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Aspheric Intraocular Lens in Cataract Surgery

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Declaration

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Abstract

This thesis, by prior publication, encompasses an overview and critical analysis of 6 publications on aspheric intraocular lenses (IOLs) carried out at St. Thomas' Hospital, Guy's & St. Thomas' NHS Foundation Trust, London between 2006-2012. The focus is on two areas: the visual and optical performance of aspheric IOLs with different values of asphericity, and their effect on posterior capsule opacification (PCO). Chapter 1 describes the history of IOLs and the evolution of aspheric IOLs. It also presents relevant optical concepts.

The three publications presented in Chapter 2 compare aspheric IOLs with spherical IOLs. The results come from two prospective, randomised, fellow-eye comparison studies: one comparing a spherical Alcon AcrySof SN60AT versus the aspheric Alcon AcrySof SN60WF (with negative asphericity), which partially corrects corneal spherical aberrations, and the other comparing the Zeiss AcriSmart 36A (with negative asphericity), which partially corrects corneal spherical aberrations, and the Bausch & Lomb Akreos MI60 (with neutral asphericity), which has zero spherical aberration. The third publication reports changes in vertical coma after implantation of all the above lenses and additionally includes data on two spherical IOLs from a previous study by our group (the three piece Alcon MA60AC IOL and the plate haptic HumanOptic MC611MI IOL). For this study, the data were divided according to their asphericity and not design. To avoid confounding from aberrometric differences due to astigmatism and surgical techniques, standard incision sizes of 2.75 mm and 2.4 mm were used in the two fellow-eye, randomised studies and a single surgeon performed all the surgeries using same incision size for each study. Results demonstrated that the aspheric IOLs significantly reduced spherical aberration, improved mesopic contrast sensitivity and reduced depth-of-focus. Asphericity differences up to 20 μm were not associated with depth-of-focus and the degree of asphericity was not associated with best-corrected distance visual acuity. The vertical coma varied within IOL groups of the same asphericity but there was no statistically significant difference between the two spherical IOLs (AcrySof

SN60AT and AcrySof MA60AC). Further critical analysis of our data already published showed no statistically significant difference in mean vertical coma between the AcrySof MA60AC (-0.060 ± 0.211μm) with that of Akreos MI60 (-0.042 ± 0.148μm) (p=0.70) and AcriSmart 36A (-0.034 ± 0.141μm) (p=0.58) even though the AcrySof MA60AC, Akreos MI60 and AcriSmart 36A IOLs had different asphericity. This may be due to the difference in the IOL designs, decentration and difference in the sample sizes between groups.

Chapter 3 discusses the findings of three publications related to posterior capsule opacification (PCO). The first publication is an in vitro study assessing posterior optic square edges of various commercially available spherical and aspherical IOLs. Results demonstrated hydrophilic IOLs had less sharp square edges compared to hydrophobic IOLs. Although these in vitro results are potentially significant, there are currently no in vivo studies on the lenses used to compare our results with. The other two publications are based on the PCO outcomes from the prospective, randomised, fellow-eye studies described above. There was no difference in the PCO rates between hydrophobic spherical AcrySof SN60AT and aspheric AcrySof SN60WF IOLs of the same design at 2 years. In contrast, we found a significant increase in the PCO with both the hydrophilic acrylic AcriSmart 36A and Akreos MI60 IOLs (one with negative asphericity and one with neutral asphericity). Variation in asphericity did not appear to be an important factor contributing to the PCO but it was apparent that the edge design and material of the IOL were important with regards to the PCO formation.

Finally, since these publications, some of manufacturers have changed their IOL models and today a majority of the IOLs have are aspheric and have a sharp edge profile. The overall, benefit of using aspheric IOLs seems to be limited as it is dependent on the natural pupil size.

Abbreviation list

AQUA: Automated Quantification of After-Cataract

BCVA: Best Corrected Visual Acuity

DCIVA: Distance corrected intermediate visual acuity

DCNVA: Distance corrected near visual acuity

EPCO: Evaluation of Posterior Capsular Opacification

ETDRS: Early Treatment Diabetic Retinopathy Study

FACT: Functional Acuity Contrast Testing

HOA: Higher order aberration

IOL: Intraocular lens

LASIK: Laser-Assisted In-situ keratomileusis

LEC: Lens Epithelial Cells

LogMAR: Log Minimal Angle of Resolution

LSF: Line Spread Function

MTF: Modulation Transfer Function

OTF: Optical Transfer Function

PCO: Posterior Capsule Opacification

POCO: Posterior capsule opacification software

PSF: Point Spread Function

PTF: Phase Transfer Function

RCT: Randomised Control Trial

RMS: Root Mean Square

SA: Spherical Aberration

YAG: yttrium aluminum garnet

Chapter 1

Introduction

1.1 History of intraocular lenses in cataract surgery

Although several types of cataract surgeries have been performed for millennia including couching, intracapsular and extracapsular cataract surgery [1-9], the existence of sophisticated optical rehabilitation after cataract surgery with visual aids has a relatively short history. The major methods now available for correcting aphakia are spectacle correction, contact lenses and intraocular lens implants (IOLs). Spectacle correction was deemed the safest method of correcting aphakia,[10] especially in a developing world setting. Although spectacle correction is functionally not nearly as good in terms of quality of visual rehabilitation compared to contact lenses and especially to intraocular lenses (IOLs), its greater availability rendered it the preferred method of optical correction in the first half of the 20th century. Contact lenses provide optical correction for aphakia[11] with less spectacle magnification compared to the undesirably magnified and distorted (pin cushion) images with aphakic spectacles. Contact lenses and IOLs also help to eliminate the ring scotoma. However, because of the high cost of contact lenses, problems with sterilization and potential complications secondary to environmental considerations, they were not commonly used particularly in the rural populations of developing countries.

Intraocular lens implantation, introduced in England by Sir Harold Ridley in 1949/1950, has emerged as a supremely successful procedure in all industrialized countries. Ridley[9, 12-20] emphasized that the surgical removal of the cataractous lens is an incomplete cure. Significant dioptric power resides in the crystalline lens, so its removal usually results in marked hypermetropia. Ridley not only understood the tremendous optical advantages that an IOL could provide but, most importantly, he had the opportunity and fortitude to apply this knowledge.

Ridley's first operation was performed on a 45-year-old woman at St. Thomas' Hospital (Guys and St. Thomas' NHS Foundation Trust) in London. He performed an extra-capsular cataract extraction[21] and temporarily inserted and judged the sizing of the IOL. He then withdrew the lens and closed the eye without a permanent insertion. The permanent implantation of the pseudophakos was done as a secondary procedure on 8th February 1950, after he was sure that the eye was quiet and suitable for implantation. Rayner Ltd manufactured the IOL. It was a Polymethylmethaacrylate (PMMA) disc, designed to be implanted within the capsular bag.

The subsequent development of IOLs is illustrated in Figure 1.1.

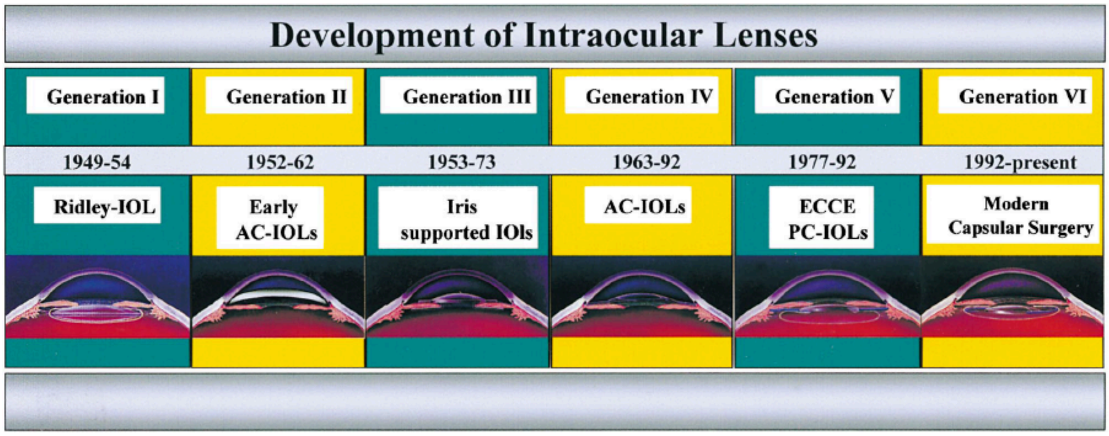


Figure 1.1. Timeline showing 6 major generations of IOLs. (Reproduced from: Evolution of Cataract Surgery and intraocular lenses (IOLs); IOL Quality. Surv Ophthalmol 2000:45:Supp 1:S53-S69)

Generation I (1949–1954) (Figure 1.1)

Ridley's first article on his IOL experience was published in 1951–1952.[12] He and his procedure were met with some hostility by his skeptical colleagues. However, good results were subsequently attained in enough cases to warrant further implantation. Other surgeons, including Warren Reese and T. Hamoi in the U.S., Edward Epstein of South Africa,[22] and S. Fyodorov of the Soviet Union continued the development making various modifications.[23] Peter Choyce, MD[24-33] who worked with Ridley on some of his earliest operations, was active in creating successful IOL designs, and he did much to enhance the acceptance of IOLs during the 1960s and 1970s when the future of implants was in doubt. Equally important, but not well known, Choyce was the first to carry out paediatric IOL implantation. Cornelius Binkhorst[34-40], deserves immense credit for his leadership in advocating the ECCE procedure[41, 42] and for re-advocating the concept of in-the-bag (capsular) fixation. These ophthalmologists provided the basis for further developments.

Generation II (1952–1962)(Figure 1.1)

Because of problems with decentration and dislocations with the Ridley lens, a new implantation site was considered—the anterior chamber, with fixation of the lens in the angle recess. This site was selected because there was little chance of dislocation. In addition, anterior chamber lenses (AC-IOLs)[15, 43-45] could be implanted after either an intracapsular cataract extraction (ICCE)[46, 47] or an ECCE. Anterior chamber placement of the pseudophakos was a relatively simpler technical procedure than placing the pseudophakos behind the iris. Unlike the original posterior chamber lens (PCIOL), the first generation of AC-IOLs was a synthesis of the ideas of many surgeons who worked on the concept at essentially the same time.[48] Baron, in France, is generally credited as the first designer and implanter of an AC-IOL. He first performed this procedure on May 13, 1952. This date marked the beginning of a long and checkered history of this lens type. Others working on this were Strampelli in Italy, Dannheim in Germany, and Ridley. New AC-IOL designs surfaced in the late 1970s and early 1980s (generation IV), with decidedly mixed results. After years of effort to improve this IOL type, much more satisfactory AC-IOLs are available (generation VI), and these were staging a comeback as a useful tool for the appropriate clinical situation. This first AC-IOL of Baron failed immediately. Predictably, the highly vaulted lens caused endothelial loss, corneal decompensation,[49] and pseudophakic bullous keratopathy, which are all conditions that have subsequently haunted numerous AC-IOL designs.[50] It took many modifications of several factors, including rigidity/flexibility, precise positioning of the optic, haptic/loop configuration,[48] and lens vaulting characteristics, to develop an AC-IOL design that would allow a reasonable prediction of long-term success. The most important advances were those of Ridley.[15] Choyce contributed greatly to the progress and development of the AC-IOL.[24-32] He designed a tissue-friendly, no-hole haptic-style footplate, and Charles Kelman[51] of New York later developed various open-loop designs that helped address the problems of IOL sizing.

Generation III (1953–1973)(Figure 1.1)

Iris-supported (iris-fixated) IOLs[52] were introduced in the late 1950s. They overcame the problems of Ridley's original PC-IOL and the AC-IOLs of the early 1950s. The displacement that sometimes occurred with the PC-IOLs and the unacceptably high rate of corneal decompensation with AC-IOLs caused some surgeons to discontinue implantation of IOLs from these first two generations (generations I and II [Fig. 1.1]). Binkhorst [34-40] was an early advocate of iris-supported IOLs. The development of his four-loop iris clip IOL was based on four premises:

1. PMMA was well tolerated within the eye, provided that it had been properly cleansed and sterilized.
2. The Ridley PC-IOL had a tendency to dislocate, leading to its disuse.
3. Most AC-IOLs were situated too close to the cornea and angle structures, and, therefore, they sometimes caused corneal decompensation.
4. Intraocular lens contact with the posterior surface of the iris did not cause complications.

Premise 4 was not entirely true, and problems with iris chafing, pupillary abnormalities, and dislocation were reported with some models of the iris-clip lens.[48] These innovations were the clear forerunners of, and, indeed, culminated in, modern capsular (in-the-bag) fixation of posterior chamber IOLs (generations V and VI).

Generation IV (1963–1992)(Figure 1.1)

While iris-supported IOLs were undergoing major modifications in the 1960s through the early 1980s, several new designs of AC-IOLs[47, 53, 54] were being introduced. Choyce continued improving his anterior chamber lens design and implanted his first Mark VIII lens in 1963. [25, 29, 31-33] This lens represented a departure from his seven earlier designs, in that it had four footplates instead of three. Strampelli had designed a four-footplate implant, that he patented, but never used. Various three- and four-point fixation, open-loop, onepiece all-PMMA designs with no positioning holes in the fixation haptics have been in use since the late 1970s and 1980s. These are the styles that work and are now being successfully implanted today. They deservedly reside in our generation VI.

Generation V (1977–1992)(Figure 1.1)

The introduction of PC-IOLS,[19, 20, 34-40, 55-62] designed to be implanted following ECCE under an operating microscope, gained momentum in the early 1970s. By 1975, John Pearce of England[57-62] began implanting a PC-IOL of this design. It was a rigid tripod design with the two inferior feet implanted in the capsular bag and the superior foot implanted in front of the anterior capsule and sutured to the iris. Dr. Steven Shearing[19, 20] of Las Vegas, Nevada, introduced a major breakthrough in early 1977 with his PC-IOL consisting of an optic with two flexible J-shaped loops. William Simcoe of Tulsa, Oklahoma, introduced his long C-looped posterior chamber lens shortly after Shearing's J-loop design appeared. Dr. Robert Sinskey of Santa Monica, California, and Dr. Richard Kratz of Newport Beach, California, and others introduced various modified J-loop designs (also termed modified C-loop by some). Dr. John Greather of Marshalltown, Iowa, and Dr. Eric Arnott of London, England, were early advocates of one-piece, all- PMMA PC-IOLs, which have become ideal choices for large-incision surgery.[63]

Generation VI (1992–2000)(Figure 1.1)

By the end of the 1980s, clinical and laboratory studies were clearly demonstrating that ECCE surgical techniques and IOL designs and manufacture had shown remarkable advancement. Older techniques, such as implantation of IOLs through can-opener capsulotomies after "simple ECCE," gave way to more modern techniques. The common denominator was and remains the achievement of safe, permanent, and secure in-the-bag (capsular) fixation of the pseudophakos. The newly developed "capsular lenses" fabricated from both rigid and soft materials,[63] along with newly perfected surgical techniques, enabled the establishment of a new generation (generation VI).

1.2 Optics

1.2.1 Measuring Optical Quality in the Eye:

1.2.1.1 Methods of assessing optical quality in the eye:

The eye, like any other optical instrument, is affected by aberrations that blur the retinal image.[64, 65] Subjects with eyes affected by large amounts of aberrations have poor spatial vision.[66] However, the impact of the eye's optical quality in subjects with excellent vision is not well understood. We may anticipate different possible scenarios: one is the idea that perfect diffraction-limited optics (zero aberrations) would produce the highest visual acuity (VA). In addition, it has also been speculated that some aberration patterns are better suited to produce good visual performance. Another option, supported by recent results showing neural adaptation to the aberrations,[67] would be that the subject's own aberrations provide the best performance. It should be pointed out that the nature and magnitude of neural adaptation is still controversial, with a recent study[68] suggesting a limited impact (approximately 12%) to the amount of higher-order aberration correction that produces the best subjective image quality.

The relationship between optical quality and visual performance has been studied in the past using computationally aberrated letters[69] and measuring VA as a function of defocus.[70] The use of adaptive-optics visual simulators provides a powerful tool to better understand this problem. The complete correction of higher-order aberrations [71] significantly improves visual performance.[72, 73]Correction of some aberration terms, in particular spherical aberration, also produces improvement in visual acuity and contrast sensitivity. [74, 75]

The three methods of assessing the visual quality, will be covered in detail below:

1) The distribution of light in the image plane is called a point-spread function (PSF) for a point source or a line spread function (LSF) for a line object. Measurements derived from these functions, such as the width (diameter of the central disc, also known as 'Airy disc') or ratio of the maximum intensity in the PSF to the diffraction-limited PSF (Strehl ratio) of

the intensity distribution can be taken as a figure of merit that captures the blurring effect.

On account of diffraction, even an ideal imaging system will have a limited spatial resolution. In the case of a uniform circular aperture, the point-spread function (PSF) is given by the Airy pattern as illustrated in the figure 1.2 below.

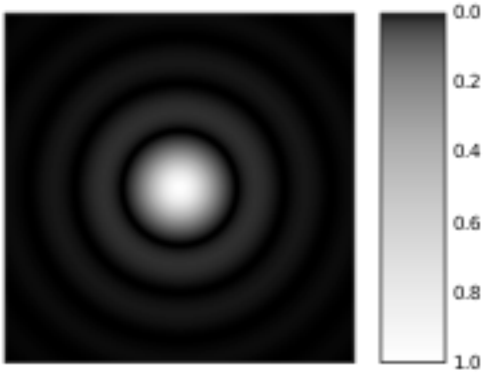


Figure 1.2. Computer generated image of the diffraction pattern from a circular aperture (Airy pattern)

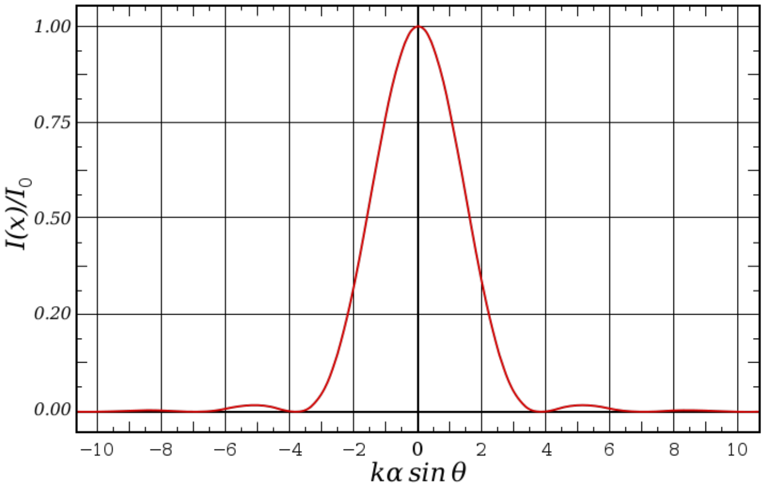


Figure 1.3. Light distribution in the Airy pattern as a function of normalized radius.

The peak intensity found at the centre of the Airy disc is the reference when calculating the Strehl ratio since it represents the maximum light intensity for the diffraction-limited case (Figure 1.3). An imperfect (aberrated) optical system, using the same physical aperture, will produce a broader PSF in which the peak intensity is reduced. The ratio of this reduced peak intensity to the diffraction-limited peak intensity is the Strehl ratio. An optical system with only minor imperfections in this sense may be referred to as "diffraction limited" as its PSF closely resembles the Airy pattern; a Strehl ratio of greater than 0.8 is frequently cited as a criterion for the use of that designation.

2) The second method quantifies the loss of contrast suffered when an image of a sinusoidal grating object is formed. The sinusoidal grating is a very useful object in optics because it contains a single spatial frequency unlike letters or more general objects. Thus, gratings allow the frequency response of the imaging system to be investigated and, in particular, its effect on just two parameters: contrast and phase. The ratio of image contrast to object contrast captures the blurring effects of diffraction and aberrations, and the variation of this ratio with spatial frequency and orientation of the grating object is called the modulation transfer function (MTF). The difference between the spatial phase of the image and the phase of the object captures the prismatic displacements induced by optical imperfections. The variation of this phase function with spatial frequency and orientation of the grating object is called the phase transfer function (PTF). Taken together, MTF and PTF define the optical transfer function (OTF) of an imaging system. Given these characterizations of an imaging system, one may use optical theory to compute the expected retinal image for any object, thus overcoming the great handicap imposed on clinicians and visual scientist by the inaccessibility of the retinal image in vivo.

3) The third method is to specify optical quality in terms of underlying optical aberrations rather than the secondary effect of those aberrations on the image quality. Such description may be made in terms of the deviation of light rays from ideal (paraxial) rays (ray aberrations) or in terms of the deviation of the optical wavefront from the ideal reference wavefront (wavefront aberrations), as is the case for most aberrometers (e.g. Hartmann-Shack). Ray and wavefront aberrations can be used to derive other measures of optical quality described above (PSF, LSF, MTF, PTF and OTF). The interdependency of these metrics has been noted in this chapter. Expressing wavefront aberrations mathematically, using Zernike polynomials, is arguably

the most useful approach for customised Excimer laser ablations since correcting any aberration reduces the root mean square wavefront aberration and improves the optical quality. It is now possible to calculate the MTF and PSF from wavefront aberrometers, which often also incorporate a topographer and autorefractor (eg. OPD Scan, NIDEK, Japan).

1.2.1.2 Principles of wavefront aberrometry:

In geometrical optics, light is considered to propagate as rays from a point source radiating in all directions. Alternatively, it is possible to consider wavefronts propagating through optical systems. These are surfaces of constant phase and to a good approximation, these surfaces are perpendicular to rays. It is, therefore, possible to consider them as surfaces at a constant optical distance from the source. For example, and importantly for the eye, an ideal wavefront from an infinitely distant source is plane such as the wavefronts emanating from an emmetropic ideal eye.

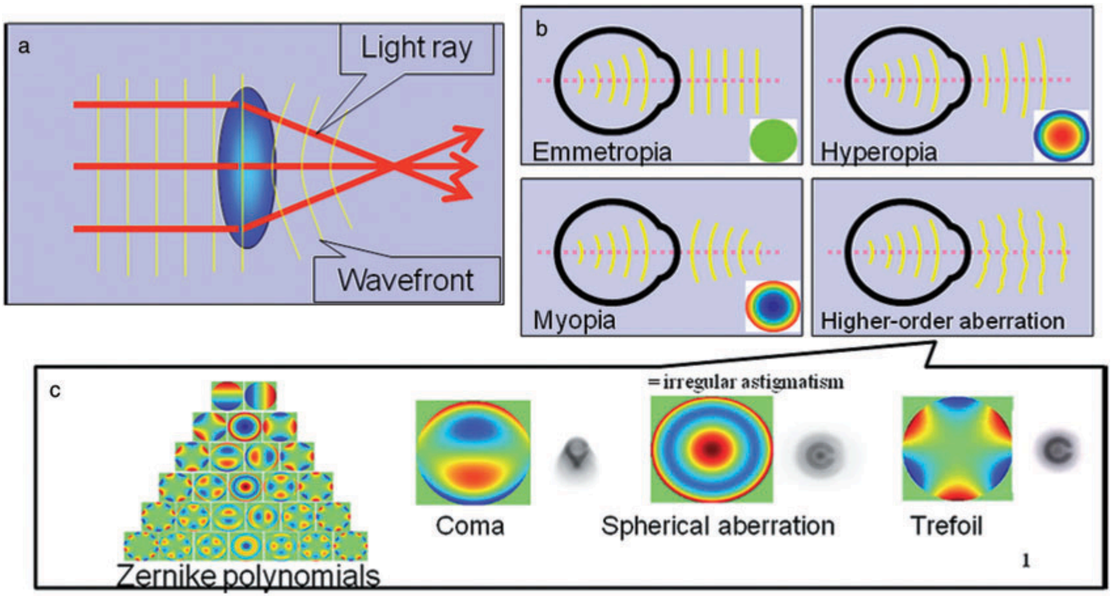


Figure 1.4. The differences in the concepts of a lens or an optical system in geometrical and physical optics (a). Effect of refractive errors on the wavefront (b). The wavefront of the perfect eye, that is an emmetropic eye without any aberrations, is shown as a perfect plane that is perpendicular to the line of sight. The wavefront in a myopic eye has a bowl-like (concave) shape with the peripheral wavefront more advanced than the central wavefront. The wavefront of the hyperopic eye has a hill-shape (convex shape) with the central wavefront more advanced than the peripheral wavefront. The wavefront of an eye with irregular astigmatism has an irregular and complex shape. The first to sixth orders Zernike

polynomials shown graphically (c). *(Reproduced from: Maeda N. Wavefront technology in ophthalmology. Curr Opin Ophthalmol 2001;12(4):294-9.)*

Although a lens is usually defined as the object that refracts the light rays (Figure 1.4a), it can also be considered as the one that transforms the shape of the wavefront. The refractive status of the eye, for example emmetropia, myopia, hyperopia and eyes with HOAs (irregular astigmatism), can be described using wavefronts as shown in Figure 1.4b.

The unit for wavefront aberrations is microns or fractions of wavelengths and this varies across the pupil, giving rise to wavefront aberration maps (figure. 1.4c). A summary measure of the overall wavefront aberration is the root mean square [76] of the wavefront errors and this is related to the Strehl ratio and other image quality measures. The purpose of wavefront analysis of the eye is to evaluate the optical quality of the eye. For this, an aberrometer or wavefront sensor is used. A corneal topographer is often used for measuring the corneal wavefront aberrations but it only estimates total corneal wavefront aberrations, as it does not consider differences in refractive indices in the epithelium and stroma or the corneal back surface.

Aberrometers are usually classified into three types.

1) The first type is based on wavefront sensing as in the Hartmann–Shack devices.[77]
2) The second type is the retinal imaging aberrometer as in the cross-cylinder aberrometer,[78] the Tscherning aberroscope[79] and the sequential retinal ray tracing method.[80]
3) The third type is a subjective aberrometer as in the spatially resolved refractometer[81] and the optical path difference method.[82]

The shape of the wavefront can be analysed by expanding it into sets of Zernike polynomials. The Zernike polynomials are a combination of independent trigonometric functions that are appropriate for describing the wavefront aberrations because of their orthogonality. The first six radial orders are shown graphically in Figures 1.4c and 1.5. The zero order has one term that represents a constant. The first order has two terms that represent tilt for the x and y axes. The second order includes three terms that represent defocus and regular astigmatism in two directions. The third order has four terms that represent coma and trefoil and, similarly, the fourth order has five terms that represent tetrafoil, secondary astigmatism and spherical aberration.

Figure 1.5 shows the expansion of Zernike terms in its usual pyramid, which is a function of the term's radial degree (or order) **n** and azimuthal frequency **m**. It is the basis for classifying aberrations as lower-order ($n \leq 2$) and higher-order ($n > 2$) in ophthalmology. Figure 1.5 shows the top 20 terms. At left: associated Zernike terms and names of aberrations; definition of the so called j-number (commonly referred to as mode), the polynomial ordering number, which is dependent on **n** (radial frequency) and **m** (angular frequency). In full notation, each term is identified in double-index notation by $\mathbf{Z_n^m}$. Finally, in so-called single-index notation, a term can be identified by its polynomial number (**j**), as $\mathbf{Z_j}$,

The individual Zernike polynomials represent a pattern for a particular aberration but not how much of that aberration is present. The amount is determined by the Zernike coefficient, which is a multiplier for the corresponding Zernike polynomial. It is a property of Zernike polynomials that the square root of the sum of the squares of the coefficients equals the RMS wavefront error. As a result any non-zero coefficient acts to increase the RMS wavefront error.

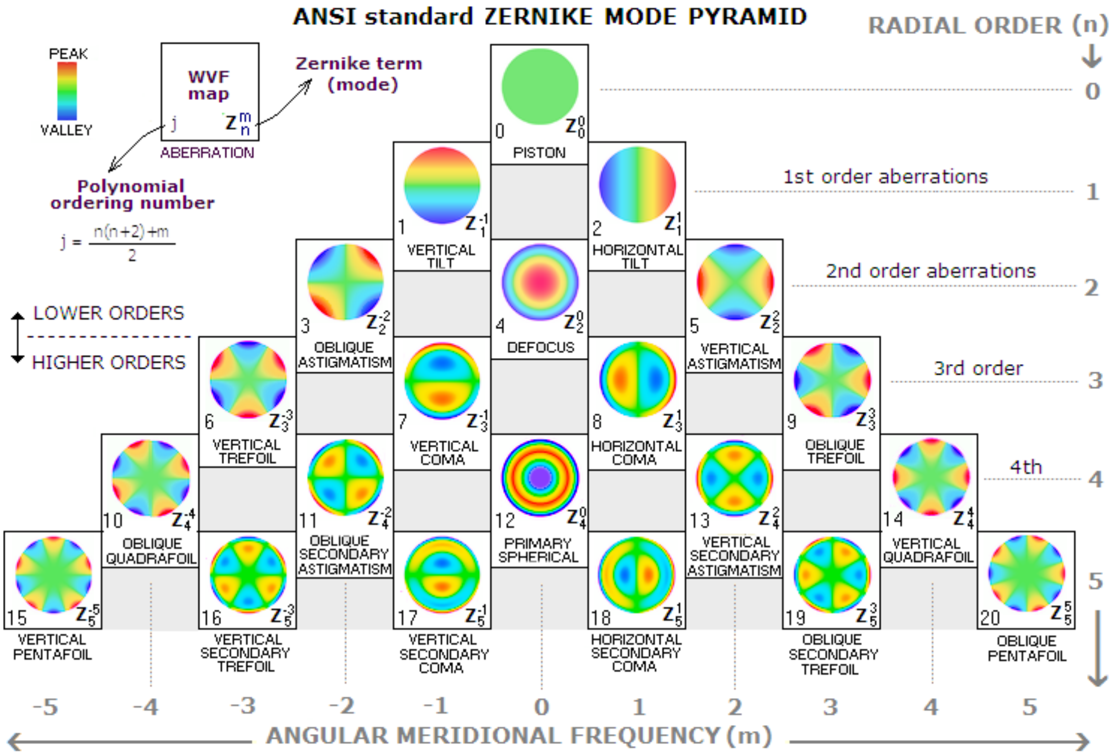


Figure 1.5. Zernike terms expansion pyramid *(Reproduced from: http://www.telescope-optics.net/monochromatic_eye_aberrations.htm)*

The polynomials can be expanded up to any arbitrary order if a sufficient number of measurements are made for the calculations. Spectacles can correct for only the second-order aberrations and not the higher-order aberrations. It should be noted that the above description applies to a single wavelength and therefore assesses the monochromatic aberrations.

It is essential to quantify the wavefront aberrations of the eye for planning surgical treatment using either the Zernike expansion or an alternative approach e.g. Fourier. The aberration coefficients can also be used to diagnose and quantify visual symptoms due to HOAs. Wavefront aberrations caused by the anterior and/or posterior corneal surfaces can be calculated using the height data of the corneal topographers.[83] Video-keratoscopes do not produce accurate height data whereas slit-scanning topographers can, but have problems with light scatter causing inaccuracies.[83] This allows relative contributions of aberrations to be assessed from cornea and lens, the major refracting elements of the eye.[83]

1.2.1.3 Aberrometry and the iTrace Dynamic Laser Refraction System

Clearly, it is not possible to directly access the retina to assess retinal image quality in the *in vivo* eye, therefore, to measure ocular aberrations, light is projected into the eye and the reflected light analysed in a double-pass phenomenon. Much work has been done to assess aberrometers and the potential error of a double pass system because a single pass of the optics creates the normal retinal image. Hartmann-Shack devices are mostly one and a half pass and use a narrow pupil for the incident beam to avoid inherent problems in double-pass systems where both the incident and outgoing beams are aberrated.

We used the iTrace aberrometer (Tracey Technologies USA), is based on laser ray tracing, which is a one and a half pass system because the laser enters the eye through a narrow aperture (the beam diameter) but exits using the whole pupil. The wavefront aberrations, PSF, MTF, and corneal topography were measured with the iTrace Dynamic Laserefraction System with Vista attachment (Tracey Technologies, USA). The iTrace aberrometer makes open-field monocular measurements by projecting a near infrared beam into the eye, which scans across the pupil. The infrared reflected out of the eye is analysed to determine the refractive error, wavefront aberration, PSF and MTF.

There are some potential advantages to the laser ray tracing approach used in the iTrace. One advantage is the sequential capture of data. This means that there is no confusion in the analysis as each point is processed separately and sequentially. Second, the pattern of laser beams projected through the entrance pupil adapts to the pupil's size; the iTrace gauges the pupil size and projects all 256 points into a pupil as small as 2.5 mm or as large as 8 mm. The third advantage is that since each point is measured separately using linear detectors, the accuracy of measuring the centre of each point increases in comparison to other aberrometers. A fourth advantage of ray tracing over other aberrometric principles is that the x-y scanner can be programmed to project any other rectilinear or polar pattern.[84]

There are many studies comparing aberrometers.[85-90] In a study carried out by Liang et al.[87], three Hartmann-Shack aberrometers were compared (WaveScan, Zywave and Ladarwave). Discrepancies were found in higher-order aberration measurements.[87] In a comparative study between the iTrace and automatic retinoscopy (Nidek OPD-Scan), important differences between the measurements of these two aberrometers were noted with the iTrace values for higher-order aberrations found to be higher. The sequential ray-tracing used in the iTrace instrument may produce less error in eyes with large aberrations compared to the Hartmann-Shack device.[88] The iTrace has also been shown to take measurements more quickly than the OPD-Scan and with less susceptibility to eye motion and tear-film artefacts.[88]

A comparative study of 6 aberrometers (iTrace, OPD-Scan, Zywave, WASCA, Multi-Spot Hartmann and Tscherning) concluded that, generally, all aberrometers produced comparable results but those which examine less than 70 data points in a 6 mm pupil had a greater variance in their measurements.[86] A further study comparing the iTrace to a Hartmann-Shack aberrometer concluded that the alignment of the aberrometer, the size of the pupil and how it compensates the accommodation, are very important.
It has also been reported that Hartmann-Shack devices can suffer from

saturation problems in corneas with high aberrations.[91] However, Xu et al,[90] assessed the precision and agreement of measurements of HOAs obtained with a ray tracing aberrometer (iTrace) and a Hartmann-Shack aberrometer (Topcon KR-1 W). They found ray tracing and Hartmann-Shack method aberrometers provided excellent repeatability but less reliable reproducibility in the measurement of HOAs (except for spherical aberration- SA). Therefore they concluded that the two aberrometers should not be interchangeable in clinical application because of the significant differences in HOA measurements between them. The system noise of the instruments may be partially responsible for the measurement inconsistency. Some researchers noted that the ray-tracing aberrometers (iTrace) may be less sensitive when measuring low values of aberrations but have more advantages when measuring high values of aberrations, compared with the Hartmann-Shack aberrometers.[90, 92] The reason may be that the ray-tracing aberrometers operate by detecting individual retinal spots, while the Hartmann-Shack aberrometers operate by detecting all the retinal spots at the same time. Thus, the ray-tracing aberrometers should be more reliable when these retinal spots are substantially larger than the instrument noise.[92] In addition to the instrument noise, there are some other factors that may account for the decreased repeatability in intra-subject measurements over time and inter-subject variability. These factors include fluctuations of accommodation, tear film changes, eye movements, etc.[93, 94] Researchers have already found that the wavefront aberrations of the eye are not static but are instead dynamic. This could be due to several reasons. The first is due to the triad of accommodation, pupil constriction and convergence, particularly in eyes with low refractive errors.[95] Dynamic changes in tear film thickness in front of the cornea could also influence the fluctuations of HOAs, which could be due to evaporation, blinking[96] and disruption of the tear film. Decreased repeatability could also be correlated to eye movements because of very slight changes in fixation.[97] It should be noted that Ray Tracing aberrometers also tend to give larger HOA values than aberrometers based on other principles. In Visser's study[89], the SA value obtained with iTrace was 0.064 ± 0.076 μm, which was significantly higher than the value obtained with an aberrometer based on the principle of slit skiascopy (OPD-Scan).[82]. Visser et al.[89] found total ocular and corneal aberrations are not comparable when measured with different aberrometers and Hartmann-Shack aberrometers showed the best repeatability for total ocular aberrations whereas iTrace for corneal aberrations. Similar results were also found in the study by Won et al.,[98] in which the ocular SA obtained with iTrace (0.038 ± 0.043 um) was significantly higher than that obtained with the OPD-Scan (0.011 ± 0.039 μm, $P < 0.001$). So were the internal coma and trefoil. Similar results were also obtained when comparing iTrace with a Tscherning Aberrometer (WaveLight).[86]

In summary, there is broad agreement between studies that wavefront total RMS values are comparable between the different aberrometers but, when higher-order aberrations are analysed, wide differences exist. Different results are found even when comparing aberrometers based on the same technology. The Hartmann-shack method uses a lenslet array to sample a large number of points across the pupil. However, Hartmann-shack aberrometry has been shown to be more difficult in highly aberrant eyes due to the crossover of spots from a lenslet to a neighboring lenslet with increasing aberrations.[99] The ray-tracing method uses sequential measurements and may therefore be more suitable to measure highly aberrant eyes.[89]

1.2.1.4 Wavefront aberrations with respect to lens and pupil size:

a) Spherical aberration and human optical system.

Almost all optical systems, whether man-made or natural, have aberrations. If an optical system is rotationally symmetric about the optical axis, it can only have spherical aberration. Therefore, if the human eye were rotationally symmetric, the only aberrations at the fovea would be spherical. However, the eye is not rotationally symmetric and the fovea is not on the optical axis. Therefore, we would expect to find other aberrations as well as spherical aberration. Measurements have confirmed these findings.[100]

Spherical aberration is included within the high order aberrations, specifically in the group of fourth order aberrations, along with quatrefoil and secondary astigmatism (Figure 1.5). Spherical aberration is the variation of cousing distance with aperture and can reduce retinal image contrast and visual quality, especially under mesopic conditions.[101] The average spherical aberration of the anterior cornea surface is positive (between +0.27 and +0.30 µm), remaining stable throughout life. The natural crystalline compensates for this positive spherical aberration, inducing a negative spherical aberration of –0.20 µm, leaving a slightly positive total aberration of +0.10 µm. Spherical aberration of the lens changes over time unlike spherical aberration of the cornea, going from negative to positive as the lens changes. This positive spherical aberration lens adds to the positive spherical aberration of the cornea, potentially impairing the visual quality of patients. Based on this concept, intraocular lenses were developed with negative spherical aberration, which simulate a young lens and can compensate for the average positive spherical aberration of the cornea. Some studies suggest that it is not necessary to correct spherical aberration completely, and in fact it is recommended to leave a slightly positive residual (+0.10 µm). A study performed on pilots of the American Air Force by Grimson et al. suggests that positive spherical aberration can be correlated with visual acuities of 20/15 or better.[102] It is impossible to completely correct the spherical aberration in all our patients as there is an interaction between much more complex aberrations than a sum of the existing spherical aberration and the intraocular lens induced aberration. Nevertheless, the objective must be directed to a final low spherical aberration, which allows the patient good contrast sensitivity. In the clinical practice, we find that the corneal spherical aberration varies greatly among individuals, especially in the presence of pathological corneas or modified ones by post-refractive surgery. In a myopic treatment with excimer laser, a central flattening of the cornea is induced, generating an oblate cornea, more flat in the center than in the periphery, inducing a positive spherical aberration (Figure 1.6).

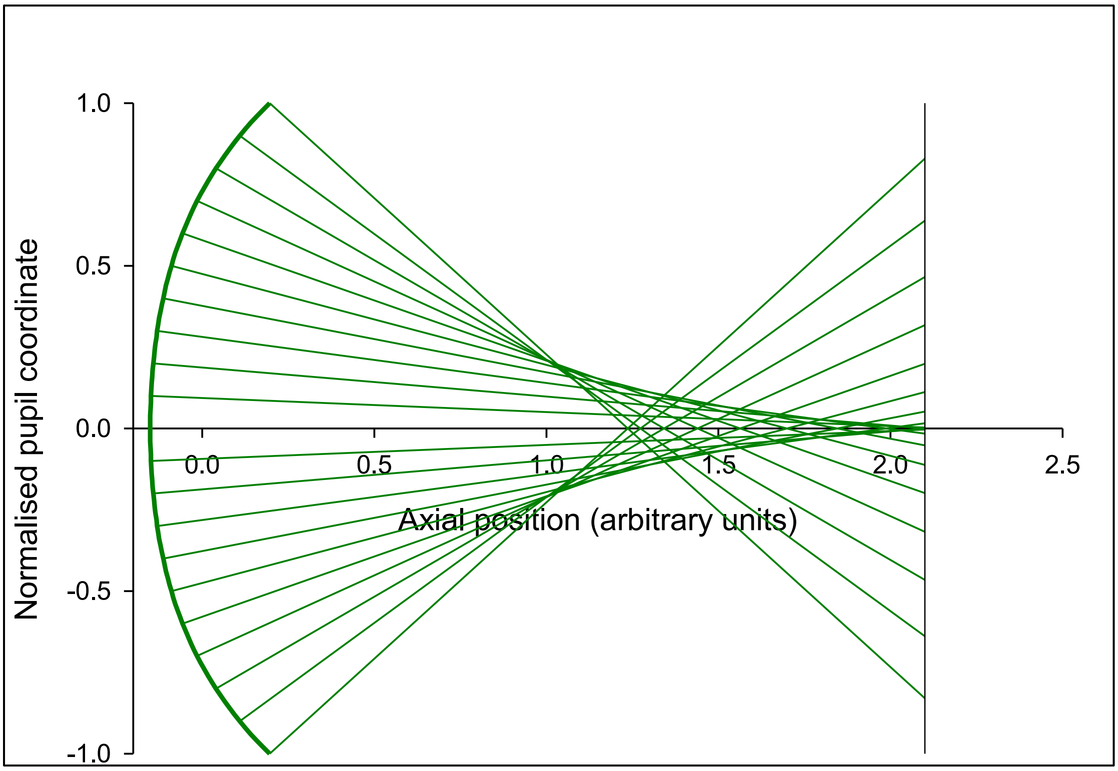


Figure 1.6. Wavefront and associated rays for positive spherical aberration. Z_2^0 = 0.1 and Z_4^0 = +0.01 (arbitrary units)

In contrast, a hypermetropic correction increases the central curvature of the anterior surface of the cornea, generating a hyperprolate cornea, inducing greater negative spherical aberration (Figure 1.7) that may contraindicate the use of an aspheric intraocular lens because instead of correcting it would worsen the existing spherical negative aberration, deteriorating the quality of vision.

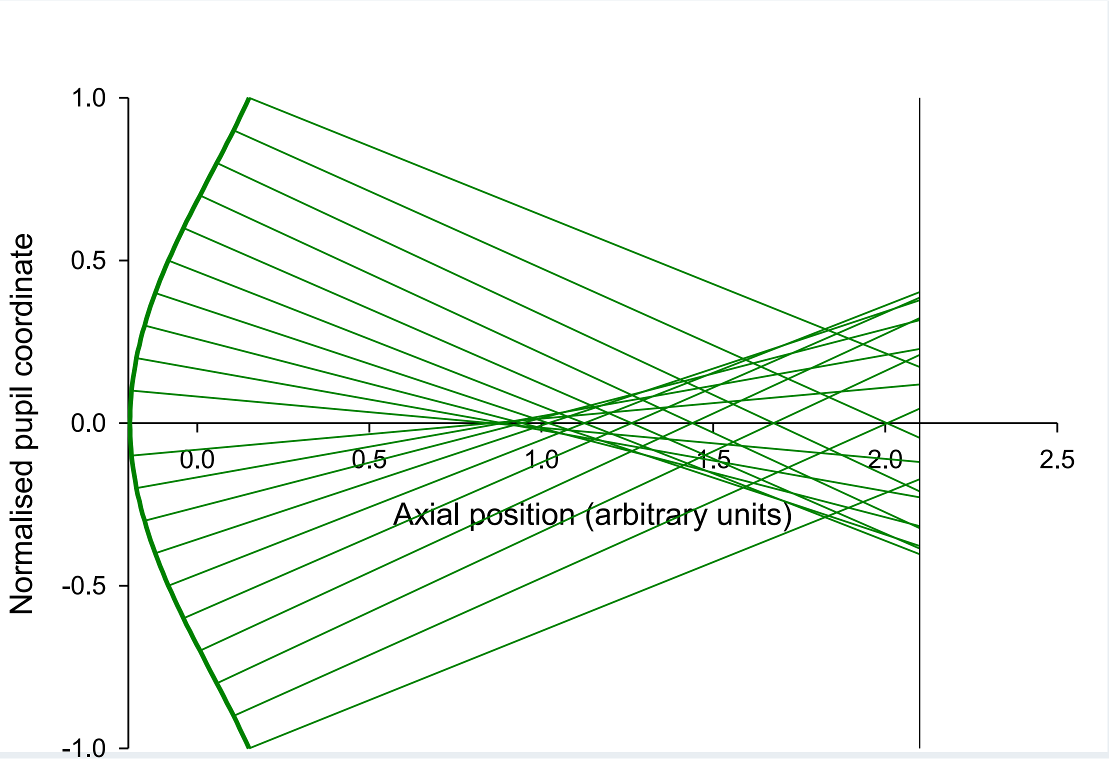


Figure 1.7 Wavefront and associated rays for negative spherical aberration. Z_2^0 = 0.1 and Z_4^0 = -0.01 (arbitrary units)

It is important to differentiate spherical aberration from corneal asphericity. Both are related but different. Asphericity quantifies how much the cornea is peripherally flattened (prolate) or steepened (oblate) from the corneal apex. Common measures of asphericity are the eccentricity, p-value or asphericity, Q. A cornea with a Q of –0.20 is not the same as a cornea with a Q of –0.45; in both cases the cornea is prolate, but the prolateness of the second case is greater, which means that the surface has a radius of peripheral curvature more flat than the first. A normal aspheric cornea has a Q factor between –0.20 and –0.45; a Q of zero would correspond to a completely spherical cornea, and a Q greater than zero corresponds to an oblate cornea. A hyperprolate cornea is considered to have a Q factor >0.6. The asphericity affects the spherical aberration with the normal human cornea having positive spherical aberration that can become negative for hyperprolate corneas. Any corneal topographer nowadays will give us the Q value. Intraocular lenses can induce positive spherical aberration, be neutral or induce negative spherical aberration to combine with the spherical aberration of the cornea.

The 'spherical' aberration of the unaccommodated eye as a whole is positive and this has been confirmed in studies.[100, 103] This is not surprising because an optical system with positive power tends to have positive spherical aberration and the aberration can be made negative only by using negative power components or aspheric surfaces or a gradient refractive index medium. The only negative power component of the eye is the posterior surface of the cornea but its power is too low to cause the aberration to go negative.[100] However, it is possible that the gradient refractive index of the lens may play an important role in the ocular aberrations.[100]

There have been a number of attempts to determine the corneal and lenticular contributions to the overall ocular aberration. [104-110] Jenkins[104] examined the lenticular aberrations of 12 subjects and found that the lenticular spherical aberration was approximately zero. El Hage and Berny[105] found that the lens had a negative spherical aberration but their single subject's corneal contribution was unusually high in a positive direction and way outside the expected range. Millodot and Sivak[109] found that the lenticular aberration was positive and similar to that of the cornea. Sivak and Kreuze[107] and Tomlinson et al.[108], found cases of both positive and negative lenticular spherical aberration, with the majority in the latter study being negative spherical aberration. Glasser and Campbell[106] found that the aberrations of younger lenses were negative and the aberrations of older lenses were positive. Smith et al.[111] studied 26 subjects and found that the lenticular aberration was negative and age-dependent, and becoming less negative with age.

The above measurements of the aberrations of the lens are difficult and contain some unavoidable errors and uncertainties, which may partly explain the range of results, although some variation is due to inter-subject variation. One can classify the methods as *in vivo* or *in vitro*. In the *in vivo* methods, one usually measures the whole eye aberration and the corneal aberration separately and the difference is the lenticular aberration. The aberration of the whole eye is measured directly (for example, with a Hartmann-Shack aberrometer). The aberrations of the cornea are calculated from its measured shape.[111] However, some investigators[105, 108, 109] took only the anterior corneal surface contribution into account and neglected the posterior surface contribution. It was assumed that this value was sufficiently low to be ignored. However, to reach aberration levels found in real eyes, Liou and Brennan,[112] in developing their model eye, had to take this contribution into account. With the *in vitro* methods, laser beams are directed through the lens which is immersed in some suitable medium. Often the incident vergence of the rays inside the eye is neglected and the rays are parallel to the axis, simulating an object at infinity. With this method, it is important to be aware that the aberrations of a lens depend on the conjugates and if the object is taken at infinity, the cornea forms the image in its back focal plane, which is about 33 mm behind it. Taking into account the anterior chamber depth of 3 mm, this puts the effective object for the lens at 30 mm behind the anterior surface and not at infinity.

Therefore, to measure the spherical aberration of a lens by the laser beam method, one should have the incident beams converging to a point about 30 mm behind the lens.[100] Alternatively, it should be demonstrated first that the spherical aberration of the lens is not sensitive to the vergence of the incident beam. Furthermore, with these in vitro methods, one has to control any change in shape of the lens in vitro, to avoid any accommodation.[100] There is strong evidence that the aberration of the eye as a whole moves in the negative direction as the eye accommodate[103, 104, 113, 114] and in fact is negative for accommodation levels greater than about 3.00 D. Using aberration theory, we can show that this change cannot come about by any change in corneal aberration with accommodation.

Accommodation is the increase in the power of the eye with an effort to focus at near. It is believed that this change in power is due to changes an increase in curvature of the crystalline lens in response to contraction of the ciliary muscle. But there is some evidence that cornea may also be contributing to these accommodative changes. The cornea is the most important refractive component of the eye, and even slight corneal changes can result in changes in vision and particularly in near vision. Conventionally it had been thought that the cornea was rigid, although some investigators proposed that the cornea had elasticity and could undergo change.[115]. In a study by Ni et al.[116], significant changes were found in the corneal curvature map with accommodation in both young and presbyopic groups, although individual variations were detected. Their results clearly showed that there were changes in corneal volumes in both young and presbyopic groups after accommodation at three zones (3.0, 5.0 and 7.0 mm zones), especially at the largest zone diameter.[116] They also observed a significant decrease in wavefront HOAs in the anterior and entire cornea with accommodation.[116] It has been suggested that the absence of HOAs induced by an adaptive optics system could result in a more accurate accommodative response.[117] Ni et al.[116] proposed that the decline in HOAs of the cornea represented a tendency to assist accommodation. Accommodation appears to induce corneal aberrations change; the spherical aberration (Z_4^0) was found to statistically significantly decrease during accommodation in anterior and entire cornea, particularly in the young group. Gambra et al.[117] demonstrated that increased aberrations, especially spherical aberration, decreased the accommodative gain. Other studies found that spherical aberration (Z_4^0) became more negative with accommodation for the whole eye.[71],[118] Since 1959, the action of extraocular muscle on cornea during accommodation was proposed.[119] The contraction of ciliary muscle was also regarded as a possible cause of the corneal changes.[120, 121] As an alternative explanation, it was suggested that intraocular pressure increased during initial accommodation, perhaps having a mild effect on the elastic cornea.[115],[122] Moreover, another study by Pierscionek et al.[123] suggested that accommodation might have some effect on corneal shape. Anatomically, it is feasible that movement of the ciliary muscle could exert slight effect on the lens, as some of the muscle fibres are in contact with the anterior sclera, which in tum extends into the cornea.[123] However, they performed the measurement over the central cornea, where any residual shape change translated to the sclera from the pull of the ciliary muscle would be least evident. The mere fact that they noted some change in the centre, the point furthest from the force, which instigated the shape change, suggests that a greater change in shape would have been found in the periphery. In terms of effect on vision, this peripheral corneal change is of course of little, if any, consequence.[123] What is of significance is that the cornea possesses sufficient malleability to deform under the action of the ciliary muscle. The suggestion was made that corneal topography may be altered either as a result of extraocular muscle tension or because of intraocular pressure.[123] It is reasonable to conclude that the change of corneal aberrations indicates that the corneal shape has changed too, and this change is beneficial for accommodation.[116, 123]

b) Coma in the human eye

Coma is the variation in magnification with aperture and occurs when a bundle of light rays enters an optical system from an off axis object if the optical system is rotationally symmetric. It can also occur on axis if there isn’t a common optical axis. Coma results in the image of an off-axis point source appearing distorted, with a comet-like tail, hence the name “coma.” Coma can be both negative (Figure 1.8) and positive (Figure 1.9).

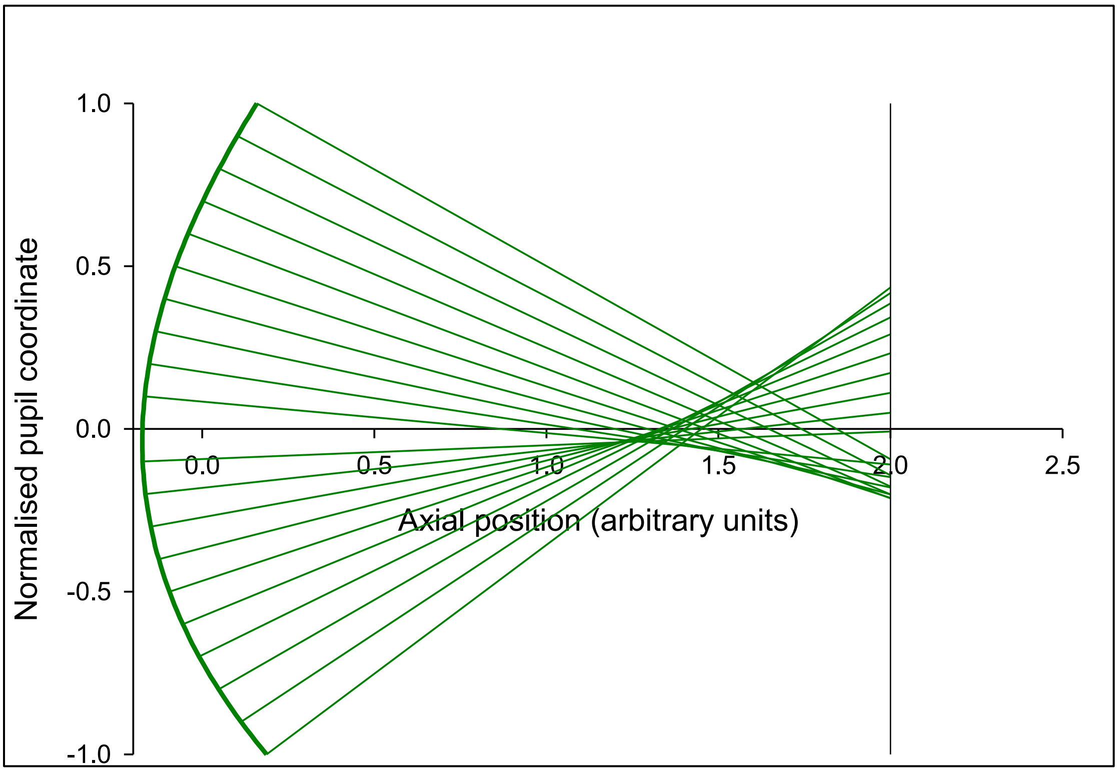


Figure 1.8. Wavefront and associated rays for negative vertical coma (tangential section). Z_2^0 = 0.1 and Z_3^{-1} = -0.005 (arbitrary units)

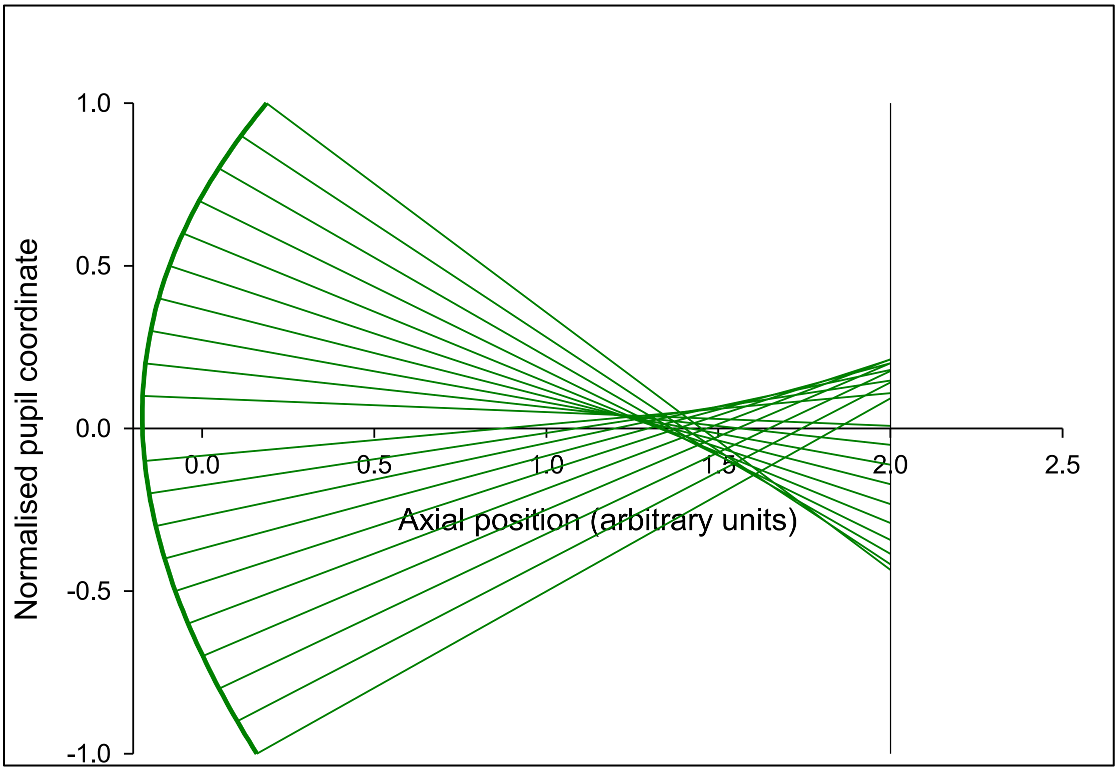


Figure 1.9. Wavefront and associated rays for positive vertical coma (tangential section). Z_2^0 = 0.1 and Z_3^{-1} = +0.005 (arbitrary units)

Comparatively little attention has been given to the 3rd-order Zernike coefficients representing coma with regards to cataract surgery. Coma is represented by the following 2 Zernike polynomials: Z_3^{-1}, which represents vertical coma, and Z_3^1, which represents horizontal coma. Wang et al.[124] computed corneal HOAs with a 6.0 mm pupil in 228 normal phakic eyes of 134 patients and found a mean total coma aberration value of 0.248 ± 0.135 µm, a mean horizontal coma Z_3^{+1} value of 0.000±0.193 µm, and a mean vertical coma Z_3^{-1} value of 0.083 ± 0.183 µm. A positive correlation between increasing age and coma has been reported.[124-126]

The ideal amount of coma required for high-quality vision remains unknown. Jet fighter pilots with supra-normal visual acuity were found to have more vertical coma than a control population.[127] Vertical coma creates multifocality along the vertical meridian. Roman letters have a majority of vertical limbs thus, vertical coma aberration enhances reading of Roman letters.[128]

In phakic eyes, several studies have investigated changes in anterior corneal wavefront aberrations as a function of age.[124-126] In their study of 102 eyes using the TMS-1 topographer (Tomey), Oshika and coauthors[126] found that for a 7.0 mm pupil, total wavefront aberrations and coma-like aberrations of the cornea correlated with age, whereas spherical-like aberrations did not vary significantly with age. In a study of 1st to 4th order aberrations in 59 eyes using the Humphrey MasterVue system (Carl Zeiss, Inc.), Guirao and coauthors[125] report that the average amount of aberration in the human cornea for a 4.0 mm pupil tended to increase moderately with age.

In pseudophakic eyes, previous studies reported that the change in corneal aberrations following cataract surgery depend on the size[129-131] and location[132] of the corneal incision and the type of the IOL.[133] Negative vertical coma of the cornea means a vertically asymmetric distribution of corneal refractive power with greater refraction located in the inferior part of the cornea.[134] In the superior incision group, corneas with a negative vertical coma preoperatively become corneas with a larger negative vertical coma postoperatively, and corneas with a positive vertical coma preoperatively become corneas with a smaller positive or a small negative vertical coma postoperatively. This means a greater flattening effect occurred in the superior cornea than in the inferior cornea. A greater flattening effect on the right side of the cornea than on the left side would induce a change in the corneal horizontal coma in the positive direction. Previous reports suggest that the surgically induced astigmatism is larger with a superior incision than that with temporal or nasal incisions.[135, 136] The smaller vertical diameter compared with the horizontal diameter of the cornea and the closer superior limbus to the visual axis could help explain their findings.[135, 136] Also, biomechanical differences between the superior cornea and temporal or nasal cornea may play a role. Another possible mechanism is that a superior cornea is likely to be affected by the upper lid pressure contrary to the temporal or nasal cornea.

We used temporal incision of 2.4 mm and 2.2 mm in the studies[137, 138] discussed in this thesis. It is likely that these incisions may have contributed to the total coma aberrations but as we did not collect the preoperative aberrometric data in our studies, this was difficult to analyse. For limbal incisions, Song et al.[139] investigated the change in corneal HOAs according to the different axes of incision location: superior, temporal, and nasal. They found that the superior incision in 2.2 mm phacoemulsification cataract surgery caused a change in the corneal vertical coma in a negative direction. Corneal trefoil changes were dependent on the incision location. They also suggested that care should be taken in particular when making an incision in the superior cornea in cases of a with-the-rule astigmatic cornea with negative vertical coma.[139] The superior incision could induce a good or bad effect on optical quality, depending on the side of the vertical coma preoperatively (ie, positive or negative).[139]

In contrast, for clear corneal incisions, Tong et al.[140] , studied the effect of incision size on the optical quality of the anterior cornea by comparing the changes in corneal wavefront aberrations between microincision cataract surgery (MICS- 1.5mm) and small-incision clear corneal cataract surgery (SICS -3mm). They found that for clear corneal incisions, cataract surgery-related changes in corneal wavefront aberrations were dependent on incision size. The MICS technique had advantages over the SICS technique in minimizing the effect of the incision size on the optical quality of the cornea. In a similar comparative study of postoperative corneal HOAs between clear corneal MICS and SICS, Yao et al.[141] found no significant differences in mean levels of total coma, total trefoil, spherical aberration, between the 2 groups. The total aberration in Yao et al.'s[141] study was equivalent to the RMS of aberrations in Tong et al.'s[140] study. The same results were observed in postoperative RMS values between the 2 groups in the study by Tong et al.[140] Tong et al.[140] also found in the MICS group, there were changes in trefoil and tetrafoil, although the magnitudes were smaller than in the SICS group. No patient in Tong et al.'s[140] study had a significant change in coma or spherical aberration. This finding is consistent with that in the study by Elkady et al.,[131] in which coma and spherical aberration were not changed in 25 patients after MICS. In Tong et al.'s study,[140] total RMS and HOA RMS were greater in the SICS group than in the MICS group, total trefoil changed more after SICS than after MICS, and 3 Zernike terms (oblique astigmatism, oblique trefoil, tetrafoil) changed more in the SICS group than in the MICS group.

c) *Pupil size and wavefront aberrations in human eye:*

Pupil size[142-145] has been shown to be an important factor for pseudoaccommodation in eyes with monofocal spherical IOLs along with factors such as age,[146] astigmatism,[147-149],[150, 151] axial length,[148, 152] axial IOL movement,[150, 153] corneal multifocality,[154, 155] and aberrations.[155]

In our case–control study[148] of factors related to uncorrected visual acuity for distance and near vision following monofocal IOL implantation, we analysed corneal astigmatism, pupil size, axial IOL movement, amplitude of accommodation, axial length, and age. Of these factors, only against-the-rule astigmatism was associated with pseudoaccommodation. A similar study by Lim et al.[156] included more factors than in previous studies, notably corneal multifocality and ocular aberrations. This study by Lim et al.[156] revealed associations of smaller pupil size and short axial length with good near vision. Previous studies also support this relationship. Nakazawa and Ohtsuki found an inverse relationship between pseudoaccommodation and pupillary diameter.[143] Why small pupil size is related to good near vision is not entirely clear, but it could be that small pupils have greater depth of focus in eyes with pseudophakia.[144, 145] The advantage of short axial length may be explained by an inverse effect of axial length on accommodation for a given amount of IOL movement. Nawa et al.[152] showed that as the posterior chamber IOL moves forward 1.0 mm, shorter eyes accommodate proportionately more than longer eyes. The accommodation per 1.0 mm of forward IOL movement varied from 0.8 D in an eye with a 27.0 mm axial length (long eye) to 2.3 D in an eye with a 21.0 mm axial length (short eye). In Lim et al.'s[156] study, the cut-off values for pupil size and axial length associated with good near vision after IOL implantation were calculated using the minimum P value approach, and the results were 2.6 mm and 23 mm respectively. Preoperative and postoperative axial lengths were not expected to differ, and changes in pupil size reported after uneventful phacoemulsification were not significant. These results suggest that good postoperative near vision may be expected if the patients have pupils less than 2.6 mm and axial lengths less than 23 mm before surgery. In contrast to these results, we[148] did not find pupil size to be a significant factor in pseudoaccommodation. The reasons for this difference may not be explained with certainty; however, differences in the devices and environments used for measurement of pupil size may potentially contribute.

Moreover, it is reported that the induced increases in ocular higher-order aberration significantly correlated with the changes in contrast sensitivity following LASIK.[157] It has been known that the amount and character of higher-order aberrations of the eye is greatly affected by the diameter of the entrance pupil.[126, 158-160] Wang et al.[160] showed that for equal increase of pupil size, not all Zernike polynomial coefficients increased. Coma aberrations increased less with pupil dilatation whereas, spherical aberration showed only a small increase from 5 – 6 mm pupil size.[160] Other higher order aberrations did not increase significantly and coma aberration was larger than spherical aberration and also larger than other HOAs.[160] It has been shown that contrast sensitivity function is also related to pupil diameter.[161, 162]

There are a lot of variations noted in several comparative studies using aspheric IOLs with regards to measuring pupil sizes and standardization of room illumination.[163-186] A few studies used Colvard pupilometer[180, 181, 187, 188] or Procyon P2000D pupillometer[171] or Haab's pupilometer.[183] A lot of studies used pupil sizes from the aberrometers such as Hartman-Shack wavefront analyzer KR-9000PW (Topcon, Tokyo, Japan),[165-167, 174, 184], Zywave IIz aberrometer (Bausch and Lomb, St. Louis, MO, USA)[168, 185], WASCA (Carl Zeiss Meditec AG, Germany),[178] iTrace (Tracy Technologies, Houston, USA)[173] and Eyetop Corneal Topographer (CSO, Scandicci, Italy).[175] One study even used the Pentacam tomographer (Oculus, Germany)[177] to assess the pupil size. Moreover, there were several studies, that did not mention how they measured the pupil size.[163, 169, 170, 172, 176, 179, 182, 186] Similarly few studies measured room illumination and standardized it.[168, 171, 174, 183]There were a couple which used ambient light of the room with standard room for all patients[174, 175] and there were several studies that did not mention the standardization of room illumination at all.[163, 169, 170, 172, 173, 176-182, 184-186] In the studies discussed in this thesis,[137, 138, 189, 190] we used ambient room illumination for measurements on iTrace aberrometer. We aim for consistency of environment and protocols in our studies, we used the same room for all pre and postoperative measurements. This allowed us to manually select the pupil diameter on iTrace aberrometer software once the image was captured and we were able to obtain aberrometric data for the desired pupil size on the software. To standardize this data capture, pupils were dilated using Tropicamide 1%. Wavefront maps were analysed using the desired pupil size on iTrace software and higher order aberration up to sixth Zernike coefficients were analysed.

1.3 Visual quality

1.3.1 Depth-of-focus

1.3.1.1 Depth-of-focus measurements

Several previous studies have assessed the depth-of-focus after implantation of aspheric IOLs and spherical IOLs.

Van Gaalen et al.[191] measured depth-of-focus by fitting a parabola through the logCS as a function of defocus curve (through-focus curve) at 6 cpd. For statistical accuracy, the r^2 value of the fitted parabola had to be at least 0.85 in both eyes and the highest contrast sensitivity value was not allowed to correspond to 1 of the 2 extreme defocus values (−2.00 D and +1.00 D) in either eye. Subsequently, depth-of-focus was defined as the dioptric range for which contrast sensitivity exceeded half its maximum value.[192] They found significantly lower spherical aberration with aspheric IOLs. However, they observed no statistically significant difference in depth-of-focus or contrast sensitivity between IOL types. Differences in testing methodology (computerized contrast sensitivity testing at several defocus levels) might explain the findings in their study.

Steinwender et al.[178] and Rocha et al.[193] evaluated depth-of-focus by having patients read ETDRS logMAR visual acuity charts at 4 m under photopic conditions through different levels of defocus induced with trial lenses (between -1.5 and 1.5 D in steps of 0.5 D) and found significantly reduced depth-of-focus with a degradation of DCIVA and DCNVA in the aspheric IOL group.

Using an adaptive optics visual stimulation, Ruiz-Alcocer et al.[194] found that the best compromise between distance visual acuity and depth-of-focus with three IOLs and the different corneal profiles relied on a certain amount of positive spherical aberration. Above a certain limit of residual positive or negative spherical aberration, visual acuity decreases worsening the depth of focus.

In another study by Thiagarajan et al.[195], depth-of-focus was measured conventionally by RAF rule to compare an aberration-free IOL with the spherical Sensar AR40e IOL. They found no differences in depth-of-focus.

1.3.1.2 Depth-of-focus calculation on the iTrace aberrometer:

Depth-of-focus measurements can also be performed on the iTrace with the patient focusing on a distant target at 4m with dilated pupils at a fixed entrance pupil size of 5.0 mm. Using software (version 3.1.1) on the iTrace aberrometer, a 3D refraction map can be derived from the PSF measurement across various pupillary diameters and the change in refractive pattern can be compared between subsequent measurements taken on a single eye. The average refraction for a circular area of 2000 µm around the points of maximum and minimum refraction at a 4.0 mm pupillary scan diameter was averaged. The difference between the maximum refraction and minimum refraction on the plot gives the value of depth-of-focus for that particular scan (Figure 1.10).

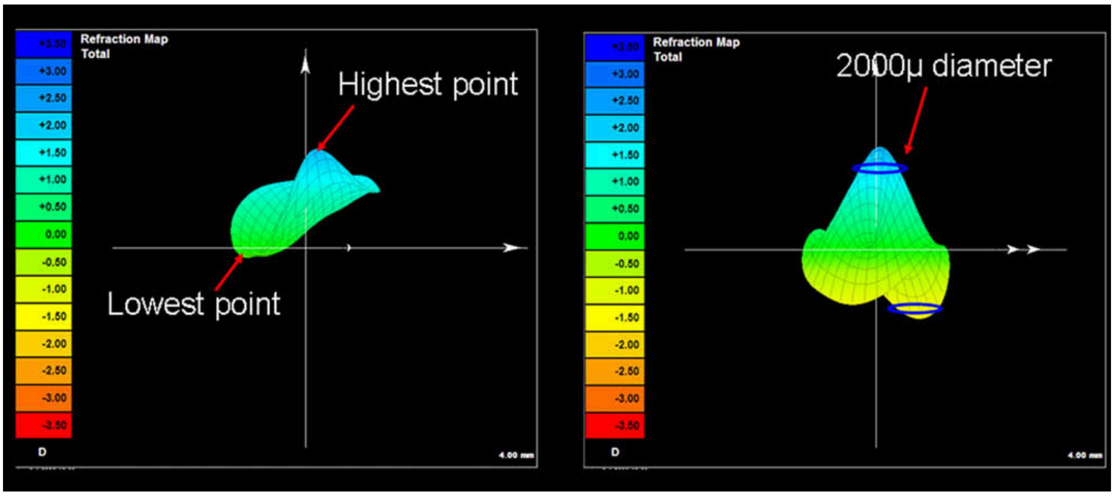


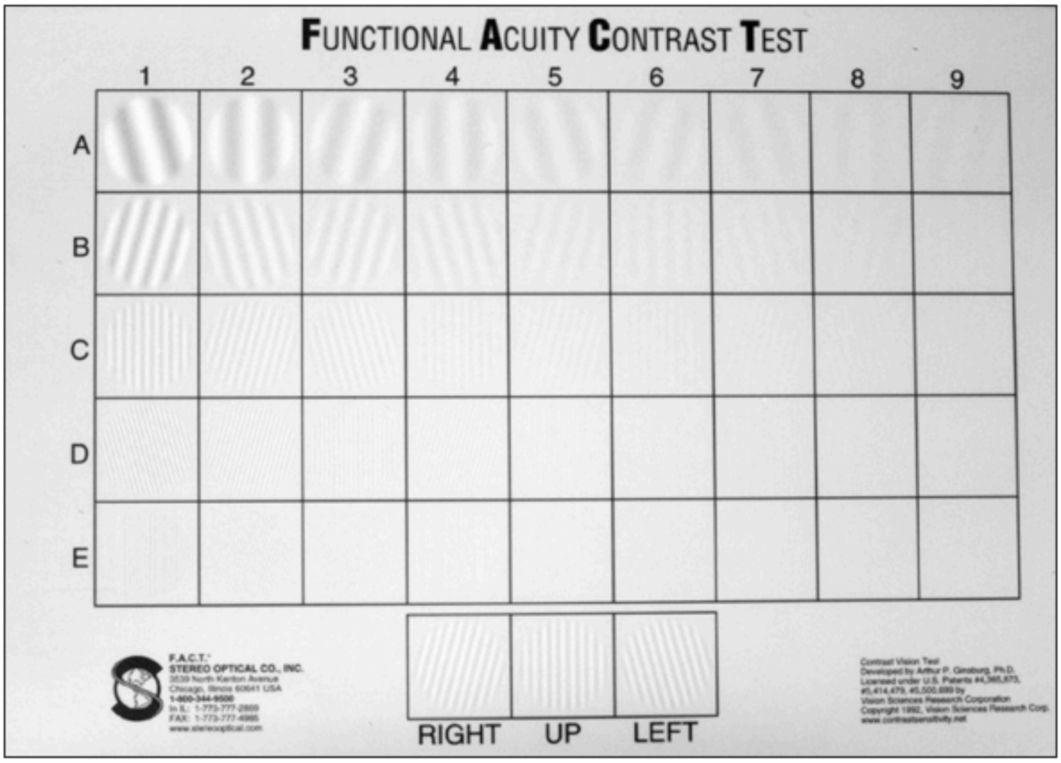
Figure 1.10. Diagram demonstrating the depth-of-focus assessment on aberrometer's software with a 4.0 mm pupil scan size. *(Reproduced from Nanavaty MA, Spalton DJ, Boyce J, et al. Wavefront aberrations, depth-of-focus, and contrast sensitivity with aspheric and spherical intraocular lenses: fellow-eye study. J Cataract Refract Surg 2009;35(4):663-71)*

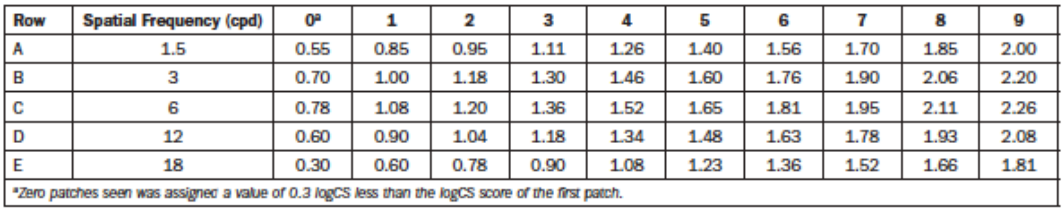
1.3.2 Contrast sensitivity assessment

Contrast sensitivity is an important measure for studying the effect of refractive procedures on quality of vision. It provides a dimension of visual quality distinct from that commonly assessed by high-contrast visual acuity and it integrates both optical and neural processing components of vision in a single function.[196, 197] Contrast sensitivity, under different lighting conditions, provides particularly important information about quality of vision for presbyopic patients who are affected by age-related changes to their crystalline lens and neural processing and for those whose cornea or lens has gone through vision-correction procedures.[196, 198-200]

The most widely used device to test contrast sensitivity is the Pelli Robson contrast sensitivity chart.[201] Like a standard Snellen visual acuity chart, the Pelli Robson chart consists of horizontal lines of capital letters but, instead of the letters getting smaller on each successive line, it is the contrast of the letters (relative to the chart background) that decreases for each group of three letters (there are two groups per line). Other, more sophisticated, devices may also be used to assess contrast sensitivity. These devices often use gratings with light and dark bars whose intensity varies sinusoidally. These gratings vary in spatial frequency, as well as contrast from target to target, to give a more thorough evaluation of how sensitive your eyes are to differences in contrast.

Clinical measurement of the contrast sensitivity function can be carried out with tests such as the Functional Acuity Contrast Test (FACT) chart in the Optec 6500 Vision Tester (Stereo Optical Co., Chicago, IL). This is a chart with sine wave gratings of varying spatial frequencies and contrast steps and the test can be carried out under photopic and mesopic conditions with and without a glare source (Figure 1.11). The graphs are plotted for mesopic and photopic lighting conditions on the chart. In our studies,[137, 138] functional acuity contrast testing was measured using the Optec 6500 Vision Tester (Stereo Optical Co., Chicago, IL) with best spectacle correction under photopic conditions (target luminance value 85 candelas cd/m^2) and mesopic conditions (target luminance value 3 cd/m^2) without glare at 3 and 6 months.





Row	Spatial Frequency (cpd)	0[a]	1	2	3	4	5	6	7	8	9
A	1.5	0.55	0.85	0.95	1.11	1.26	1.40	1.56	1.70	1.85	2.00
B	3	0.70	1.00	1.18	1.30	1.46	1.60	1.76	1.90	2.06	2.20
C	6	0.78	1.08	1.20	1.36	1.52	1.65	1.81	1.95	2.11	2.26
D	12	0.60	0.90	1.04	1.18	1.34	1.48	1.63	1.78	1.93	2.08
E	18	0.30	0.60	0.78	0.90	1.08	1.23	1.36	1.52	1.66	1.81

[a] *Zero patches seen was assigned a value of 0.3 logCS less than the logCS score of the first patch.*

Figure 1.11**.** The FACT chart in the Optec 6500 vision tester (Stereo Optical Co., Chicago, IL) that consists of sine-wave grating patches at 9 contrast levels and 5 spatial frequencies. The corresponding log10 unit of contrast sensitivity (logCS) scores for the FACT chart are presented. This demonstration of the FACT chart reprinted with permission from Vision Sciences Research Corporation. *(Reproduced from: Lin L, van de Pol C, Vilupuru S, Pepose JS. Contrast Sensitivity in Patients with Emmetropic Presbyopia Before and After Small-aperture Inlay Implantation. J Refract Surg. 2016 Jun 1;32(6):386-93.)*

1.3.3 Optical and Visual Quality:

We are able to get more accurate information on the quality of vision in human eyes employing modern optical and adaptive optics principles. Optical quality of an eye can be tested using objective and subjective measures. Wavefront analysis, point-spread function (PSF), modulation transfer function (MTF), Strehl ratio and objective depth-of-focus are all parameters affected by the quality of an optical system, whereas visual acuity, contrast sensitivity, straylight and subjective depth-of-focus also incorporate retinal and cortical processing.

Optical and image quality can be described in 3 alternative domains[202] (Figure 1.12): (1) The pupil function which depends on pupil transmittance and wavefront aberrations; [203] [203] [203] the image of a point source (Point Spread Function or PSF); and (3) the Optical Transfer Function in the frequency domain.

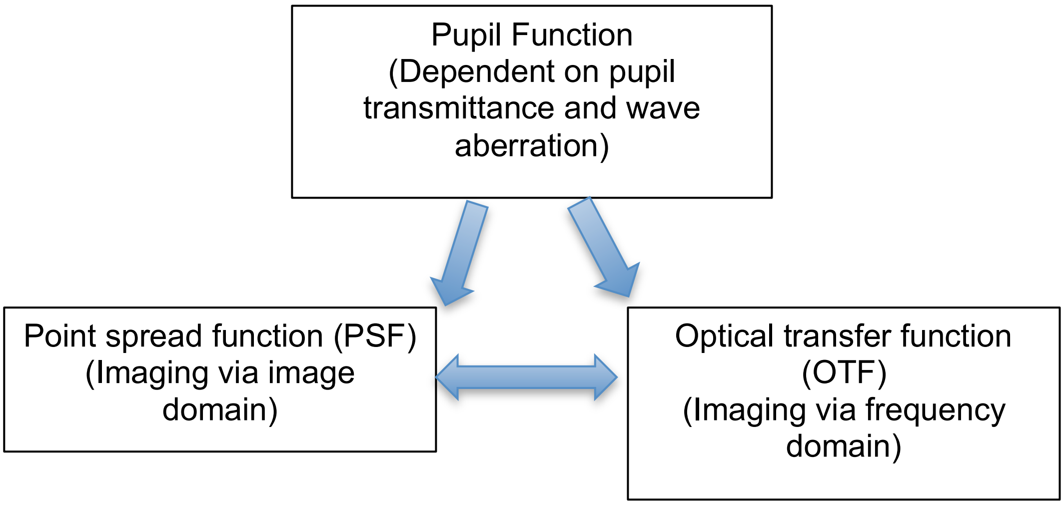


Figure 1.12. The interconnected domains affecting optical and image quality.

The Optical Transfer Function (OTF) has two components: the Modulation Transfer Function (MTF), which is the amplitude component and the Phase Transfer Function (PTF), which contains information about phase shift. The MTF includes diffraction and aberrations but not phase.

The MTF is the ratio of image contrast to object contrast as a function of spatial frequency and optical engineers evaluate optical systems by measurement of the MTF. It can be measured by directly imaging the PSF on the retinal surface[204] or by calculating the PSF from the wavefront or ray tracing.[205] The MTF of the human eye is dependent on pupil diameter[206] because larger pupil diameters include more aberrations, particularly spherical aberration.

In the wave theory of light, all points of light that originate from the same point source and that are oscillating in the same state or phase are termed a "wavefront". This implies, to a good approximation, that a wavefront is a surface at constant optical distance from a source. In an ideal optical system (paraxial case) the wavefront is spherical. An optical aberration can be defined as a departure of the performance of an optical system from paraxial optics and for the wavefront aberration, it is the optical distance between the real and ideal wavefront. As described in chapter 2, analysis of wavefront aberrations in eyes has been widely used to isolate the effect of lower-order aberrations and higher-order aberrations (HOAs), as well as the contributions of individual aberrations to optical quality.

The quality of an optical system can also be quantified in terms of the Point Spread Function (PSF). The PSF of an optical system is the intensity distribution of the image for a point object. A measure of optical quality based on the PSF that has been applied to the eye is the Strehl ratio, which is the ratio of the central maximum illuminance of the PSF in the aberrated eye to the central maximum that would be found in the corresponding aberration-free optical system.[207] It is, therefore, a measure of the fractional drop in the peak PSF and it depends on the wavefront error. A Strehl ratio of 1 indicates a diffraction-limited optical performance.[207]

Visual performance following intraocular lens implantation can be assessed in different ways. Contrast sensitivity measures not only the optical quality of the retinal image but also the retinal and cortical processing of this image by the patient. The PSF beyond the central 1 degree is of functional importance and is called intraocular straylight. It causes disability glare and many other visual symptoms. This is described in more in detail in this chapter.

1.4 Aspheric intraocular lenses

1.4.1 Effect of asphericity on optical and visual quality

In order to achieve the best quality of vision, cataract surgery must consider other aspects of vision beyond Snellen acuity, such as contrast sensitivity and wavefront error. As a result, IOL manufacturers have incorporated advanced optics and refractive technology towards this objective since over a decade now.

In 1999, Holladay, demonstrated that side effects of myopic LASIK were likely to be due to the fact that the procedure turned a prolate cornea into an oblate one with an asphericity, or Q-value, more akin to that of a frog than of a predator eagle.[208] We also know that, with aging, contrast sensitivity decreases. This is first noted at the higher spatial frequencies and then at all the spatial frequencies.[209]

The loss of functional vision can decrease quality of life and compromise vision for everyday tasks such as driving even despite of good Snellen acuity[210] and the onset of cataract exacerbates any pre-existing functional vision problems. Traditional spherical IOLs typically add positive spherical aberration, keeping total spherical aberration similar to that found in the ageing natural lens.

Some studies [137, 211, 212] have argued that an advantage of positive spherical aberration in the ageing eye is an increased depth-of-focus. The corollary to that is that sharpening distance vision by correcting spherical aberration with an aspheric IOL might worsen near and intermediate vision.

However, recent publications[211-215] refute this argument. Nishi has also shown a significant negative correlation between range of accommodation and spherical aberration.[211] In other words, lower spherical aberration is correlated with better accommodation. Wang and Koch recently demonstrated that when all aberrations were corrected, eyes with zero spherical aberration have the best depth-of-focus.[212] If spherical aberration was not zero, they also found that slightly negative spherical aberration, rather than slightly positive SA, provided better depth-of-focus.[212] A newer Mini Well IOL (SIFI Meditech, Italy), is based on spherical aberration.[213-215] This IOL is a progressive multifocal aspheric IOL with an equivalent addition of +3.00 D. Its optical design is based on the introduction of an appropriate spherical aberration at the pupil's center and the control of high-order aberrations at the pupil's periphery to increase the depth-of-focus to generate a progressive multifocality. Its optical design consists of 3 zones. The inner and middle zones have different spherical aberrations with opposite signs, whereas the outer one is a monofocal zone. [213-215]

1.4.2 Introduction of the first aspheric IOL

Corneal topography measurements on 71 cataract patients showed that the average SA of the human cornea was +0.27 microns at a 6 mm pupil diameter.[216] This was subsequently confirmed in several other studies.[124, 132] A model cornea based on these measurements was used to design IOLs having a fixed amount of negative SA to compensate for the positive SA of the average human cornea.

From these modeling experiments, the Tecnis Z9000 wavefront-designed IOL (AMO, Santa Ana, CA, USA) was manufactured. In testing of 25 patients aged 60 and older implanted with the Tecnis aspheric IOL, total ocular SA was not significantly different from zero, so the lens was effective in reaching the intended target.[217]

A prospective, randomised, American study showed a 78% gain in peak contrast sensitivity with the new lens with mesopic contrast sensitivity approximately equivalent to photopic contrast sensitivity with a spherical lens[218]. Early European studies also showed that aspheric IOLs could improve visual quality.[187, 219]

Driving simulations were also conducted as part of the US Food and Drug Administration clinical trials to determine the impact of the lens on functional vision. The FDA approved the Tecnis lens in 2004, with the unprecedented claim that it was likely to offer a meaningful safety benefit for elderly drivers and others with whom they share the road. Moreover, it was claimed that the improvement in functional vision might improve patient safety for other situations in which visibility is low.

1.4.3 Development of aspheric IOLs:

Since 2004, other lens manufacturers have introduced new aspheric IOLs with varying asphericity. The IOLs can broadly be classified as spherical, spherically neutral or aspheric IOLs. So-called spherical IOLs have positive spherical aberration and, therefore, add to the positive corneal spherical aberration. Spherically neutral IOLs are designed to have zero spherical aberration so that the contribution to ocular spherical aberration comes from the cornea. Aspheric IOLs have negative spherical aberration designed to compensate the positive spherical aberration of the average human cornea.

1.4.4 Literature review of studies published on aspheric IOLs.

Multiple studies have compared IOLs from different platforms.[163, 166, 168-177, 187, 188, 220] and some of the intra-individual (bilateral) studies have evaluated whether the eye with the aspheric IOL or the eye with the spherical IOL was subjectively perceived as better.[163, 168, 169, 187, 221] The implanted IOLs differed in the haptics, material or edge design, all of which are factors that may influence optical quality.[222, 223] To analyse the effect of aspheric IOL implantation on vision irrespective of these factors, some studies have been conducted with platform-identical IOLs.[137, 169, 174, 221, 224-232] A meta-analysis performed by Schuster et al.[233] analysed whether and to what extent aspheric IOLs produce different results compared to spherical IOLs in terms of best-corrected visual acuity (BCVA), contrast vision, and visual quality. For BCVA, Schuster et al.[233], found no evidence that newer aspheric IOLs were superior over earlier implant designs with regards to BCVA. For contrast sensitivity, a small effect was calculated for 1.5 to 6 cpd under photopic light conditions and a moderate to high effect was calculated under mesopic light conditions. [233]

With regard to contrast sensitivity, Schuster et al. [233] reported that there was a statistically significant difference at spatial frequencies between 3 and 18 cpd for photopic light conditions, but none at the low spatial frequency of 1.5 cpd. However, contrast sensitivity was better with aspheric IOLs at all spatial frequencies under mesopic light conditions. The effect size was strongest at 18 cpd.[233]

Schuster et al.[233] also found that the reduction of the spherical aberration itself appears to be more important despite the difference in the asphericity of different aspheric IOLs and this difference in asphericity did not lead to different contrast sensitivity results. However, two RCTs[234, 235] found no difference in the contrast sensitivity measurements after the implantation of different aspheric IOLs, whereas a separate study did demonstrate a significant difference.[236] This could be because the implantation of aspheric IOLs changes the ocular spherical aberration,[237] whereas higher-order aberrations such as coma[190] or trefoil are not influenced,[163, 173] which may also influence the contrast sensitivity.

Reducing the spherical aberration not only increases contrast sensitivity but also reduces myopic shift when the pupil size increases.[188, 227, 238] Three studies showed that there was no myopic shift in the aspheric IOL group, whereas the spherical IOL group exhibited a myopic shift of approximately -0.5 D. This difference might be of importance when light conditions change and the pupils dilate and will also influence the depth-of-focus. Several authors have proposed IOL selection according to the degree of corneal spherical aberration.[217, 239, 240] Ocular spherical aberrations can be corrected in a manner that is tailored to each individual.[217, 240] To investigate the role of pupil size in aspheric IOL selection, Yamaguchi et al[236] performed a study that included 30 eyes implanted with 4 types of IOLs. They evaluated the impact on pupil size with regard to reductions in spherical aberration via linear regression and concluded that if a patient's pupil under mesopic conditions is smaller than 3.0 mm, an aspheric IOL will not reduce ocular spherical aberration. In eyes with a larger pupil under mesopic conditions, the IOL's impact on spherical aberration will increase.[236] This observation highlights the importance of pupil size in the selection of a particular IOL for an individual. Studies including younger patients may be assessed with this assumption, because corneal spherical aberration remains stable with age,[241] but mesopic pupil size decreases.[242]

Spherical aberration can be helpful for reading purposes. One study reported decreased distance-corrected intermediate and near visual acuity after aspheric IOL implantation (aspheric lens: AcrySof IQ).[243] This finding is concordant with a more technical study where the depth-of-focus assessment was performed using aberrometer software which yielded similar results[137] but could not be reproduced by 2 other studies using the TECNIS and the AcrySof IQ lenses.[226, 244]

Ideally, individuals with particularly high mesopic vision requirements, such as airplane pilots, hunters, lorry drivers, or populations in Nordic countries with prolonged twilight hours, may perceive such a visual benefit. Standardised questionnaires are a very useful tool to evaluate a patient's subjective outcomes. However, Schuster et al.[233] found that the subjective perception of visual quality is still heterogeneous even when standard questionnaires were used. Overall, aspheric IOL implantation might be a good choice for patients with high demands in terms of contrast vision.

Most clinical trials in ophthalmology use visual acuity measured by an eye chart to assess changes in vision related to experimental conditions. However, as clinicians and researchers are aware, objective measurement of visual acuity (and/or visual field) may not adequately describe the total impact of a treatment on a patient's visual world. Patient-reported outcomes (PROs) are the measurement of patients' perception of the impact of a disease and its treatment(s), which are typically reported via a questionnaire.[245] Growing evidence indicates the importance of vision-related PROs in clinical trials for evaluating medical drugs and devices, not only for medical product labelling, but also to expand the understanding of clinical trial outcomes.[246-249] PROs are increasingly being accepted as the primary endpoints of clinical trials in health research.[250-252] The U.S. Food and Drug Administration [253] has also endorsed PROs as key clinical trial endpoints owing to the notion that such clinical trials ultimately guide patient care.[254] Therefore, it is critical that data collected by PROs are accurate and reliable, which is only possible when patients are able to understand the questions asked and select response categories that represent their status. Poorly understood questions, or underutilized rating scale categories can seriously impair the accuracy and reliability of PRO measurements.[255-257] Hence, a number of cataract surgery outcome questionnaires have been developed, most of which measure the difficulty people have performing daily activities because of their vision; this trait is known as visual functioning, visual disability, or, more literally, vision-related activity limitation. There are several questionnaires in the literature[258] and newer ones[259] are evolving. We did not have subjective questionnaires in our protocol when we conducted the studies[137, 138, 189, 190] however, studies on newer lenses would benefit from subjective questionnaires and indeed they may be an essential requirement for approval.

1.5 Posterior Capsule Opacification

Posterior capsular opacification (PCO) is the most common complication following cataract surgery.[260-264] PCO is caused by lens epithelial cells (LECs) that remain in the equator of the capsular bag after surgery. The LECs first proliferate at the periphery where they produce a Soemmering's ring, after which they migrate across the posterior capsule into the visual axis, leading to opacification of the centre of the posterior capsule resulting in reduced visual acuity.[76, 265] Progression in surgical techniques and intraocular lens design has reduced PCO but has not eliminated it and prevalence rates show that between 20% to 40% of the patients currently report a decline in visual acuity related to PCO from 2 to 5 years postoperatively.[265] The most common and effective treatment for PCO is laser capsulotomy, a treatment which is not complication-free, with the reported complications including cystoid macular edema, retinal detachment, and damage to the lens itself.[266-268] Although extremely rare, but retinal detachment following Nd:YAG laser capsulotomy is a recognised complication.[269-272] Various approaches have been investigated to reduce the prevalence of PCO. These have included mechanical and pharmaceutical techniques as well as different lens shapes and materials. [273-278] Although there has been a reduction in the prevalence of PCO, prevention of this complication remains elusive.

PCO after routine cataract surgery with any IOL will affect the optical quality and visual outcomes[279]. There are several IOL materials available and acrylic remains more popular among ophthalmic surgeons. Much is known about the 2 types of acrylic IOLs; hydrophobic and hydrophilic. There is evidence that hydrophobic acrylic IOLs have more glistenings[280] and hydrophilic IOLs have more intralenticular calcification.[281] Hydrophilic acrylic is known to cause more PCO compared to hydrophobic acrylic IOLs,[278] and increased PCO causes increased light scatter.[282] As a result, there is conflict between the requirements for reducing PCO and factors that affect optical quality.

1.5.1 Measuring Posterior Capsule Opacification:

Posterior capsule opacification (PCO), the most common complication of modern cataract surgery, has a reported incidence of 20 to 50% within 5 years of surgery.[55] Lens epithelial cell (LEC) proliferation, migration, and metaplasia,[283] are the pathogenic mechanisms of PCO and strategies for prevention have focused on modifying postoperative LEC cell behavior. These have included various surgical techniques,[284-286] drugs,[287, 288,289-300] capsule polishing[301-304] and intraocular lens designs.[305-309]

There are a number of published methods for quantifying PCO which can be classified as either indirect or direct systems. Direct systems look at the PCO by imaging it whereas indirect systems rely on other methods to indirectly quantify PCO.

1.5.1.1 Indirect quantification of PCO:

Some clinical studies have used the neodymium:YAG (Nd:YAG) laser capsulotomy rate as the outcome measure.[305, 306, 308, 309] This is an indirect measure of PCO, indicative of the visual disturbance produced by LEC proliferation and migration onto the central posterior capsule and visual axis. The Nd:YAG laser capsulotomy rate is dependent on the subjective threshold of visual disability at which the patient demands and the surgeon offers laser treatment; financial factors and access to equipment can also influence this decision. These subjective factors limit the validity of conclusions from clinical studies that use the Nd:YAG capsulotomy rate as an index of PCO.

1.5.1.2 Direct quantification of PCO using bespoke systems:

Evaluation of PCO would be more accurate if an objective and quantitative direct measurement of LEC proliferation on the posterior capsule could be made. Such a measure could also potentially increase the sensitivity to detect small changes in PCO potentially reducing the length of follow-up needed for clinical studies. Several methods to measure and quantify PCO have been proposed in the literature. The 3 commonly described methods are EPCO, [307, 310] POCO[311] and AQUA[312]. All 3 systems require capturing digital reflected light images and subjective grading of PCO using software.

a) EPCO Analysis (Evaluation of Posterior Capsular Opacification)

EPCO was introduced in 1997 by Tetz et al[307, 310] and is commercially available. It is a computer-assisted system based exclusively on the morphological assessment of PCO. It incorporates planimetric and grading assessment. The density of the opacification behind the IOL is graded clinically as follows: 0= none; 1= minimal; 2= mild; 3= moderate; 4= severe. The individual PCO score is calculated by multiplying the opacification grade by the fraction of capsule area involved behind the IOL optic. The selection process and grading of areas are subjective.

b) POCO System (Posterior capsule opacification software)

With the computer-based POCO system, developed at St. Thomas' Hospital and King's College in London,[311] the images are evaluated using pixel analysis based on texture differences. This is customized, automated software and is not freely available. Analysis results in a percentage of opacification area from 0% to 100%. Different opacification densities are not directly accounted for but are incorporated through the texture analysis.

c) AQUA System (Automated Quantification of After-Cataract)

The AQUA software is also based on texture analysis.[312] The outcome measure, the inhomogeneity of the image, is based on statistical texture analysis. To calculate the inhomogeneity of the texture of an image, a gray level co-occurrence matrix (GLCM) of the bitmap of the image is built. The GLCM belongs to 2nd-order statistics, which deal with the probability that 2 pixels connected by a position operator (eg, the relative position of the 2 pixels) have 2 gray levels. A GLCM is a square matrix with a side length corresponding to the number of gray levels of a bitmap. The grading is performed using the GLCM entropy, which is a measure of inhomogeneity. The GLCM is computed for 1 of the 3 color channels (RGB), currently the red channel.

d) POCOman:

Bender *et al*.[313] described a new interactive software program, POCOman, for the semi-objective assessment of PCO. The software is free to download and free for any user. Digital images of the posterior capsule, acquired by any technique, were analysed by the observer to determine the percentage area of PCO and a severity score assigned. The system was validated by comparing it to clinical slit lamp evaluation of PCO and automated POCO system analysis using a library of 100 images taken from archives. They found that an image could be analysed in approximately 2 minutes. The results of the POCOman system correlated well with the results of the automated POCO system and clinical evaluation.

e) Friedman *et al*.[314] system:

Friedman *et al*.[314] developed a digital imaging and analysis technique by taking retroillumination images of the posterior capsule for assessing the extent of PCO. The images were analysed using an available image analysis software program. Automated analysis of images correlated well with clinical grading both at slit lamp examination and when looking at the images themselves. Analysis of images taken at different times showed high reproducibility and the system was able to identify progression of capsular opacity over a 2 year period with a mean increase of 15.8% in progressors versus an increase of 0.6% in non-progressors. They concluded that their technique was reliable, easy to use, and could detect small changes in PCO over time.

f) <u>Clinical method using slit lamp</u>:

Elgohary *et al.*[315] compared the effect of PCO on visual function in patients with monofocal and multifocal IOLs. They graded the PCO using the following grading scale whilst examining the patients.

Grade I (mild)	The outlines of the optic nerve head and main retinal vessels (±retinal striations) are clearly distinguishable
Grade II (moderate PCO)	The outlines of the optic nerve head or of the main retinal blood vessels are blurred
Grade III (severe or dense)	The optic nerve head and blood vessels are barely visible

Table 1.1. Grades of PCO *((Reproduced from: Elgohary MA, Beckingsale AB. Effect of posterior capsular opacification on visual function in patients with monofocal and multifocal intraocular lenses. Eye (Lond) 2008;22(5):613-9.)*

A total of 33 consecutive patients with clinically significant PCO, 24 with monofocal, and nine with multifocal IOLs were recruited in their study.[315] There was no significant difference between the proportions of patients with different PCO grades in the two groups. At presentation, high- and low-contrast distance visual acuity was significantly greater in the multifocal group, whereas near VA and contrast sensitivity were similar. The effect of PCO on visual function in the two groups is comparable, although patients in the multifocal group presented with earlier loss of visual function.

Findl *et al*.[312] compared four methods for quantifying PCO—a fully automated analysis system (Automated Quantification of After-Cataract [AQUA]), subjective grading by four experienced and four inexperienced examiners, subjective Evaluation of Posterior Capsular Opacification (EPCO) system and posterior capsule opacification software (POCO). The objective AQUA score correlated well with subjective methods, including the EPCO system. The POCO system, which assesses PCO area, did not adequately describe PCO intensity and includes a subjective step in the analysis process. Aslam *et al*.[316] analysed the various systems of PCO grading published in literature and concluded that no single system could be considered the gold standard and it is difficult to comment on the advantages of one system over another.

1.5.1.3 Direct quantification of PCO using commercially available imaging systems:

a) Scheimpflug system:

Lasa *et al*.[317] described a method to objectively document PCO using Zeiss Scheimpflug tomography and computerised image analysis. They examined 42 eyes with clear capsules (group A) and 27 with PCO (group B). The eyes in group A had significantly better visual acuity, lower mean capsular densitometry readings, and thinner capsules.

Grewal *et al*.[318] developed a method to quantify PCO in eyes after cataract surgery and IOL implantation using Image J software (Image processing and analysis in JAVA by NIH) on images obtained using Scheimpflug Pentacam® tomograms and compared its validity with slit lamp retroillumination image analysis using POCOman software. In a study of 124 pseudophakic eyes of 124 patients, they found good correlation between the two methods and Pentacam tomograms were easier to obtain, free of flash reflections, and they allowed more objective analysis in comparison with the retroillumination method.

b) Ocular coherence tomography systems (OCTs):

Moreno-Montanes *et al.*[319] evaluated PCO in humans after cataract surgery with IOL implantation by using optical coherence tomography (OCT-1). A total of 66 eyes with PCO and 20 eyes with a normal posterior capsule were analysed using a 3 mm long horizontal scan of the posterior capsule. Peak intensity (PI) and posterior capsule thickening (PCT), with PCT indicating the distance between two reflectivity spikes with an approximate axial resolution of 10 μm were obtained and compared with VA and PCO type. PCT was found in PCO eyes whereas no second spike appeared in control eyes. Worse VA correlated significantly with larger PCT. They concluded that OCT-1 is useful to quantify and discriminate between different types of PCO and that PCT may be a previously unrecognized factor in visual acuity degradation.

1.5.2 Factors affecting Posterior Capsule Opacification:

PCO is affected by many factors[320] including changes in the IOL design. The most important of these changes developed to control PCO is a square edge profile but other factors such as optic size, haptic design and IOL material play significant roles.[321-323] Low PCO rates, particularly fibrotic changes, were initially reported with Acrysof IOLs; Nishi identified the square edge profile as the underlying factor.[324] Buehl and associates showed that a hydrophobic, acrylic IOL exhibited a marked reduction of PCO when the optic was modified from a round edge design to a square posterior edge.[325]

There are two theories as to why a square edge prevents migration of LECs onto the posterior capsule; these are the “contact cell inhibition theory” which postulates that LECs cease to proliferate on meeting a square edge and the “compression theory” which postulates that capsular contraction pushes the IOL against the posterior capsule and produces a pressure barrier at the optic edge inhibiting LEC migration. Mathematical modeling suggests that a square edge profile produces a greater pressure barrier on the posterior capsule in comparison to a round edge;[326] this is supported by in vitro LEC culture experiments by Nagamoto.[327]

Fibrosis on the anterior capsule shrinks the capsular bag after surgery, forcing the posterior IOL surface against the posterior capsule which produces the pressure barrier within a month of surgery and before LECs have had time to migrate from the peripheral capsule.[320] This process would be enhanced by factors such as haptic angulation and IOL-capsular adhesion.[323] It would also explain why silicone round-edge IOLs are associated with low PCO rates.[320] As silicone has been shown to induce more marked anterior capsular fibrosis than other materials,[328] one would postulate that in these eyes there is more shrinkage of the bag and a greater pressure of the IOL edge against the capsule, therefore, anterior capsular fibrosis in this situation works to the advantage of the IOL. Furthermore, Khalifa showed that polishing of the anterior capsule removes LECs, reduces anterior capsular fibrosis, and conversely is associated with more PCO (pearl formation PCO) 2 years later.[329]

Despite square-edge optic lenses, some patients still require Nd:YAG capsulotomy; recent reports suggest YAG rates in the order of 1% to 4% at 2 years.[330] Wren et al.[320] demonstrated that 65% of patients with a 5.5 mm square-edged IOL had clear posterior capsules and only one patient (1.7%) from this cohort required capsulotomy at one year. The main identifiable cause of PCO formation in these patients relates to the capsulorrhexis contact with the IOL as, within the limited parameters of this study, Wren et al.[320] found no relationship between the amount of PCO and the patient’s age, gender or axial length, but they found the PCO was increased if there was loss of IOL/rhexis contact. Analysis of images shows that LECs invade the capsule in this area explaining the reason for PCO in 13 eyes (61.9%) of the 21 eyes with PCO. Other authors have found that there is more PCO in this situation.[329, 331] Complete contact of the rhexis with the lens provides equal forces of capsular pressure around the IOL circumference. If there is loss of contact of the rhexis with the lens, unequal forces of capsular fibrosis will produce an uneven pressure profile on the capsule which could allow LECs to migrate and proliferate under the IOL. Probably the worst situation would be when the rhexis sits “half on and half off” the IOL which causes the greatest imbalance of capsular fibrosis. It is notable that Wren et al.[320] found more PCO in those patients groups with between 4 and 9 clock hours of loss of rhexis contact. This was further substantiated by another study.[332]

Meacock et al noticed that larger optic IOLs have a lower PCO rate and this might, in retrospect, be explained by the fact that it is easier to get the rhexis on the IOL with a larger optic.[322] Better injector technology now allows larger optic IOLs to be inserted through smaller incisions and this should encourage the transition to use of larger optic IOLs. These results show that the comparative success of an IOL in preventing PCO cannot be judged in isolation from surgical technique.[321]

As discussed in chapter 2, asphericity was introduced as a new concept in the IOL technology in early 2000s. Whether the asphericity of the IOL optic design affects the square edge profile of the IOL (an important factor for PCO prevention) was unknown and this led us to perform an invitro study described in Section 3.5. How the different aspheric designs (AcrySof SN60WF) compare with the conventional spherical IOLs (AcrySof SA60AT) on the market with regards to the PCO was yet to be understood and this led us to study this in the paper described in Section 3.6. Whether different hydrophilic acrylic aspheric design of IOLs differ in the PCO rates was studied in the paper described in Section 3.7.

1.6 Rationale for conducting our studies

Conventional spherical IOL implantation after cataract surgery provides excellent visual acuity outcomes but contrast sensitivity in pseudophakic eyes can be affected by spherical aberration. This is because conventional spherically-surfaced IOLs have positive spherical aberration which combines with the positive spherical aberration of the cornea to reduce optical quality as noted above. Aspheric IOLs with a modified optic geometry can induce negative spherical aberration and were designed to compensate for the spherical aberration of the cornea to improve optical performance. The Tecnis Z9000 IOL is the first wavefront-designed (aspherical) IOL used in clinical practice in 2002.[218] Its purpose is to correct the positive spherical aberration of the cornea resulting in a pseudophakic eye with zero spherical aberration and thus reproducing the aberration condition in young eyes. Following this development, other companies have started producing aspheric IOLs with different asphericities.

The results of studies comparing various aspheric and spherical IOLs vary widely due to the variation in study designs and methods.[333] Although there is evidence that IOLs with negative spherical aberration reduce the depth-of-focus by reducing the multifocality,[137, 243] there are no studies comparing the visual and optical outcomes after implanting conventional IOLs with spherical aberration with negative spherical aberration of different amounts, that can compensate for the corneal spherical aberration fully or partially. Various groups have previously published studies that compare conventional spherical IOLs with different aspheric IOLs employing different protocols and follow-up times[163, 166, 168-177, 187, 188, 220] but there are no studies performed by the same group with the same protocol comparing the variety of IOLs with different spherical aberration profiles.

1.7 Thesis Synopsis and Aims

Following the overview of visual and optical performance of IOLs and PCO in the preceding two sections, Chapter 2 discusses the results of three papers published on the comparison of visual and optical outcomes after implantation of different aspheric and spherical IOLs[137, 138].

Chapter 3 investigates PCO more fully by discussing three further papers showing that not all ‘square edge’ IOLs are the same with regards to sharpness of the ‘square edge’,[334] the difference in PCO performance between aspheric and spherical IOLs[189] and the difference in PCO performance between two different hydrophilic acrylic (Akreos MI60 and AcriSmart 36A) IOLs with difference asphericity.[335] And finally, Chapter 4 provides a discussion of the results in the wider context of modern cataract surgery.

This thesis, therefore, presents and discusses a coherent body of publications on areas that affect the visual and optical performance of intraocular lenses in human eyes.

Chapter 2

Effect of Aspheric Lenses on Optical Quality and Visual Performance

2.1 Introduction

The initial concept of an IOL to correct the spherical aberration of the cornea came from a better understanding of the nature of the optical aberrations in the young eye and how aging modifies these aberrations. The relative contribution of the cornea and the lens to the retinal image has attracted the attention of scientists since Thomas Young in the 19th century.[336] In 1973, El Hage and Berny[105] measured corneal spherical aberration using a photokeratoscope and ocular spherical aberration using a Foucault knife-edge test. They observed that the corneal values were more positive than the total eye values, which they concluded were the result of negative values for the lens spherical aberration. A coupling of other higher-order aberrations between the cornea and lens was discovered later.[64, 337] In addition to spherical aberration, horizontal corneal coma is mostly compensated by the crystalline lens.[338, 339] This mechanism in the young eye resembles an aplanatic optical design in which both spherical aberration and coma are corrected.

Changes with age result in reduced optical image quality in the eye.[340] Whether this change is a consequence of changes at the cornea, lens or both, is clearly relevant to refractive procedures that alter these optical components. There is evidence that corneal aberrations are relatively stable with age,[125, 126] but the lens[106] changes from negative spherical aberration values in the young eye to more positive values in the older lens. This supports the hypothesis of a loss of the balance between aberrations of the cornea and the lens as a consequence of the changes in the ageing human crystalline lens. This was first demonstrated experimentally in a study[341] in which corneal and ocular aberrations as a function of age were measured simultaneously. Results demonstrated that normal ageing disrupted the balance of spherical aberration and coma between the cornea and lens compared to that present in younger subjects. With this understanding of aberration coupling in the older eye, Navarro et al[342] further evaluated eyes after IOL implantation. In their experimental studies of the in vivo optical quality of eyes implanted with IOLs, they showed that the objective retinal image quality appeared to be similar to that in normal patients of the same age.[342] This result was unexpected because IOLs were manufactured with theoretically perfect and ideal optical quality standards[343] and they have better optical quality than the isolated older human lens with theoretically imperfect optical quality. The compensation of aberrations in the eye provided an explanation to this apparent paradox and, more interestingly, a potential solution.[344] The best IOL would not be a perfect (aberration-free) lens but rather the IOL with aberrations opposite to those of the corneal aberrations, mimicking the situation in the young eye. These ideas opened a new era in the optical design of IOLs.

It should be mentioned that aspheric IOLs had been suggested earlier for the purpose of improving retinal quality in pseudophakic eyes[345] but not in the context of a proper understanding of the compensation of aberrations. Since then, aspheric-optic technology has been used to deliberately vary the spherical aberration of the eye and, therefore, retinal image quality. For example, IOLs have now been designed with negative spherical aberration with a mean value similar to that of the cornea but of opposite sign (Tecnis IOL, Abbott Medical Optics, USA) in an attempt to remove spherical aberration from the average eye and maximize retinal image quality. The path to the discovery of this technology is a good example of how better understanding of the basic optics of the eye has led to an improvement in patients’ quality of vision.

The papers presented as part of this thesis in sections 2.2 to 2.4 are all related to the effect of aspheric IOLs on the optical quality of the eye and its corresponding visual performance. Section 2.2 describes our study analyzing wavefront aberration, depth-of-focus and contrast sensitivity using a fellow-eye, randomised comparison between aspheric (Alcon AcrySof IQ) and spherical (Alcon AcrySof Natural) intraocular lenses following standard cataract surgery. Both these lenses have a yellow filter and are therefore block blue light blocker. In the second study, we discuss the effect of the asphericity of intraocular lenses on vertical coma in section 2.3. In section 2.4 we describe our study comparing two different designs of aspheric IOLs that can be implanted through smaller incision sizes (microincision) (Acrsmart 36A and Bausch & Lomb MI60). The negatively asphric IOLs (Alcon AcrySof IQ and Acrismart 36A IOL) are described in chapter 2.

The papers described in sections 2.2 to 2.4 were from randomised fellow-eye studies performed at the Department of Ophthalmology, St. Thomas' Hospital, Guys' & St. Thomas' NHS Foundation Trust, London between 2006 and 2008. All the participants signed informed consent for participation in these studies and the studies had all the necessary approvals from the research and ethics committees and followed the tenets of the Declaration of Helsinki.

2.1.1 Alcon AcrySof IQ and Acrismart 36A IOLs:

The Acrysof IQ IOL (SN60WF, Alcon, Fort Worth, TX) was designed to partially compensate for the SA of a model eye. The lens has an aspheric posterior optic design with a thinner centre. It induces -0.15 microns of SA, compared to the -0.27 microns induced by the Tecnis lens, leaving approximately 0.1 micron of positive SA in the average eye. A few months later the AcriSmart 36A was launched by Carl Zeiss, Germany, which had the same asphericity as AcrySof IQ IOL but with a different lens design and material.

Awwad et al. showed that the Acrysof IQ aspheric IOLs reduce the positive ocular spherical aberration observed in pseudophakic and elderly eyes, especially at larger pupil diameters (6 mm), with no notable increase in coma.[346] With a 6.0mm pupil, total SA post-implantation was very close to predicted levels, at 0.09 ± 0.04 microns, compared to 0.43 ± 0.12 microns for patients implanted with Acrysof spherical IOLs ($p<0.0001$). However, it must be noted that a natural pupil size of 6 mm is not common and with advancing age the pupil size decreases. Moreover, larger the pupil, the issue of directional cone sensitivity needs to be considered. This issue is discussed further in this thesis on pages 92-93 in Chapter 4.

In another prospective study, the aspheric AcrySof IQ IOLs provided significantly better contrast sensitivity at all spatial frequencies during mesopic testing, with and without glare, than two other spherical Acrysof lenses.[230]

2.1.2 Bausch & Lomb Akreos MI60

A third aspheric IOL, the Akreos MI60 (Bausch & Lomb, Rochester, NY) was designed to be SA neutral, not adding to or subtracting from the corneal SA. Akreos MI60 is a newer microincision hydrophilic acrylic IOL with the same asphericity as its parent the Akreos Adapt AO. The Akreos Adapt AO lens is an aspheric acrylic IOL that is with aberration neutral. As a result, it does not add further aberrations to the patient's eye. This leaves the slight, naturally occurring positive aberration from the cornea, providing better depth-of-field. Because the AO lens has no relationship to the average or actual SA in the eye, it may be less dependent on centration. Altmann et al. found that the optical performance of a model eye was not affected by decentration of the AO, even when the lens was decentered by as much as 1.00 mm.[347] In this decentration model, the lens performed better than both a spherical IOL and an aspheric IOL designed to compensate SA (Tecnis).

Tolerance levels for the Tecnis aspheric lens require that it be decentered less than 0.4 mm and tilted less than 7 degrees in order to provide optical performance superior to that of a spherical lens.[216] Later studies have shown that the above values applied to monochromatic light only. In a real-world situation where polychromatic light is present, the above values nearly double, with about 0.8 mm of decentration and more than 10 degrees of tilt being tolerated.[348] A number of published studies over the past decade or more have shown that with a continuous curvilinear capsulorrhexis and in-the-bag IOL implantation, modern cataract surgery results in average tilt and decentration that is typically well within such tolerance limits.[349-351]

This concept was later added to all Bausch & Lomb lenses including the Akreos MI60, which was studied by us in detail and discussed later in this chapter.

2.2 Analysis of wavefront aberration, depth-of-focus and contrast sensitivity by the way of fellow-eye randomised comparison between aspheric and spherical intraocular lenses

Nanavaty MA, Spalton DJ, Boyce J, Saha S, Marshall J. Wavefront aberrations, depth-of-focus, and contrast sensitivity with aspheric and spherical intraocular lenses: fellow-eye study. J Cataract Refract Surg. 2009 Apr;35(4):663-71

Spherical aberration of the incident rays of light induces multiple focal points along the axis of an optical system. These multiple focal points contribute to the depth-of-focus after spherical IOL implantation, and residual spherical aberration can improve the depth-of-focus in eyes with spherical IOLs compared with that in eyes with aspheric IOLs.[243, 352] Vertical coma, Z_3^{-1}, may also be beneficial for reading function as the Roman alphabet uses verticals more than horizontals and verticals are better imaged in the presence of Z_3^{-1}.[155, 211, 353, 354] We designed this study to compare the quality of vision after fellow-eye implantation of a spherical IOL and an aspheric IOL by assessing wavefront aberrations, in vivo MTF, depth-of-focus and contrast sensitivity until 12 months follow-up.

Major findings:

1) At 3 and 6 months, there was no significant difference in 100% and 9% BCVA or photopic contrast sensitivity.
2) Mesopic contrast sensitivity was better and total and internal spherical aberrations were significantly less with the aspheric IOL.
3) Total and internal eye vertical coma was reduced with aspheric IOL.
4) Total MTF was not significantly different between groups.
5) The aspheric IOL group had 0.46 D less depth-of-focus than the spherical IOL group at 6 months. Distance corrected near acuity was

significantly better with the spherical IOL.

Study limitation:

1) This study did not formally assess the subjective outcomes of the patient through a validated questionnaire. To reduce the participant's fatigue, we did not include questionnaires. However, during the conduct of the study none of the recruited patients reported any subjective difference between the two IOLs. Interesting, a very few studies[172, 238] published on this subject included subjective questionnaires. Perhaps a questionnaire would have been useful to identify whether the difference in the contrast sensitivity and depth-of-focus was subjectively noticeable between the eyes in this fellow-eye study. Also questionnaire on the night vision would be more appropriate. A study comparing Tecnis (AMO, USA) (negatively aspheric) and Softport IOL (Bausch & Lomb, Rochester, USA) (aberration neutral) showed Tecnis to have better subjective night vision scores.[238] As stated earlier in the thesis in Chapter 1, there are several questionnaires in the literature for patient reported outcomes after cataract surgery[258] and newer ones[259] are evolving. We did not have subjective questionnaires in our protocol when we conducted the studies[137, 138, 189, 190] however, studies on newer lenses nowadays might not be approved without subjective questionnaires.
2) We did not measure subjective near and intermediate vision or depth-of-focus curves and only measured objective depth-of-focus. The investigators considered that the lengthy investigations involved for contrast sensitivity testing, aberrometry, 100% and 9% visual acuities, etc. precluded further tests.

Clinical implications:

The results in our study may imply that although asphericity of an IOL significantly improves mesopic contrast sensitivity, this may be at the expense of multifocality. However, the loss of depth-of-focus with the studied design of aspheric lens was only 0.46D. Whether this is significant for the patients is still debatable.

2.3 The effect of intraocular lens asphericity on vertical coma

Nanavaty MA, Spalton DJ, Marshall J. Effect of intraocular lens asphericity on vertical coma aberration. J Cataract Refract Surg. 2010 Feb;36:215-21.

Oshika et al[155] report that coma appears to contribute to apparent accommodation and it has been postulated that an age-related increase in corneal coma counteracts the normal onset of presbyopia.[126] The findings of Oshika et al [155] were confirmed by Nishi et al,[211] who found that vertical coma was responsible for a larger range of pseudo accommodation. Because of the beneficial effects of coma, Oshika et al[155] have suggested that coma might be induced with keratorefractive surgery. However, other studies found a degradation in contrast sensitivity from coma after keratorefractive surgery.[355-358] This has changed significantly in the past 15 years with advent of newer laser platforms and techniques. A recent meta-analysis by Wen et al.[359] comparing all newer platforms and techniques for laser refractive surgery has confirmed that corneal stromal ablation procedures (LASIK and FS-LASIK) rank highest in relation to efficacy, predictability, and safety, but surface treatments (PRK, T-PRK, LASEK, and Epi-LASIK) are superior in terms of image quality (ocular aberrations and contrast sensitivity). They also showed that in terms of ocular aberrations, the superiority of surface ablation surgery is most evident for a 6-mm pupil diameter.[359]

In a prospective, randomized, fellow-eye comparison of an aspheric IOL and a spherical IOL[137] we found that the aspheric IOL predictably reduced spherical aberration, thereby improving mesopic contrast sensitivity. However, we also found reduced vertical coma and reduced distance-corrected near visual acuity in eyes with the aspheric IOL. Bellucci et al[360] and Kim et al[173] also found reduced vertical coma after implantation of aspheric IOLs. Clinical studies of HOAs have not discussed the changes in vertical coma in detail. Therefore, we designed a non-randomised clinical observational study to analyse the effect of differences in IOL asphericity on vertical coma. This study recruited 200 eyes of 100 patients. 92 eyes had a spherical IOL, 32 eyes had a spherically neutral IOL, and 76 eyes had an aspheric IOL.

Major findings:

1) Vertical coma Z_3^{-1} and spherical aberration Z_4^0 values were highest with the spherical IOLs and lowest with the aspheric IOLs. Conventional spherical IOLs induced more vertical coma than newer aspheric and spherically neutral IOLs.
2) There was no difference in horizontal coma aberration between the 3 IOL groups.
3) There was no correlation between IOL power and vertical coma.
4) Vertical coma enhances the depth-of-focus; thus, newer aspheric and spherically neutral designs of IOLs may negatively affect uncorrected near vision.

Study limitations:

One limitation is that ours was a retrospective observational study analysing the data from 2 separate randomised fellow-eye controlled studies. There was a difference in sample sizes in the spherical, spherically neutral, and aspheric IOLs, with more eyes having an AcrySof SN60AT IOL in the spherical group and an AcrySof SN60WF IOL in the aspheric group. This may introduce some bias. However, our study gives an in-depth analysis of aberrations by placing eyes with different IOLs in broad groups according to the sphericity of the IOL optic. Preoperative aberrometry was not performed, therefore, the theoretical possibility of pre-existing aberrations influencing the postoperative aberration profile cannot be ruled out. Finally, this study was not designed to look at the effect of vertical coma aberration at various pupil sizes. iTrace machine measures the aberrometry at the patients natural pupil size but the software has a capability to give aberrometric values computed for various fixed pupil diameters after the measurements are stored on the system.

Clinical implications:

The technology of aberration-correcting IOLs is promising but should not be generalized to all patients. Discussion of the pros and cons becomes questionable in light of the fact that pupil size normally decreases with age.[242] Yamaguchi et al[128] found a mean mesopic pupil size of 3.60 ± 0.57 mm and a mean photopic size of 2.9 ± 0.50 mm in a pseudophakic population with a mean age of 68 ± 9.6 years.

The other interesting finding of this study is the fact that we found no statistically significant difference ($p=0.0520$) between the mean vertical coma of 44 eyes with Alcon AcrySof SN60AT (-0.165 ± 0.208μm) and 24 eyes implanted with the Alcon AcrySof MA60AC (-0.060 ± 0.211μm). It should be noted that from the same company with the same material and same spherical aberration profile and with same optic diameter. Furthermore, there was no significant difference in mean vertical coma between the Alcon AcrySof MA60AC (-0.060 ± 0.211μm) and the Akreos MI60 (-0.042 ± 0.148μm) ($p=0.7089$) and also the AcriSmart 36A (-0.034 ± 0.141μm) ($p=0.5829$). This suggested that although the Alcon AcrySof MA60AC (Spherical), Akreos MI60 (spherically neutral) and AcriSmart 36A (negatively aspheric) IOLs had different asphericity they induced similar vertical coma (Appendix 2, Table 2). This may be due to the difference in the designs as explained below and difference in the sample size of the three IOL groups. It is also of note that we found positive vertical coma values with the HumanOptics MC611MI spherical IOL, which has a plate haptic design.[190] This difference may be due to slight tilt and decentration of the IOL inside the capsular bag. Tilt and decentration of intraocular lenses (IOLs) are known to deteriorate image quality, particularly with aspheric IOLs.[345, 360, 361] Several investigators have performed laboratory tests to identify the maximum decentration and tilt possible before the performance of the Tecnis aspheric IOL (Advanced Medical Optics) becomes inferior to that of a spherical control IOL. Holladay et al.[216] calculated the critical amount of decentration for the aspheric Tecnis IOL to be 0.4 mm, while tilt is critical at 7.0 degrees. Using a more physiological eye model, Piers et al.[348] calculated an even greater range of decentration (0.8 mm) and tilt (10 degrees) before the performance of the Tecnis IOL performs more poorly than a spherical control IOL.

However, a study comparing 3 piece and single piece AcrySof IOLs found no difference in tilt and decantation of the IOLs. [362]. A majority of the aberrometers will measure the aberration once the eye is focused on a target. This means that the aberration will be measured on the visual axis rather than the pupillary axis. Also it is known that the intraocular lenses and crystalline lenses may not be centered on the pupil axis and the capsular bag may not be centered to the visual or pupil axis.[363] Therefore, slight decentration of any IOL with regards to visual axis (even if it is centered in the capsular bag or the pupil axis) will lead to some comatic aberration.

The question is whether mild malpositioning of IOLs in the pseudophakic eye has an impact on image quality. With increasing decentration, the model eye of Dietze and Cox[364] with an aspheric IOL showed an increase of asymmetrical 3rd-order aberrations at a much faster rate than the spherical IOL. On the other hand, it was recently reported that tilting of the natural aspheric lens has surprisingly little effect on foveal image quality because corneal and internal coma cancel each other out in phakic eyes due to opposite signs of corneal and internal coma.[339, 365] Mester et al.[363] found this compensation effect in the young eyes of the crystalline lens group in their study comparing tilt and decentration in aspheric IOL with young eyes of crystalline lens patients. Furthermore, they also found that all crystalline lenses were displaced to the temporal side of the pupil centre (mean 0.07 mm) and all IOLs, to the nasal side of the pupil centre (mean 0.06 mm) with some downward decentration (mean 0.16 mm) in the crystalline lens group.[363] In the IOL group, there was almost no mean vertical decentration detectable. With respect to the fixation axis, lenses in both groups were significantly tilted to the temporal side and up (ie, top of the lens tilted more toward the back and bottom tilted more toward the front).[363]

Moreover, the effect of tilt and decentration on induced coma through the lens is negligible when the aspheric surface is close to the pupil.[366] The closer the distance, the less effective the influence of asphericity on coma. This could be an advantage of the prolate aspheric surface of the Tecnis IOL, which is on the front of the lens. The effect might therefore be different for aspheric IOLs with a different shape factor or IOL power or with IOLs that have the aspheric surface on the posterior surface of the lens.[363].

In our studies although the Akreos MI60 and AcriSmart 36A had plate haptic designs, we found a difference in coma between them (Akreos MI60 is aspherically neutral and AcriSmart 36A is negatively aspheric).[138, 190] This could be due to aberration-free IOLs being less sensitive to decentration and tilt than aberration-correcting IOLs but provided better image quality than spherical IOLs.[367] Aberration correcting IOLs have the potential to provide diffraction-limited imaging quality when perfectly aligned.[367]

With age the pupil size decreases[242] and hence the effect of asphericity of the IOLs decrease. Age-related cataract remains the main indication for cataract surgery, hence the practical benefits of aspheric IOLs in older patients with smaller pupils is debatable. Intraocular lenses should be customized to the patient's visual requirements and ophthalmic parameters, such as natural photopic and mesopic pupil size. For example, a patient who drives a lot particularly at night may benefit from an aspheric IOL, which improves mesopic contrast sensitivity. A person who is an occupational reader or a computer worker may receive more benefit from a conventional spherical IOL. As stated in Chapter 1 and earlier in this chapter, this again highlights the importance of questionnaires not only for research studies but also for clinical decision-making.

2.4 Comparing two different designs of aspheric IOLs that are designed to go through smaller incision sizes (microincision).

Nanavaty MA, Spalton DJ, Gala KB. Fellow-eye comparison of 2 aspheric microincision intraocular lenses and effect of asphericity on visual performance. J Cataract Refract Surg. 2012 Apr;38(4):625-32.

Microincision cataract surgery has evolved so that phacoemulsification can be performed through incisions 1.5 mm or smaller,[129] inducing considerably less corneal astigmatism than surgery using conventional corneal incisions.[368-370] The development of microincision cataract surgery has led to a new generation of microincision IOLs that can be implanted through sub-2.0 mm incisions. These newer IOLs, which can be implanted through smaller incisions, are also aspheric in design. Several studies[137, 168, 187, 230, 238, 371-373] have shown that decreasing spherical aberration with aspheric IOLs improves retinal image quality and mesopic contrast sensitivity. The results in studies comparing various aspheric and spherical IOLs vary widely due to the wide variation in study designs and methods.[333] Although there is evidence that negatively aspheric IOLs reduce the depth-of-focus by reducing the multifocality,[137, 243] there is no study comparing the visual and optical outcomes after grouping these IOLs according to their inherent ability to induce spherical aberration (ie, spherical, spherically neutral, and negatively aspheric IOLs) and that are implanted by and followed up with the same protocol by the same investigators.

This was a dual-phase study. The first part was a prospective randomised fellow-eye controlled analysis of visual performance, wavefront aberration, and depth-of-focus after implantation of a negatively aspheric and spherically neutral hydrophilic acrylic aspheric (Akreos MI60 and AcriSmart 36A) IOL.

The second part compared visual performance, wavefront aberration, and depth-of-focus after grouping various IOLs into 3 groups: spherical, spherically neutral and negatively aspheric, as well as using the data from the first part of this study and from a prospective randomised fellow-eye controlled study comparing the same parameters with standard aspheric and spherical IOLs.[137, 189]

Major findings:

1) In part 1, there was no difference in 100% or 9% BCVA, distance corrected near visual acuity (DCNVA), or depth-of-focus between the Akreos MI60 and AcriSmart 36A IOLs. Total spherical aberration was lower with the aspheric IOL.
2) In part 2, the BCVA and DCNVA were not different between the spherical, spherically neutral or aspheric IOLs. Total spherical and vertical coma aberrations decreased with increasing IOL asphericity. Depth-of-focus (4.0 mm pupil) also decreased with increasing asphericity and was significant between the spherical IOL and aspheric IOLs. The DCNVA did not differ between groups.
3) Asphericity of IOLs did not affect distance visual acuity. The difference in depth-of-focus was significant only between negatively aspheric and spherical IOLs. Asphericity differences up to 20 μm did not influence depth-of-focus.

Study limitations:

1) One limitation is that part 2 of this study was a retrospective observational study.
2) The incision sizes used in Part 2 of this study were 2.75mm and 2.4mm. However, we combined the data from various studies for these two incision sizes, as we believe that the difference in astigmatism between them would not be clinically significant.
3) There was a difference in sample sizes in the spherical, spherically neutral and aspheric IOLs, with more eyes having an AcrySof SN60AT IOL in the spherical group and an AcrySof SN60WF IOL in the aspheric group. This may introduce some bias, however, our study gives an in-depth analysis of aberrations by placing eyes with different IOLs in broad groups according to the sphericity of the IOL optic.
4) Preoperative aberrometry was not performed, therefore, the theoretical possibility of pre-existing aberrations influencing the postoperative aberration profile cannot be ruled out.
5) We did not assess the preoperative pupil size in our studies included in this project, and this is a limitation. However, it is debatable whether cataract surgery significantly affects the natural pupil size.

Clinical implications:

Our group (same investigators) conducted two randomized studies with various aspheric IOLs. One study comparing Acrysof IQ and Acrysof Natural[137] and another comparing two hydrophilic acrylic lenses (Akreos MI60 versus Acrismart 36A).[138] However all these lenses had different asphericity. The aim of both these randomized studies were to assess the impact of aberrations on visual quality when other factors such as the surgeon and surgical techniques were standardized. This is the reason why we used the same surgeon and same incision size in both these randomized studies. As there are no randomized studies performed by the same group with same standardized protocol with IOLs with varying asphericity, we decided to give a comparative overview of performance of all these lenses in part 2 of this paper.[138]

It is well known that the pupil size normally decreases with age.[242] The benefits of aspheric IOLs should be carefully balanced against their potential disadvantages because a reduction in spherical aberration and vertical coma may affect the depth-of-focus. In patients with small pupils, the advantages of increased contrast from the correction of spherical aberration are doubtful; so are the effects of reduction in depth-of-focus from HOAs. The relative merits of asphericity and better mesopic contrast sensitivity in patients with larger pupils have to be balanced with a potential loss of depth-of-focus in these eyes. A difference of up to 20 µm in asphericity of the IOLs appears not to produce a significant difference in depth-of-focus. Hence, it becomes imperative to customise the IOLs for the patient's visual requirements, taking into account photopic and mesopic pupil size and the advantages and disadvantages of aspheric and spherically neutral IOLs, which should be weighed against the patient's requirements and daily activities.

2.5 Conclusions:

This chapter summarises the findings of our publications comparing aspheric IOLs with spherical IOLs. We conclude that aspheric IOLs significantly reduce spherical aberration, improving mesopic contrast sensitivity. Results demonstrated that vertical coma was also reduced with aspheric IOLs. The reduced spherical aberration may be responsible for reduced depth-of-focus with aspheric IOLs, which could be disadvantageous for near tasks. The difference in depth-of-focus was significant only between negatively aspheric and spherical IOLs. Asphericity differences up to 20 µm did not influence depth-of-focus. We also conclude that the conventional spherical IOLs induced more vertical coma than newer aspheric and spherically neutral IOLs. Vertical coma aberration enhances the depth-of-focus, thus, newer aspheric and spherically neutral designs of IOLs may negatively affect uncorrected near vision. Moreover, asphericity of IOLs did not affect best-corrected distance visual acuity. Since the publication of our studies, Schuster et al[374, 375] in a detailed systematic review with meta-analysis and other later studies as described in table 2, have shown that aspheric monofocal IOL implantation resulted in less ocular spherical aberration and fewer ocular HOAs than spherical IOLs. This might explain the better contrast sensitivity in patients with aspheric IOLs.

Author	**Year**	**N**	**Aspheric IOL**	**Spherically neutral IOL**	**Spherical IOL**	**BCVA**	**Contrast vision**
2015	Raina et al.[179]	40	Alcon AcrySof SN60WF	-	Alcon AcrySof SN60AT	No diffrence	Better with aspheric IOL
2014	Li et al.[376]	60	Alcon AcrySof ReSTOR SN6AD3	-	Alcon AcrySof ReSTOR SN60D3	No difference in BCVA	Better with aspheric IOL
2010	De Vries et al.[377]	92	Alcon AcrySof ReSTOR SN6AD3	-	Alcon AcrySof ReSTOR SN60D3	No difference in BCVA	No difference between the IOLs
2010	Jafarinasab et al.[378]	68	AMO Tecnis (n=17) Alcon AcrySof IQ (n=17)	B&L Akreos AO (n=17)	AMO Sensar (n=17)	No difference in BCVA	AMO Tecnis & Alcon AcrySof IQ gave better contract vision at smaller pupil sizes
2010	Nochez et al.[379]	25	Zeiss AcriSmart 36A	Zeiss AcriSmart 46LC	-	No difference in BCVA	Better contrast sensitivity with AcriSmart 36A

Table 2.1. Comparative studies between aspheric and spherical IOLs.

Chapter 3

Posterior Capsule Opacification for Aspheric Intraocular Lenses

3.1 Introduction

While the quest to eliminate PCO continues, technological advancements in the field of cataract and refractive surgery have led to the development of newer aspheric IOLs that are well recognised to improve mesopic contrast sensitivity.[74, 75] Aspheric IOLs have aspheric surfaces, either anteriorly or posteriorly, depending on the manufacturer. There is little evidence on whether the aspheric design of the IOL could cause a clinically significant change in the development of PCO . [189, 335, 380-382]

Biber et al[382], in their study, compared PCO rates and the impact of PCO on visual performance between three IOL models (multifocal spherical AcrySof SN60D3, monofocal spherical AcrySof SN60AT and monofocal aspherical AcrySof SN60WF) in 225 eyes (75 in each group), all of which were single-piece hydrophobic acrylic IOLs. Patients had a mean follow-up of 15.9 ± 6.5 months. Posterior capsule opacification was diagnosed clinically by retrospective chart review and the length of time that this occurred after surgery was recorded. The PCO rate was found to be 42.7% at 13.1 ± 7.1 months postoperatively in the multifocal spherical group, 28.0% at 14.9 ± 9.5 months in the monofocal spherical group, and 14.7% at 10.3 ± 5.3 months in the monofocal aspheric group. The YAG capsulotomy rate with the multifocal spherical group (25.3%) and monofocal spherical group (17.3%) was higher than the monofocal aspheric group (4%).[382] Although they did not report a significant difference in mean postoperative duration at the time of performing YAG laser capsulotomy, laser capsulotomy was performed earlier in the monofocal aspheric IOL groups (approximately 9 months postoperatively) compared to multifocal spherical and monofocal spherical IOL (approximately 13 months postoperatively).[382] The authors[382] postulated that the reduction in PCO with aspheric IOLs in their study was because of the difference in design of the IOLs. They state that the posterior surface of the aspheric IOL is more convex centrally than that of the relatively flat spherical IOLs and postulate that a decrease in the convexity of the posterior surface of the spherical IOL reduces the potential for contact between the IOL and the posterior capsule thereby creating a potential space for lens epithelial cells to migrate and proliferate. [382] This is, in fact, erroneous as the AcrySof SN60WF has an aspheric posterior surface which is less convex that the anterior surface of the same IOL or the posterior surface of the spheric AcrySof SN60AT IOL. Their results are therefore more likely to reflect the retrospective study design.

YAG capsulotomy rates with other aspheric IOLs such as the Akreos AO IOL (Bausch and Lomb, Rochester, NY, USA) are reported to be 35% at 1 year by Alio´ et al.[383] and 1.4% with Tecnis Z9000 IOL (Abbott Laboratories, Abbott Park, North Chicago, IL, USA) at approximately 40 months by Ram et al.[384] whereas in a study on the Restor (AcrySof SN60D3; Alcon Laboratories) multifocal IOL Shah et al.[385] found a capsulotomy rate of 15.49% at a mean follow-up of 22 months. None of these studies can be compared because of the huge variation in the IOL design and material, lack of universal guidelines for performing laser capsulotomy, individual patient requirements, surgeon perception, availability of equipment and financial factors.

Although the aspheric IOL is thinner than its corresponding spherical IOL, the edge profile and edge thickness are very similar. We believe that a square edge profile produces its effect by compression of the edge against the posterior capsule as the bag fibroses and collapses after surgery thereby creating a mechanical pressure barrier to the lens epithelial cell migration.[326] In theory, reduced IOL thickness could cause less compression of the IOL against the posterior capsule as there is less IOL volume to push against the capsule. If this is the case, a reduction of 9% does not appear to affect PCO performance.

In summary, from the above studies, it was difficult to ascertain whether asphericity of IOL was a major factor influencing the development of PCO during the first 2 years after surgery.

Section 3.2 describes a comparison in an *in vitro* study analyzing the square edges of commercially available aspheric and spherical IOLs. We discuss the effect of asphericity on PCO in a clinical study in section 3.3 and in section 3.4 we describe our study comparing two different designs of hydrophilic (Akreos MI60 and AcriSmart 36A) aspheric IOLs that can go through smaller incision sizes.

Publications described in sections 3.2 through to 3.4 were from randomised fellow-eye studies performed at the Department of Ophthalmology, St. Thomas' Hospital, Guys' & St. Thomas' NHS Foundation Trust, London, between 2006 and 2008. All the participants signed informed consent for participation in these studies and the studies had all the necessary approvals from the research and ethics committees and followed the tenets of the Declaration of Helsinki.

3.2 Comparison of square edges of various aspheric and spherical IOLs that are commercially available

Nanavaty MA, Spalton DJ, Boyce J, Brain A, Marshall J. Edge profile of commercially available square-edge intraocular lenses. J Cataract Refract Surg. 2008 Apr;34(4):677-86

Posterior capsule opacification (PCO) remains the main complication of cataract surgery. As described in Section 3.3 above, its development is multifactorial, involving patient factors, surgical technique,[386-388] intraocular lens design, and possibly IOL material.[277, 278, 321, 389, 390] This study was designed to evaluate the edge profile of several commercially available IOLs using scanning electron microscopy [391]. All IOLs are marketed as having a ‘‘square-edged’’ profile. Using purpose designed software, we measured the IOLs edge sharpness and edge thickness.

We scanned the IOL with a standardized technique and measurements as described in the main publication (Appendix 4). In brief, the edge profile was calculated as shown in the figure 3.1 below.

For every consecutive pixel P on the posterior optic edge,

PR = PL = 40 pixels and angle ROL = 45 degrees.

Sharper optic edge = Smaller r and the smallest value for r is taken to be the 'sharpest' point of the edge, defining its profile.

Figure 3.1. Schematic diagram to show the principle of measuring the radii of curvature of the posterior optic edge (r = radius). *(Reproduced from* ***Nanavaty MA****, Spalton DJ, Boyce J, Brain A, Marshall J. Edge profile of commercially available square-edge intraocular lenses. J Cataract Refract Surg. 2008 Apr;34(4):677-86)*

Major findings:

1. The repeatability of the scanning technique was excellent (radius of curvature= ±0.10 μm).
2. The radius of curvature of posterior optic edges ranged from 7.6 to 23.1 μm.
3. Hydrophilic acrylic IOLs (except the HumanOptics MC Microlens 611 MI-B and 1CU) had radii of curvatures more than 10.0 μm of the posterior optic edge compared with hydrophobic acrylic and silicone IOLs (<10.0μm) except the Hoya AF-1 (19.9 μm).
4. Alcon AcrySof single-piece (SN60WF), HumanOptics 1CU, and AMO Clariflex CLRFLXC IOLs had the thinnest optic edges in the hydrophobic, hydrophilic and silicone groups respectively.

Study limitation:

3) There are several hundred IOLs available across the globe. This study only analysed the most popular IOLs of major IOL companies as it was beyond the scope of this study to analyse each and every IOL available on the international market.
4) There will be several new models and designs of IOLs coming to the market in future and the findings of these studies may not apply to those new designs in future.

Clinical implications:

1. Commercially marketed square-edged IOLs differed in the sharpness of the posterior optic edge.
2. Asphericity did not appear to be a factor affecting the square edge
3. Hydrophobic acrylic and silicone IOLs have sharper posterior optic square edge than most hydrophilic acrylic IOLs. This probably reflects difference in manufacturing techniques.
4. Differences in posterior optic edge profile may explain variation in posterior capsule opacification performance with different IOLs and materials.
5. Since the publication of this study, several companies have changed or started manufacturing IOLs with sharper edges. In 2018, we published the part 2 of this study to see how square are the edges of the 'square edged' IOLs since 2008.[392] In our recent part 2 paper we concluded that commercially marketed square-edged IOLs still differed in the sharpness of the posterior optic edge. More hydrophobic IOLs have rounder edges than those studied 10 years ago. Variations in the edge profile of hydrophobic IOLs were by far greater compared to the hydrophilic IOLs.[392]

3.3 PCO performance of aspheric and spherical IOL with same design and material

Nanavaty MA, Spalton DJ, Gala KB, Dhital A, Boyce J. Effect of intraocular lens asphericity on posterior capsule opacification between two intraocular lenses with same acrylic material: a fellow-eye study. Acta Ophthalmol. 2012 Mar;90:e104-8

There are numerous published studies on the visual and optical performances of these aspheric IOLs[137, 187, 218, 221, 230, 238, 371, 373, 393] but there is limited published literature on influence of the IOL asphericity on PCO. PCO performance of the spherical AcrySof SN60AT IOL has already been published[394]. We designed this prospective, randomised, fellow-eye controlled study to compare the spherical AcrySof SN60AT and an aspheric AcrySof SN60WF (Alcon Labs, Fort Worth, TX, USA), which are both single-piece IOLs made of same acrylic material, to evaluate the impact of asphericity on visual acuity and PCO outcomes.

We conducted a prospective, randomised, fellow-eye controlled study to analyse the effect of IOL asphericity on PCO by comparing two IOLs which were made of same hydrophobic acrylic.[189] They had similar designs except that the aspheric IOL is 9% thinner[395] and had a posterior aspheric surface (Figure 3.2).

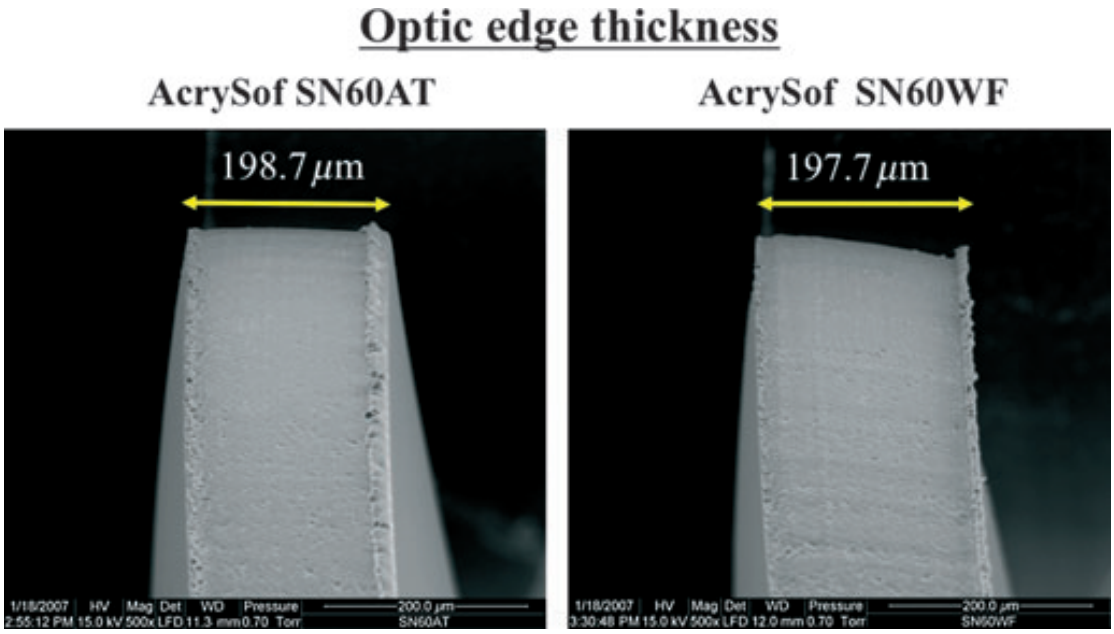


Figure 3.2. Environmental scanning electron microscopy pictures of the optic edge thickness of spherical AcrySof SN60AT and an aspheric Acrysof SN60WF *(reproduction of images from:* ***Nanavaty MA****, Spalton DJ, Gala KB, Dhital A, Boyce J. Effect of intraocular lens*

asphericity on posterior capsule opacification between two intraocular lenses with same acrylic material: a fellow-eye study. Acta Ophthalmol. 2012 Mar;90(2):e104-8).

Major findings:

1. At 1, 3, 6, 12 and 24 months, 47 (94 eyes), 47 (94 eyes), 44 (88 eyes), 42 (84 eyes) and 41 (82 eyes) patients were followed-up respectively. Hundred per cent and 9% contrast LogMAR BCVA was not significantly different between the two IOLs.
2. Percentage area PCO scores (mean ± SD) at 1, 3, 6, 12 and 24 months with the spherical IOL was 5.82 ± 9.89, 7.76 ± 16.83, 7.21 ± 12.46, 9.29 ± 18.25 and 14.39 ± 25.42, respectively, and with an aspheric IOL was 8.91 ± 12.79, 5.97 ± 10.32, 5.15 ± 7.92, 7.68 ± 11.18 and 12.18 ± 20.10, respectively.

Study limitations:

1. Like any surgical study, it is hard to implement a double-masked design for this prospective, randomised study where surgeries were performed by the same surgeon and this could be a potential limitation.
2. Unlike previous studies,[383-385] it was not possible to compare the YAG laser capsulotomy rates in our study as the number of patients needing YAG capsulotomy were relatively small in our study.
3. For this study we calculated the sample size based on the information from previous publication as there were no publications similar to what we intended to study. For this calculation, the mean PCO of group one (AcrySof SN60AT in this study) was presumed to be nine [394] and mean PCO for group two (AcrySof SN60WF in this study) was speculated to be 18. A standard deviation of 15 was presumed for both groups. For achieving 80% power with the type 1 error of 5%, the sample size was calculated to be 44 in each group. Considering 18– 20% dropout at follow-up visits, we decided to enroll 52 patients bilaterally.[189]

   However, if we calculate the required sample size now after the publication of this study, the mean PCO score of group one (AcrySof SN60AT) was 14.39 ± 25.42 and group two (AcrySof SN60WF) was

12.18 ± 20.10, for achieving 80% power with the type 1 error of 5%, the sample size comes up to 1286 in each group. This will clearly be impossible to achieve in a limited time frame.

Clinical implications:

1. Posterior capsule opacification was not significantly different between the spheric and aspheric IOLs in this fellow-eye, randomised comparison.
2. Additional asphericity on the existing model of IOL does not influence PCO performance.

3.4 Comparing the PCO performance of two different designs of aspheric IOLs with same material (hydrophilic) that are designed to go through smaller incision sizes (microincision).

Nanavaty MA, Spalton DJ, Gala KB, Dhital A, Boyce J. Fellow-eye comparision of posterior capsule opacification between 2 aspheric microincision intraocular lenses. J Cataract Refract Surg. 2013 May;39(5):705-11

The development of MICS has required the development of a generation of microincision intraocular lenses (IOLs) that can be implanted through sub-2.0 mm incisions, and it is important that these IOLs perform at least as well as IOLs designed for conventional incisions. Until recently, available microincision IOLs did not match the standards of conventional IOLs.[5–8] In a previous study comparing a single-piece microincision IOL and a conventional IOL,[396] we found equivalent visual performance but more posterior capsule opacification (PCO) with the microincision IOL as a result of its plate-design characteristics.

We designed this prospective randomised fellow-eye comparison study to evaluate the difference in PCO performance between 2 hydrophilic aspheric IOLs which are designed to be inserted through smaller incisions, the Acri.Smart 36A (Carl Zeiss Meditec AG, recently renamed the CT Asphina

509M), which corrects 0.17 μm of spherical aberration, and the Akreos MI-60 (Bausch & Lomb), which is spherical aberration neutral. Both IOLs can be implanted through a 1.8 mm incision. We also compared the PCO performance of these 2 hydrophilic Akreos MI60 and AcriSmart 36A IOLs with that of a single-piece hydrophobic acrylic spherical IOL (Acrysof SN60AT, Alcon Laboratories, Inc.) using information from our database.

Major findings:

1. High contrast BCVA was significantly better at 12 months and low contrast (9%) BCVA was better at 6, 12, and 24 months ($P < .05$) with the negatively aspheric IOL.
2. One eye in each group with microincision IOLs developed capsule phimosis at 1 month (No specific cause found to be responsible for capsular phimosis).
3. Neodymium:YAG capsulotomies were required by 2 years in 2 eyes with a negatively aspheric IOL and 8 eyes with an aspherically neutral IOL.
4. At 24 months, the mean PCO score remained less than 10% with the conventional spherical IOL, whereas it increased with time in the negatively aspheric IOL (up to 16%) and the aspherically neutral IOL (up to 23%).

Study limitations:

1. Like any surgical study, it is hard to implement a double mask design to this prospective, randomised study where the same surgeon performed surgeries and this could be a potential limitation.
2. There are several different models of hydrophilic acrylic aspheric (Akreos MI60 and AcriSmart 36A) IOLs with different haptic and optic designs. The findings of our study, which used hydrophilic IOLs of a particular design, do not necessarily apply to all IOL designs of newer IOLs.
3. A retrospective critical analysis of sample size based on our finding was very different to the actual sample size we used. If we consider the mean difference in PCO between the two groups of the IOLs studies in

this publication as 11.63% ± 30.5% at 2 years,[335] for achieving 80% power with the type 1 error of 5%, the sample size comes up to 109 eyes in each group. However, due to the lack of previously published data on the subject at the time when we conducted these studies, the sample sizes were calculated by assuming the difference between the PCO scores of the IOLs.

Clinical implications:

1. Single-piece hydrophilic acrylic (Akreos MI60 and AcriSmart 36A) IOLs have equivalent visual performance but more PCO than hydrophobic acrylic (AcrySof SA60AT and AcrySof SN60WF) IOLs.
2. There were significant variations in PCO performance with hydrophilic acrylic IOLs that may be attributable to difference in edge designs.
3. Modern aspheric hydrophilic acrylic IOL designs had more PCO than a conventional IOL (AcrySof SA60AT and AcrySof SN60WF) over a longer-term follow-up.

3.5 Conclusions:

This chapter summarises the findings of our publications assessing posterior optic square edges of various commercially available spherical and aspherical IOLs. We found that the asphericity of the IOLs was not related to the sharpness of the posterior optic edges of the IOLs. We also found that hydrophilic acrylic IOLs had less sharp square edges compared to hydrophic acrylic IOLs.

We also compared PCO rates of conventional hydrophobic spherical and aspheric IOLs of the same material and design and found no difference in the PCO rates between the two IOLs at 2 years. We compared PCO performance of 2 aspheric hydrophilic (Akreos MI60 and AcriSmart 36A) IOLs with different asphericity and found more PCO with both these hydrophilic IOLs compared to hydrophobic acrylic IOLs and variation of asphericity did not appear to be an important factor contributing to the PCO. In retrospect, with regards to the sample size of these studies[189, 335] a retrospective power calculation indicates significantly larger numbers of participants would be required to reach significance although the data on which to base the power calculation was not available prior to the study. We must also consider that the lenses compared were of different designs and materials, which will also influence the development of PCO significantly.

Chapter 4

Discussion and Conclusions

4.1 Discussion on aspheric IOLs.

Since the publication of our work[137, 138, 190], several comparative studies[178-186, 397] have supported our findings. Yadav et al.[185] conducted a study comparing the safety and efficacy of a relatively low cost locally manufactured spherical IOL (Acriol EC, Caregroup IOLs, India) with an aspheric IOL (AcrySof IQ, Alcon Laboratories, USA) on 205 eyes of 137 patients. They found no significant difference in the mean postoperative BCVA up to 12 months in either group. The contrast sensitivity, wavefront aberrations and PCO were comparable between the groups except for higher-order aberrations and spherical aberration which were higher in eyes with the spherical Acriol EC. Furthermore, a prospective, non-randomised study by Xu et al.[184] of 105 patients (210 eyes) compared patient-reported outcomes after implantation of the aspheric ZA9003 (AMO, USA), or the aspheric MCX11 ASP IOL (HumanOptics AG, Germany) or a spherical IOL (HQ-201HEP, Hexavision, France). They concluded that the implantation of an aspherical IOL could improve vision-related quality of life compared with a spherical IOL. However, there were no statistically significant differences in vision-related quality of life between aspheric IOLs with different magnitude of negative spherical aberration. In a paediatric population, Raina et al.[398] compared the optical performance of aspheric IOLs versus spherical IOLs after cataract surgery. Their results suggest that aspheric IOLs compensate for the spherical aberration of pediatric eyes. In comparison to spherical IOLs, eyes with aspheric IOLs had decreased ocular aberrations, particularly spherical aberration, which contributed to better contrast sensitivity in these eyes. Furthermore, Eppig et al.[181] evaluated the index of contrast sensitivity (ICS) in eyes after cataract surgery with various intraocular lens designs. They compared the area under the log contrast sensitivity curve (AULCSF) in 395 eyes of 198 patients (age of 73.1 ± 7.86 years) receiving 11 different aspheric IOL designs (aberration-free and correcting) and a spherical IOL as a control group. From the contrast sensitivity, they calculated the ICS according to Haughom and Strand[399]. With aberration-correcting IOLs, ICS was statistically better than with aberration-free or spherical IOLs, whereas the latter two showed no significant difference at 3 months. Espindola et al.[397] in a prospective clinical study enrolling 25 patients with bilateral cataract (50 eyes) using either aspheric (Akreos AO, Bausch & Lomb, USA) or a spherical (Akreos Fit, Bausch & Lomb, USA) IOL also found that aspheric IOLs significantly reduced spherical aberration and HOAs, improving mesopic contrast sensitivity. Similar results were also shown in a study by Naripthaphan et al.[182] who compared visual and aberrometric outcomes of 2 toric IOLs, a spherical lens (AcrySof Natural, Alcon Laboratories, USA) and an aspheric IOL (AcrySof IQ, Alcon Laboratories, USA) at 3 months after implantation in 44 eyes. They concluded that both groups had similar clinical effectiveness for unaided visual acuity, aided visual acuity and astigmatism correction but aspheric IOLs had significantly less spherical aberration.

In our studies,[137, 138, 190] we found contrast sensitivity to be better with aspheric IOLs in mesopic conditions only but Yagci et al.[186] using a Rayner 620H spherical IOL (Rayner, UK) in one eye and a Rayner 920H aspheric IOL in the contralateral eye in a randomised prospective comparative study of 60 eyes (30 patients) showed that the aspheric IOL significantly reduce HOAs and resulted in better levels of contrast sensitivity under photopic conditions. Crnej et al.[180] compared the ocular wavefront of eyes with aspheric (Tecnis, Z9000, AMO, USA) and silicone spherical optics (CeeOn Edge, 911A, AMO, Santa Ana, CA, USA) after cataract surgery. They took into account the patients' pupil size under reading conditions and after pupil dilatation in a prospective, randomized, bilateral, intra-individual, controlled study which was patient and examiner masked, in 60 eyes of 30 patients. They found that the effect on visual function was detectable for mesopic contrast sensitivity but there was no difference in visual acuity. The spherical aberration was found to be significantly lower under physiological pupil conditions as well as when recalculated for the capsulorrhexis size and under pharmacological dilatation.

We did not study the difference in depth-of-focus outcomes between aspheric and spherical IOLs in eyes with different axial lengths[137, 138, 190] but Steinwender et al.[400] evaluated whether hyperopic patients with short axial length and high dioptric intraocular lens power can achieve a higher depth-of-focus after implantation of a monofocal spherical or aspheric IOL than emmetropic patients. They concluded that implantation of a monofocal spherical IOL resulted in an increased depth-of-focus without significant degradation of distance visual acuity or contrast sensitivity. Interestingly there were no differences in the depth-of-focus between hyperopic eyes and emmetropic eyes. Another study by Nishi et al.[183] assessed the amplitude of pseudo accommodation and higher-order aberrations with three types of implanted monofocal IOLs: aspheric yellow (AcrySof IQ); spheric yellow (AcrySof Natural); and spheric clear (AcrySof single piece) in 60 patients. The pseudo accommodation was measured by the lens-loading method and the postoperative ocular higher-order aberrations were measured with a Hartmann-Shack wavefront analyser through natural and 4 mm pupils. Their results suggest that the spherical aberration and selective spectral transmission of IOLs may work together to increase the amplitude of the pseudo accommodation.

There have been a couple of non-comparative cohort studies published assessing quality of vision after aspheric IOL implantation since our publications[137, 138, 190]. Kretz et al.[401] evaluated the quality of vision in respect to high order aberrations and straylight perception after implantation of an aspheric, aberration-correcting, monofocal IOL in 21 patients (34 eyes) aged 50 to 83 years. The straylight was measured with C-Quant (Oculus, Germany). They concluded that implantation of an aspherical aberration correcting monofocal IOL after cataract surgery resulted in very low residual higher order aberration [71] and normal straylight. Nochez et al.[402] assessed the impact of ocular aberrations on objective vision quality and depth-of-focus in 30 patients (54 eyes) who had received an aspheric monofocal IOL (Acri.Smart, Carl Zeiss, Germany). Aberrometry measurements were performed under mesopic conditions with a 6.0 mm pupil using a Wavescan aberrometer. Objective evaluation of optical vision quality was performed using the Optical Quality Analysis System II (Visionmatrix, Spain). The 3 measurements were the MTF: the objective depth-of-focus which was computed as the focus range at which Strehl ratio did not fall below 50% of the maximum and the objective scatter index. Three ocular aberrations (2nd-order astigmatism, trefoil and spherical aberration) seemed to interact with objective contrast sensitivity and depth-of-focus, whereas residual spherical aberration exerted opposite effects on image quality in individual patients.

In our studies[137, 138, 190] we did not aim to categorise the outcomes based on the pre-existing refractive error. Fang et al.[403] evaluated the postoperative visual quality of cataract patients with extreme myopia after implantation of aspheric intraocular lenses (IOLs) in 33 eyes. They concluded that the aspheric IOLs provided good visual outcomes in cataract patients with extreme myopia. These patients should undergo careful evaluation to determine the maculopathy severity level before surgery.

We excluded any eyes with previous corneal refractive surgery in our studies.[137, 138, 190] Ruiz-Alcocer et al.[404] studied the outcomes of aspheric IOL implantation in the presence of normal, hyperopic and myopic corneal ablation profiles post corneal laser refractive surgery. They analysed the visual quality of the AcrySof IQ (Alcon Laboratories, USA) IOL when combined with different corneal profiles in 10 eyes (10 participants) with no prior history of refractive or cataract surgery. An adaptive optics visual simulator was used to simulate the wavefront aberration pattern of an aspheric aberration-correcting IOL. Normal corneas (group A), low and high myopic corneal ablations (groups B and C, respectively) and low and high hyperopic corneal ablations (groups D and E, respectively) were also simulated. Monocular distance visual acuities at 100, 50 and 10 per cent of contrast were measured. The results suggested that the aspheric aberration-correcting IOL studied provides comparable results when it is combined with normal corneas and with corneas with simulated low myopic ablations. Their study suggested that when negative amounts of residual spherical aberration after cataract surgery are expected to be achieved, IOLs with more positive spherical aberration should be considered. Wang et al.[405], using theoretical simulation in 106 eyes of 80 patients, conducted a study to determine the optimum amount of spherical aberration in IOLs to maximize optical quality in eyes with previous hyperopic corneal surgery. The amount of spherical aberration in the IOL was varied to produce residual ocular spherical aberration ranging from -0.50 to +0.50 µm. With the use of the Zernike Tool Program, the polychromatic point-spread function with Stiles-Crawford effect was calculated for 6.0 mm and 4.0 mm pupils and defocus of 0.00 dioptre (D), -0.50 D, and +0.50 D. The IOL spherical aberration at which maximum image quality was achieved was determined. They suggested that the amount of IOL spherical aberration producing the best image quality in eyes with previous hyperopic corneal surgery, varied widely and could be predicted on the basis of the full spectrum of corneal HOAs.

We did not correlate our outcomes with the biometric data in our studies[137, 138, 190] but Whang et al.[406] studied the effect of biometry on outcomes of aspheric IOLs. They analysed internal spherical aberration in pseudophakic eyes that underwent aspheric IOL implantation, and investigated the relationships between biometric data and the effectiveness of aspheric IOL implantation. They found that the corrective effect of an aspheric IOL is influenced by preoperative axial length and postoperative anterior chamber depth. Not only the amount of negative spherical aberration on the IOL surface but also the preoperative axial length should be considered to optimize spherical aberration after aspheric IOL implantation.

In our study on aspheric hydrophilic (Akreos MI60 and AcriSmart 36A) IOLs, we used a standard incision size of 2.4 mm temporal side with coaxial cataract surgery for both the hydrophilic IOLs as the aim was to compare the visual outcomes only.[138] Von Sonnleithner et al.[407] analysed the clinical outcome and higher-order aberrations (HOAs) after 1.4-mm biaxial cataract surgery (B-MICS) and implantation of a new aspheric Incise® IOL MJ14T (Bausch & Lomb, Rochester, N.Y., USA) IOL in 157 eyes of 106 patients. They assessed the aberrations using the iTrace aberrometer (Tracey Technologies, Houston, Tex., USA). They found that the aspheric IOL was safely implanted through a 1.4-mm incision and showed similarly good postoperative outcomes in comparison to our outcomes with coaxial phacoemulsification.

From our studies, we suggested further research on analysis of customizing the aspheric IOLs based on patients' needs and patients' pre-existing ocular parameters.[137, 138, 190] Li et al.[408] investigated the distribution and changes in spherical aberration (Z_4^0) in patients with age-related cataract before and after phacoemulsification. They found that the corneal Z_4^0 varied significantly among cataract patients. They recommended that patients' corneal Z_4^0 should be considered when choosing an aspheric IOL as it increases slightly with age and hence customization of aspheric IOLs is important. Al-Sayyari et al.[409] published a study analysing the postoperative results of targeting zero spherical aberration by selecting the best-fit aspheric IOL based on preoperative corneal spherical aberration of patients with phacoemulsification surgery in 53 eyes. They concluded that customised selection of aspheric IOLs based on the eyes corneal spherical aberration has no significant importance comparing their results with the non-selected group.

We already know that the higher order aberrations can be measured with an aberrometer such as a Hartmann-Shack wave front sensor and they can be corrected with an adaptive optics system.[410] The benefits of correcting higher order aberrations in an adaptive optics system have been demonstrated.[410] However, there are some important caveats about the visual benefit that can be realized in ordinary vision. First, the benefits are reduced when the pupil is small. The visual benefit would be largest in younger patients in which the pupil is large, and in situations such as night driving. It is also important to recognize that the eye's higher order aberrations change substantially with accommodation in phakic eyes and we do not understand pseudoaccommodation in pseudophakic eyes well despite many studies[148, 149, 155, 354] having examined this. This means that a higher order correction for distance vision may not be appropriate for near viewing and vice versa even in pseudophakic eyes. There remain important questions about the accuracy with which customized, higher order correction can be delivered with intraocular lenses and laser refractive surgery. As just one example, there will be less tolerance to decentrations of the eye during surgery when higher order aberrations are corrected than when only defocus and astigmatism are corrected. This lack of tolerance may induce complex higher order aberrations which may or may not be beneficial.[410] As shown in our studies[137, 138, 190, 335] these vary with different designs of IOLs and the amount of asphericity they have. Moreover, the variability of the optical quality of the eye is very large, and some people will derive much more visual benefit than others. Abnormal eyes, such as those that suffer from large amounts of spherical aberration due to laser refractive surgery, or keratoconic eyes, stand to gain the most from customization methods with laser correction platforms.[410] As these methods are constantly refined, there is good reason to believe that many normal eyes, especially those with large pupils and large amounts of higher order aberrations, will see important improvements in visual performance with customized correction. With the rapid development of wave front sensing technology, we now have the tools to screen such patients easily. The remaining challenge is to perfect the correction methods to maximize the visual benefit for the largest number of patients. However, with regards aspheric IOLs for cataract surgery, as the volumes of the patients needing these are very high, it is not cost-effective to customize the IOLs for each patient undergoing cataract surgery based on their higher order aberrations and pupil size.

There are no studies on the impact of directional sensitivity of retinal photoreceptors at different pupil size on aberrations and quality of vision in pseudophakic eyes with aspheric IOLs. It is widely accepted that the cone photoreceptors exhibit directional sensitivity,[411] which is well known as Stiles–Crawford effect. [412,413] Simply stated, the Stiles–Crawford effect is the fact that a beam of light entering peripheral regions of the pupil does not appear as bright as light entering near the center of the pupil, and it can be explained by the waveguide properties of the retinal photoreceptors, particularly the cones. Atchison and co-authors[414-417] have reported the influence of the Stiles–Crawford effect on visual performance based either on experimental measurements or on eye models. For a photopic pupil, the hypothesis of uniform pupil transmission is effective in predicting the influence of aberrations and defocus on the eye’s visual performance, when the Stiles–Crawford effect can be ignored. But for a larger pupil size, the impacts of defocus on visual performance predicted by the above hypothesis do not agree with the experimental data measured on actual human eyes, and then the Stiles–Crawford effect could be introduced to interpret the discrepancies between the predicted results and the experimental data. Furthermore, a greater amount of higher-order aberrations were measured after refractive surgery as the pupil size increases,[160] especially for the aberrations of peripheral regions of the pupil. So the Stiles–Crawford effect may have a larger ability to compensate for the higher-order aberrations of the postoperative eyes, and be more likely to ameliorate the impacts of aberrations on visual performance when pupils are larger. Increase of higher-order aberrations accounts for only a proportion of the discrepancy between the theoretical and experimental visual performance. This discrepancy can also be attributed to the Stiles–Crawford effect. The Stiles–Crawford effect originates at the retina. Vohnsen Iglesias extended the common waveguide theory of photoreceptors to formulate a theory of the Stiles–Crawford effect in order to investigate in detail the relationship between the Stiles–Crawford effect and its optical counterpart.[418] They found that the finite width of photoreceptors not only leads to a slight broadening of the effective PSF but also reduces the impact of aberrations on the visual sensation produced.[419] From the optic theory, when light passing through the edge of a large pupil plays a significant role in degrading retinal image quality, the reduced effect of this light by apodization will improve image quality. Furthermore, Atchison revealed that the Stiles–Crawford effect could improve spatial visual performance for healthy eyes.[415, 417] Given all the above evidence on Stiles–Crawford effect, it is likely that the overall benefit of asphericity of the IOL for patients may be very small apart from slightly increased mesopic contrast sensitivity.

In our studies, we did not access intermediate vision or near vision but in retrospect these measurements could have given more information on the intermediate and near additions required after the spherical versus aspherical IOLs. Data indicate that some positive spherical aberration may provide better depth of focus.[420] Some studies found that the depth of focus was significantly larger in eyes with spherical IOLs compared with negative spherical aberration aspheric IOLs.[243, 352] In a comparison of the Tecnis Z9000 IOLs and the Akreos AO IOLs, Johansson *et al.*[234] reported that the latter provided a larger depth of focus. They also showed that a higher amount of spherical aberration resulted in a better depth of focus. Santhiago *et al.*[421] reported a comparison of the Akreos AO IOLs and the Akreos Fit IOLs, he found there was a significantly different amount of spherical aberration between the 2 IOLs while the depth of focus was similar. Gong et al.[422] compared the depth of focus amongst 3 groups of patients based on corneal spherical aberration. They divided patients according to the value of preoperative corneal SA. Eyes with corneal spherical aberration <0.10µm were assigned to group A, those with 0.10 ≤corneal spherical aberration <0.20µm to Group B, and those with 0.20≤ corneal spherical aberration <0.35µm to Group C. After implantation of a spherical aberration-free IOL that does not generate negative spherical aberration to compensate for the positive spherical aberration of the cornea in all three groups, they found a higher amount of spherical aberration in the optical system, which produced no significant reduction in depth of focus.[422] They also suggested that the difference of spherical aberration among groups was not large enough to cause changes in depth of focus.[422]

Since the introduction of IOLs with aspheric surfaces, improvements in the optical performance of monofocals IOLs have been minor. However, this could be set to change with the introduction of advanced technology monofocal IOLs such as the TECNIS Eyhance IOL, model ICB00, from Johnson & Johnson Vision (USA). With the naked eye the TECNIS Eyhance refractive IOL (ICB00) is indistinguishable from the TECNIS® Monofocal lens ZCB00 and refers to the same base geometry as for other TECNIS® IOLs. The TECNIS Eyhance IOL, unlike other monofocal lenses, is not based on a spherical-aberration (SA) based or zonal design, but the continuous power profile is created with a higher order asphere. In our recent study evaluating early experience with the new Tecnis Eyhance monofocal IOL in eyes with co-existing pathologies in 10 consecuitive patients [including a patient with corneal astigmatism needing limbal relaxing incision (n=1), previous macula-on retinal detachment (n=2), previous trauma with irregular pupil (n=1) and mild corneal guttate (n=1)], we found mean LogMAR (Snellen equivalent) BCVA and DCIVA were 0.07±0.13 (20/20) and 0.49±0.11 (20/60) respectively. 20/60 is equivalent to J7 or 10pt font in MicroSoft Word (MicroSoft Inc, USA).[423] Several other leading IOL manufacturers are working on similar designs of monofocal IOLs to give added benefit to intermediate vision.

Finally, there are no published studies or analysis directly comparing the cost-effectiveness of aspheric and spherical monofocal IOLs. Since these aspheric IOLs have been on the market for a long time now, the cost is not too dissimilar to the conventional spherical IOLs. Today, almost every company manufacturing IOLs will have majority of their IOL models based on an aspheric design. As it is hard to find the real cost difference in manufacturing aspheric and spherical IOLs in the literature, it is hard to justify whether the benefit of slightly improved contrast sensitivity at a larger pupil size is worth the costs involved.

4.2 Discussion on PCO.

Since our study on analysis of square edge designs of a wide range of IOLs, Brockmann et al.[424] evaluated commercially available 1- and 3-piece IOLs with scanning electron microscopy (SEM). In their study seven +23.0 dioptre IOLs of different design and material, and from different manufacturers, were chosen for a detailed assessment. Scanning electron microscopy was used at standardised magnifications to assess the IOL characteristics. The particular focus was the optic edge, the optic surface, the haptic–optic junction and the haptic. They found that all IOLs were of high manufacturing quality. Surface irregularities of 2 IOLs were attributed to the manufacturing technique. Methods for implementing the haptic–optic junction were diverse. Furthermore, Werner et al.[425] evaluated the microstructure of the edges of currently available hydrophilic acrylic IOLs in terms of their deviation from an "ideal" square as a follow-up of preliminary in vitro studies of experimental PMMA IOLs and commercially available foldable hydrophobic IOLs. In this study they had 24 designs of hydrophilic acrylic IOLs. For each design, a +20.0 dioptre (D) IOL and a +0.0 D IOL (or the lowest available plus dioptric power) were evaluated. The IOL edge was imaged under scanning electron microscopy (SEM) using an environmental microscope and standardised technique. The photographs were imported to a digital computer program and the area above the posterior-lateral edge, representing the deviation from a perfect square, was measured in square microns. They concluded that the microstructure of the optic edge of currently available square-edged hydrophilic acrylic IOLs showed a large variation of the deviation area from a perfect square. Buehl and Findl[426] conducted a systematic review of the literature based on Cochrane methodology to summarise the effects of intraocular lens geometry, including modifications of the IOL optic (especially optic edge design) and haptics, on the development of PCO. Twenty-six prospective randomised controlled trials with a follow-up of at least 12 months were included. In 5 of 7 studies, visual acuity was better in sharp-edged IOLs than in round-edged IOLs. The PCO score was significantly lower with sharp-edged IOLs but did not differ significantly between 1-piece and 3-piece open-loop IOLs. Because of the significant difference in the PCO score, sharp-edged IOL optics should be preferred to round-edged IOL optics.

We did not find any difference in PCO between the aspheric AcrySof IQ and AcrySof SN60AT at 2 years. Leydolt et al.[427] compared the incidence and intensity of PCO over 3 years in a randomised study comparing an aspheric Tecnis ZCB00 (AMO, USA) continuous-optic-edge IOL in 1 eye and spherical Acrysof SA60AT (Alcon Laboratories, USA) interrupted-optic-edge IOL in the other eye. They concluded that both IOLs had comparable PCO and Nd:YAG rates 3 years postoperatively. The optimised barrier function of the continuous-optic-edge IOL and the material properties of the interrupted-optic-edge IOL seemingly outbalanced the effect on lens epithelial cell migration and proliferation beneath the optic. Similar findings were also reported by Johansson[428] in a prospective, randomised, intra-individual, comparative trial with 50 cataract patients receiving either an AcrySof IQ® SN60WF (Alcon Laboratories, USA) or a Tecnis® ZCB00 (AMO, USA) IOL in the first operated eye and the second eye received the IOL type. Visual outcomes, PCO over time and the need for Nd:YAG laser treatment, were similar for the two IOLs. Anterior capsule fibrosis/contraction and glistenings were more pronounced with the AcrySof SN60WF IOL. In another study, Nixon and Woodcock[429] compared PCO in eyes with 1 of 2 models of 1-piece acrylic IOLs. This paired-eye study evaluated patients who had implantation of a aspheric Tecnis AAB00 (AMO, USA) IOL with a continuous optic edge in 1 eye and an AcrySof spherical SA60AT or aspheric SN60WF (Alcon Laboratories, USA) IOL with an interrupted optic edge in the fellow-eye. Posterior capsule opacification was assessed using the EPCO system. Eyes with an IOL with a continuous 360-degree square edge had significantly less PCO than eyes with an IOL with a square edge that was interrupted at the optic-haptic junction.

4.3 Conclusions:

In our prospective randomised studies[137, 138, 190] comparing aspheric (AcrySof SA60WF) vs. spherical (AcrySof SN60WF) IOLs and comparing two hydrophilic acrylic (Akreos MI60 and AcriSmart 36A) IOLs with different asphericity, we found that there was no significant differences in high contrast and low contrast (9%) BCVA or photopic contrast sensitivity between aspheric and spherical IOLs. However, mesopic contrast sensitivity was statistically significantly better and total and internal spherical aberrations were significantly less with the aspheric IOL. Vertical coma Z_3^{-1} and spherical aberration Z_4^0 values were highest with the spherical IOLs and this was not IOL power dependent. Conventional spherical IOLs induced more vertical coma than newer aspheric and spherically neutral IOLs. There was no difference in horizontal coma aberration between the 3 IOL groups. Vertical coma enhances the depth-of-focus and hence the aspheric IOL group had less depth-of-focus than the spherical IOL group at 6 months. Distance corrected near acuity was significantly better with the spherical IOL. We found no significant difference in the depth-of-focus between the IOLs with different asphericity. The difference in depth-of-focus was significant only between negatively aspheric and spherical IOLs (spherical IOLs had significantly better than negatively aspheric IOLs). Difference in IOL asphericity of up to 20 µm did not influence depth-of-focus.

The results in our studies may imply that, although asphericity of an IOL significantly improves mesopic contrast sensitivity, this may be at the expense of depth-of-focus. However, the loss of depth-of-focus with the studied design of aspheric lens was only 0.46 D for a pupil size of 4mm. Whether this is significant for patients is still debatable. The result may also imply that the technology of aberration-correcting IOLs is promising but may not be generalizable to all patients. Discussion of the depth-of-focus of aspheric IOLs must also include the fact that pupil size normally decreases with age.[242]

However, despite the advancement in the IOL technology with regards to asphericity, the issue of posterior capsule opacification affecting the visual quality still remains. In our in vitro study,[334] comparing the square edges of commercially available square edge designs, we found that commercially marketed square-edged IOLs differed in the sharpness of the posterior optic edge. Asphericity did not appear to be a factor affecting the square edge with hydrophobic acrylic and silicone IOLs showing sharper posterior optic square edge than most hydrophilic acrylic IOLs. This may be due to difference in manufacturing techniques. These differences in posterior optic edges may be responsible for the variation in posterior capsule opacification performance with different IOLs and materials. In the clinical study[189] comparing PCO we found that the PCO was not significantly different between the spherical and aspheric IOLs in this fellow-eye, randomised comparison. Additional asphericity on the existing model of IOL does not influence PCO performance.

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