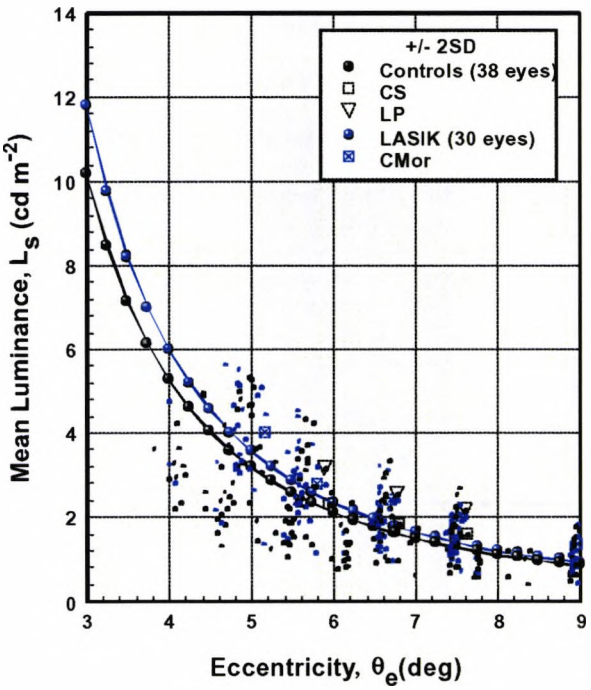

Figure C-1.1: Measured scatter data for control and LASIK groups.

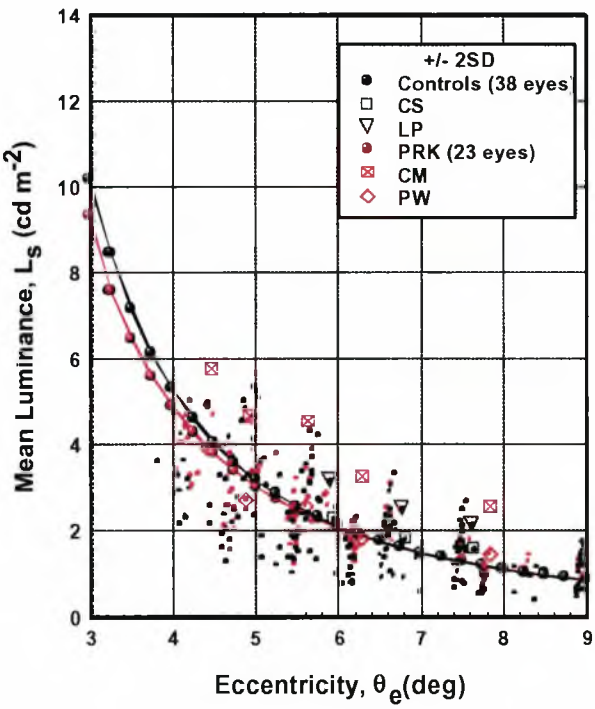

Figure C-1.2: Measured scatter data for control and PRK groups.

C.2 Absolute contrast detection thresholds

The methods used to assess the contrast detection and contrast acuity thresholds of the three subject groups are described in chapter 5.

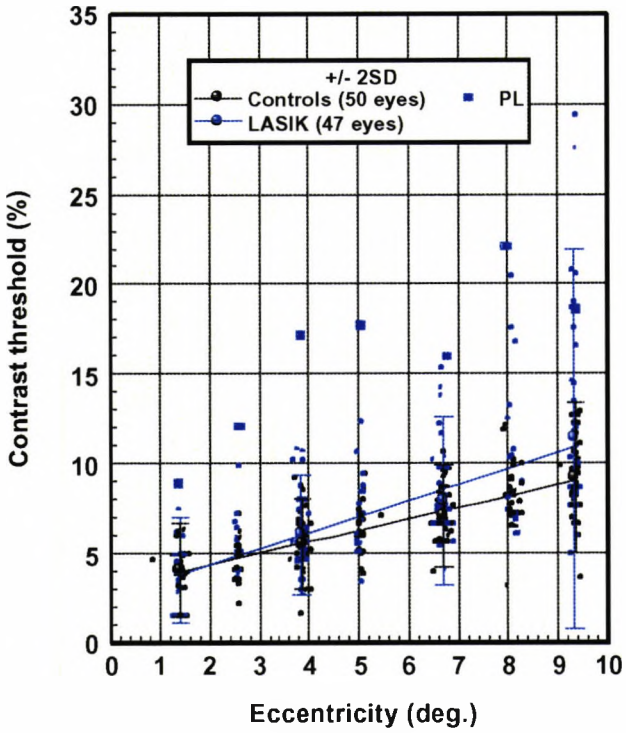

Figure C-2.1: Measured absolute contrast detection data for control and LASIK groups.

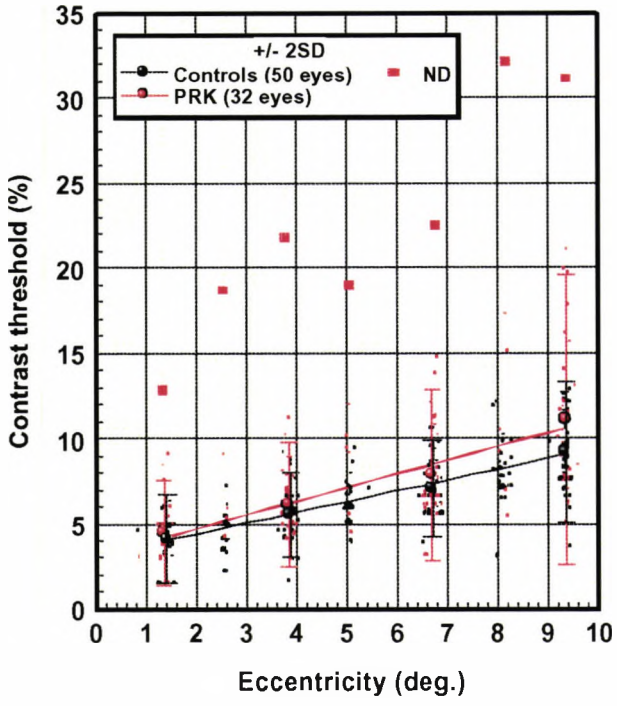

Figure C-2.2: Measured absolute contrast detection data for control and PRK groups.

C.4 Visual Search

The methods used to assess visual search performance for the three subject groups are described in chapter 6.

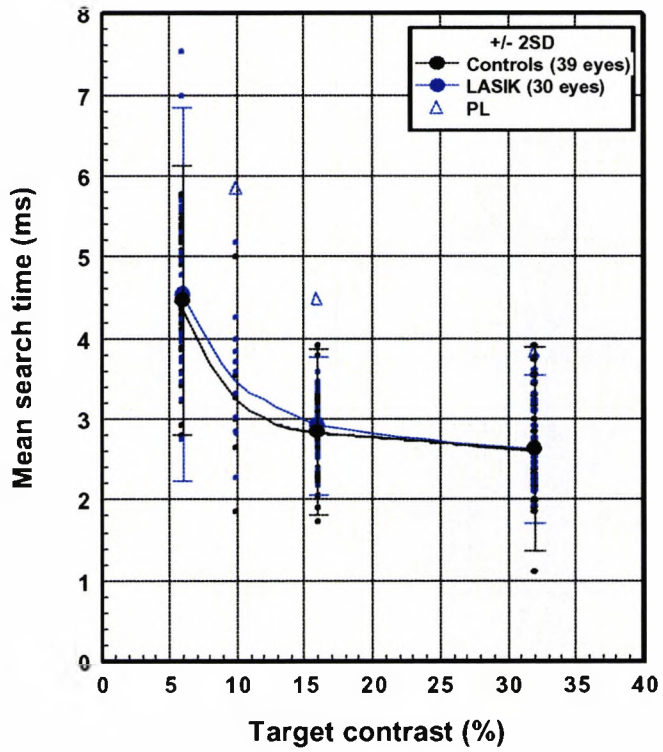

Figure C-4.1: Measured visual search data for control and LASIK groups

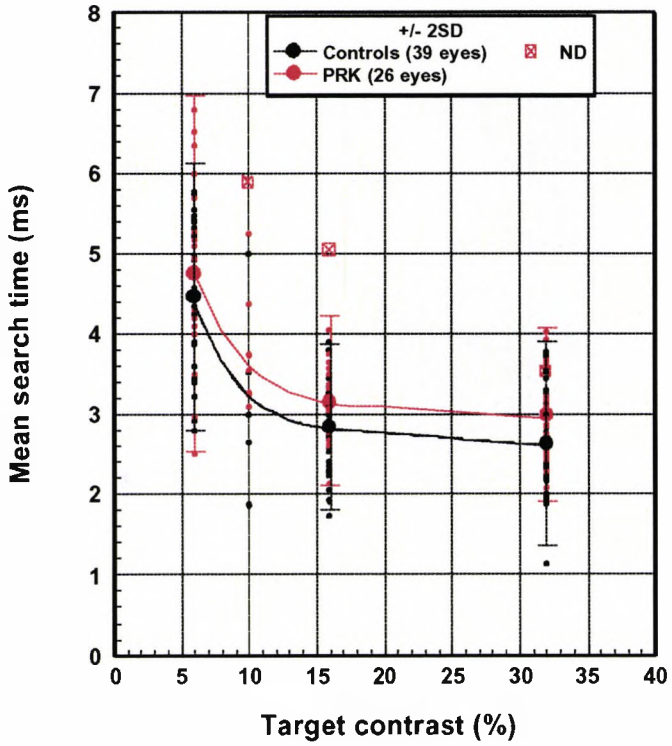

Figure C-4.2: Measured visual search data for control and PRK groups

C.3 Contrast acuity thresholds

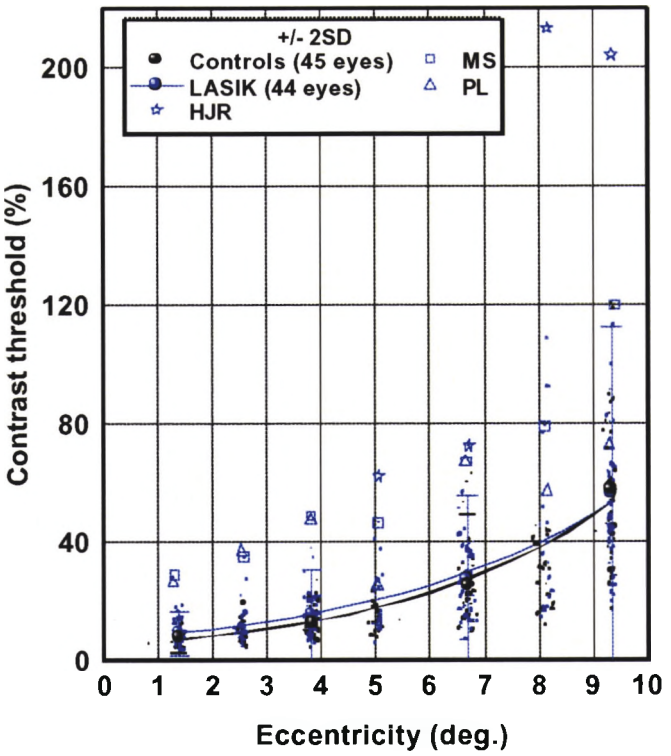

Figure C-3.1: Measured contrast acuity data for control and LASIK groups.

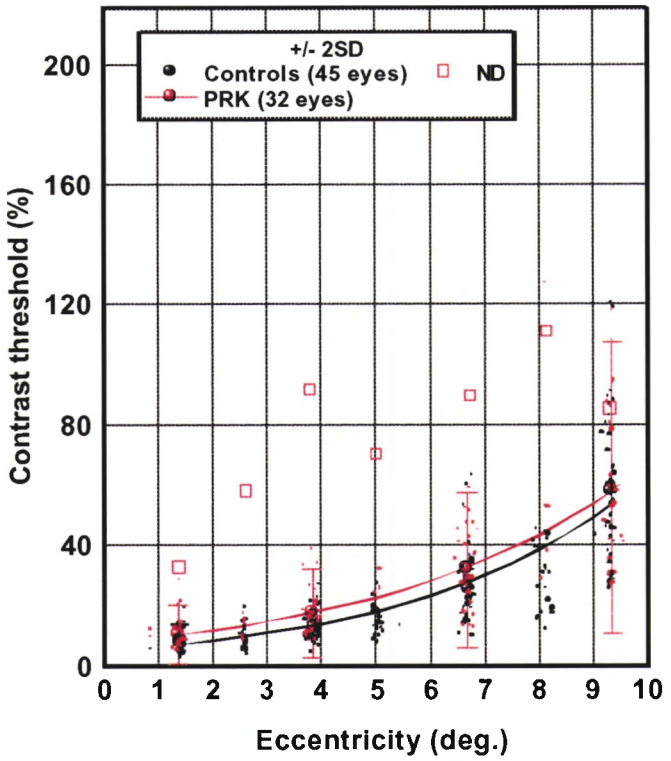

Figure C-3.2: Measured contrast acuity data for control and PRK groups.

Appendix D: Outliers

The following tables describe all subjects who were identified as outliers from their group, in one or more experiments. Data within the normal range can be assumed for all other tests unless listed as not available. Possible explanations are given based on the patient's clinical characteristics. Ablation zone and photopic pupil data indicate the diameter in each case.

D.1 Control subjects

Subject details	Outlier for test	Comments or possible explanation for outlier status
CS Age 38 Refractive error: +3.50/-1.00x180 Visual acuity: $6/6^{-1}$	Forward light scatter (low scatter index, n)	The subject found it difficult to appreciate flicker for the innermost scatter annulus leading to reduced precision at this glare angle (large standard error). This may have affected the scatter function leading to an apparently abnormal distribution of straylight.
LP Age 34 Refractive error: -6.25DS Visual acuity: 6/4 Photopic pupil: 6.4 mm	Forward light scatter (low scatter index, n)	Large pupil – scatter originating from the mid-peripheral cornea may have influenced the distribution of forward scatter, particularly since the subject was a soft contact lens wearer.

Subject details	Outlier for test	Comments or possible explanation for outlier status
PMF Age 69 Refractive error: +1.00/-0.50x105 Visual acuity: 6/6 Photopic pupil: 4.6 mm	Glimpse duration	Measured levels of forward scatter were within the normal range and significant aberrations in a normal subject are unlikely for a pupil size of 4.6mm, suggesting that optical factors are not the major cause of the increased mean glimpse duration. A reduction in the attentional field size with age (Haegerstrom-Portnoy et al., 1999) and possibly an age-related reduction in saccade speed/visual information processing speed may explain the long mean glimpse duration value.

TableD-1: Outliers from the control group

D.2 LASIK subjects

Subject details	Outlier for test	Comments or possible explanation for outlier status
CMor Age 31 Preoperative refraction: -2.50/-1.00x100 Follow-up: 11 weeks Visual acuity: 6/5 Ablation zone: 6.0 mm Photopic pupil: 6.6 mm Fine interface haze	Forward light scatter (low scatter index, n)	The appearance of low-grade inflammation (haze) in the corneal interface is likely to have influenced the scatter function of the eye. Visual performance was not affected.
HJR Age 34 Preoperative refraction: -5.00/-0.75x10 Follow-up: 1 week Visual acuity: 6/6 Ablation zone: 6.0 mm Photopic pupil: 6.5 mm Complains of poor quality night vision and halos.	Contrast acuity No visual search or glimpse data available	His symptoms are likely to be associated with the mismatch between the pupil and ablation zones, particularly under low illumination. Light is refracted by the untreated cornea. Sub-clinical flap oedema and irregularity are likely to be present at one week post-LASIK

Subject details	Outlier for test	Comments or possible explanation for outlier status
MS Age 57 Preoperative refraction: +3.50/-0.50x100 Follow-up: 1 week Visual acuity: 6/7.5 Ablation zone: 6.0 mm Photopic pupil: 4.6 mm	Contrast acuity No scatter, visual search or glimpse data available	High incidence of corneal irregularity following treatment for hypermetropia. Examined at one week post-surgery when flap oedema and irregularity are common
PL Age 42 Preoperative refraction: –8.00/-1.25x67 Follow-up: 37 months Visual acuity: $6/6^{-2}$ Ablation zone: 4.8 mm Photopic pupil: 4.1 mm	Contrast detection Contrast acuity Visual search	Subject reports poor quality vision and glare at night. Often wears rigid contact lens to improve visual quality, implicating corneal irregularity. Mean glimpse duration for subject PL within the normal range.

Table D-2 Outliers from the LASIK group

D.3 PRK subjects

Subject details	Outlier for test	Comments or possible explanation for outlier status
CM Age 41 Preoperative refraction: -2.00DS Follow-up: 10 weeks Visual acuity $6/5^{+3}$ Ablation zone: 6.5 mm Photopic pupil: 4.4 mm	Forward light scatter High integrated straylight parameter (k') and low scatter index (n)	Cornea exhibited grade 2.5 stromal haze (backscatter), which is not uncommon at 10 weeks post-PRK. This was associated with both an increase in the quantity and alteration of the distribution of forward light scatter. All measures of visual performance fell within the normal range.
ND Age 38 Preoperative refraction: -7.75/-1.25x165 Follow-up: 5 years Visual acuity: $6/9^{+2}$ Ablation zone: 5.0 mm Photopic pupil: 5.6 mm	Contrast detection Contrast acuity Visual search Glimpse duration	Measured levels of forward light scatter were normal. The pupil was larger than the treated zone. Combined with the relatively high degree of myopia treated, this subject is likely to be suffering from significant aberrations leading to a reduction in visual performance.

Subject details	Outlier for test	Comments or possible explanation for outlier status
PW Age 47 Preoperative refraction: -4.00/-0.50x170 Follow-up: 6 years Visual acuity: $6/6^{-1}$ Ablation zone: 6.0 mm Photopic pupil: 5.6 mm Grade 0.5 stromal haze	Forward light scatter (low scatter index, n)	Despite the long follow-up time, slight corneal haze (backscatter) persists. This 'scarring' is likely to be caused by alterations in the regular arrangement of collagen fibres and the deposition of abnormal collagen. It is therefore not surprising that forward light scatter is affected.

Table D-3 Outliers from the PRK group

D.4 Discussion

When considering outliers, it should be remembered that the refractive surgery subjects recruited for the study were classified by the operating surgeon as having had a successful outcome (section 3.4). Those with poor high contrast acuity associated with surgical complications were excluded.

All three refractive surgery subjects who were identified as outliers for forward scatter, also exhibited increased levels of backscatter in the form of stromal haze. Only one subject of the three (CM) was an outlier on the basis of a high integrated straylight parameter (k'). All three exhibited a reduced scatter index value (n), indicating a greater angular spread of straylight in the eye. Visual performance remained within the normal range for all three of these subjects. This suggests that changes in forward light scatter, (increased quantity of increased spread), do not necessarily lead to a significant reduction in visual performance. There is evidence that the increase in contrast acuity thresholds and visual search times exhibited by the PRK group is related to an increase in both the quantity and

distribution of forward light scatter but aberrations and small angle scatter are also likely to play an important role.

Those refractive surgery subjects who were outliers for one or more measures of visual performance had almost exclusively undergone surgery for =–5.00D of myopia. The treatment of higher degrees of myopia is associated with a greater degree of induced aberrations (Hersh et al., 1996b). In addition, topography plots indicated induced corneal irregularity in some outliers (PL and ND). No topography plot was available for subject MS although he was treated for hypermetropia, which is more likely to induce irregularity than myopic treatments due to the creation of a mid-peripheral corneal gutter. Two subjects (ND and HJR) were treated using an ablation zone smaller than their photopic pupil diameter, which would be expected to lead to a marked increase in spherical aberration. None of these subjects were outliers for forward scatter although small angle scatter cannot be ruled out as a possible explanation for reduced visual performance.

Only two subjects were outliers for absolute contrast detection thresholds since detection thresholds are relatively insensitive to optical degradation. Both subjects (ND and PL) exhibited a significant reduction in visual performance and were significant outliers for all other tests. Subjects MS and HJR were only outliers for the contrast acuity threshold test but may have been outliers for visual search performance and glimpse duration had they been available for further testing.

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