FUNCTIONAL NEAR VISION ASSESSMENT IN PRESBYOPIA

NAVNEET GUPTA

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An ageing population means that there is an increasing prevalence of associated eye problems, of which the most common non-pathological condition is presbyopia. Although this is correctable by several techniques, few provide spectacle-free clear near vision similar to pre-presbyopes. Therefore, the development of presbyopia corrections continues and in order to obtain evidence of benefit of one technique over another, evaluations and comparisons must be made in a consistent manner. However, from the reviews presented in this thesis it is apparent that this is often not the case. The aim of this thesis therefore was to develop standards of best practice for the subjective assessment of near visual function in presbyopia.

Near visual acuity (VA) is a quick and simple measure but an assessment of the maximum reading speed and the smallest print size that can maintain this are equally important, to gain a better reflection of real world visual function. These metrics are dependent on the amplitude of accommodation (AoA) and often this must be evaluated using subjective techniques. Defocus curves are less susceptible than the push-up/push-down test to the influence of blur tolerance but their implementation must be standardised such that letter sequences and the order of lens presentation are randomised, to avoid memory effects, whilst the AoA should be quantified as the range of defocus for which only the best VA is maintained. In addition to such clinical assessments, subjective questionnaire evaluations are also important, to determine whether at least an individual's needs are met. The Near Activity Visual Questionnaire (NAVQ) developed in this thesis can be used for this.

Using these standardised near vision metrics it is shown that visual performance with monovision and multifocal contact lenses is comparable whilst initial outcomes of single optic 'accommodating' intraocular lens implantation are unlikely to be sustained in the long-term.

Keywords: Visual Acuity and Reading
Amplitude of Accommodation
Questionnaire
Presbyopic Contact Lenses
Accommodating Intraocular Lenses

DEDICATION

For my dear family – mum Sushma, dad Naresh and brother Bhupinder – thank you for being there to ride the highs and lows with me over the past three years.

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Finally, a special thank you to Amy Whiskens, with whom I shared an office for the duration of our PhDs; it is a tremendous support to have someone go through similar experiences at the same time as you.

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CHAPTER 1

The Origins and Correction of Presbyopia

1. Introduction

The life expectancy of humans has increased considerably over the past 100 years as a result of significant advances in medicine and technology. The population is also now ageing, with the proportion of those aged under 16 declining and the proportion aged 65 and over increasing, in the UK (The Office for National Statistics 2007). This longevity of life is accompanied by a preponderance of disorders that are typically attributed to the ageing process. Indeed, the eyes are no exception to this and of particular interest is the condition of *presbyopia*. Coined from the Greek term meaning 'old eye', presbyopia represents an age-related decline in the ability to maintain clear visual focus at near and is especially intriguing since its effects do not coincide with other age-related systemic deficits or even other ocular deficits (Pierscionek and Weale 1995, Weale 1995).

There are several techniques that can be used to correct presbyopia, as reviewed in this Chapter, with each aiming to provide clear distance and near visual function. In order to gauge the relative benefits of one technique over another, it is important to accurately evaluate the near visual ability that each confers without the need for additional aids. However, as is evident from the proceeding Chapters, there is a lack of standardisation in methods used for conducting common near vision assessments, making such comparisons difficult if not impossible. This thesis therefore aims to optimise the methodology of such near vision assessments in order to provide standards of best practice that ought to be applied. First, the most useful measures of near visual acuity (VA) and reading ability are investigated (Chapter 2). Second, the measurement of defocus curves to quantify the subjective amplitude of accommodation (AoA) is optimised (Chapter 3). Third, a new questionnaire to evaluate subjective perceptions of near visual ability and satisfaction with presbyopic corrections is developed (Chapter 4). The outcomes of these investigations are then applied to the evaluation of visual function with a new presbyopic contact lens (Chapter 5), a prototype single optic 'accommodating' intraocular lens (IOL) (Chapter 6), and the long-term visual outcomes of a single optic 'accommodating' IOL (Chapter 7). Finally, the implications of this research, and future possibilities, are discussed (Chapter 8).

1.1 Accommodation and Presbyopia

The ability of the eye to alter its dioptric power so that objects viewed at a variety of distances can be clearly perceived is known as *accommodation*. It was first suggested by Young in 1801 that this ability was conferred by a suspended lens in the eye (cited in Atchison 1995), whilst the AoA was first quantified by Donders in 1864 (cited in Rabbetts and Mallen 2007). His findings however, were superseded by those of Duane (1922), who studied a large sample of 4200 eyes. Duane reported no differences in the AoA between males and females, as measured using the subjective push-up/push-down test (see section 3.1.7.3, Chapter 3), but found that the binocular AoA was greater than the monocular AoA, most likely due to increased ciliary muscle contraction that arises from convergence in the binocular state. Indeed, this was supported by Glasser and Kauffman (1999) who found a reduction in the AoA when convergence was restricted. Of particular interest was the finding that whilst the AoA gradually declines with age, the rate of decline reduces beyond an age of 40 years (Figure 1.1). This was supported by Hamasaki et al. (1956) and by the objective measurements (the minus-lens induced change in refractive error) of Anderson et al. (2008) (Figure 1.1). It is likely, according to Duane (1922), that this reflects the increasing influence of *depth of focus* (DoF) that is associated with age-related pupil miosis (see section 3.1.1, Chapter 3), which may offset the loss of accommodation.

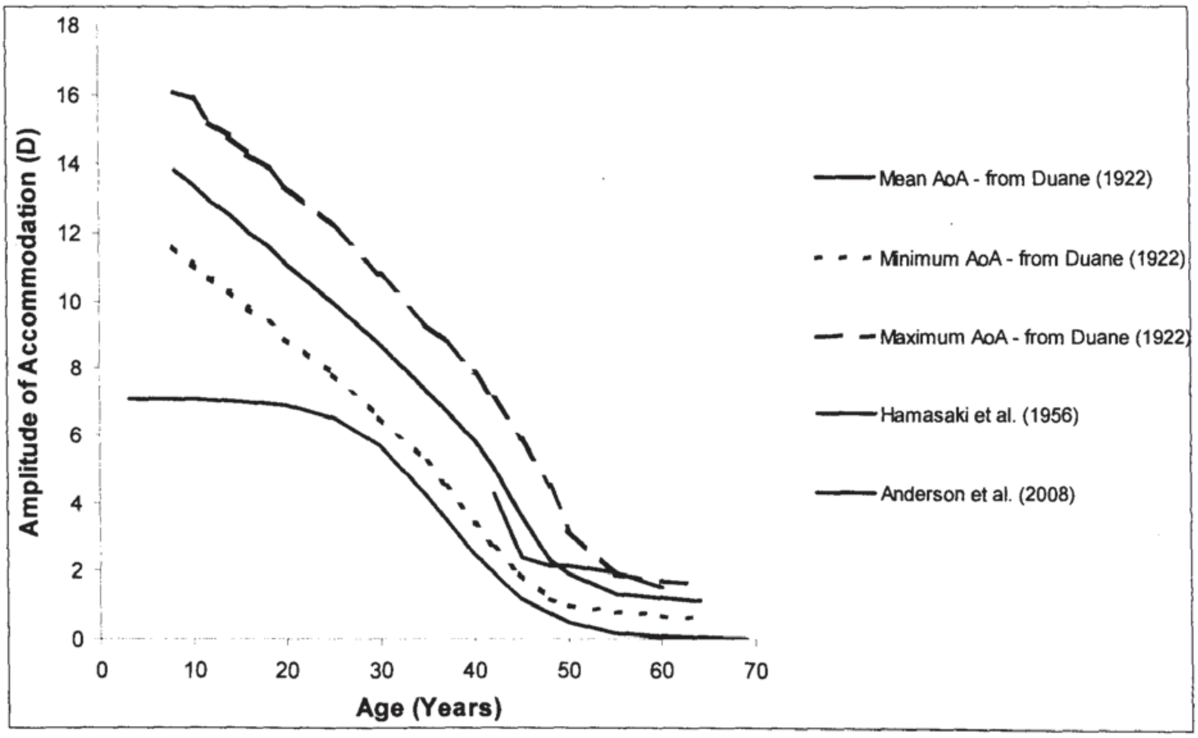

Figure 1.1 Change in the amplitude of accommodation (AoA) with age – *produced from data presented in Duane (1922), Hamasaki et al. (1956), and Anderson et al. (2008)*

NB. Anderson et al. only measured the AoA up to an age of 40 years; beyond this, data was pooled from the studies of Hamasaki et al. (1956), Koretz et al. (1989), Wold et al. (2003) & Ostrin & Glasser (2004)

In comparison to these cross-sectional studies, longitudinal studies instead suggest a linear decline in the AoA with age, at a rate of 0.40D per year (Hofstetter 1965), until this ability is lost completely by the age of 50 years (Ramsdale and Charman 1989). This disparity may be due to the susceptibility of cross-sectional studies to inter-individual variations in the onset of presbyopia, which may cause an average non-linear change in the AoA from an age of 40 years (Ramsdale and Charman 1989). It may also relate to differences in the use of non-standardised methods of measuring the AoA. Of importance however, is the notable problem that presbyopia poses, since the ability to maintain clear visual focus at near is lost approximately two-thirds of the way through the human lifespan. Discovering and correcting the cause(s) of presbyopia is therefore the subject of extensive research.

1.1.1 The Accommodation Apparatus

The primary ocular structures that are involved in the function of accommodation are the *ciliary muscle*, the *zonules of Zinn* and the *crystalline lens* (Figure 1.2). Other structures including the iris and vitreous may also be involved but there is currently insufficient evidence in support of this (see section 1.1.2).

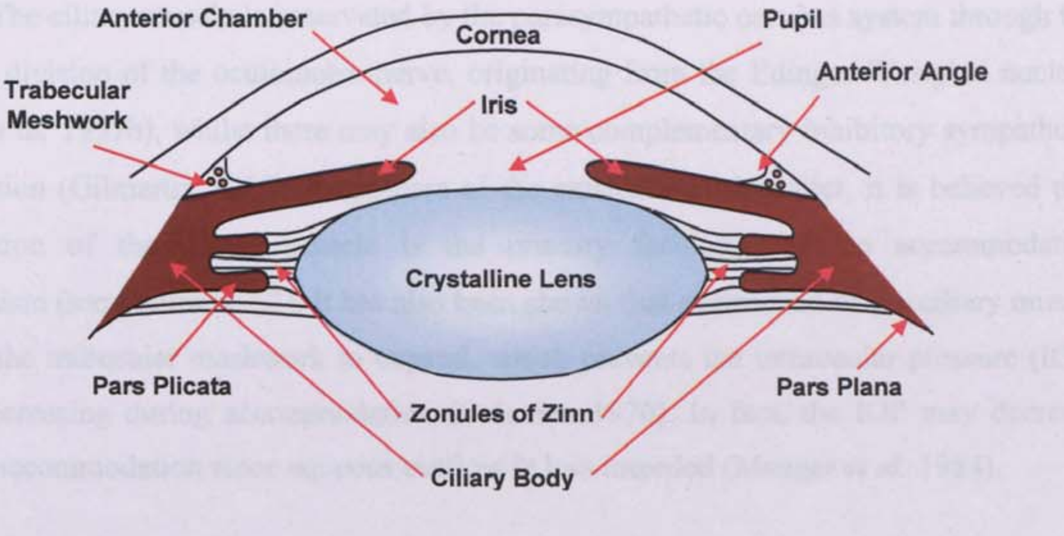

Figure 1.2 The accommodation apparatus in relation to other anterior eye structures – *produced based on a photograph in Bron et al. (1997a)*

1.1.1.1 The Ciliary Body & Muscle

The ciliary body is a highly vascular and pigmented ring of tissue that internally lines the anterior aspect of the eye at the region between the iris, to which it actually gives rise, and the choroid, with which it is continuous (Atchison 1995, Snell and Lemp 1998).

The posterior aspect of the ciliary body, the *pars plana*, has a smooth flat surface, which allows attachment with the vitreous. In contrast, the anterior aspect of the ciliary body, the *pars plicata*, comprises 70-80 finger-like processes that act as a connecting site for the zonules of Zinn. It is here that aqueous solution is produced whilst the ciliary muscle is also found in this region, occupying approximately 67% of the anterior ciliary body volume (Snell and Lemp 1998, Shea *et al.* 1999). The ciliary muscle comprises three distinct types of fibres. *Longitudinal* fibres are located adjacent to the sclera and are the most prevalent (41-69%), whilst *radial* fibres are found underneath these and *circular* fibres, the least prevalent (4-24%), are the most internal and anterior (Flugel *et al.* 1990, Bron *et al.* 1997b). The differentiation between these fibres improves with age since an increase in connective tissue content increases their separation (Pardue and Sivak 2000).

Whilst the ciliary muscle is classified as *smooth muscle*, it is in fact functionally atypical since it possesses fast contraction and relaxation properties that are more typical of *skeletal muscle* (Pardue and Sivak 2000, Croft *et al.* 2001). It is thought that these features are conferred by dense neural innervation (Schachar and Anderson 1995) and an abundance of mitochondria, which produce rapid reaction (0.34±0.06 seconds) and response (0.82±0.12 seconds) times for changes in accommodation with changes in fixation (Heron and Winn 1989). The ciliary muscle is innervated by the parasympathetic nervous system through the inferior division of the oculomotor nerve, originating from the Edinger-Westphal nucleus (Bron *et al.* 1997b), whilst there may also be some complementary inhibitory sympathetic innervation (Gilmartin 1986). Regardless of the existence of the latter, it is believed that contraction of the ciliary muscle is the primary facilitator of the accommodative mechanism (see section 1.1.2). It has also been shown that contraction of the ciliary muscle causes the trabecular meshwork to expand, which prevents the intraocular pressure (IOP) from increasing during accommodation (Coleman 1970). In fact, the IOP may decrease during accommodation since aqueous outflow is less impeded (Mauger *et al.* 1984).

1.1.1.2 The Zonules of Zinn

The zonules of Zinn, also known as *suspensory ligaments* but from this point referred to as *zonules*, are fibres that connect the crystalline lens to the ciliary body. Each zonule comprises many collagen fibrils, whilst elastic proteins confer recoil properties that are essential for accommodation (see section 1.1.2) (Atchison 1995, Bron *et al.* 1997a).

Scanning electron microscopy suggests that the zonules are attached to the crystalline lens capsule in three distinct groups. Equatorial zonules arise from the pars plicata and attach approximately 1.5mm anterior and posterior to the lens equator, whilst anterior and posterior zonules arise from the pars plana, with the former coursing anteriorly to the pre-equatorial aspect of the lens and the latter extending longitudinally towards the posterior, post-equatorial aspect of the lens (Bron *et al.* 1997a). Equatorial zonules appear to be finer and fewer in number than anterior and posterior zonules, although the distinction of these three groups has been questioned and suggested to be merely an artefact of tissue processing; instead all of the zonules may form a single uniform structure that inserts into the lens equator (Glasser and Campbell 1998). Of importance is that the insertions of the zonules into the crystalline lens have been shown to alter with age (Farnsworth and Shyne 1979) whilst the strength and number of fibres also reduces (Bron *et al.* 1997a); together, these changes may therefore contribute to the onset of presbyopia (see section 1.1.3).

1.1.1.3 The Crystalline Lens

The crystalline lens is a biconvex transparent structure that is suspended by the zonules immediately behind the iris and in front of the vitreous (Saude 2003). It is composed of approximately 65% water and 35% protein (*crystallins*) (Atchison 1995, Schachar 2006). The avascular nature of the lens allows light to pass to the retina unimpeded but this also means that oxygen and nourishment must instead be obtained from the aqueous. The primary role of the lens is to allow alterations in dioptric power of the eye so that incident light from various distances of regard can be focussed onto the retina. The power of the unaccommodated lens is approximately 16.00D and this is attributed to its high refractive index (1.39-1.42), which is conferred by crystallins (Bron *et al.* 1997a, Shea *et al.* 1999). The axial thickness of the unaccommodated lens is approximately 4.0mm whilst the equatorial diameter is approximately 10.0mm (Snell and Lemp 1998); the maximum power and axial thickness that can be achieved depends upon the age of the individual.

The lens structure can be divided into stratified layers, which represents the manner whereby fibres are continually produced in an onion-like configuration throughout the human lifespan (Oyster 1999, Shea *et al.* 1999). These layers can be categorised into the *capsule* (see section 1.1.1.3.1), the *epithelium* (see section 1.1.1.3.2), the *cortex* (see section 1.1.1.3.3) and the *nucleus* (see section 1.1.1.3.3) (Bron *et al.* 1997a, Saude 2003).

1.1.1.3.1 The Lens Capsule

The capsule is the most external part of the crystalline lens. It comprises predominantly collagen fibres that form a complex matrix to allow changes in lens shape when subjected to stress forces. The lack of elastin fibres is counter-intuitive to the capsule's very elastic behaviour, but it is thought that this property is achieved by virtue of a *coiled* configuration that the collagen fibres have, which allows them to behave like a 'spring' (Bron *et al.* 1997a, Krag and Andreassen 2003). Indeed, this type of characteristic is paramount to the universally accepted mechanism of accommodation (see section 1.1.2).

The capsule envelops the whole lens structure but in a non-uniform manner. The posterior capsule is thinnest (2.8μm) and the anterior capsule is more substantial (15.5μm), but the greatest thickness occurs at the equatorial region (20.0μm) (Bron *et al.* 1997a, Saude 2003). This distribution is thought to reflect the need for a strong attachment between the lens and the ciliary body at the equatorial region, with the zonules shown to penetrate deeply here (Krag and Andreassen 2003). Also, it has been suggested that an extra membrane exists on the external capsule surface during embryological development, but this then retracts during the first two decades of life to remain in the equatorial region only (Seland 1974). With increasing age, the anterior capsule thickness increases but the posterior capsule thickness does not (Fisher 1969). This is likely to reflect life-long growth of the lens epithelium, which is most abundant anteriorly and which itself forms the capsule; the posterior capsule in contrast has no epithelium (see section 1.1.1.3.2). The mechanical strength of the capsule also reduces with age (Krag *et al.* 1997), primarily due to an increase in inclusion bodies (Seland 1974) but perhaps also due to changes in amino acid and collagen fibre content, which therefore alters the capsule structure (Peczon *et al.* 1980). These changes may also contribute to the onset of presbyopia (see section 1.1.3.2).

1.1.1.3.2 The Lens Epithelium

The lens epithelium is located directly under the capsule but it is found only on the anterior lens surface. Posteriorly, the epithelium is only present during embryological development, to initiate primary fibre growth, and once these cells lose their nuclei they become enveloped within the lens structure (Shea *et al.* 1999, Saude 2003). The epithelium comprises a single layer of cells that perform different functions and consequently this produces a variation in cellular morphology (Bron *et al.* 1997a).

Central cells are flat and display relatively little mitotic activity as they are mainly involved with the refraction of light; these cells however do not lose their ability to divide and in fact do so if, for example, the epithelium is damaged. In contrast, peripheral cells are cuboidal in shape and differentiate into those that will synthesize crystallins and those that will become actively mitotic to produce new lens fibres; the latter cells are arranged such that their nuclei remain in the equatorial region whilst they elongate in a concentric fashion, running parallel to the lens surface (Snell and Lemp 1998). Fibres that are produced by the lens are not shed from the structure but are instead compressed and eventually become part of the lens cortex and nucleus (Bron *et al.* 1997a).

1.1.1.3.3 The Lens Cortex and Nucleus

The adult lens is estimated to contain about 3.6 million fibres, the majority of which are found in the cortex, which surrounds the nucleus (Oyster 1999). Although there is no definitive demarcation between the two regions, differences in light scatter are observable due to differences in cellular structure; these are referred to as *zones of discontinuity* and they reflect the growth pattern of the lens throughout life (Koretz *et al.* 1994, Oyster 1999).

Cortical fibres are hexagonal in shape (Atchison 1995, Saude 2003) and are regularly and densely arranged so that lens transparency can be conferred. An abundance of *gap junctions* helps to maintain this, as does the high solubility of crystallins, whilst the former also provides a means for metabolic transfer with the aqueous (Bron *et al.* 1997a, Oyster 1999, Shea *et al.* 1999). With increasing age, there is no relocation of lens position but the axial and equatorial lens thicknesses have been shown to increase, with this being seven times greater in the cortex than in the nucleus (Dubbelman *et al.* 2003). In addition, it has been shown, by Magnetic Resonance Imaging (MRI), that the anterior cortical thickness increases more than the posterior cortical thickness (Strenk *et al.* 2004).

The nucleus is the most central aspect of the lens and with increasing age, a yellow discolouration is observed due to the absorption of ultraviolet (UV) light by *chromophores* (pigments) within the structure (Shea *et al.* 1999, Saude 2003). An ageing nucleus is also found to contain an increasing concentration of insoluble proteins, which are derived from the cross-linking (binding) of crystallins (Bron *et al.* 1997a). These changes have been implicated as possible contributors to the mechanism of presbyopia (see section 1.1.3.2).

1.1.2 The Mechanism of Accommodation

The mechanism of accommodation has been the subject of much research for over 200 years. It is not fully understood how the process is mediated but the theory proposed by Helmholtz in 1855, and later modified by Fincham in 1937, is generally accepted by most (Atchison 1995, Gilmartin 1995, Glasser and Kaufman 1999, Croft *et al.* 2001, Glasser 2006). This theory suggests that when the eye is fixating a near object, innervation of the ciliary muscle causes it to move anteriorly and away from the sclera. This causes a reduction in diameter of the ciliary muscle collar, a ring that the muscle forms around the crystalline lens, and this instigates a loss of tension in the equatorial and anterior zonules. Subsequently, elastic properties of the lens capsule enables an axial thickening of the lens nucleus, but not the cortex (Dubbelman *et al.* 2003), a reduction in the lens equatorial diameter by 11-12% (Glasser and Kaufman 1999), and a decrease in the radius of curvature of the anterior lens surface; the posterior lens surface remains unaffected since this is constrained by the vitreous. These changes result in a more spherical lens shape, which produces an increase in positive power (Figure 1.3).

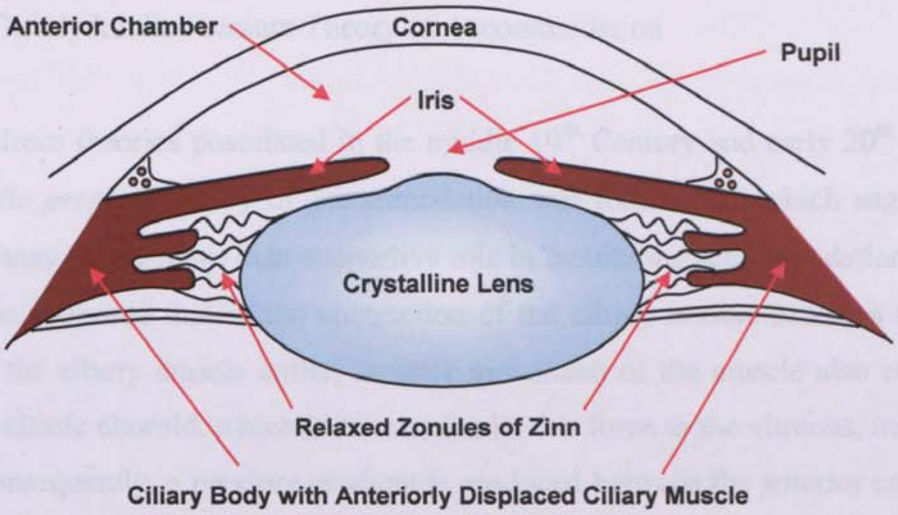

Figure 1.3 State of the anterior ocular structures during accommodation – *produced based on a photograph in Bron et al. (1997a)*

When fixation alters to a distant object, the posterior zonules, which remain under tension during accommodation (Glasser and Kaufman 1999), function as an elastic sling to reverse the process with the aid of the elastic properties of the choroid (Tamm *et al.* 1991, Weale 2000). The ciliary muscle is pulled posteriorly and towards the sclera, causing the diameter of the ciliary muscle collar to increase and restoring tension in the equatorial and anterior zonules. This then allows the lens to return to its flat and minimally curved state.

Where Helmholtz suggested that the iris plays a role in regulating the change in shape of the anterior lens surface, Fincham revealed that similar changes in lens shape occurred in subjects with aniridia. However, a reduction in the AoA by as much as 40% has been reported in eyes with total iridectomy, leading to the suggestion that the iris sphincter muscle may actually pull the ciliary muscle further forward and inward than the maximum force of ciliary muscle contraction alone (Crawford *et al.* 1990). Fincham, and later Glasser et al. (2001), also confirmed that elastic properties of the lens capsule were responsible for producing changes in lens shape, since its removal resulted in a loss of accommodation. Indeed, this also confirmed the small role that the posterior lens surface plays in accommodation, due to the lower capsule thickness here (see section 1.1.1.3.1).

Recent evidence suggests that a decrease in the radius of curvature of the cornea may also occur as a result of ciliary muscle contraction and that this may contribute to accommodative ability by producing an increase in corneal refractive power (Yasuda and Yamaguchi 2005). However, there is little further evidence to support this. Also unclear is the role that the vitreous has in the accommodation process (see section 1.1.2.1).

1.1.2.1 The Hydraulic Pressure Theory of Accommodation

Originating from theories postulated in the middle 19th Century and early 20th Century, a new *hydraulic pressure theory* of accommodation was formulated, which suggested that the vitreous may play a more than supportive role in facilitating accommodation (Coleman 1970). It was proposed that whilst contraction of the ciliary muscle causes a decrease in diameter of the ciliary muscle collar, anterior movement of the muscle also concurrently pulls on the elastic choroid, which in turn transmits this force to the vitreous, increasing its pressure. Consequently, a pressure gradient is produced between the anterior and posterior chambers of the eye, the presence of which was confirmed by investigations on primate eyes (Coleman 1986). Accordingly, it was proposed that this gradient, the creation of which may be aided by increased aqueous outflow through expansion of the trabecular meshwork, causes the vitreous to push the lens anteriorly in a hydraulic fashion, producing an increase in positive power i.e. accommodation. Tension in the lens zonules was suggested to *increase* during accommodation, since these provide an anchor for the lens, whilst the anterior zonules act to decrease the radius of curvature of the anterior lens surface; the posterior lens surface is not affected due to resistance from the vitreous (Coleman 1986).

The hydraulic pressure theory of accommodation has been mathematically modelled and, according to Coleman, proven to discount Fincham's belief that elasticity of the lens capsule alone is sufficient to create changes in lens shape for accommodation (Coleman and Fish 2001). However, the primary limitation of this model is that, theoretically, the hydraulic effect ought to be short-lived since the pressure gradient should re-stabilise as more aqueous solution is produced by the ciliary body, resulting in a return of the lens to its unaccommodated state and position. Furthermore, it was reported that the AoA in one eye of a 32-year-old individual after total vitrectomy was the same as the contralateral eye containing natural vitreous (Fisher 1983).

1.1.2.2 Schachar's Theory of Accommodation

The most recent and perhaps controversial theory of the accommodative mechanism is that proposed by Ronald Schachar (Schachar 1992). In contrast to Helmholtz's theory, Schachar suggested that contraction of the ciliary muscle causes an *increase* in equatorial zonule tension and that this causes an *increase* in equatorial lens diameter, resulting in an increase in peripheral lens volume and a bulging of the central anterior lens surface (Schachar 1992). Schachar's theory rules out any role for the anterior lens capsule and instead suggests that only the equatorial zonules act to transmit the force of ciliary muscle contraction to the peripheral region of the lens (Schachar and Bax 2001).

Schachar purportedly found evidence in support of his theory by revealing that stretching the sclera at the region of the ciliary muscle of bovine eyes produced a reversible and repeatable increase in optical power, a decrease in focal length, and an increase in lens equatorial diameter (Schachar *et al.* 1993a). He then used mathematical models to reveal that this mechanism was feasible for human eyes (Schachar *et al.* 1993b) and later added further support by showing that this mechanism produced similar changes in the shape of a gel-filled balloon model (Schachar *et al.* 1994). Following this, Schachar proposed a new hypothesis for zonule function during accommodation, suggesting that only the equatorial zonules are involved and that the anterior and posterior zonules only provide mechanical support for the lens (Schachar 1994). Schachar (1994) also suggested that age-related shift of zonule insertions into the lens *away* from the equator (Farnsworth and Shyne 1979) was evidence of a change required to maintain this support for an increasingly thicker lens. This function is in contrast to Helmholtz's theory, which suggests that all of the zonules act in unison and hence relax and stretch together.

Using ultrasound biomicroscopy, Schachar found support for his hypothesis that the lens equator moves *towards* the sclera during accommodation (Schachar *et al.* 1995, 1996b). He then suggested that contraction of the radial and longitudinal fibres of the ciliary muscle ensures that only the muscle in the region of the equatorial zonules curls towards the sclera, whilst contraction of the circular fibres releases tension on the anterior and posterior zonules to prevent axial lens movement (Schachar and Anderson 1995). It was then shown that the amount of equatorial zonule movement during accommodation (100μm) was producible within the physiological limits of the force of ciliary muscle contraction suggested by Fisher (1977), whilst the force required to move all three zonule types would cause the *whole* lens to flatten (Schachar and Bax 2001, Schachar 2004).

Schachar's theory of accommodation is not met with widespread acceptance, especially since it is considered that errors were made when assessing zonule and lens movement during accommodation, by not imaging exactly the same part of the ciliary body each time (Glasser and Kaufman 1999). Schachar's theory is also based on a definite division of the zonules into three types, which, as mentioned in section 1.1.1.2, is not at all certain. In contrast to Helmholtz's theory, Schachar also suggests that the equatorial diameter of the lens increases during accommodation. Since visualisation of this region can be impeded by the opaque iris with Schiempflug imaging (e.g. Dubbelman *et al.* 2005), iridectomies have been performed on experimental monkey eyes and the lens diameter has been found to *decrease* during accommodation (e.g. Glasser *et al.* 2006). This finding is supported by techniques not requiring iridectomies, including ultrasound biomicroscopy (e.g. Storey and Rabie 1985) and MRI (Strenk *et al.* 1999, Jones *et al.* 2007, Kasthurirangan *et al.* 2008).

1.1.3 The Mechanism of Presbyopia

Most studies that have investigated the mechanisms of accommodation and presbyopia have used primate eyes, such as the rhesus monkey, as these are the closest model to human eyes (Bito *et al.* 1987, Koretz *et al.* 1987b). However, the lack of a perfect animal model and the inability to carry out human measurements *in vivo*, for ethical reasons, prevents substantial progress on understanding the true aetiology of presbyopia from being made. Several studies have sought to determine the fundamental cause(s) of presbyopia, as reviewed previously (Atchison 1995, Gilmartin 1995, Croft *et al.* 2001, Glasser *et al.* 2001), and these can be categorised into *extralenticular* (see section 1.1.3.1) and *lenticular* (see section 1.1.3.2) theories.

1.1.3.1 Extralenticular Theories of Presbyopia

Extralenticular theories of presbyopia suggest that age-related changes in the structures surrounding the crystalline lens are the primary cause of a reduced ability to create a change in lens shape for accommodation. Of primary interest is the possibility that ageing of the ciliary muscle results in a reduced force of contraction and therefore a reduced ability to release tension in the zonules (Duane 1922). This is supported by the finding that the number of cells in the ciliary muscle reduces with age (Bron *et al.* 1997b). However, it appears highly unusual that the ciliary muscle should lose its ability to contract completely by the age of 50 years when no other muscle system in the body does so at this age (Croft and Kaufman 2006). Indeed, studies have in fact shown that the ciliary muscle does not lose its force of contraction with age (Swegmark 1969, Poyer *et al.* 1993, Strenk *et al.* 1999, Pardue and Sivak 2000, Strenk *et al.* 2006, Hermans *et al.* 2008) and that it may actually increase between the ages of 30 and 50 years (Fisher 1977).

It has also been shown that neuromuscular innervation of the ciliary muscle in adult rhesus monkeys (approximately equal to 84 human years) is not diminished compared to younger animals (Gabelt *et al.* 1990) and therefore reduced muscular contractility as a result of this is unlikely to be a cause of presbyopia. Furthermore, since convergence remains unaffected, a weakness of the ciliary muscle would cause the accommodative convergence to accommodation (AC/A) ratio to increase with age (Strenk *et al.* 1999). Whilst more recent investigations support this (Bruce *et al.* 1995, Ciuffreda *et al.* 1997), older studies have found little or no change (Morgan and Peters 1951, Tait 1951), although measurement of AC/A ratios beyond the age of 45 years is not considered to be entirely reliable due to the impairment of near visual ability (Strenk *et al.* 1999).

It has been suggested that a reduction in ciliary muscle *mobility* may occur with age, as a direct consequence of increasing rigidity that arises from an increase in tendon thickness and an increasing presence of collagen fibrils in the normally elastin-rich posterior attachment of the ciliary muscle to the globe (at Bruch's membrane of the choroid) (Tamm *et al.* 1991). These changes may carry mechanical implications on the ability of the ciliary muscle to move away from the sclera during accommodation (Tamm *et al.* 1991, 1992). Indeed, if Helmholtz and Fincham are correct, this movement is fundamental to the release of zonule tension, which is required to produce an accommodative change in lens shape (Atchison 1995).

The reduced mobility of the ciliary muscle may also be due to changes in the muscle structure itself, since it has been shown that the muscle becomes shorter anteriorly, longer posteriorly, and increases in thickness with age (Pardue and Sivak 2000). Furthermore, the proportion of longitudinal fibres in the ciliary muscle decreases with age whilst radial fibres increase (Pardue and Sivak 2000). As a result of these changes, the diameter of the ciliary muscle collar reduces, causing a reduction in zonular tension and a resultant limitation in movement of the muscle and lens (Neider *et al.* 1990, Strenk *et al.* 2006).

Alterations to the zonules themselves with age have also been implicated as possible contributors to presbyopia. It has been reported that as a direct consequence of age-related anterior and tangential shift of the zonule insertions into the lens (Farnsworth and Shyne 1979), the force that can be applied to the lens may decrease, resulting in a subsequent loss of accommodative ability (Koretz and Handelman 1983). It has also been suggested that alteration of zonule position during prolonged near work as a pre-presbyope may stimulate excessive mitosis in the lens epithelium, which changes the lens substance in this region and therefore reduces the ability to accommodate in later life (Bito *et al.* 1965).

Under the hydraulic pressure theory of accommodation, age-related changes in the vitreous may also cause a reduction in accommodation due to the reduced efficacy of pressure gradients (Coleman 1986, Croft and Kaufman 2006). However, there is insufficient evidence to support this. In fact, there is a general lack of certainty with all extralenticular causes of presbyopia, primarily since these changes do not explain the magnitude of accommodation loss (Croft and Kaufman 2006). Therefore, lenticular changes are instead considered to be the most likely causes of presbyopia.

1.1.3.2 Lenticular Theories of Presbyopia

Lenticular theories of presbyopia were suggested by Hess and Gullstrand in the early 20th Century and by Fincham in 1937 (cited in Atchison 1995). Both theories suggest that due to an increase in thickness and rigidity with age, the crystalline lens is less amenable to changes in shape when subjected to the forces of ciliary muscle contraction. The theories differ however, since Fincham suggested that ciliary muscle contraction is maximal at the highest AoA achievable, whilst Hess and Gullstrand suggested that the ciliary muscle continues to contract even after the maximum AoA has been reached.

There is evidence to support of each of these theories since the AC/A ratio should increase with age if the Hess-Gullstrand theory is correct (Bruce *et al.* 1995, Ciuffreda *et al.* 1997), whilst this ought to remain unchanged if Fincham's theory is correct (Morgan and Peters 1951, Tait 1951). Regardless of this, several changes in the lens structure and its properties have been suggested to be the primary cause(s) of presbyopia. For example, the thickness of the lens capsule is known to increase with age, causing a consequential change in its mechanical properties (see section 1.1.1.3.1). Under the Helmholtz and Fincham theories of accommodation, this may carry important implications on the capsule's ability to create a change in lens shape. However, these alterations do not coincide with the observed reduction in the AoA with age (Fisher 1973), whilst more recent evidence suggests that changes in capsule elasticity are independent of age (Ziebarth *et al.* 2008); the capsule is therefore unlikely to contribute to presbyopia in a significant way.

Whilst Fisher and Pettet (1973) found no age-related change in the water content of the lens, this was in contrast to the findings of Siebinga et al. (1991). However, both studies agreed that the nuclear fibres of the lens might increasingly resist deformation. This may be related to the increased binding of *α-crystallins* (Bracchi *et al.* 1971), which is an important protein that confers lens flexibility (Heys *et al.* 2007). Presbyopia may therefore reflect a reduced ability of the force of ciliary muscle contraction to change the shape of an increasingly inflexible or rigid lens (Glasser and Campbell 1998, Glasser and Kaufman 1999). In addition, due to mitosis in the lens epithelium (see section 1.1.1.3.3), the lens mass has been shown to increase at a rate of 1.33mg per year from a birth weight of 180mg, and therefore the force required to instigate changes in lens shape also increases (Glasser and Campbell 1999). This is further supported by findings that the axial thickness of the unaccommodated lens increases with increasing age, with estimates of the rate ranging variably from 13μm per year (Koretz *et al.* 1989) to 24μm per year (Dubbelman *et al.* 2001), or by a total of 1.0mm between the ages of 20 years and 60 years (Brown 1973).

In addition to the increase in lens rigidity, there is also an age-related decrease in the radius of curvature of the unaccommodated anterior lens surface (Brown 1974, Koretz *et al.* 1984, 1987a, 1989, Glasser and Campbell 1999, Dubbelman and Van der Heijde 2001, Dubbelman *et al.* 2005). However, in contrast to the expected myopic change in refraction that ought to occur, there is instead an observed *increase* in focal length of the lens (Glasser and Campbell 1998, 1999).

It is possible that the myopic change in refraction is countered by an adult form of the *emmetropization* process, whereby the axial length of the eye decreases to compensate for this change (Grosvenor 1987). However, it is very unlikely that the adult eye will change in this manner, especially since it is well past the growth phase of ocular development. It is therefore more readily supported that the myopic change in refraction is offset by changes in refractive index within the lens. Indeed, several studies have confirmed this presence of a refractive index gradient and in particular that this alters with age (Pierscionek 1990, Smith *et al.* 1992, Hemenger *et al.* 1995, Augusteyn 2008, Augusteyn *et al.* 2008, Kasthurirangan *et al.* 2008). Moffat et al. (2002) for example revealed a refractive index gradient to exist in both the equatorial and axial meridians of the lens and that these reduce with age, at a rate of 0.00034±0.0006 per year, due to changes in the composition of the lens nucleus. Whilst supporting this change, others have actually found no significant change in the refractive index of the nucleus itself (Jones *et al.* 2005, 2007) and it may therefore be that changes in refractive index only occur in the lens cortex (Pierscionek 1990, Kasthurirangan *et al.* 2008).

1.1.3.3 Schachar's Theory of Presbyopia

Founded on his theory of the accommodative mechanism (see section 1.1.2.2), Schachar proposed that presbyopia might be caused by age-related growth of the lens in the equatorial region, which consequently reduces the space between the lens equator and the ciliary muscle (referred to as the *circumlental space*) and therefore reduces tension in the equatorial zonules. In effect, this reduces the ability of the ciliary muscle to induce accommodation (Schachar 1992, 2006). There is evidence from an MRI study to suggest that the equatorial diameter of the lens increases with age (Kasthurirangan *et al.* 2008), whilst Schachar has mathematically matched the age-related decline in the AoA to the age-related increase in lens equatorial diameter (Schachar 2008). In addition, Schachar has shown that increasing the space between the lens equator and the ciliary muscle may increase the AoA (see section 1.4.5) (Schachar 1992, Schachar *et al.* 1995).

Schachar's theory of presbyopia is dependent on the lens maintaining its flexibility with age, but as described in section 1.1.3.2, this is highly unlikely (Charman 2005). In addition, studies have shown very little improvement in the AoA by Schachar's proposed method of correcting presbyopia (see section 1.4.5) and therefore disagree with his theory.

Glasser and Kauffman (1999) found that Schachar's method of presbyopia reversal may actually restrict ciliary muscle contraction and hence reduce the AoA, whilst Coleman and Fish (2001) have shown by mechanical modelling that this method does not increase the AoA according to the hydraulic pressure theory. Furthermore, another MRI study revealed that as opposed to an increase in the equatorial lens diameter with age, the diameter of the ciliary collar reduces instead (Strenk *et al.* 1999). Schachar's theory of presbyopia, just as his theory of accommodation, is therefore not readily accepted (Pierscionek *et al.* 2001).

1.1.3.4 The Bito & Miranda Theory of Presbyopia

Most elastic tissues in the human body are comprised of components that function in an agonist/antagonist relationship. Equal deterioration in the condition of each component, for example with age, would result in no net effect since the equilibrium would still be maintained. If however one of the elastic components resists deterioration more than the other, there would no longer be equilibrium and there would be a shift towards one direction. Bito and Miranda (1989) applied this theory to Helmholtz's theory of accommodation and suggested that the crystalline lens and the zonules form an elastic equilibrium such that relaxation of tension in the latter causes a relaxation of the lens into a more spherical shape i.e. accommodation. They then hypothesised that extralenticular changes with age result in a greater loss of elasticity in the zonules e.g. by loss of ciliary muscle contractility and/or mobility, compared to the loss of elasticity that may be associated with lenticular growth. The lens therefore experiences reduced resistance to taking an accommodated state, since the zonules no longer possess the elastic force required to pull the lens into its minimally curved state. Bito and Miranda thus hypothesised that presbyopia represents a loss in ability of the crystalline lens to 'unaccommodate' and that changes in the refractive index of the lens that have been observed (see section 1.1.3.2) would explain why there is no myopic shift in refraction.

The Bito and Miranda hypothesis for presbyopia would also fit Coleman's Hydraulic Pressure theory of accommodation since reduced elasticity of the choroid with age would reduce the transmission of the force of ciliary muscle contraction to the vitreous, which is required to produce a change in lens shape (Bito and Miranda 1989). Although this theory is plausible, recent evidence strongly suggests that the ciliary muscle is not likely to lose its contractile force with increasing age, and therefore lenticular changes appear to be the prime contributors to presbyopia (see sections 1.1.3.1 and 1.1.3.2).

1.2 Spectacle Correction of Presbyopia

The origin of spectacles is unknown since their invention appears to have occurred through a progressive process involving several people in different locations over a long period of time (Cashell 1971). Some credit the discovery to Marco Polo in China in 1270, although it has been suggested that convex lenses were first used in Europe as reported by the English friar Roger Bacon in circa 1262 (Cashell 1971).

Until the late 17th Century to middle 18th Century, most spectacles were positioned and held in front of the eyes by hand. However, owing to the introduction of printed press and the subsequent increasing popularity of reading (The Foundation of the American Academy of Ophthalmology 2007), the use of materials such as wood, leather and steel meant that spectacle frames could be manufactured with straps or rigid arms that reached around the head or behind the ears (Cashell 1971). Since then, substantial advances have been made in spectacle frame and lens designs, although single-focus near lenses still provide the simplest form of spectacle correction of presbyopia. Aside from this, the most notable contributions to the spectacle correction of presbyopia were the introduction of bifocal (see section 1.2.1) and varifocal (progressive addition) lenses (see section 1.2.2).

1.2.1 Bifocal & Trifocal Spectacle Lenses

Although full aperture, single-focus lenses provide the biggest field of view and optimal visual function for the presbyope, there is the inconvenient need to change between different pairs of spectacles for changes in distance of regard. Bifocal lenses overcome this problem and although Benjamin Franklin is accredited with their invention in 1784, their true origin is not certain as Franklin merely stated that he was "*happy in the invention of double spectacles*" (cited in Letocha 1990). The Franklin *split bifocal* (Figure 1.4) comprises two half lenses that are held together in a frame, with the top half used for distance vision and the bottom half used for near vision. As the two half lenses are entirely separate, the optical centres of each can be positioned in such a way that these are coincident with the pupil centre, which prevents unwanted prismatic effects and ensures optimal visual function (Letocha 1990, Jalie 2003). Indeed, this is important since changes of gaze from distance to near vision can lead to the perception of images jumping to new locations, as a result of the prism induced by the near segment (Fowler and Petre 2001).

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Figure 1.4 A replica of the original Franklin split bifocal spectacles – ***reproduced with permission from: © The College of Optometrists (British Optical Association Museum, LDBOA1999.5499)***

In the 1880s, the split bifocal design was improved upon by a *cemented* design, where a separate near lens segment was attached to the lower half of a distance lens (Fowler and Petre 2001). The major drawback of this modification however, lay in the fact that the adhesive used to join the segment to the distance lens readily wore-off and caused the segment to detach. In the 1960s, the adhesive was replaced with more durable UV-cured epoxy resins, and these lenses, now commonly known as *fused bifocals*, excelled (Jalie 2003). Fused bifocals can be manufactured with a variety of segment shapes, whilst high refractive index materials can allow the lens thickness to be minimised (Fowler and Petre 2001, Jalie 2003).

Soon after the introduction of fused bifocals, an alternative *solid* design was established. These are made from one material yet incorporate both distance and near refractive powers through the creation of each respective curve on one lens surface. The remaining surface can then be used to create an astigmatic refractive correction. *Upcurve* solid bifocals carry predominantly a near vision correction, with a small segment placed in the top half of the lens for distance vision. In contrast, the more common *downcurve* solid bifocals carry predominantly a distance vision correction and have a near vision segment in the lower half of the lens (Jalie 2003). Solid bifocals are principally manufactured from plastic materials, although glass solid bifocals can also be manufactured. The segment shapes of solid bifocal lenses can be made similarly to fused bifocals (Jalie 2003) and when the near segment occupies the entire lower half of the lens, an *executive* or *E-style* bifocal is created. This is perhaps the closest design to the Franklin split bifocal that can be achieved and this also provides the largest field of view for distance and near vision of all bifocal lenses. Furthermore, control over prismatic effects can be achieved by ensuring that the centre of curvature for each of the refractive zones is aligned with the segment top (Fowler and Petre 2001).

Segmented bifocals, the most preferred of which is the *D-segment*, are the most successful of all spectacle corrections for presbyopia, and this success increases as the magnitude of the near addition increases (Eichenbaum *et al.* 1999). However, as the magnitude of the near addition increases, the range of clear vision for the ageing presbyopic bifocal wearer reduces. Trifocal lenses are able to overcome this problem and are particularly beneficial, for example, for use with computers and for reading music (Callina and Reynolds 2006). These lenses are manufactured in a similar fashion to bifocal lenses but instead carry three regions of refractive power, with an additional intermediate segment placed just above the near segment. This region typically has a power of 50% of the near addition, although this can be altered to suit the individual's needs. As with bifocals however, trifocal lenses can suffer from 'image jump' whilst the range of clear vision may still not encompass the whole range from distance to near (Fowler and Petre 2001, Jalie 2003).

1.2.2 Varifocal (Progressive Addition) Lenses

Progressive addition lenses (PALs) are more commonly known as *varifocals* and take the principle of trifocal lenses a step further by blending the refractive zones to create a progressive power change and the cosmetic appearance of a single vision lens (Callina and Reynolds 2006). The first varifocal lens design was patented by Owen Aves in 1907 and comprised a conical rear lens surface, with an ellipsoid front lens surface whose radius of curvature decreased towards the bottom of the lens and therefore resulted in an increase in positive power (Meister and Fisher 2008). The Aves design however did not allow for the correction of astigmatism and it wasn't until 1920 that Poullain and Cornet improved upon this design by introducing the first single surface varifocal, in which the lens surface geometry resembled that of an 'elephant's trunk' (Sullivan and Fowler 1988).

It wasn't until 1962 that the next significant development in varifocal lens design was achieved. At this time, the 'elephant's trunk' surface geometry was found to be similar to two cylindrical surfaces superimposed with their axes orientated at 45° and 135° respectively. In this configuration, the central vertical meridian, known as the *umbilical meridian,* possesses increasing spherical power from top to bottom, whilst points located laterally away from this were found to be sphero-cylindrical, representing zones of increasing distortion. Of importance was that this design simplified the construction of a single progressively powered surface, which in turn allowed for the creation of an astigmatic correction on the remaining surface, when needed (Sullivan and Fowler 1988).

It was Maitenaz who introduced the first successful varifocal lens, the *Varilux 1*, in 1966 (Maitenaz 1966). This lens provided large and stable regions of distance and near power by virtue of commencing the progressive surface, following the 'elephant's trunk' design, from the bottom edge of a spherical distance vision lens. The lens was characterised by a steep and abrupt transition from distance vision to near vision, with notable areas of peripheral distortion that were primarily limited to the near zone (Figure 1.5a). In 1972, this design was superseded by Maitenaz's *Varilux 2* design, which minimised the distortion in the near zone by virtue of a longer transition from distance to near, which spread the peripheral distortion over a larger area (Figure 1.5b) (Fowler and Petre 2001, Sheedy *et al.* 2006). Today, a variety of varifocal lenses can be manufactured, differing in the length of the progression, the width of the refractive zones and the amount and location of distortion (e.g. see Sheedy *et al.* 2006).

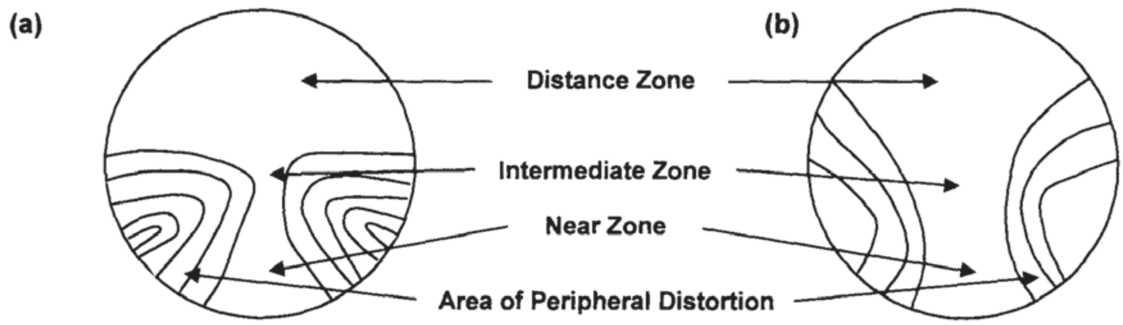

Figure 1.5 Astigmatism plots displaying the type of progression expected of (a) Varilux 1 lens and (b) Varilux 2 lens – *reproduced and modified from Meister and Fisher (2008)*

Although the progressive power change of varifocal lenses reduces 'image jump' compared to bifocal lenses, the intermediate and near zones may only be small whilst neck strain may occur during reading (Eichenbaum *et al.* 1999). Also, the need for larger head movements may cause visual quality to deteriorate (Sheedy *et al.* 1987), which can reduce success, especially as the near addition increases (Eichenbaum *et al.* 1999).

1.2.3 Other Presbyopic Spectacle Lenses

Liquid crystals possess characteristics of both solids and liquids and their use in spectacle lenses for presbyopia has been suggested (Fowler and Pateras 1990). The passage of an electric current through a sheet of crystals will align these such that there is a resulting increase in refractive index. If such a sheet is then sandwiched between two convex or concave lenses, a change in refractive power can be achieved (Fowler and Pateras 1990).

The use of diffractive optics may improve near visual ability but overall clarity may reduce since light is then split between two foci (Charman 1993). In addition, liquid crystals are susceptible to changes in temperature, resulting in fluctuations in refractive index and therefore lens power. The crystals may also not align accurately, causing light scatter, whilst response and recovery times may be undesirably long (Fowler and Pateras 1990).

An alternative *deformable* lens has been described whereby a fluid filled cavity is sandwiched between one or two expandable surfaces (Sullivan and Fowler 1988, Pateras *et al.* 1993). The application of pressure either to the lens surface(s) or directly to the liquid results in expansion of the surface(s), creating a change in curvature and therefore a change in lens power. Although Schachar suggested a power change of 7.00D may be achievable (Schachar *et al.* 1996a, 1998), the original lens designed by Wright in the 1970s only produced a power change of 1.00D; furthermore, poor reproducibility and limited repeat deformations meant that these lenses did not become very popular (Pateras *et al.* 1993).

1.3 Contact Lens Correction of Presbyopia

Contact lens corrections for presbyopia can be classified into *simultaneous vision* and *alternating vision* designs, with each comprising various alternatives as summarised in Figure 1.6; *monovision* however, can be classified within both groups (see section 1.3.1).

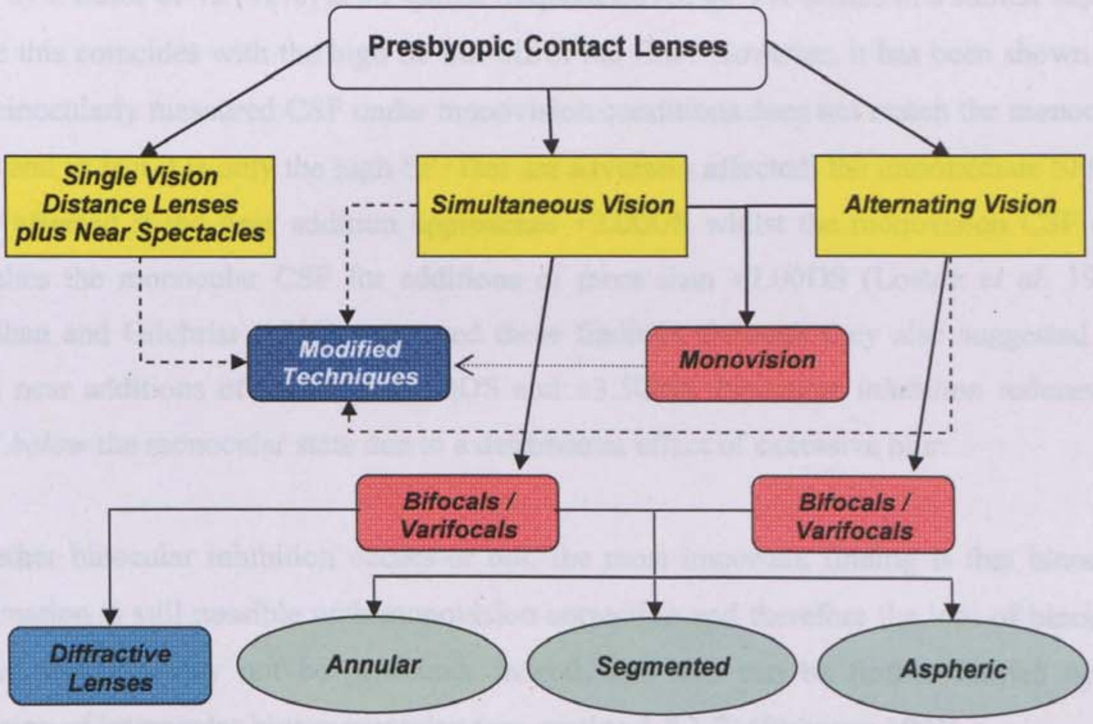

Figure 1.6 Functional and design classification of presbyopic contact lens options

1.3.1 Monovision

Monovision with contact lenses was first described by Westsmith in the 1960s (cited in Josephson *et al.* 1990), and this is achieved by intentionally focussing one eye for optical infinity (distance vision) and the other eye for a near point dependent on the individual's preferred working distance(s). Consequently, this results in a loss of the best binocularly balanced refractive correction, since with both eyes open the visual cortex is presented with two opposing images (Johannsdottir and Stelmach 2001). However, the process of *binocular summation* (see section 1.3.1.1) may still allow binocular simultaneous vision whilst the process of *interocular blur suppression* (see section 1.3.1.2) may mean that visual perception can instead alternate between the two eyes (Benjamin and Borish 2006); monovision can therefore be classified as providing simultaneous *or* alternating vision.

1.3.1.1 Binocular Summation

Contours from the retinal image of each individual eye are combined within the visual cortex and contrast information derived from the binocular percept is then used to drive visual function. This process, known as *binocular summation*, provides better object detection compared to monocular vision. Campbell and Green (1965) revealed that as a result of this, the binocular contrast sensitivity function (CSF) is better than the monocular CSF by a factor of $\sqrt{2}$ (42%) at all spatial frequencies (SFs); VA differs in a similar fashion since this coincides with the high SF cut-off of the CSF. However, it has been shown that the binocularly measured CSF under monovision conditions does not match the monocular CSF and in fact it is only the high SFs that are adversely affected; the intermediate SFs are only affected if the near addition approaches +2.00DS whilst the monovision CSF only matches the monocular CSF for additions of more than +2.00DS (Loshin *et al.* 1982). Pardhan and Gilchrist (1990) supported these findings although they also suggested that with near additions of between +1.50DS and +3.50DS, *binocular inhibition* reduces the CSF *below* the monocular state due to a detrimental effect of excessive blur.

Whether binocular inhibition occurs or not, the most important finding is that binocular summation is still possible with monovision correction and therefore the loss of binocular visual function may not be profound. Indeed, this loss can be further limited by the function of interocular blur suppression (see section 1.3.1.2) (Simpson 1991).

1.3.1.2 Interocular Blur Suppression

Interocular blur suppression is a cortical phenomenon that enables out-of-focus elements of the retinal images to be ignored and for in-focus elements to dominate perception. It is a fluid process that can alternate between the eyes when gaze is changed from distance vision to near vision and vice versa. The resulting suppression scotoma represents reduced sensitivity to stimulation, not an absolute loss, which is limited to a particular region of the visual cortex (although the retina is often referred to instead) (Simpson 1991).

Interocular blur suppression is governed primarily by retinal image contrast such that when edge detection becomes too difficult, as a result of increased blur, there will be an increased need to suppress the blurred elements (Schor *et al.* 1987). Bright objects are more difficult to suppress than dim objects since the contrast of the former is higher, making edge detection relatively simple and the perception of blur more difficult (Schor *et al.* 1987). In contrast, large amounts of anisometropia produce more noticeable retinal defocus, as a result of larger relative retinal blur circles, which facilitates their suppression (Collins and Goode 1994a). Simpson (1991) in fact reported that suppression does not occur for up to 0.50DS of defocus, whilst greater defocus is required for larger targets. Heath et al. (1986) suggested that suppression is more difficult when viewing objects at near, primarily due to pupil miosis which reduces retinal blur circle size. However, this latter point is disputed since retinal image contrast is independent of pupil size (Collins and Goode 1994a). Perhaps of greatest importance is that subjective reports of ghosting, glare or haloes by monovision patients when viewing car headlights at night, for example, can be explained by inadequate interocular blur suppression since this essentially reflects an inability to suppress small, bright objects (Johannsdottir and Stelmach 2001).

1.3.1.3 Ocular Dominance

The primary visual cortex is arranged into columns of cells denoting the manner whereby cells are grouped by similarity of function and according to how their input originates from one particular eye. These are known as *ocular dominance columns* and although their exact role in visual function is not fully understood, it is thought that they begin the process of combining the two retinal images into a single binocular percept (Crowley and Katz 2002, Horton 2006). Where cells responding to one particular eye predominantly drive visual function, there is said to be strong *ocular dominance*.

In the presence of strong ocular dominance, alternate interocular blur suppression with monovision can become difficult since perception must alternate away from the favoured eye; this can reduce the range of clear vision (Schor and Erickson 1988). Indeed, it is a convention to correct the vision of the dominant eye for the most frequently used viewing distance, under the belief that this will aid interocular blur suppression of the less frequently used eye (Gasson and Morris 2003). However, this may not be necessary since little difference in VA was reported when the dominant eye was corrected for distance vision or near vision (Robboy *et al.* 1990), whilst this was also true for stereoacuity, even in unsuccessful monovision wearers (Erickson and McGill 1992). Furthermore, it has been suggested that ocular dominance is actually a fluid and adaptive phenomenon, which can make the identification of this very difficult (Evans 2007). In contrast, it has been reported that strong ocular dominance is highly inversely correlated to symptoms of ghosting, which indicates poor interocular blur suppression (Collins and Goode 1994b). Therefore, monovision success may not be predictable from the presence or absence of ocular dominance.

1.3.1.3.1 Identification of Ocular Dominance

A *sensory* test of ocular dominance was described by Schor et al. (1987) and required the individual to alter the back-illumination of an aperture viewed on a white diffusing surface, whilst wearing monovision correction, until it was perceived clearly i.e. the contrast was reduced to induce interocular suppression. The order of the lenses with which the contrast needs to be reduced the least represented the sensory dominant eye (Schor *et al.* 1987, Robboy *et al.* 1990). This type of test however is not commonly used today.

The *acuity method* involves assessing the change in best binocular distance and near VA when the near addition (positive lens) is placed in front of each eye in turn. The condition under which the best VA is obtained indicates the acuity dominant eye, since suppression is more readily achieved (Robboy *et al.* 1990). The most popular method of assessing ocular dominance however, is known as the *sighting method* (Westin *et al.* 2000). This involves the individual simply pointing towards a distant target with the two first fingers of their hands joined together to form a gun shape, or by viewing a target through a hole. The eyes are then alternately closed to identify the eye with which the target is most closely aligned with the fingers, or the hole, which indicates the sighting dominant eye. This test however may be influenced by the *handedness* of the person (Benjamin and Borish 2006).

1.3.1.4 Adaptation & Long-term Effects

Adaptation of the presbyopic visual system to monovision correction relates to the development of interocular blur suppression, a process that can take up to three weeks to occur (Josephson *et al.* 1990). However, there is a suggestion that the visual system does not adapt to this type of correction at all, since there was no observed improvement in VA, stereoacuity or occupational task performance, two months after monovision fitting (Sheedy *et al.* 1988, Schor *et al.* 1989, Sheedy *et al.* 1993). The long-term use of monovision correction (one year or more) however, may induce anisometropic changes in the refractive error of the eyes, with 1.25DS of induced anisometropia causing a permanent 0.50DS increase in anisometropia (Wick and Westin 1999). This finding is particularly unusual since the adult eye is well past the growth phase of ocular development and therefore the change cannot be attributed to a process akin to disruption of the emmetropization process in young primates (monkeys) (Hung and Smith 1996, Smith and Hung 1999, Smith *et al.* 1999). Indeed, this effect has not yet been explained (Wick and Westin 1999) and since there is very little further evidence in support of this in the literature, it is unclear as to whether this is a widespread phenomenon to cause concern.

1.3.2 Simultaneous Vision Lenses

Simultaneous vision contact lenses produce both distance and near images on the retina at the same time, through the incorporation of two or more refracting powers within the lens optic (Figure 1.7) (Gasson and Morris 2003). Visual perception therefore switches attention from one image to the other (distance to near and vice versa), without movement of the lens or the eye (Evans and Thompson 1991).

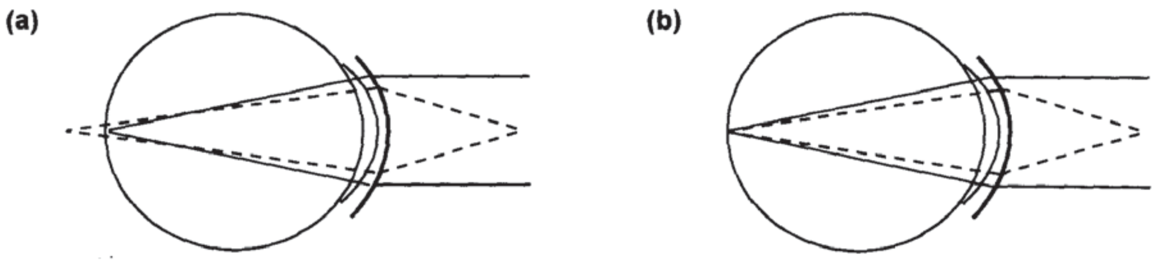

Figure 1.7 **(a) A single vision distance contact lens on a presbyopic eye. Distance light (—) is focussed onto the retina but near light (----) is not**
(b) A simultaneous vision contact lens on a presbyopic eye. Both distance light (—) and near light (----) are focussed onto the retina

As shown in Figure 1.6, simultaneous vision lens designs can broadly be classified into *annular*, *segmented* and *aspheric* designs. A fourth group, *diffractive lenses*, are discussed separately since these do not employ solely refractive optics (see section 1.3.2.4).

Annular lenses, also referred to as *concentric* bifocals, comprise a central zone of refractive power surrounded by a ring of an alternative refractive power, both of which are found within the optic zone of the lens; this in turn occupies a significant proportion of the pupil area (Borish and Soni 1982). Annular lenses may follow a 'centre-distance' approach, whereby the central zone carries the distance refractive power and the peripheral ring carries the near refractive power, or a 'centre-near' design whereby the reverse is true (Stein 1990). The main advantage of annular lenses is that they are free to rotate on the eye without causing detriment to vision, whilst the lens thickness can be minimised since there is no need for stabilisation; this in turn also reduces production costs. The main disadvantage of this design is that visual performance is dependent upon pupil size and illumination (see section 1.3.2.2) (Borish and Soni 1982). Furthermore, where astigmatic corrections are incorporated, some form of stabilisation will be required, which overcomes the primary advantage of this design.

Segmented lenses were originally manufactured similarly to solid bifocal spectacle lenses but these were later replaced by fused designs incorporating a high refractive index near segment. This manufacturing change allowed various segment shapes to be created, although it is still convention for the segment to be located in the lower half of the lens (Borish and Soni 1982). As with annular lenses, both distance and near refractive zones are found within the optic zone of the lens and therefore visual performance is equally subject to variations in pupil size and illumination (see section 1.3.2.2). In addition, the location of the near zone in the lower half of the lens means that some form of stabilisation is required to prevent variation of vision with segment position. Consequently, segmented designs are instead more usually encountered as alternating vision contact lenses (see section 1.3.3).

Aspheric lenses do not carry distinct distance and near refractive zones but instead possess elliptical surfaces that emanate from a central spherical refractive zone. This creates a gradual power variation towards the periphery of the lens, akin to varifocal spectacle lenses. As such, objects viewed at a variety of distances can potentially be seen clearly (Borish and Soni 1982), whilst the magnitude of near power can be altered by varying the rate of change in power (surface curvature) across the lens (Charman and Saunders 1990).

The use of aspheric surfaces is associated with reduced flare, glare and prismatic effects, the latter of which reduces 'image-jump' (Erickson *et al.* 1988). Unfortunately however, aspheric lenses may not perform as intended, since it has been shown that the desired power profile and near addition magnitude may not actually be created (Campbell *et al.* 1993). Furthermore, the performance of aspheric lenses is still dependent on pupil size, whilst centration is also of utmost importance (see sections 1.3.2.2 and 1.3.2.3).

1.3.2.1 The Stiles Crawford Effect

It is known that rays of light that enter the eye through peripheral parts of the pupil are not as visually effective as central, paraxial rays. At points 7.0-8.0mm from centre of the pupil, photoreceptors possess only 33.3% of the luminous efficiency of central photoreceptors and as such, centrally incident light appears more prominent (Stiles and Crawford 1933). This is known as the *Stiles-Crawford Effect* and is thought to reflect the finding that foveal photoreceptors are orientated with their long axis pointing towards the pupil centre, which optimises the capture of centrally incident light as opposed to peripherally incident light (Laties *et al.* 1968). Furthermore, studies on the reflectance of retinal light suggest that there is a wave-guide property of cone photoreceptor outer segments, which 'channel' centrally incident light towards photo-pigment more successfully than peripheral light (Figure 1.8) (Snyder and Pask 1973, van de Kraats *et al.* 1996). The consequence of this for simultaneous vision contact lenses lies in the fact that their performance is dependent on adequate perception of both centrally and peripherally incident light. For the centre-distance lens therefore, reduced sensitivity to peripheral light will cause detriment to near vision whilst for the centre-near design, this will cause detriment to distance vision.

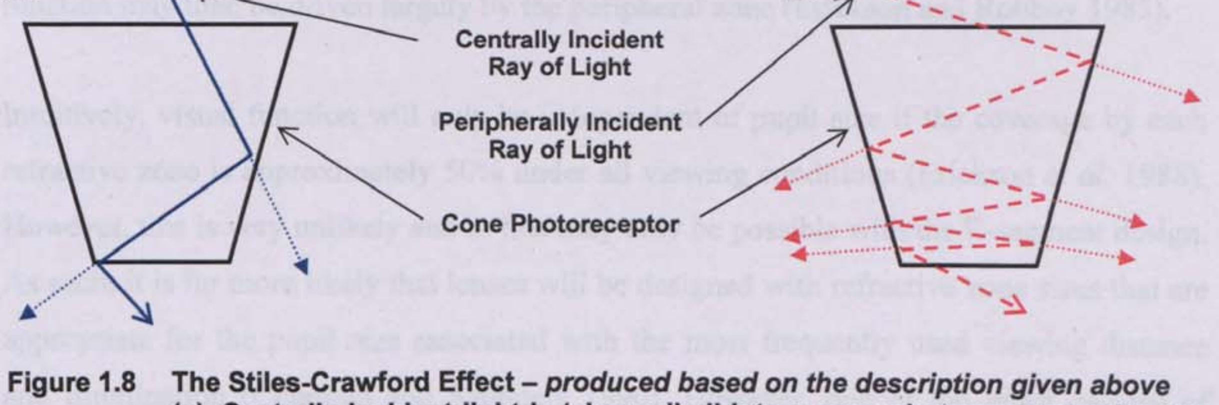

Figure 1.8 The Stiles-Crawford Effect – *produced based on the description given above*
(a) Centrally incident light is 'channelled' into a cone photoreceptor, with little light being reflected (⇢), optimising stimulation of the photoreceptor
(b) Peripherally incident light experiences greater reflection (⇢), which reduces stimulation of the photoreceptor

1.3.2.2 Pupil Size Dependency

The variation of pupil size with viewing distance and illumination means that coverage of the pupil by each of the refractive zones of a simultaneous vision contact lens will also change. In bright illumination or near gaze, pupil miosis will reduce the relative coverage by the peripheral lens zone, causing deterioration of near vision with a centre-distance lens or distance vision with a centre-near lens. Conversely, low illumination or distance gaze will cause pupil dilation, resulting in increasing influence of the peripheral refractive zone to the detriment of the central refractive zone (Figure 1.9) (Borish 1988).

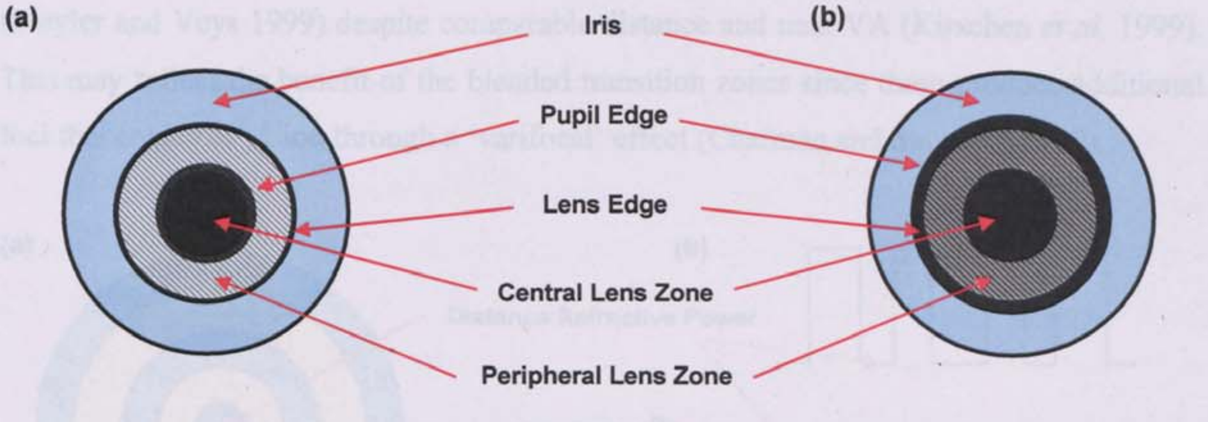

Figure 1.9 Pupil dependency of simultaneous vision contact lenses – *produced based on the description in Borish (1988)*
(a) Small pupil sizes will result in greater influence of the central zone
(b) Large pupil sizes will result in greater influence of the peripheral zone

There is also added complication from the Stiles Crawford Effect (see section 1.3.2.1), which in essence reduces the 'effective' pupil size. Consequently, it has been proposed that this problem may be countered, especially for centre-near designs, by concentrating a high degree of power within a small central zone (Erickson *et al.* 1988). Conversely, visual function may then be driven largely by the peripheral zone (Erickson and Robboy 1985).

Intuitively, visual function will only be independent of pupil size if the coverage by each refractive zone is approximately 50% under all viewing conditions (Erickson *et al.* 1988). However, this is very unlikely and in fact may only be possible with the E-segment design. As such, it is far more likely that lenses will be designed with refractive zone sizes that are appropriate for the pupil size associated with the most frequently used viewing distance and illumination (Charman and Saunders 1990). However, one of the latest designs of annular bifocal contact lenses has purportedly achieved independence from pupil size.

The Acuvue™ bifocal (Johnson & Johnson Vision Care Inc., Jacksonville, FL., USA.) (Figure 1.10a) is a centre-distance lens that is marketed as being 'pupil-intelligent' by virtue of five alternating concentric rings of distance and near refractive power. Pupil coverage by each refractive zone is believed to be approximately equal for all viewing conditions, although this is not quite achieved practically since a pupil diameter of 6.5mm results in 65% coverage by the distance zone, whilst this is 50% for a pupil diameter of 3.7mm (Meyler and Veys 1999). The main cause of this relates to the *stabilised soft moulding* manufacturing process that is used, which blends the refractive zones into each other instead of producing precise transitions (Figure 1.10b) (Hough 2002). Despite this, initial reported success was high (Key and Yee 1999) and out-weighed that of monovision (Meyler and Veys 1999) despite comparable distance and near VA (Kirschen *et al.* 1999). This may reflect the benefit of the blended transition zones since these produce additional foci that enhances vision through a 'varifocal' effect (Charman and Saunders 1990).

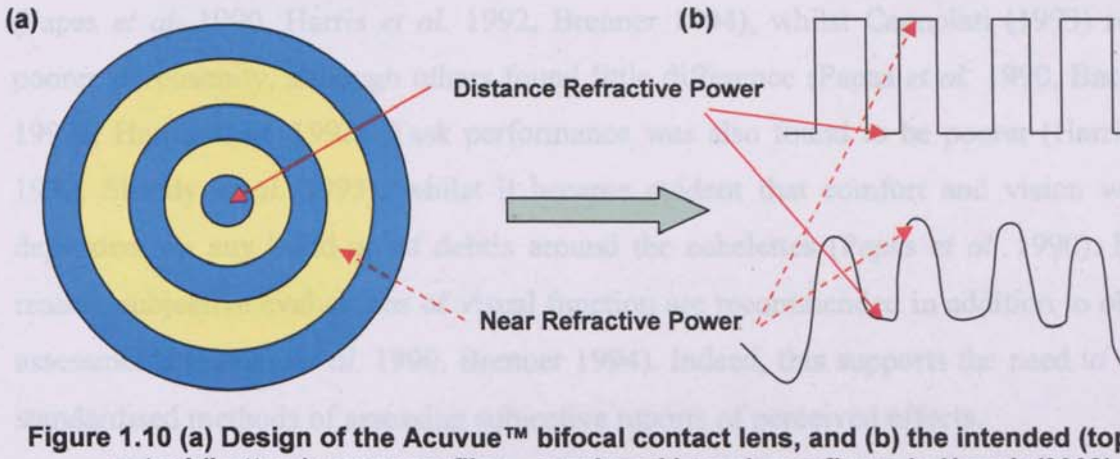

Figure 1.10 (a) Design of the Acuvue™ bifocal contact lens, and (b) the intended (top) and actual (bottom) power profiles – *produced based on a figure in Hough (2002)*

1.3.2.3 Lens Centration

Decentration of annular and segmented bifocal lenses typically causes symptoms of flare and glare when light is reflected from the junctions of the refractive zones (Erickson *et al.* 1988). Decentration of aspheric lenses may cause similar symptoms but primarily as a result of the astigmatic images that they produce; this is also dependent on the type of ellipsoidal curve used and on the eccentricity from the lens centre. If the pupil centre and optical centre of the lens are no longer coincident, the pupil will be presented by a larger astigmatic image, which will degrade retinal image quality and therefore visual performance. However, there may be some benefit in this since there will be a resultant increase in DoF or *pseudoaccommodation* (see section 1.4.4) (Charman and Walsh 1988).

1.3.2.4 Diffractive Lenses

The inherent ability of light to bend around obstacles can be used in simultaneous vision contact lens designs to produce a near visual focus on the retina. Such *diffractive* lenses achieve this through concentric rings of *echelettes*, whilst refractive optics are used to create the distance focus; if the rings are closely spaced and/or a large number of rings is present, the amount of diffraction increases and therefore a stronger near power is produced (Cohen 1993). Although diffractive lenses are considered to be pupil size independent, retinal blur circle size and therefore image quality has still been found to vary with these (Charman and Saunders 1990). Consequently, visual function with the only diffractive lenses that have been manufactured, the soft Hydron Echelon™ (Allergan Inc., Irvine, CA., USA.) and the rigid gas permeable (RGP) Diffrax™ (Allergan Inc., Irvine, CA., USA.) lenses, was not found to be substantially different to other presbyopic contact lenses. Indeed, contrast sensitivity/low contrast VA was shown to be adversely affected (Papas *et al.* 1990, Harris *et al.* 1992, Brenner 1994), whilst Cagnolati (1993) reported poorer stereoacuity, although others found little difference (Papas *et al.* 1990, Back *et al.* 1992a, Harris *et al.* 1992). Task performance was also found to be poorer (Harris *et al.* 1992, Sheedy *et al.* 1993), whilst it became evident that comfort and vision was also dependent on any build-up of debris around the echelettes (Papas *et al.* 1990). For this reason, subjective evaluations of visual function are recommended in addition to objective assessments (Young *et al.* 1990, Brenner 1994). Indeed, this supports the need to develop standardised methods of assessing subjective reports of perceived effects.

1.3.3 Alternating Vision Lenses

Instead of providing all of the functionality for distance and near vision within a central optic that occupies a large proportion of the pupil area, alternating vision lenses exhibit an amount of movement or *translation* so that in primary gaze, good centration allows for clear distance vision whilst upon down gaze, the lens in front of each eye translates so that the pupils are then presented with the near zone. Binocular fusion is therefore retained whilst visual function is then independent of pupil size (Evans and Thompson 1991).

Annular and aspheric designs (see section 1.3.2) are the simplest of all alternating vision lenses since these do not require any form of stabilisation, with free rotation of the lens not having any impact on the position of each refractive zone relative to the pupil.

Segmented designs in contrast, typically place the near zone in the lower half of the lens and therefore, although translation occurs in the same manner, some form of stabilisation is required to maintain segment position for down gaze. Stabilisation is usually achieved by *prism ballasting*, where a base down prism in the order of 0.75Δ to 1.50Δ is generated in the lower half of the lens so that gravitational effects from the increased mass keeps the lens orientated in that position. Alternatively, the upper half of the lens can be polished in order to decrease the thickness here. More commonly, this is combined with *truncation*, where the top and bottom edges of the lens are cut to be flat, producing a rectangular shape that orientates according to the action of the eyelids (Figure 1.11) (Borish and Soni 1982).

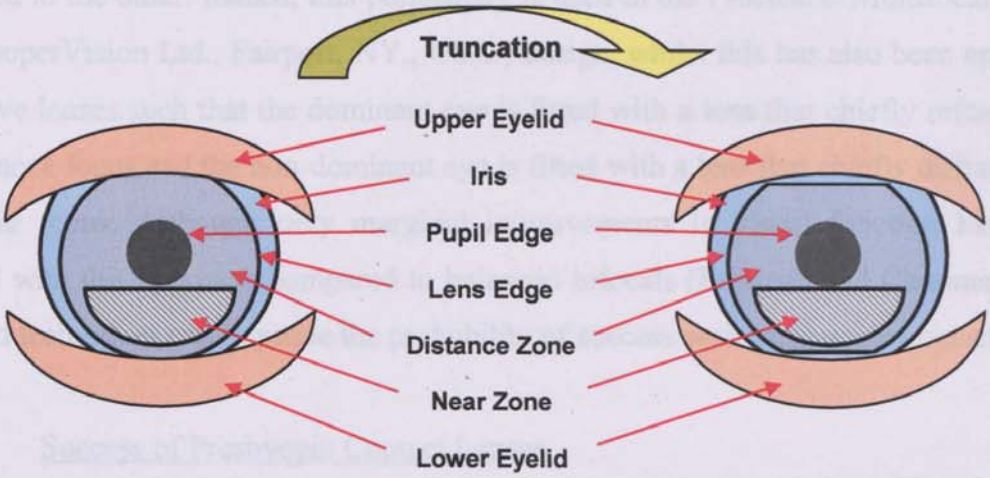

Figure 1.11 Lens truncation creates flat top and bottom edges so that the eyelids can act to prevent lens rotation – *produced based on a description in Borish and Soni (1982)*

Translation was thought to occur due to the lower eyelid acting as a physical 'stop' to prevent downward lens movement upon down gaze. In fact, the upper eyelid actually plays a more important role in applying 'lift' to the upper aspect of the lens to prevent downward movement (Borish and Soni 1982). Soft alternating lenses however, have been shown to function poorer than RGP equivalents (Robboy and Erickson 1987), mainly due to their large total diameter, which creates a 'draping' effect that limits their movement to up to 0.5mm and therefore prevents adequate translation (Robboy and Cox 1988). In contrast, RGP lenses move relatively freely, allowing better prediction of visual performance (Ames *et al.* 1989). In both cases however, near vision is only possible in down gaze and therefore the use of such lenses is precluded where near vision is required in primary or up gaze. Also, the complexity of RGP lens fitting can increase time expense and lens costs (Stein 1990), whilst issues of poor initial on-eye comfort may prevent these types of lenses from being a first choice option to correct presbyopia. Indeed, this perhaps explains why soft simultaneous vision lenses are instead preferred (Gussler *et al.* 1992).

1.3.4 Modified Techniques

Modified techniques usually involve the combination of two different designs of simultaneous vision contact lenses or a combination with monovision correction (Stein 1990). The correction can then be tailored to meet the individual's specific needs. For example, the occasional contact lens wearer may have a distance vision lens fitted to one eye and a centre-near simultaneous vision lens fitted to the other, allowing for occasional improvement in near vision when this is required. Alternatively, one may have a centre-distance simultaneous vision lens fitted to one eye and a centre-near simultaneous vision lens fitted to the other. Indeed, this philosophy is used in the Proclear® Multifocal contact lens (CooperVision Ltd., Fairport, NY., USA.) design, whilst this has also been applied to diffractive lenses such that the dominant eye is fitted with a lens that chiefly refracts light to a distance focus and the non-dominant eye is fitted with a lens that chiefly diffracts light to a near focus. Although only marginal improvements in visual function have been reported with this approach compared to balanced bifocals (Freeman and Charman 2007), modified techniques can improve the probability of success with presbyopic contact lenses.

1.3.5 Success of Presbyopic Contact Lenses

The success of presbyopic contact lenses depends upon the definition used. Jain et al. (1996) for example, defined success as *the percentage of patients that managed to accept monovision after three or more weeks of acclimatization*, and reported a mean success rate of 76% from previous studies. In contrast, Back et al. (1989) used a more prescriptive approach, defining success as *full-time wear of lenses plus an intention to continue after completion of the study*. Monovision success was therefore found to be 66.7% whilst for simultaneous vision lenses this was 42.3%. Such prescriptive definitions however do not account for successful wear by occasional users, whilst financial implications after participating in a 'free' study are also not considered. These success rates are therefore likely to be inaccurate (Back *et al.* 1992b). The most common reasons for failure relate to aspects of visual function, including poor VA and stereoacuity (Erickson and McGill 1992), whilst subjective reports of ghosting, a person's age (Back 1995) and occupational needs should also be considered (Westin *et al.* 2000). Standardised assessment of visual function, especially at near, is required to aid such evaluations, although acceptance is purportedly highest in those who are motivated and have personality traits such as perseverance, conscientiousness, and a sense of realism (du Toit *et al.* 1998).

1.4 Surgical Correction of Presbyopia

The surgical correction of presbyopia provides a more permanent alternative to the techniques that have previously been described. In fact, the most common techniques of monovision (see section 1.4.1) and multifocal vision (see section 1.4.2) have evolved from contact lens counterparts (Charman 2003) and this was made possible by the advent of cataract surgery and IOL implantation, first carried out by Sir Harold Ridley in 1949 (cited in Davies *et al.* 2006). Indeed, interest in these techniques has now grown to include IOL designs that may restore the pre-presbyopic AoA to the presbyopic eye (see section 1.4.3) (Packer *et al.* 2006), whilst other techniques such as *pseudoaccommodation* (see section 1.4.4), *scleral expansion* (see section 1.4.5) and the use of gel-like substances to mimic the natural crystalline lens (see section 1.4.6) have also been suggested.

1.4.1 Monovision

Originating from the principles described in section 1.3.1, monovision can be surgically induced by implanting an IOL aimed at providing an emmetropic post-operative refraction in one eye and an IOL aimed at providing a myopic post-operative refraction of up to 3.00D (depending on the individual subject's needs) in the other. Visual results with such an approach are comparable to contact lenses, with many being spectacle independent and highly satisfied (Greenbaum 2002). This procedure is usually performed on those subjects undergoing cataract extraction, although it can also be used with Clear Lens Extraction (CLE) where the healthy crystalline lenses of a high myope (e.g. Fernandez-Vega *et al.* 2003) or of a high hypermetrope (e.g. Preetha *et al.* 2003) are removed and are replaced with IOLs. It is perhaps more common however, for surgical monovision correction to be induced through excimer laser corneal refractive surgery.

Excimer laser refractive surgery involves the use of energy released by excited molecules such as Argon Fluoride to break organic bonds within the cornea, in order to restructure its shape through a process called *photo-ablation*. In myopic eyes, a relatively flatter central cornea is created whilst in hypermetropic eyes, a relatively flatter peripheral cornea is created (Stevens and Steele 1993). Photorefractive Keratectomy (PRK), first described by Trokel in 1983 (cited in Stevens and Claoue 1996), and Laser assisted *in-situ* Keratomileusis (LASIK), first described by Pallikaris in 1990 (cited in Horn 1999), are perhaps the most common excimer laser refractive surgery techniques that are used today.

In contrast to PRK in which Bowman's layer of the cornea is ablated, LASIK involves the creation of an anterior corneal flap to allow ablation of the stroma. Consequently, the latter is associated with less corneal scarring and improved healing time (Naroo and Charman 2000). In either case, the aim of surgery is the same as monovision with IOLs, and visual results are equally comparable, with improved near vision reported (Wright *et al.* 1999, Goldberg 2001) and an expected reduction in stereoacuity occurring with increasing anisometropia (Fawcett *et al.* 2001, Kirwan and O'Keefe 2006). Success with the excimer laser approach is comparable to contact lenses (Jain *et al.* 2001), if not better (Reilly *et al.* 2006), particularly with increasing age (Miranda and Krueger 2004), whilst aniseikonia (in the order of 5-8%) is not thought to be a reason for failure, since this is less compared to spectacles; failure is instead attributed to poor binocular fusion (Crone and Leuridan 1975) or perhaps correction of the non-dominant eye for distance vision (Cox and Krueger 2006).

Surgical monovision provides an opportunity to treat one eye at a time, allowing the potential for success and the appropriate near addition power to be gauged, particularly if a contact lens trial has not been carried out (Hom 1999, Epstein *et al.* 2001, Sippel *et al.* 2001). It is also possible to carry out additional treatment(s) to either enhance or reverse monovision (Wright *et al.* 1999). The excimer laser approach also allows facilitation of binocular adaptation, since myopic regression that usually occurs after surgery will gradually create the 'near eye' (Hom 1999). The procedure is however contraindicated in those with progressive myopia, due to likely post-operative progression, whilst there are also risks of complications such as flap abnormalities, corneal ectasia, and irregular astigmatism with LASIK (Davis *et al.* 2000, Melki and Azar 2001), corneal scarring, induced astigmatism and glare with PRK (Seiler *et al.* 1994, Stein 2000) and more general complications, also applicable to cataract surgery and CLE, such as keratitis, retinal detachment and macular oedema. It is therefore important that all potential patients are educated on these issues first, with motivation and occupational needs assessed (Baikoff 2004) and a contact lens trial conducted (Sippel *et al.* 2001, Evans 2007).

1.4.2 Multifocal Vision

The surgical creation of multifocal vision follows the same principles as simultaneous vision contact lenses (see section 1.3.2) and can be achieved either through multifocal IOL implantation (see section 1.4.2.1) or by corneal refractive surgery (see section 1.4.2.3).

1.4.2.1 Multifocal Intraocular Lenses (IOLs)

Multifocal IOLs are a popular choice for the surgical correction of presbyopia due to the substantial improvement in near vision that can be gained compared to single vision IOLs (Leyland and Zinicola 2003), independently of ciliary muscle action and capsular bag mechanics (Lane *et al.* 2006). Multifocal IOLs were popularised in the early 1990s by the Array™ multifocal IOL (Advanced Medical Optics - AMO, Santa Ana, CA., USA.) (Steinert *et al.* 1992, Negishi *et al.* 1996, Weghaupt *et al.* 1996, Javitt *et al.* 1997), a refractive design that is still used today (Packer *et al.* 2002, Sen *et al.* 2004, Chen *et al.* 2007, Mester *et al.* 2007), and the 3M diffractive IOL (Vision Care, St. Paul, MN., USA.) (Gimbel *et al.* 1991, Akutsu *et al.* 1992, Gray and Lyall 1992, Auffarth *et al.* 1993, Lindstrom 1993), which has now been superseded by more advanced designs.

1.4.2.1.1 Refractive Multifocal IOL Designs

The AMO Array™ multifocal IOL is a centre-distance annular design containing five concentric rings of alternating distance and near refractive power on the anterior surface (Steinert *et al.* 1992). The refractive zones are contained within a central 4.7mm optic, with 50% of incident light focussed for distance vision and 37% of incident light focussed for near vision (Steinert *et al.* 1999), producing a near addition of +2.80D at the spectacle plane (Arens *et al.* 1999, Brydon *et al.* 2000, Sasaki 2000, Leyland *et al.* 2002). There are aspheric transitions between each refractive zone, which are thought to reduce photic phenomena such as haloes and glare and which benefit intermediate vision (Steinert *et al.* 1999). The design philosophy of this IOL has since been modified with the creation of the ReZoom™ multifocal IOL (AMO, Santa Ana, CA., USA.). This IOL also has a centre-distance zonal-progressive design, containing five alternate zones of distance and near refractive power with aspheric transitions. However, the central optic is 6.0mm in diameter and a near addition of +2.60D is conferred at the spectacle plane. These alterations are thought to maximise distance vision, particularly in low light conditions (Lane *et al.* 2006), and improves intermediate visual performance (Chiam *et al.* 2007, Pepose *et al.* 2007).

Unlike simultaneous vision contact lenses, it appears that multifocal IOLs tend to take a centre-distance design approach since there are only descriptions of the latter design in the literature to date. This may relate to the fact that IOL implantation is more permanent and therefore the need to re-operate, in case there is rejection, needs to be minimised.

1.4.2.1.2 Diffractive Multifocal IOL Designs

Diffractive IOLs can follow an asymmetric design whereby one eye is implanted with a distance-biased IOL and the other eye is implanted with a near-biased IOL. This system was originally described in 1993 (Jacobi and Eisenmann 1993) and was experimented with until 1999 (Jacobi *et al.* 1999), but is now used by the Acri.Twin® asymmetric IOL (Carl Zeiss Meditec AG, Jena, Germany). The distance-biased Acri.Twin® IOL focuses 70% of incident light for distance vision, and 30% for near vision, whilst the reverse is true for the near-biased counterpart (Alfonso *et al.* 2007d). Overall, a near addition of +3.20D is achieved at the spectacle plane (Jacobi *et al.* 1999) and the primary benefit of this system is that the near-biased IOL can be substituted for a distance-biased IOL for those who have a greater demand for distance vision (Fernandez-Vega *et al.* 2007b).

Alternative diffractive IOL designs include the Tecnis® ZM900 IOL (AMO, Santa Ana, CA., USA.), which incorporates an aspheric surface (Mester *et al.* 2007) that improves distance VA and contrast sensitivity compared to conventional IOLs (Bellucci *et al.* 2005), and the Acri.LISA® IOL (Carl Zeiss Meditec AG, Jena, Germany), which incorporates refractive optics (Alfonso *et al.* 2007b). Perhaps the most significant modification however is *adopisation*, whereby the spacing between the diffractive rings varies from the centre of the IOL to the periphery. Adopisation is a key feature of the AcrySof ReSTOR® IOL (Alcon Labs, Fort Worth, TX., USA.) (Figure 1.12) and is such that ring spacing reduces from 1.3µm at the centre of the optic to 0.2µm in the periphery (Souza *et al.* 2006). This is thought to increase the proportion of incident light that is focussed for distance vision, improving visual performance particularly in those with large pupils (Blaylock *et al.* 2006), and reducing photic phenomena (Lane *et al.* 2006).

Figure 1.12 The ReSTOR® Multifocal IOL (Alcon Labs., Forth Worth, TX., USA.) – *reprinted from Davison & Simpson (2006) ©2006 with permission from Elsevier*

1.4.2.1.3 Visual Performance of Multifocal IOLs

Multifocal IOLs perform expectedly similarly to simultaneous vision contact lenses as they too produce superimposed retinal images. Furthermore, their performance is restricted by the same factors (see section 1.3.2) although there is added importance of pupil size since it has been shown that this can vary quite considerably, by 0.5-1.0mm, post-operatively compared to pre-operatively (Koch *et al.* 1996). Consequently, it can be difficult to predict post-operative visual potential due to varying influences of the peripheral refractive zone (Hayashi *et al.* 2001, Salati *et al.* 2007). Diffractive IOLs ought to out-perform refractive IOLs in this respect, due to their pupil independent design, but it has been reported that VA and the CSF vary according to pupil size with these IOLs also (Alfonso *et al.* 2007a).

Distance vision with refractive multifocal IOLs is reportedly comparable to single vision IOLs (Weghaupt *et al.* 1996, Hayashi *et al.* 2000, 2001), if not better (Nijkamp *et al.* 2004, Sen *et al.* 2004), whilst substantial improvements in near vision (Weghaupt *et al.* 1996, Hayashi *et al.* 2000, Javitt *et al.* 2000, Hayashi *et al.* 2001, Nijkamp *et al.* 2004) and the range of clear vision (Sen *et al.* 2004, Bi *et al.* 2008) were also shown. These findings are also true of diffractive IOLs (Allen *et al.* 1996, Chiam *et al.* 2006), but there appears to be no difference in reading speed and the critical print size (CPS) (see section 2.2.1, Chapter 2) (Souza *et al.* 2006). Whilst distance vision is comparable between refractive and diffractive designs (Walkow *et al.* 1997, Weghaupt *et al.* 1998, Alio *et al.* 2004, Schmidinger *et al.* 2006, Chiam *et al.* 2007, Mester *et al.* 2007, Pepose *et al.* 2007, Renieri *et al.* 2007), near vision appears to be superior with the latter (Walkow *et al.* 1997, Chiam *et al.* 2007, Mester *et al.* 2007, Pepose *et al.* 2007, Renieri *et al.* 2007). Similarly, reading acuity and speeds are better with diffractive IOLs than refractive IOLs, perhaps due to a greater affect on retinal image contrast by the aspheric transitions of the latter (Richter-Mueksch *et al.* 2002, Hutz *et al.* 2006, 2008). These studies however did not assess for differences in the CPS and this supports the need to standardise such visual assessments.

As expected, the CSF is adversely affected with both refractive and diffractive IOLs compared to single vision IOLs (Ravalico *et al.* 1993, Allen *et al.* 1996, Hayashi *et al.* 2000, 2001, Souza *et al.* 2006), most likely due to superimposed retinal images and increased aberrations (Zeng *et al.* 2007), and possibly due to short-term corneal haze after surgery (Montes-Mico and Charman 2001). As a consequence, visual problems may occur with night driving and in overcast conditions (Winther-Nielsen *et al.* 1995).

The difference in CSF however, may not be clinically significant (Weghaupt *et al.* 1996) since this can improve between six months (Montes-Mico and Alio 2003) and two years after surgery (Avitabile *et al.* 1999). The near CSF may also be better than single vision IOLs (Olsen and Corydon 1990), or worse (Montes-Mico *et al.* 2004), whilst differences can be minimised through adopisation of diffractive designs (Alfonso *et al.* 2007c, Vingolo *et al.* 2007) or by the use of aspheric surfaces (Toto *et al.* 2007). In fact, some report no differences at all in the CSF between multifocal and single vision IOLs (Sen *et al.* 2004), even in the presence of glare (Schmitz *et al.* 2000), and whilst there may be no differences between different multifocal designs (Ravalico *et al.* 1993, Walkow *et al.* 1997, Renieri *et al.* 2007), some suggest the diffractive design to be better (Mester *et al.* 2007, Pepose *et al.* 2007) whilst others have found the refractive design to be better (Pieh *et al.* 1998).

Symptoms of haloes and glare with multifocal IOLs are subject to individual tolerances (Hunkeler *et al.* 2002) and whilst one study reported these to be comparable to single vision IOLs (Dick *et al.* 1999), Pieh et al. (2001) found significantly larger halo sizes with multifocal IOLs, suggesting support for all of the studies that have reported greater photic symptoms with multifocal IOLs, regardless of design (Gimbel *et al.* 1991, Steinert *et al.* 1999, Haring *et al.* 2001, Leyland *et al.* 2002, Alio *et al.* 2004, Nijkamp *et al.* 2004, Sen *et al.* 2004, Chiam *et al.* 2006, Souza *et al.* 2006, Chiam *et al.* 2007, Mester *et al.* 2007, Renieri *et al.* 2007, Vingolo *et al.* 2007, Palmer *et al.* 2008). Adopisation however may minimise these symptoms (Alfonso *et al.* 2007c, Chiam *et al.* 2007).

Spectacle independence with multifocal IOLs is comparable to monovision (Chen *et al.* 2007), although Slagsvold et al. (2000) reported a spectacle independence rate of 54% eight years after surgery. Other estimates vary from 30-40% (Javitt *et al.* 1997, 2000, Leyland *et al.* 2002, Pineda-Fernandez *et al.* 2004) to 88-95% (Shoji and Shimizu 2002, Claoue 2004) with refractive IOLs, and from 50% (Allen *et al.* 1996, Kohnen *et al.* 2006) to 80-93% (Walkow and Klemen 2001, Chiam *et al.* 2007, Vingolo *et al.* 2007, Goes 2008) with diffractive IOLs. Success however will depend on the individual's expectations and perceptions and therefore standardised measurement of these is required to determine this. Bilateral IOL implantation may maximise visual function (Shoji and Shimizu 2002) and may improve quality of life (QoL) (Blaylock *et al.* 2008), whilst the range of correctable refractive errors can be increased through piggyback techniques (Gayton and Sanders 1993), whereby a single vision IOL is concurrently implanted with a multifocal IOL (Donoso and Rodriguez 2001, Akaishi and Tzelikis 2007, Akaishi *et al.* 2007).

1.4.2.2 Corneal Multifocal Vision

Advances in LASIK techniques now mean that it is possible to create a multifocal cornea, akin to multifocal IOLs. Originally described by Vinciguerra et al. (1998a, 1998b) the technique involves the use of a variable diaphragm to create semi-circular ablation zones, just below the pupil centre, with varying depth from the centre to the periphery. This creates a varifocal progression such that the central cornea is steepest, creating a near addition to correct presbyopia, whilst the peripheral cornea is flattest, correcting distance vision (Epstein *et al.* 2001). Although visual outcomes may be stable over a period of at least two years after surgery (Vinciguerra *et al.* 1998a, 1998b), the need for absolute precision and a relatively small pupil size to achieve maximal near visual performance means that this technique has not become popular (Epstein *et al.* 2001). Furthermore, the limited range of correctable refractive errors compared to IOL implantation means that the latter is instead preferred (Hoffman *et al.* 2004).

It is also possible to create multifocal vision through the use of small-diameter corneal inlays. These are hydrogel lenses, 1500-2000μm in diameter and 30-60μm in thickness, with a power of +1.50DS to +3.50DS, which are implanted into the stroma at 70% depth to create simultaneous vision. These inlays can improve near vision for the presbyope, with no significant impact on the CSF, but distance vision may decline (Keates *et al.* 1995).

1.4.3 'Accommodating' Intraocular Lenses (IOLs)

It is increasingly evident that ciliary muscle contractility and mobility is retained in presbyopia (see section 1.1.3.1) whilst this function may increase after cataract extraction (Park *et al.* 2008). Furthermore, based on observations in the 1980s that conventional single vision IOLs can move within the capsular bag, by up to 0.7mm, upon contraction of the ciliary muscle, it was hypothesized that an accommodative effect could be obtained by implantation of an IOL specially designed to move axially within the bag (Dick 2005). This hypothesis, also referred to as the *optic-shift principle*, forms the fundamental theory behind 'accommodating' IOLs (Baikoff 2004, Doane 2004), and carries the primary advantage of potentially increasing the AoA without producing the visual compromise and photic phenomena that are associated with multifocal vision (for example with multifocal IOLs and contact lenses) (Dick and Dell 2006). Such 'accommodating' IOLs can be categorised as *single optic* (see section 1.4.3.1) and *dual optic* (see section 1.4.3.2) designs.

1.4.3.1 Single Optic 'Accommodating' IOLs

The BioComFold 'accommodating' IOL (Morcher® GmbH, Stuttgart, Germany) was the first single optic design to be marketed in the early 1990s (Dick 2005). This IOL has a 5.8mm biconvex optic with perforated haptics that are angled anteriorly by 5° to 10° in a discontinuous ring (Figure 1.13) (Beiko 2007, Menapace *et al.* 2007). An 'accommodative' effect is produced when compression of the capsular bag upon ciliary muscle contraction pushes the haptics inwards and the optic forwards; elastic properties of the IOL allow it to return to its original position when the ciliary muscle relaxes (Doane and Jackson 2007). This IOL purportedly produces a significantly larger optic shift than a conventional single vision IOL but the reported AoA (2.10±0.58D) was similar with both types of IOL (Legeais *et al.* 1999). This may be because there is no apparent advantage of the haptic design compared to other 'accommodating' IOLs (Findl *et al.* 2003).

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Figure 1.13 The BioComFold 'accommodating' IOL (Morcher® GmbH, Stuttgart, Germany) – ***from the website: http://www.morcher.com/webcontent/englisch/index3.php, accessed 18:05, 24/07/2008***

The AT-45 'accommodating' IOL (Bausch & Lomb Corp., Rochester, NY., USA.) is manufactured from a silicone material and has a square-edged optic with a diameter of 4.5mm. Two plate haptics are hinged immediately adjacent to the optic and have a tapered thickness to allow maximum flexibility for anterior optic movement; polyamide loops at the ends of the haptics provide stability within the capsular bag (Figure 1.14) (Beiko 2007, Doane and Jackson 2007).

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Figure 1.14 The Crystalens AT-45 'accommodating' IOL (Bausch & Lomb Corp., Rochester, NY., USA.) ***– reprinted from Cumming et al. (2006) ©2006 with permission from Elsevier***

The AT-45 'accommodating' IOL was designed based on the hydraulic pressure theory of accommodation (see section 1.1.2.1), whilst a relatively small optic diameter was selected to maximise the axial distance that could be travelled by the optic, thus maximising the potential AoA (Cumming *et al.* 2001, Dick 2005, Dick and Dell 2006, Beiko 2007, Menapace *et al.* 2007). The mechanism of action is supported by ultrasound biomicroscopy (Marchini *et al.* 2004) although pilocarpine stimulation reportedly caused a *backward* optic shift, possibly due to the large haptics (Koeppl *et al.* 2005). It is perhaps for this reason that there are conflicting reports regarding the AoA that is conferred by this IOL, with estimates ranging from, on average, 1.00D (Marchini *et al.* 2004) to 1.75D (Macsai *et al.* 2006) according to the defocus curve method (see section 3.1.7.4, Chapter 3). However, this disparity may also have arisen due to differences in the methodology used, which adds support for the need to standardise such AoA measurements. Initial performance with this IOL was however better than a conventional single vision IOL, and was comparable to a multifocal IOL, with distance VA being 0.10 logarithm of the minimum angle of resolution (logMAR) and distance-corrected near VA being Jaeger (J) 3 (Cumming *et al.* 2001).

Distance VA with this IOL appears to remain consistent for up to one year after implantation (Alio *et al.* 2004, Marchini *et al.* 2004, Macsai *et al.* 2006) and although there may be a decline in distance-corrected near VA (Marchini *et al.* 2004), a retention is more likely (Alio *et al.* 2004, Koeppl *et al.* 2005, Cumming *et al.* 2006, Macsai *et al.* 2006). Contrast sensitivity remains expectedly unaffected (Pepose *et al.* 2007) but photic phenomena of haloes, glare and flare have still been reported (Alio *et al.* 2004) despite no effect on retinal image quality with axial optic movement (Hunter *et al.* 2006). These symptoms typically increase if the pupil diameter exceeds the optic diameter (Dick and Dell 2006) and it is for this reason that the AT-45 model was modified into the AT-50 model, which comprises a 5.0mm optic diameter. An AT-52 model is also available, which has the same 5.0mm optic as the AT-50 model, but the inclusion of longer haptics allows for greater stability in those eyes that have a larger sulcus to sulcus length (Doane and Jackson 2007). One must also consider that a unique post-operative complication may occur with these IOLs whereby capsular fibrosis causes asymmetric anterior vault of the optic, resulting in optic tilt, induced astigmatism and reduced VA (Jardim *et al.* 2006).

Although visual performance with the AT-45 'accommodating' IOL is comparable to that of the 1CU 'accommodating' IOL (HumanOptics AG, Erlangen, Germany) (Figure 1.15), the latter has been shown to provide a larger AoA (Buratto and Di Meglio 2006).

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Figure 1.15 The 1CU 'accommodating' IOL (HumanOptics AG, Erlangen, Germany) – *reprinted from Heatley et al. (2005a) ©2005 with permission from Elsevier*

The 1CU 'accommodating' IOL is a single-piece design that has a 5.5mm biconvex optic and four opposing flexible haptics that are thinner at the junction with the optic (Dick and Dell 2006, Beiko 2007, Menapace *et al.* 2007). This IOL was designed based on the Helmholtz theory of accommodation (see section 1.1.2) (Dick and Dell 2006) and support for this mechanism has been found by observation of a greater reduction in anterior chamber depth (ACD) with this IOL compared to a conventional single vision IOL (Findl *et al.* 2004, Kuchle *et al.* 2004, Sauder *et al.* 2005). Kriechbaum et al. (2005) however suggested that the maximum achievable optic movement is restricted by tonic forces of the ciliary muscle, which cause the optic to vault further forward than would be desired in the unaccommodated state. Indeed, Findl et al. (2004) suggested that only up to 0.50D of accommodation would be possible due to this, as confirmed by a clinical trial (Schneider *et al.* 2006). However, the accompanying distance VA (-0.02 to 0.02 logMAR) and distance-corrected near VA (0.30 to 0.56 logMAR) were favourable (Kuchle *et al.* 2002, Vargas *et al.* 2005, Schneider *et al.* 2006).

Distance VA with the 1CU IOL is maintainable six months after implantation and although an AoA of 1.00D to 2.00D has been reported (Kuchle *et al.* 2004, Sauder *et al.* 2005), this may decline by approximately 0.50D over this period (Mastropasqua *et al.* 2003), possibly causing a decline in distance-corrected near VA also (Langenbucher *et al.* 2003b, 2003c). In fact, the AoA may decline to as low as 0.06D (Dogru *et al.* 2005) or 0.04D (Hancox *et al.* 2006) over two years, resulting in deterioration of near vision and reading ability (Heatley *et al.* 2005a). Others however, suggest visual results to be stable for up to two years after implantation (Kuchle *et al.* 2003), with distance VA of 0.00 logMAR, distance-corrected near VA of 0.52 logMAR to 0.72 logMAR and an AoA of 0.44D to 1.40D reported (Claoue 2004, Kriechbaum *et al.* 2005, Wolffsohn *et al.* 2006a). These conflicting results again provide support for the need to standardise vision assessments.

Of importance is that improvements in near vision with single optic 'accommodating' IOLs are not thought to be due to magnification effects (Langenbucher *et al.* 2003a). However, in order to assess the actual visual function of these IOLs, one must ascertain the amplitude of true pseudophakic accommodation that is conferred, using both objective and subjective techniques (Langenbucher *et al.* 2003a, 2003b, 2003c). Pilocarpine has often been used to determine the maximum capability, but this is unlike natural stimulation by the ciliary muscle and therefore leads to an over-estimate of the AoA (Kuchle *et al.* 2002, Findl *et al.* 2003, Baikoff 2004, Schneider *et al.* 2006). For example, Kriechbaum et al. (2005) reported an anterior optic movement of 0.01±0.03mm with physiological stimulation, but a significantly larger movement of 0.20±0.14mm with pilocarpine stimulation. It is therefore evident from this that single optic 'accommodating' IOLs may actually only provide small improvements in near VA and AoA compared to conventional single vision IOLs (Hancox *et al.* 2006, Schneider *et al.* 2006, Findl and Leydolt 2007). Furthermore, the 'accommodative' ability of these IOLs is adversely impacted upon by *posterior capsular opacification* (PCO). PCO is caused by the proliferation and migration of lens epithelial cells across the IOL surface and this is associated with a loss of capsular elasticity, which may reduce anterior optic movement (Mastropasqua *et al.* 2003, Dogru *et al.* 2005, Heatley *et al.* 2005a, Dick and Dell 2006, Menapace *et al.* 2007). PCO is more common in IOLs manufactured from hydrophilic materials (Heatley *et al.* 2005b), but this can be reduced by ensuring that at least 30% of the optic is covered by the anterior capsule after capsulorrhexis (Vargas *et al.* 2005), whilst square-edged optics can provide a more effective barrier to epithelial cellular migration than round-edged optics (Nishi *et al.* 2000, Hayashi and Hayashi 2005). A lack of this barrier at the haptic-optic junction however, can increase PCO here (Hancox *et al.* 2007).

The AoA is also dependent on the axial length of the eye, dioptric power of the IOL and the power of the cornea (Nawa *et al.* 2003, Beiko 2007). Nawa et al. (2003) for example revealed that myopic eyes may only achieve 0.80D of accommodation per millimetre of optic movement compared to 2.30D in hypermetropic eyes. This was confirmed by Lehrer et al. (2003) after implantation of a +31.00D IOL in a highly hypermetropic eye. In view of this, several mathematical models have been proposed to assess the potential function of these IOLs, taking into account factors such as ACD and axial length of the eye (Missotten *et al.* 2004), corneal thickness and curvature (Langenbucher *et al.* 2004), and capsule thickness, elasticity and diameter (Heatley *et al.* 2004). In fact, it has become apparent from these that a larger AoA can be obtained by dual optic 'accommodating' IOLs instead.

1.4.3.2 Dual-Optic 'Accommodating' IOLs

The first dual optic 'accommodating' IOL was described in 1990 (Hara *et al.* 1990) and comprised a rigid shell of two lenses, 6.0mm in diameter and 4.4mm apart, attached together by a spring. The anterior optic of the IOL provided the refractive power required by the eye whilst the posterior optic provided stability for the IOL when in the capsular bag; the spring allowed the optics to be compressed together by the force of the capsular bag elasticity. Upon release of this elastic spring force, a forward movement of the anterior optic conferred 'accommodation' (Hara *et al.* 1990). The design of this IOL was later modified to introduce flexible polyvinylidine haptics in place of the spring, but fibrosis of the capsule led to a loss of accommodative power (Hara *et al.* 1992).

Interest in dual optic 'accommodating' IOLs has only recently returned since mathematical models have shown that a significantly larger AoA can be achieved with relatively smaller optic movement compared to single optic counterparts (Beiko 2007). Indeed, up to 2.40D of 'accommodation' per millimetre of optic movement can be obtained, independently of the axial length of the eye and the refractive power of the IOL (Langenbucher *et al.* 2004), whilst estimates of up to 4.00D have also been suggested (Ho *et al.* 2006). Dual optic 'accommodating' IOLs can comprise two positive lenses or one positive and one negative lens, with the positive lens being in either the anterior or posterior position. An increase in positive power ('accommodation') is then conferred by an increase in optic separation and it has been shown that this is greatest when a positive anterior optic is combined with a negative posterior optic (Rana *et al.* 2003).

The first dual optic IOL design of note, the Synchrony IOL (Visiogen Inc., Irvine, CA., USA.) is mathematically calculated to confer 2.20D of accommodation per millimetre of optic separation (McLeod *et al.* 2003). The Synchrony IOL is manufactured from a silicone material, the anterior optic of which has a diameter of 5.5mm and a power of between +30.00D and +35.00D, whilst the posterior optic has a diameter of 6.0mm and a power selected according to that required to achieve an emmetropic refraction (Dick 2005). The optics are joined by three spring-like haptics and a maximum separation of 3.7mm is possible when the ciliary muscle contracts and the capsular bag collapses (Beiko 2007). Changes in magnification associated with lens translation are limited to 2.5% and therefore any improvement in near vision is unlikely to be due to this, whilst aniseikonia in single eye treatments is all but eliminated as a result of this (McLeod 2006, McLeod *et al.* 2007).

Initial visual outcomes with the Synchrony IOL were promising and appeared to be better than the single optic alternative, with a mean distance VA of 0.04±0.06 logMAR, distance-corrected near VA of 0.15±0.14 logMAR and an AoA of 3.22±0.88D reported (McLeod 2006). One-year post implantation, all subjects managed to achieve at least 0.30 logMAR distance VA and J3 near VA, whilst the AoA was sustained (Ossma *et al.* 2007). Unfortunately, the Synchrony IOL is prone to *intralenticular opacification*, as opposed to PCO, whereby epithelial cellular migration *in-between* the optics can reduce the AoA (McLeod *et al.* 2007). The design of the IOL is therefore currently being modified, perhaps to allow circulation of aqueous solution between the optics (Menapace *et al.* 2007).

The Sarfarazi dual optic IOL (Bausch & Lomb Corp., Rochester, NY., USA.), appears to be very similar to the Synchrony IOL. It comprises a highly powered positive anterior optic which is coupled by three spring-like haptics to a low negatively powered posterior optic, with both optics having a diameter of 5.0mm and being manufactured from silicone (Sarfarazi 2006). Unlike the Synchrony IOL however, the Sarfarazi IOL makes use of the SofPort® Aspheric Advanced Optics system (Bausch & Lomb Corp., Rochester, NY., USA.), which reduces aberrations and improves contrast sensitivity (Sarfarazi 2006).

To date, all dual optic 'accommodating' IOL designs remain experimental with little clinical data available. However, great potential has been shown by these IOLs and it may only a matter of time before they become more widespread.

1.4.4 Pseudoaccommodation

Pseudophakes implanted with conventional single vision IOLs can reportedly achieve good uncorrected near vision, most likely due to anterior optic movement (Lesiewska-Junk and Kaluzny 2000, Altan-Yaycioglu *et al.* 2002). However, others disagree (Hardman Lea *et al.* 1990, Tsorbatzoglou *et al.* 2006), especially since better than expected near vision has been observed even where the optic of 'accommodating' IOLs moves backwards, which is contrary to the hypermetropic change in refraction that occurs (Gonzalez *et al.* 1992, Muftuoglu *et al.* 2005). These findings have been attributed to *pseudoaccommodation* (Dick 2005), which is primarily conferred by DoF (Ravalico and Baccara 1990) and not a change in ACD (Nakazawa and Ohtsuki 1983, 1984), although other causes are also possible. Elder et al. (1996) for example, suggested that pseudoaccommodation will be conferred if an individual has a good ability to decipher blur.

Corneal changes are the most likely contributors to pseudoaccommodation, since it has been shown that contraction of the ciliary muscle with near vision causes an increase in corneal curvature, and this corresponds to an increase in power by as much as 0.40D (Pierscionek *et al.* 2001). Even likelier than this however, is a residual corneal multifocal effect that may arise following cataract or corneal refractive surgery (McDonnell *et al.* 1988). Fukuyama et al. (1999) for example, found an increase in corneal multifocality six months after implantation of conventional single vision IOLs, compared to pre-operatively, and this was highly correlated to the AoA. Oshika et al. (2002) concurred with this and also suggested that aberrations such as *coma* may contribute.

The intentional creation of an irregular cornea has in fact been proposed as a correction for presbyopia (Moreira *et al.* 1992). Indeed, against-the-rule astigmatism is perhaps a more likely cause of pseudoaccommodation than optic shift and DoF (Nanavaty *et al.* 2006), and therefore low levels of myopic astigmatism could be used to improve near vision akin to simultaneous vision contact lenses, whereby the anterior and posterior focal points of the astigmatic image form the foci for near and distance vision, respectively (Datiles and Gancayco 1990). Indeed, letters are deemed to be more recognisable if the vertical elements are clear compared to the horizontal elements (Friedman 1940), and this would result if against-the-rule astigmatism is induced (Huber 1981). This would also follow the natural age-related change in astigmatism that occurs (Trindade and Pascucci 2006).

An induced refractive error of 0.25DS of myopia with 0.50-0.75DC of myopic astigmatism has been suggested as the optimum to correct presbyopia (Sawusch and Guyton 1991), although others have suggested that spectacle independence and good binocular near vision can be achieved with 1.50DC (Verzella and Calossi 1993) to 2.00DC of astigmatism, with uncorrected distance VA being 6/12 (Snellen) and uncorrected near VA being N8 (see section 2.1.4.1, Chapter 2) (Bradbury *et al.* 1992). Savage et al. (2003) instead suggested that a greater benefit can be gained by inducing low degrees of spherical myopia, although there was little difference in QoL and vision at distance, intermediate and near compared to the astigmatism approach. Hayashi et al. (2000) in fact suggested that there is no pseudoaccommodative advantage to be gained with inducing astigmatism, whilst a detrimental effect is likely if more than 1.00DC of astigmatism is induced in those with multifocal IOLs. Hayashi et al. (2003) also suggested that pseudoaccommodative effects may reduce with age, most likely due to a reduction in visual perception, and therefore the potential usefulness of these techniques may be limited for the older presbyope.

1.4.5 Scleral Expansion

In accordance with his theories of accommodation and presbyopia (see sections 1.1.2.2 and 1.1.3.3), Schachar proposed that increasing the circumlental space could restore the function of the ciliary muscle and equatorial zonules that is required for accommodation (Schachar 1992). He proposed that this could be achieved by expanding the sclera in the region of the ciliary muscle, or by reducing the length of the zonules, or by reducing the equatorial lens diameter (Schachar 2001). Of these options, expansion of the sclera was the most feasible since all that was required was modification of the existing scleral buckle technique that was used for the treatment of rhegmatogenous retinal detachment (Kaufman 2001). Instead of being used to push the sclera closer to the retina however, polymethyl methacrylate (PMMA) bands implanted within the sclera could be used to lift the sclera away from the underlying ciliary body, thus increasing the circumlental space and restoring zonular tension (Marmer 2001, Ostrin *et al.* 2004).

In his original trials, Schachar (1992) revealed that scleral expansion could produce 10.00D of accommodation. The procedure however was associated with several complications, including dislocation and/or extrusion of the band, inconsistency of band placement, and an acute increase in IOP (Kleinmann *et al.* 2006). More seriously, anterior segment ischemia was observed due to blockage of the anterior ciliary vascular supply (Marmer 2001). The procedure was therefore modified so that four individual segment bands were implanted, one in each of the oblique quadrants of the eye (Schachar 2001). These PMMA *scleral expansion bands* (SEBs) are 1380µm wide, 925µm deep and 5500µm long, with grooves that provide grip to prevent migration (Kleinmann *et al.* 2006).

SEBs can reportedly produce 10.00-15.00D of accommodation (Marmer 2001) although an AoA of 1.30-7.00D is more typical, depending on the position of SEB implantation (Schachar 2001). Initial results of a Food and Drug Administration (FDA) trial were promising, with considerably more subjects achieving 6/12 (Snellen) or better near VA compared to an unoperated control group (Kleinmann *et al.* 2006). The literature however, appears to be unanimous in the view that there is little accommodative function to be regained with SEBs. Mathews (1999) for example, measured the objective accommodation dynamics after SEB implantation and found the lens to be immobile, with an absence of the typical micro-fluctuations observed in pre-presbyopes. Any improvement in near vision was therefore attributed to pseudoaccommodation instead (see section 1.4.4).

Ostrin et al. (2004) reported that although a 50-year-old male subject who received bilateral SEB implants was satisfied and did not require reading aids 19 months after surgery, his near vision had declined significantly over this period of time. Furthermore, the AoA was comparable to age-matched 'normal' controls, as assessed using a variety of subjective and objective techniques. Satisfaction with SEBs is also reportedly comparable to monovision, despite a lack of improvement in subjective AoA and near vision compared to unoperated controls (Malecaze *et al.* 2001, Qazi *et al.* 2002). These evaluations however, may not have been conducted using standardised techniques and questionnaires.

An alternative *anterior ciliary sclerotomy* (ACS) technique has also been described to create scleral expansion. Originally proposed by Spencer Thornton in 1997, ACS involves making incisions in the sclera overlying the ciliary muscle, as opposed to inserting SEBs (Hamilton *et al.* 2002). Incisions up to 3.0mm long and up to 100% of the scleral thickness can produce an initial improvement in the AoA but this readily declines over the proceeding months (Fukasaku and Marron 2001). This deterioration occurs due to closure of the incisions through wound healing, and therefore silicone plugs must be used to keep the incisions open. This modification produces an AoA of 1.50D, which is maintainable at least one year after surgery (Fukasaku and Marron 2001), but the AoA and quality of near vision is not significantly better compared to pre-operatively (Hamilton *et al.* 2002).

1.4.6 Phaco-ersatz

In accordance with evidence that indicates ciliary muscle and zonule function to be maintained with increasing age (see section 1.1.3.1), it has been suggested that presbyopia may be correctable by replacing the ageing crystalline lens with a material that mimics, both in behaviour and physical properties, the pre-presbyopic lens. This idea was first tested in the mid-1960s (Kessler 1964) but was not physically possible due to limitations of the surgical technique that was used for cataract extraction at the time. It wasn't until *extracapsular cataract extraction* (ECCE) and *phacoemulsification* were developed that the feasibility of this idea was established in the mid-1980s, since these techniques allowed the capsular bag to be retained in cataract extraction. Coining the name *phaco-ersatz* for the technique of re-filling the capsular bag with a soft transparent material, whilst leaving the zonules untouched, Parel et al. (1986) discovered that a silicone-based polymer was the most ideal substitute material for the lens, owing to the similarity of the average refractive index (approximately 1.402), specific gravity (approximately 0.97) and biocompatibility.

Although it was found that 10.00-11.50D of accommodation would be possible with phaco-ersatz (Haefliger *et al.* 1987), this technique is unfortunately limited by the problem of PCO, which cannot be treated with Neodymium-doped:Yttrium Aluminium Garnate (Nd:YAG) laser, unlike conventional IOLs, since the material would bulge from the capsulotomy and capsule contraction would alter the optical properties (Norrby *et al.* 2006). In addition, extensive leakage of silicone from the capsular bag is often observed, whilst homogeneous spreading of the silicone cannot be ensured, which may cause multifocal effects, and long-term material degradation may also occur (Charman 2003).

Several attempts have been made to combat the primary limitations of phaco-ersatz. For example, it was suggested that pre-cured silicone could be used to prevent leakage of silicone but it was found that the physiological speed of accommodation was not maintained (Haefliger *et al.* 1987). Later work by Nishi et al. (1992) suggested that an inflatable silicone balloon could be used to house the silicone in order to prevent leakage, although they were only able to measure an AoA of 6.00D in one primate eye out of several that were operated on, since dense PCO was observed in all of the other eyes. In addition, the AoA was not maintained at one year after surgery (1.70-1.80D), primarily due to PCO and subsequent balloon rigidity (Nishi *et al.* 1993). Nishi et al. (1997) then suggested that a double-plated silicone sheet could be used to plug the leakage of silicone and whilst experiments on the eyes of monkeys suggested that this was successful, the AoA was still significantly poorer compared to pre-operatively, and dense PCO was again observed (Nishi and Nishi 1998, Koopmans *et al.* 2003, 2004). Most recently, it has been suggested that 'accommodating' IOLs with square-edged optics can be implanted to perform the function of plugs to prevent leakage of silicone from the capsular bag, whilst the square-edged optic ought to minimise PCO (Nishi *et al.* 2008). Trials on rabbit and pig cadaver eyes revealed success on both of these fronts, although such use of IOLs effectively prevents changes in surface curvature from occurring and the result, in essence, is therefore a dual-optic 'accommodating' IOL (Nishi *et al.* 2008).

1.4.7 Developments in Surgical Presbyopia Reversal

Surgical techniques such as 'accommodating' IOLs and phaco-ersatz are as yet in their infancy but are perhaps the most feasible corrections for presbyopia due to the magnitude of the AoA that can potentially be restored, with minimal optical detriment. Current interest therefore substantially lies in evolving and perfecting these techniques.

The SmartLens (Medennium Inc., Irvine, CA., USA.) for example, is a concept IOL that is a rigid rod, 30.0mm long and 2.0mm wide, which transforms into a gel-like substance at body temperature after implantation in the capsular bag (Doane 2004). It is an entirely cohesive material and purportedly behaves just like the natural crystalline lens (Doane and Jackson 2007). The NuLens 'accommodating' IOL in contrast, comprises a flexible material that is sandwiched between two rigid surfaces, the most anterior of which has a central hole (Ben-Nun and Alio 2005). With application of pressure to the IOL by the capsular bag upon ciliary muscle contraction, the flexible material is forced through the hole causing it to bulge in a spherical fashion. The diameter of the hole, flexibility and refractive index of the material, and the amount of applied pressure, determine the change in refractive power that can be generated (Ben-Nun and Alio 2005). Preliminary results in monkey eyes indicate a potential AoA of 40.00D can be achieved, with pharmacological stimulation, whilst 50% of this ability persists after 18 months (Ben-Nun 2006).

The Light Adjustable lens (LAL) (Calhoun, Pasadena, CA., USA.) is an IOL containing partially polymerised silicone-based macromers and a bonded photosensitizer. Upon exposure to a particular wavelength of light, the photosensitizer causes polymerisation of the macromer and a subsequent change in refractive power, the amount of which depends on the exposure time. The correction of presbyopia however, is as yet theoretical since delivery of the desired wavelength of light to the lens has not been perfected whilst a changeable refractive state from distance vision to near vision, and vice versa, has also not been achieved. Furthermore, the cornea and aqueous may act as barriers to the photosensitizer, creating differential power distributions in the lens (Olson *et al.* 2006).

The FlexOptic IOL (AMO, Santa Ana, CA., USA.) is a single optic 'balloon' that is implanted within the capsular bag such that contraction of the ciliary muscle creates an increase in its curvature. The lens supposedly mimics the change in shape of the natural crystalline lens during accommodation and purportedly provides an AoA of 3.00D; however no clinical trials have as yet been conducted (Doane and Jackson 2007).

Other notable developments that have arisen for the surgical correction of presbyopia relate to corneal refractive surgery techniques used for the creation of monovision. The minimally invasive Conductive Keratoplasty (CK) technique for example, which was originally used for the correction of hypermetropia, has now been applied to the correction of presbyopia (Allamby and Heaven 2003).

CK involves the application of radio-frequency energy (approx. 350Hz) to the corneal surface for a short duration of time (0.6 seconds) such that as the radio-frequency waves propagate through the cornea, a resultant heating of the surrounding stromal tissue occurs in a cylindrical fashion, for a depth of up to 80% (500μm) (Allamby and Heaven 2003). As a consequence, the stromal collagen fibres shrink due to contraction, becoming permanent if the temperature exceeds 65°C (Du *et al.* 2007). The application of CK in a ring of spots in the peripheral cornea will therefore cause shrinkage of the collagen here, producing a net steepening of the central cornea and inducing myopia for monovision (Du *et al.* 2007).

The results of CK are consistent with LASIK but it has the advantage of being less invasive (Cox and Krueger 2006). It has also been confirmed that the improvement in near vision is not inadvertently produced by corneal multifocality or through increased spherical aberration (SA) (Hersh 2005). Furthermore, 76% of subjects were reportedly 'satisfied' or 'very satisfied' after CK monovision, with anisometropia of 2.00D, whilst 85% of subjects were reported to have a distance VA of 6/7.5 (Snellen) or better and the results were stable over a period of six months after surgery (McDonald *et al.* 2004).

1.5 Conclusion

It is evident from this review that presbyopia is a multifactorial phenomenon. Research aimed at explaining the fundamental mechanism underlying the accommodation process is ongoing and is vital to understanding the cause(s) of presbyopia. In particular, there is still uncertainty over the actual anatomical and physiological arrangement of the ciliary muscle and zonular apparatus that results in the accommodative process. All that is certain is that some form of attachment is required, and is present, for the forces of ciliary muscle contraction to be transmitted to the crystalline lens to allow for a change in lens shape. Until this process is definitively explained however, one can only rely on postulated theories for the purpose of designing new techniques that restore accommodative ability or improve the near range of clear vision for the presbyopic eye. As these are produced however, accurate comparisons of the visual outcomes of each can only be conducted if visual measurements are performed in a consistent and standardised manner. As is evident from the reviews presented in subsequent Chapters however, this isn't always adhered to, with many variations occurring from one study to another. The next Chapter therefore begins the process of standardisation by investigating the most useful near VA and reading metrics that ought to be assessed when evaluating presbyopic corrections.

1.6 Explanation of Experimental Work

The studies described in the proceeding Chapters of this thesis are presented in an order that best describes standardisation and optimisation of near vision assessment in presbyopia (Chapters 2, 3 and 4). Examples of the implementation of these findings are then applied to the evaluation of presbyopic corrections after this (Chapters 5, 6 and 7).

Data for the studies in Chapters 5, 6 and 7 were collected first, whilst the study described in Chapter 3 was conducted concurrently with Chapter 6. Accordingly, all of the near vision and reading assessments that are described in Chapter 2 (near VA with uppercase letters, lowercase letters, and words, reading acuity, CPS, and CPS reading speed) were measured on *all* of the subjects that participated in these studies (apart from Chapter 3) whilst this was also true for the full 26-Item questionnaire (before Rasch Analysis) described in Chapter 4. However, the data were analysed in Chapters 2 and 4 *first*, along with Chapter 3, so that the terms of standardising near vision assessment could be derived. Once these data were analysed, the findings were applied to the reporting of the studies in Chapters 5, 6 and 7 with respect to this standardisation and optimisation.

As an example, near VA was measured with uppercase letters, lowercase letters, and words, whilst reading acuity, CPS, and CPS reading speed were also measured, for all subjects in Chapter 5. This was so that data could be collected with a view to being analysed in Chapter 2 first. Subsequently, the findings of redundancy of some of these metrics in Chapter 2 meant that they were not reported for the actual study in Chapter 5. Also, all defocus curves in Chapter 6 were initially measured with randomised letter sequences and lens presentation order, until data were analysed in Chapter 3. Thereafter, the defocus curves were measured for Chapters 5 and 7 according to the findings of Chapter 3, which in fact indicated that this ought to be the preferred method of measurement anyway. Consequently, there was no error in the methodology for Chapter 6.

The reason that the studies were conducted in this order was primarily due to the limitations of recruiting large subject numbers, in effect for these studies to be conducted three times. In particular, 'accommodating' IOL implantation and multifocal contact lens fittings are not very common and therefore it was not possible to recruit two separate cohorts of each of these to participate in Chapters 2 and 4 for standardisation, and then to recruit further separate cohorts of each for Chapters 5, 6 and 7 thereafter.

CHAPTER 2

Comparison of Near Visual Acuity and Reading Metrics in Presbyopia

2. Introduction

A measurement of VA is instinctively incorporated into any description of visual function as it represents the ability of the visual system to resolve spatial detail i.e. to discriminate two stimuli as being separate. The smallest detail that can just be resolved (*threshold of resolution*), in terms of its angular subtense at the eye, is referred to as the *minimum angle of resolution* (MAR) and the reciprocal of this represents VA (Kniestedt and Stamper 2003, Jackson and Bailey 2004). The limit of MAR was thought to be one arc minute (1') (Hartridge 1922) but VA can actually be better than this (Elliott *et al.* 1995), whilst finer discriminations such as depth and vernier assessments are also possible from higher orders of cortical processing (Westheimer 1979b, Skottun 2000). Near VA can be measured in many ways (see section 2.1) but near visual function can also be described in terms of reading ability (see section 2.2). A comparison of these forms the focus for this Chapter.

2.1 Measurement of Near Visual Acuity

Perhaps the simplest method of measuring near VA is in terms of one's ability to resolve print types that are typically encountered in daily life, e.g. newspapers, or bible print; due to large variation however, there is little resultant consistency for near VA to be compared from one person to another and therefore the system is no longer used (Jose and Atcherson 1977). Many of the alternative measures of near VA also appear to be riddled with inherent drawbacks that preclude their clinical and scientific usefulness (see sections 2.1.1 to 2.1.4). However, there is certainly a clear advantage for a logarithmic system (see section 2.1.5).

2.1.1 Equivalent Snellen & Decimal Notation

The *Equivalent* or *Reduced Snellen system* is based on the distance Snellen chart (Figure 2.1) and is such that near VA is recorded as a Snellen fraction, which describes the distance at which a particular size of optotype subtends a visual angle of 5' at the eye (denominator) compared to the working distance used (numerator) (Linksz 1975).

Figure 2.1 A modern Snellen chart – *photographed at the Aston University Optometry Clinic*

Near VA can also be expressed in decimal form whereby the Snellen fraction numerator is divided by the denominator. However, despite the simplicity of this system in detecting common causes of visual impairment, such as refractive error, amblyopia, cataract and macular disease (McGraw *et al.* 1995), the Snellen chart has many inherent design flaws that can impede its clinical usefulness (Kniestedt and Stamper 2003, Hussain *et al.* 2006). For example, changes in optotype size follow an arithmetical progression and therefore there is no consistent interval between each level of VA. In particular, optotypes corresponding to poorer levels of VA are often omitted, which reduces the accuracy of the scale and can lead to missed changes in VA due to pathology (Jackson and Bailey 2004). There is also no consistent task requirement since those with poorer VA are required to read fewer optotypes compared to those with better VA. Although this is mainly due to space limitations of printing several large letters on a single line, crowding effects will vary whilst the accuracy of VA measurement is reduced since, for example, 89% of optotypes must be correctly identified on the line representing a MAR of 1' (6/6 Snellen) compared to only 50% on the line representing a MAR of 6' (6/36 Snellen) if one mistake is allowed (McGraw *et al.* 1995). Those with poorer VA may also memorise the optotype sequences with repeated VA measures and this can lead to over-estimates of the true VA.

Near VA is often measured at non-standard working distances due to large inter-individual variations in preference (Mehr and Freid 1976). However, due to the lack of a regular progression for changes in letter sizes and the lack of a regular spacing relationship between optotypes and lines of acuity on a Snellen chart, VA measures cannot be easily equated to a standardised working distance. Furthermore, this also prevents individual letters from contributing in their own right to the measured VA, which is considered to be a finer scale of measurement and is important to detect clinically significant changes (Bailey *et al.* 1991, Bailey 1993). Such disadvantages have therefore resulted in reducing popularity of the Equivalent Snellen system (Bailey 1982).

2.1.2 Jaeger Notation

Eduard Jaeger's system for measuring near VA provides highly correlated measures to the Equivalent Snellen system and although it is commonly used today, due to its simplicity and familiarity, it is often criticised for its lack of reproducibility (Bailey 1982). Jose and Atcherson (1977), for example, measured the size of Jaeger (J) print types on a variety of near vision charts and found substantial variation between the charts, by as much as a factor of two for a single type size. Such variability has even been reported within the same manufacturer and it appears that the only consistency lies in the expression of smaller print sizes with smaller 'J' numbers (Bailey 1982). The cause of this variability has been attributed to changes in font styles with time, particularly since the original font used by Jaeger became obsolete. Manufacturers therefore had to select the closest possible match based on visual inspection (Law 1951). Ultimately therefore, near VA measured with the Jaeger system is not comparable and should not be used (Mehr and Freid 1976).

2.1.3 AMA System, A Series & M Units

The *American Medical Association (AMA) system* follows the Equivalent Snellen system but denotes working distances in inches rather than in metres. Since the metric system is now followed, the AMA system is now considered redundant (Bailey 1978). The *A Series Chart* (Keeler Ltd., Windsor, UK.) was introduced in 1956 (cited in Tunnacliffe 1993a) and comprises twenty rows of letters, ranging in size from A1 to A20 and following a geometric progression such that each row is a factor of 1.25 (approximately 0.10 logarithmic units) larger than the previous row. However, this chart was not received with great popularity since the design was based on the Jaeger system and hence issues relating to poor reproducibility were applicable to this chart also (Mehr and Freid 1976).

The *M Unit* notation for near VA was introduced by Sloan and Habel in 1956 (cited in Rabbetts 2007c). This system describes the distance at which letters of a known height subtend a visual angle of 5' at the eye. It is similar to the Equivalent Snellen system in that the M Unit corresponds to the denominator of the Snellen fraction. As such, a 6M optotype subtends 5' at six metres, whilst its physical height is the same as the letters on the 6/6 row of the Snellen chart (8.73mm). As with the Equivalent Snellen system, the M Unit must be accompanied with a working distance at which the measurement was made.

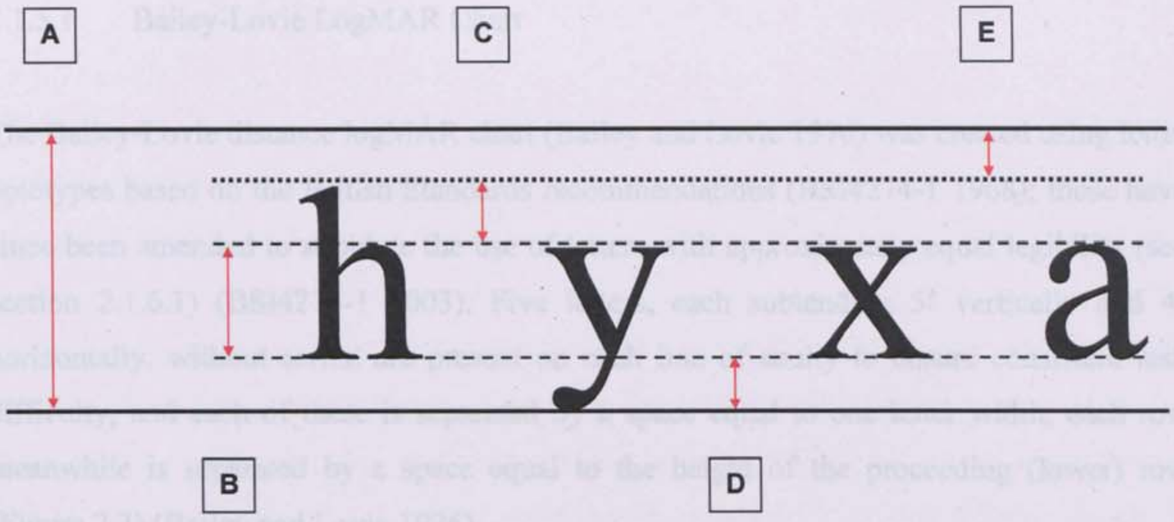
The benefit of the M Unit notation is that near VA measured at non-standard working distances can be equated to other working distances. For example, a near VA of 0.4/1.00M indicates that letter sizes of 1M (1.46mm) were read at a distance of 40cm and this equates to 0.3/0.75M or 0.5/1.25M (Rabbetts 2007c). Near VA expressed in Equivalent Snellen can also be converted into M Unit approximations by multiplying the denominator of the Snellen fraction by 0.02, or by measuring the 'x' height' of the Snellen letter (see section 2.1.4) and then multiplying this by 0.688 (Bailey 1982).

2.1.4 Point System & N-Notation

The *Point system* is most commonly encountered in the form of the Royal College (formerly the Faculty) of Ophthalmologists standardised reading cards (Law 1952). These cards are printed in the *Times New Roman* font, selected due to its familiarity, and comprise passages of text in lowercase words in Point sizes of 5, 6, 8, 10, 12, 14, 18, 24, 36 and 48. Each of these is labelled in the form 'N*y*', where '*y*' denotes the Point size of the print, and it is from this that the Point system has become known by its common name of *N-notation* (Law 1951). Near VA in N-notation is then recorded as the smallest 'N*y*' paragraph that can be read and the corresponding working distance used (Law 1951, 1952).

In the Point system, one Point (Figure 2.2 'A') measures 1/72 of an inch (0.035cm). However, letters do not follow a geometric or a linear progression for changes in size. In fact, it is only the *x-height* (Figure 2.2 'B') of the letters that follows a linear relationship. This is because even though not all letters have ascenders or descenders, (Figure 2.2 'C' and 'D' respectively) their existence is still accounted for within a Point, whilst a *Leading* (Figure 2.2 'E'), which is a space that governs spacing between rows of letters, is also included (Law 1951, Bailey 1978, Tunnacliffe 1993a). Therefore, whilst the Point size may be consistent for different letters, the overall physical size of these may not be.

The widespread use of the Times New Roman font, especially with modern computers, means that there is little problem posed for consistent chart reproduction whilst the content can be varied for different charts and for each passage of text to remove memory effects. However, as with the Snellen system, N-notation optotypes do not follow a regular progression for actual letter size or for letter and line spacing and therefore accurate inter-individual comparisons of near VA to a standardised working distance cannot be made.



A = Total Point size
B = 'x'-height of a letter
C = Height of the ascender
D = Height of the descender
E = Height of the Leading – a space allowance that determines row spacing

Figure 2.2 Nomenclature for Point size – *reproduced and modified from Tunnacliffe (1993a)*

2.1.5 Logarithm of the Minimum Angle of Resolution (logMAR)

It was evident as early as the 1950s that changes in letter size on acuity charts ought to follow a regular progression (Ogle 1953). Indeed, Westheimer (1979a) suggested that a logarithmic (geometric) progression ought to be used as opposed to linear, exponential or reciprocal scales, primarily since each value on a logarithmic scale is related to adjacent values by a specific ratio. A change by one unit therefore represents a change by a specific factor and in terms of the logarithm of the MAR (*logMAR*) this represents a change by a factor of 10, i.e. the base of the logarithm, which corresponds to a ratio of 1.259 (Jackson and Bailey 2004).

The logMAR notation was first used in the Sloan distance VA chart, which comprised optotypes from a set of ten uppercase letters (C, D, H, K, N, O, R, S, V and Z), selected to provide a mixture of vertical, horizontal and oblique elements but with approximately equal legibility to Landolt rings; the logarithmic progression however, was only applied to letter size variation and not for the spacing between letters and between lines (Sloan 1959). Therefore there was little benefit gained over previous chart designs and by the time this was attended to (Sloan 1980), the more successful Bailey-Lovie chart had been introduced.

2.1.5.1 Bailey-Lovie LogMAR Chart

The Bailey-Lovie distance logMAR chart (Bailey and Lovie 1976) was created using letter optotypes based on the British Standards recommendations (BSI4274-1 1968); these have since been amended to stipulate the use of letters with approximately equal legibility (see section 2.1.6.1) (BSI4274-1 2003). Five letters, each subtending 5' vertically and 4' horizontally, without serifs, are present on each line of acuity to ensure consistent task difficulty, and each of these is separated by a space equal to one letter width; each row meanwhile is separated by a space equal to the height of the proceeding (lower) row (Figure 2.3) (Bailey and Lovie 1976).

Figure 2.3 The Bailey-Lovie distance logMAR chart – *photographed at the Aston University Optometry Clinic*

Computerised Bailey-Lovie logMAR charts, such as the *Test Chart 2000 Pro* (Thomson Software Solutions, Hatfield, Herts., UK.) (Thomson 2005) are also now available, whilst a near VA chart (Figure 2.4) was also introduced employing word optotypes instead of letter optotypes to better reflect everyday reading activities (Bailey and Lovie 1980). The words are randomly ordered so that contextual influences are avoided, whilst their familiarity allows for use with young children (Bailey and Lovie 1980). The *face validity* of the chart however has been questioned since a logMAR progression is not used for line spacing whilst each line of acuity has a variable number of words, with variable difficulty, which may create variation in task difficulty (Wolffsohn and Cochrane 2000b).

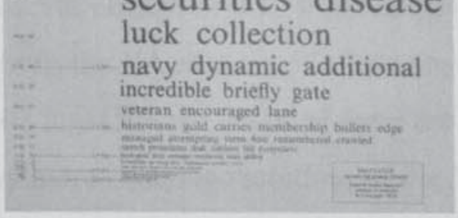


Figure 2.4 The Bailey-Lovie near logMAR chart – *photographed at the Aston University Optometry Clinic*

2.1.5.2 Other Near LogMAR Acuity Charts

In order to overcome the limitations of the Bailey-Lovie near logMAR chart relating to the variable difficulty of words (see section 2.1.5.1), the *Practical Near Acuity Chart* (PNAC) was created. This provides a quick but accurate measure of the VA threshold, which can then be checked against real world reading tasks such as maps and newsprint on the reverse, to ensure that this translates to actual near ability (Wolffsohn and Cochrane 2000b). The *Institute of Optometry Near Test Card* (IONTC) is similar to the PNAC but instead uses a column of single words to determine the VA threshold whilst paragraphs of text adjacent to these are then used to assess reading fluency (Evans and Wilkins 2001).

The *Early Treatment of Diabetic Retinopathy Study* (ETDRS) *Near LogMAR Chart 2000* (Precision Vision™, La Salle, IL., USA.) (Figure 2.5) is similar to the Bailey-Lovie near chart but uses the single uppercase letter optotype designs of Sloan (Ferris *et al.* 1982).

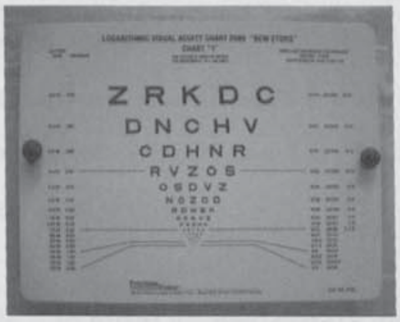


Figure 2.5 The Early Treatment of Diabetic Retinopathy Study (ETDRS) near logMAR chart – *photographed at the Aston University Optometry Clinic*

2.1.5.3 Advantages of LogMAR Charts

The logMAR system is more reliable, accurate and quicker than the Snellen system for VA measurement and it is also amenable to statistical analysis (Lovie-Kitchin 1988). This is made possible by its design features, which essentially mean that each line of acuity is a scaled version of other lines on the chart. This also means that VA measurements taken at non-standard working distances can be equated, since each change in working distance by a factor of 1.259 is equal to a VA change of 0.10 logMAR (Bailey and Lovie 1976, Bailey 1980). Each letter contributes to the VA measure if a letter-by-letter scoring system is used (Hazel and Elliott 2002) (0.02 logMAR per letter, as there are five letters per 0.10 logMAR line of acuity), which allows more accurate recording of the VA end-point if correct letter identification spreads over more than one line, as is often the case (Bailey 1980).

The logMAR system also aids the detection of 'malingering' patients, also known as *visual conversion reactions*, since these patients are not likely to be familiar with the use of non-standard working distances and may therefore restrict themselves to the same line of acuity when the chart is placed at different distances; if VA were truly reduced then this should vary according to the change in working distance (Evans and Wilkins 2001).

2.1.6 Choice of Optotype & Measurement of VA

Word optotypes on near VA charts may be preferred to single letters as they better relate to everyday near vision tasks, for example reading newspapers and books, whilst they can also be more easily understood by those who are unfamiliar with the concept of VA (Bailey 1978). However, problems may still arise if patients are unable to read through disability or a language disorder (Evans and Wilkins 2001). Furthermore, it has been shown that the magnitude of VA measured with single optotypes (letters in most cases) is lower compared to when word optotypes are used (Sheedy *et al.* 2005). This difference may arise from the possibility that the perception of words is a higher order cortical task than the perception of single optotypes, as reflected by the finding that uppercase letters are more legible than lowercase letters (Arditi and Cho 2007), which are in turn 10-20% more legible than words (Sheedy et al. 2005).

The cause of this variation in legibility is not certain but a cortical origin has been proposed whereby delayed photoreceptor recovery or fatigue from stimulation may create prolonged after-images with complex targets (e.g. words), preventing distinct and equal visualisation compared to simple targets (e.g. letters) (Sanford 1888). Legibility is typically ascertained by determining the frequency of correct identification of a particular letter from a specific number of attempts. Such research (sections 2.1.6.1 and 2.1.6.2) has revealed that not all letters are of equal legibility, due to variations in size and form. This is of particular importance for VA measurements since a consistent standard of measure cannot be assumed if optotypes are not equally discernible. Only 'Landolt C' and 'Illiterate E' optotypes provide constant legibility since it is only the *orientation* that is altered when these optotypes are employed. In fact, these optotypes form the standard reference against which all others are now compared (Bailey 1998). However, the corresponding 4-alternate forced choice system that results may artificially over-estimate VA, by 0.01-0.04 logMAR (Bailey 1998), preventing widespread success and use of these charts for research.

When measuring VA, one must also consider the influence of contour interaction. This describes the spatial interference of adjacent contours (for example letter limbs or bars) on a centrally fixated optotype, which may impair or even eliminate visual resolution (Flom *et al.* 1963a). It is thought that this is a cortical phenomenon, since the effects vary between 'normal' and amblyopic eyes (Flom *et al.* 1963b, Simmers *et al.* 1999) whilst there is also evidence of interocular transfer (Flom *et al.* 1963a). In essence, the interaction of adjacent optotypes on acuity charts may be detrimental to the measured VA, with this being worst if letters are narrowly spaced (Liu and Arditi 2001). VA measured with single optotypes may therefore be better compared to if a line of optotypes is presented or if a whole chart is presented (Morad *et al.* 1999).

2.1.6.1 Legibility of Uppercase Letters

The relative letter legibility of the Snellen uppercase letters, as determined by Coates in 1935 and Woodruff in 1947, is shown in Table 2.1 (Bennett 1965). It is evident that there is great variation in letter legibility and as such it was stipulated by the British Standards (BSI4274-1 1968, 2003) that only a pre-defined set of letters ought to be used for VA assessments, based on those with approximately equal legibility (Table 2.1).

Snellen Letter	**Legibility According to Coates** ***from Bennett (1965)***	**Legibility According to Woodruff** ***from Bennett (1965)***	**British Standard Letter Legibility (5' x 4' non-serif)** ***from Bailey (1998)***
A	1.36		
B	0.53	0.81	
C	0.97	0.84	
D	1.10	0.91	0.99
E	1.08	1.01	1.00
F	1.05		0.95
G	0.79	0.80	
H	0.58	0.98	0.97
K	1.07		
L	1.36	1.26	
N	0.70	1.01	1.01
O	1.00	0.95	
P	1.10	1.07	1.01
R	0.94		0.92
S	0.55		
T	1.24	1.12	
U		1.08	1.03
V		0.85	1.01
Y		0.80	
Z	1.00	1.05	1.10

Table 2.1 The relative legibility of uppercase letters as determined by different sources

Despite these recommendations however, some notable differences still remain, with the letters 'F' and 'H' for example considered to be the most difficult and 'E' and 'R' the least (McMonnies and Ho 2000). It has therefore been recommended that all ten letters be used in a randomised order on every line of acuity (McMonnies and Ho 1996, 2000), although the probability of 'correct-guesses' through the resulting 10-alternate forced choice system may then be unacceptably high (McMonnies 1999).

2.1.6.2 Legibility of Lowercase Letters

The relative legibility of lowercase letters, as listed in Table 2.2 in order of least to most difficult, can vary by as much as 56% (Sanford 1888).

Letter	Percentage Correct Identification (%)	Letter	Percentage Correct Identification (%)	Letter	Percentage Correct Identification (%)
m	90.9	b	70.4	u	55.2
w	88.1	y	70.4	s	53.0
f	84.4	h	69.9	t	46.5
p	84.3	d	68.3	n	46.2
q	80.9	g	68.2	e	46.2
r	78.7	x	63.0	c	45.1
j	77.6	a	60.8	o	44.9
v	71.0	i	60.6	z	34.1
k	70.9	l	58.6		

Table 2.2 The relative legibility of lowercase letters – *data from Sanford (1888)*

This variability has primarily been attributed to the presence of ascenders and descenders, which can create confusion groups that hinder letter identification. For example, the letters 'b, d, h, and p' are often confused whilst this is true for the groups 't, f, i and l', 'a, s, z and x', 'c, e and o', 'n, m and u' and 'r, v and w' (Dunn-Rankin 1968, Bouma 1971). On the other hand, the presence of ascenders and descenders can act as perceptual cues that aid the identification of letters that have these over letters that do not.

2.1.7 Effect of Font Style on Near VA

The x-height of letters varies from one font to another and as such it can be difficult to obtain comparable measurements of near VA if optotypes are printed in different fonts (Bullimore 1997), even if the logMAR notation is used (Hazel and Elliott 2002). Of further interest is the effect of serifs on letter legibility. These refer to little finishing strokes on letters (Figure 2.6) that may not be present on all font types (Sanford 1888).

B b H h

Figure 2.6 Serifs are finishing strokes on letters

The presence of serifs can create letter confusions since they may unintentionally look like one another. However it has been reported that there is little measurable effect on VA if all optotypes are printed in the same font, although differences may occur if comparisons are made between fonts that have serifs and those that no not, since resulting variations in letter spacing can alter contour interaction effects (Arditi and Cho 2005). This was supported by Sheedy et al. (2005), especially when electronic displays are used, although the size of serifs can be altered so that they have little effect on VA measures.

2.2 Measurement of Reading Ability

Reading is a crucial part of life, being the central function for learning, communication, daily living tasks and leisure (Legge *et al.* 1985, Schneck and Haegerstrom-Portnoy 2003). It is stated to be one of two fundamental factors that define visual ability, the other being mobility (Massof *et al.* 2007). As such, an assessment of reading performance is a better descriptor of real world vision than a measure of VA alone. However, VA affects reading performance since the latter is dependent on an *acuity reserve*. This refers to the difference in threshold print size between that which *can* be read and that which one *would like* to be able to read; a larger reserve indicates a better ability to comfortably read finer text (Whittaker and Lovie-Kitchin 1993) without adversely affecting reading rate (Legge *et al.* 1985). However, reading is not solely a visual function and in fact relies on other cortical processes such as memory and comprehension (Just and Carpenter 1980). As such, although assessment of reading ability with semantic sentences is more representative of the real world (Bailey and Lovie 1980, Mansfield *et al.* 1993), true near visual ability can be over-estimated through contextual elements, and the measure is then no longer solely one of visual resolution (Wolffsohn and Cochrane 2000b, Evans and Wilkins 2001).

The use of standardised reading tests has become important to assess reading ability (see section 2.2.1) and in fact are effective in discriminating the cause of visual impairment due to, for example, cataract and age-related macular degeneration (AMD) (Stifter *et al.* 2005).

When assessing reading performance in presbyopes, one must consider that reading speed naturally declines with age from 130 words per minute (wpm) in young adults to 58 wpm for those aged 85 or over (Schneck and Haegerstrom-Portnoy 2003). This deterioration has been attributed to age-related deficits that occur in visual functions such as contrast sensitivity, due to changes in the ocular media (Owsley *et al.* 1983), as well as deficits in cognitive ability such as cortical processing (Lott *et al.* 2001) and oculomotor function (Akutsu *et al.* 1991). Indeed, pursuit eye movements are important for reading but deteriorate with age despite good VA (Long and Crambert 1990).

2.2.1 The Minnesota Near Reading Chart

The Minnesota Near Reading (MNRead) chart (Lighthouse Low Vision Products, Long Island City, NY., USA.) was originally created to assess dynamic reading ability in low vision patients and involves measuring the time taken for subjects to read aloud contextual sentences of various sizes as they appear on a computer screen at different rates, as quickly but as comfortably as possible. Although this test is objective and repeatable, it is time consuming to administer and requires a computer (Legge *et al.* 1989). Since there is little difference between dynamic and static reading and little difference between oral and silent reading (Legge *et al.* 1989), an alternative static printed MNRead chart was designed (Mansfield *et al.* 1993). The very first chart was printed in a high contrast Courier font and comprised 18 sentences that followed a logMAR progression for changes in optotype size and for spacing, with each matched for the number of characters (60) and frequency of words (10) (Mansfield *et al.* 1993). The chart has since been modified to increase the range of print sizes (1.30 logMAR to -0.60 logMAR in 0.10 logMAR steps) and is printed in the more familiar Times New Roman font, in both positive and negative polarity (Figure 2.7).

Figure 2.7 The Minnesota Near Reading (MNRead) chart (Lighthouse Low Vision Products, Long Island City, NY., USA.). *Left*: side 1 of the positive polarity chart, *Centre*: side 2 of the positive polarity chart, *Right*: side 2 of the negative polarity chart – *photographed at the Aston University Optometry Clinic*

The MNRead chart can be used to describe reading ability through four specific metrics. *Reading acuity* was originally defined as the smallest print size that can be read without errors and regardless of speed (Mansfield *et al.* 1993) but this definition was later re-assigned to *word acuity* whilst reading acuity was re-defined to account for any errors that are made; reading acuity can then be calculated using Equation 2.1 (Rumney 1998).

$$\text{Reading Acuity (logMAR)} = 1.4 - [s \times 0.1] + [e \times 0.01] \qquad \textbf{Equation 2.1}$$

where s is the total number of sentences on the chart that the patient attempted
e is the total number of errors made

Reading speed (in wpm) is calculated for each sentence using Equation 2.2 based on the time taken to read the sentence, in seconds (Rumney 1998).

$$\text{Reading speed (wpm)} = \frac{[60 \times (10 - e)]}{t} \qquad \textbf{Equation 2.2}$$

where e is the total number of errors made in reading a particular sentence
t is the time, in seconds, taken to read that particular sentence

The *critical print size* (CPS) is defined as the smallest logMAR print size that supports the maximal reading speed; the latter is then referred to as the *CPS reading speed* (Rumney 1998). Although this can be determined from inspection of the recorded times, it can also be determined from a graph plotting the reading speed (y-axis) against the corresponding print size (x-axis); the CPS is then taken as the point at which the maximal reading speed begins to reduce (Figure 2.8). Of importance is that the CPS represents the most comfortable print size that can be read by an individual (Rumney 1998).

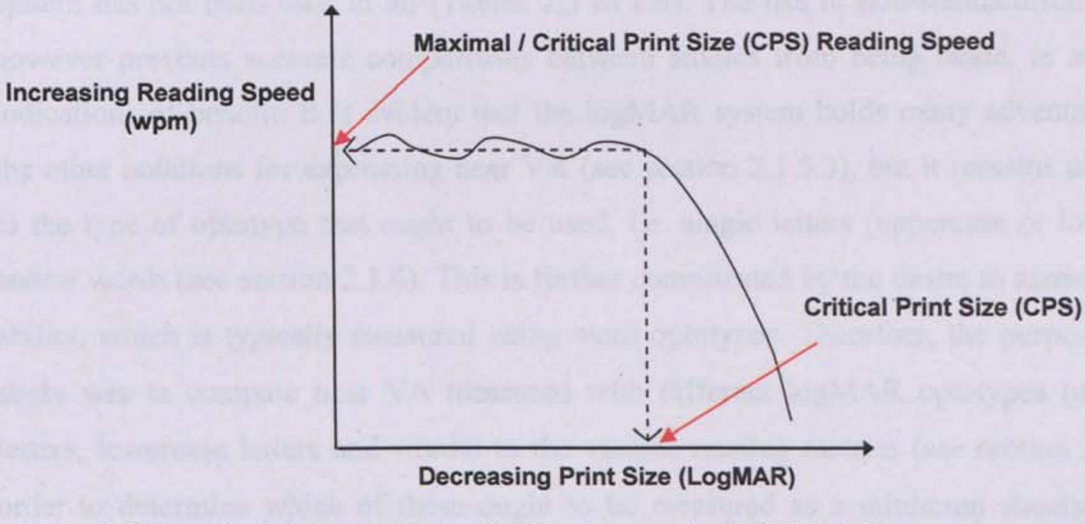


Figure 2.8 Graphical determination of critical print size (CPS) is taken as the point at which the maximal reading speed begins to reduce

Assessment of reading ability with the MNRead chart is repeatable but subject to variation with different working distances, despite a logMAR design; a Badal system (see section 3.1.7.2, Chapter 3) removes this difference, suggesting that there are inherent flaws in chart production (Subramanian and Pardhan 2006). It has also been suggested that maximal reading speed can be reliably determined as the median of the first three sentences (Rice *et al.* 2005), although all of the sentences need to be read anyway, to assess the other metrics.

2.2.2 Other Reading Tests

The Bailey-Lovie near logMAR chart, the PNAC and the IONTC (see sections 2.1.5.1 and 2.1.5.2) can all be used to assess near VA, CPS and reading speed, but not reading acuity as is possible with the MNRead chart. In contrast, other charts that can assess reading performance do not explicitly aim to describe visual resolution. *The Pepper Visual Skills for Reading Test* (VSRT) for example was developed for the purpose of assessing how reading is affected by macula problems, such as AMD, and to aid in the rehabilitation of such individuals by testing the effects of increased contour interaction (Baldasare *et al.* 1986). The *Rate of Reading Test®* on the other hand was created to investigate the effects of visual stress on reading speed, as encountered in Meares-Irlen Syndrome, and the benefit of coloured overlays or lenses against this (Evans *et al.* 1996, Wilkins *et al.* 1996).

2.3 The Study Aim

Previous studies that have investigated visual outcomes of various presbyopic corrections have reported different notations to express near visual resolution, although the M Unit system has not been used at all (Tables 2.3 to 2.6). The use of non-standardised systems however prevents accurate comparisons between studies from being made, to assess for indications of benefit. It is evident that the logMAR system holds many advantages over the other notations for expressing near VA (see section 2.1.5.3), but it remains unclear as to the type of optotype that ought to be used, i.e. single letters (uppercase or lowercase) and/or words (see section 2.1.6). This is further complicated by the desire to assess reading ability, which is typically measured using word optotypes. Therefore, the purpose of this study was to compare near VA measured with different logMAR optotypes (uppercase letters, lowercase letters and words) to the various reading metrics (see section 2.2.1), in order to determine which of these ought to be measured as a minimum standard, when assessing the near visual function conferred by different presbyopic corrections.

Author(s)	Aim of Study	Equivalent Snellen or Decimal	Jaeger	Point System (N Notation)	LogMAR (Optotype)	Reading Metrics	Other
Gimbel et al. (1991)	Evaluation of the 3M diffractive IOL		✓				
Akutsu et al. (1992)	Evaluation of the 3M diffractive IOL				✓ (Letters)	✓ (Speed)	
Gray & Lyall (1992)	Evaluation of the 3M diffractive IOL			✓			
Knorz et al. (1993)	Comparison between the TrueVista bifocal IOL, 3M diffractive IOL and the Nordan aspheric varifocal IOL	✓					
Auffarth et al. (1993)	Evaluation of the 3M diffractive IOL	✓					
Allen et al. (1996)	Comparison of the 3M diffractive IOL to a single vision IOL		✓				
Weghaupt et al. (1996)	Evaluation of the Array refractive IOL		✓				
Negishi et al. (1996)	Evaluation of the Array refractive IOL	✓					
Walkow et al. (1997)	Comparison of the 3M diffractive IOL to the Array refractive IOL		✓				
Arens et al. (1999)	Evaluation of the Array refractive IOL	✓					Nieden Scale
Avitabile et al. (1999)	Evaluation of the 811E diffractive IOL		✓ (Reported)		✓ (Letters) (Measured)		
Jacobi et al. (1999)	Evaluation of an asymmetric diffractive IOL		✓				Nieden Scale
Hayashi et al. (2000)	Evaluation of the Array refractive IOL	✓					
Javitt et al. (2000)	Comparison of the Array refractive IOL to a single vision IOL	✓	✓				
Slagsvold (2000)	Long-term results of the 3M diffractive IOL		✓				
Leyland et al. (2002)	Comparison of the Array refractive IOL to the TrueVista IOL				✓ (Words)		
Richter-Mueksch et al. (2002)	Comparison of the 811E diffractive IOL to the Array refractive IOL					✓ (Acuity & Speed)	
Shoji & Shimizu (2002)	Evaluation of a concentric refractive IOL		✓				
Baikoff et al. (2004)	Evaluation of the Newlife bifocal IOL						Parinaud's Scale
Sen et al. (2004)	Evaluation of the Array refractive IOL	✓					
Pineda-Fernandez et al. (2004)	Evaluation of the Array refractive IOL		✓				
Nijkamp et al. (2004)	Comparison of the Array refractive IOL to a single vision IOL						De Nederlanders reading chart
Alio & Mulet (2005)	Evaluation of an anterior chamber multifocal IOL	✓					Holladay
Schmidinger et al. (2005)	Evaluation of the Acri.Tec TwinSet diffractive IOL				✓ (Letters)		
Tsorbatzoglou et al. (2006)	Evaluation of the AcrySof ReSTOR diffractive IOL		✓				
Blaylock et al. (2006)	Evaluation of the AcrySof ReSTOR diffractive IOL				✓ (Letters)		
Souza et al. (2006)	Evaluation of the AcrySof ReSTOR diffractive IOL				✓ (Letters)	✓ (Speed)	

Table 2.3 Near vision metrics used in the evaluation of multifocal IOLs

Author(s)	Aim of Study	Equivalent Snellen or Decimal	Jaeger	Point System (N Notation)	LogMAR (Optotype)	Reading Metrics	Other
Chiam et al. (2006)	Evaluation of the AcrySof ReSTOR diffractive IOL	✓	✓	✓			
Hutz et al. (2006)	Comparison of the Array, Tecnis and ReSTOR multifocal IOLs					✓ (Acuity & Speed)	
Schmidinger et al. (2006)	Comparison of the Array refractive IOL to the Acri.Twin and 811E diffractive IOLs				✓ (Letters)		
Vingolo et al. (2007)	Evaluation of the AcrySof ReSTOR diffractive IOL		✓ (Reported)		✓ (Letters) (Measured)		
Fernandez-Vega et al. (2007a)	Evaluation of the AcrySof ReSTOR diffractive IOL	✓					
Alfonso et al. (2007b)	Evaluation of the Acri.LISA diffractive IOL				✓ (Letters)		
Toto et al. (2007)	Comparison of the ReSTOR and Tecnis diffractive IOLs		✓		✓ (Letters)		
Mester et al. (2007)	Comparison of the Tecnis diffractive IOL to Array refractive IOL						Cardiff Acuity Test
Fernandez-Vega et al. (2007b)	Evaluation of the Acri.Twin diffractive IOL				✓ (NR)		
Alfonso et al. (2007d)	Evaluation of the AcriTwin diffractive IOL				✓ (NR)		
Akaishi et al. (2007)	Piggyback implantation of the Tecnis diffractive IOL		✓				
Chiam et al. (2007)	Comparison of ReSTOR diffractive IOL to ReZoom refractive IOL	✓	✓				
Hutz et al. (2008)	Comparison of the Array, Tecnis and ReSTOR multifocal IOLs				✓ (Words)	✓ (Speed)	

Table 2.3 cont. Near vision metrics used in the evaluation of multifocal IOLs. *"NR" = Not Reported*

Author(s)	Aim of Study	Equivalent Snellen or Decimal	Jaeger	Point System (N Notation)	LogMAR (Optotype)	Reading Metrics	Other
Claoue (2004)	Comparison of the Array refractive multifocal IOL to the 1CU 'accommodating' IOL	✓		✓			
Alio et al. (2004)	Comparison of the Array and Acri.Tec TwinSet multifocal IOLs to the Crystalens AT-45 'accommodating' IOL	✓	✓				
Pepose et al. (2007)	Comparison of the ReZoom and ReSTOR multifocal IOLs to the Crystalens AT-45 'accommodating IOL'	✓ (Reported)			✓ (Words) (Measured)		
Patel et al. (2008)	Comparison of the Crystalens AT-45 IOL to the Acri.Smart multifocal IOL and LASIK	✓					
Harman et al. (2008)	Comparison of the 1CU 'accommodating' IOL to the Array refractive multifocal IOL and a single vision IOL				✓ (Words)	✓ (CPS & Speed)	

Table 2.4 Near vision metrics used in the comparison of various presbyopic IOLs

Author(s)	Aim of Study	Equivalent Snellen or Decimal	Jaeger	Point System (N Notation)	LogMAR (Optotype)	Reading Metrics	Other
Legeais et al. (1999)	Evaluation of the BioComFold IOL						Parinaud's Scale
Cumming et al. (2001)	Feasibility of the Crystalens AT-45 IOL		✓				
Kuchle et al. (2002)	Evaluation of the 1CU IOL	✓	✓				
Langenbucher et al. (2003b, 2003c)	Evaluation of the methods of assessing accommodation of 'accommodating' IOLs	✓					
Kuchle et al. (2003)	Stability of the 1CU IOL	✓	✓				
Mastropasqua et al. (2003)	Evaluation of the 1CU IOL		✓				
Kuchle et al. (2004)	Evaluation of the 1 CU IOL	✓					
Marchini et al. (2004)	Performance and mechanism of the Crystalens AT-45 IOL		✓				
Dogru et al. (2005)	Early results of the 1CU IOL	✓					
Heatley et al. (2005a)	Comparison of the 1CU IOL to a single vision IOL		✓			✓ (Speed)	
Sauder et al. (2005)	Evaluation of the 1CU IOL		✓				Nieden Scale
Vargas et al. (2005)	Effect of capsulorrhexis size on the 1CU IOL	✓					
Kriechbaum et al. (2005)	Measurement of accommodation of the 1CU IOL				✓ (Words)		
Koeppl et al. (2005)	Evaluation of the Crystalens AT-45 IOL shift		✓		✓ (NR)		
Schneider et al. (2006)	Comparison of the 1CU IOL to a single vision IOL				✓ (Words)		
Hancox et al. (2006)	Comparison of the 1CU IOL to a single vision IOL		✓			✓ (Speed)	
Wolffsohn et al. (2006a)	Evaluation of the 1CU IOL				✓ (Words)		
Wolffsohn et al. (2006b)	Evaluation of the KH3500 IOL				✓ (Words)		
Cumming et al. (2006)	Evaluation of the Crystalens AT-45 IOL	✓ (Reported)	✓ (Reported)		✓ (Words) (Measured)		
Macsai et al. (2006)	Evaluation of the Crystalens AT-45 IOL	✓					
Buratto & Di Meglio (2006)	Early results of the 1CU and Crystalens AT-45 IOLs		✓				
McLeod (2006)	Biomechanics and performance of a dual-optic IOL	✓ (Measured)			✓ (Reported)		
Ossma (2007)	Pilot evaluation of a dual-optic IOL	✓ (Measured)	✓ (Reported)		✓ (Reported)		
Marchini et al. (2007)	Comparison of the 1CU and Crystalens AT-45 IOLs		✓				
Sanders & Sanders (2007)	Evaluation of the KH3500 IOL	✓	✓				

Table 2.5 Near vision metrics used in the evaluation of 'accommodating' IOLs. *"NR" = Not Reported*

Author(s)	Aim of Study	Equivalent Snellen or Decimal	Jaeger	Point System (N Notation)	LogMAR (Optotype)	Reading Metrics	Other
Erickson & Robboy (1985)	Evaluation of a hydrophilic concentric bifocal lens	✓					
Robboy & Erickson (1987)	Evaluation of five soft alternating lens designs	✓					
McGill et al. (1987)	Evaluation of soft simultaneous vision lenses	✓					
Jones & Lowther (1989)	Effect of near zone size & pupil size on vision	✓					Landolt C's
Papas et al. (1990)	Comparison of the Echelon diffractive lens to monovision		✓				
Van Meter et al. (1990)	Evaluation of three bifocal lenses		✓				
Sheedy et al. (1991)	Evaluation of task and visual performance with concentric bifocal lenses				✓ (Letters)		
Harris et al. (1991)	Evaluation of patient response to bifocal lenses				✓ (Letters)		
Back et al. (1992a)	Comparison of visual performance with three presbyopic lens systems				✓ (Letters)		
Gussler et al. (1992)	Evaluation of two multifocal contact lens designs		✓				
Zandvoort et al. (1993)	Evaluation of a new multifocal lens design	✓					
Brenner (1994)	Comparison of a diffractive lens to a front surface aspheric lens		✓				
Back (1995)	What factors influence monovision success?				✓ (Letters)		
Bierly et al. (1995)	Clinical experience with the SimulVue bifocal lens		✓				
Meyler & Veys (1999)	Description of the Acuvue bifocal Lens			✓			
Key & Yee (1999)	Prospective evaluation of the Acuvue bifocal lens		✓				
Kirschen et al. (1999)	Comparison of the Acuvue bifocal lens to monovision	✓ (Measured)			✓ (Reported)		
Fisher et al. (1999)	Comparison of the Focus Progressive multifocal lens to the Acuvue bifocal lens				✓ (NR)		
Guillon et al. (2002)	Comparison of a multi-zone bifocal to a multifocal lens				✓ (Letters)		
Situ et al. (2003)	Re-fitting monovision wearers to bifocal lenses				✓ (Letters)		
Soni et al. (2003)	Contrast sensitivity with multifocal lenses				✓ (Letters)		
Lakkis et al. (2005)	Evaluation of the Menifocal-Z alternating lens				✓ (NR)		
Richdale et al. (2006)	Comparison of a multifocal lens to monovision				✓ (Letters)		
Freeman & Charman (2007)	Comparison of modified monovision to diffractive lenses			✓			

Table 2.6 Near vision metrics used in the evaluation of presbyopic contact lens corrections. *"NR" = Not Reported*

2.4 Method

Near VA was measured with uppercase letter optotypes using the ETDRS logMAR chart (see section 2.1.5.2) and with lowercase letter optotypes using a purpose designed logMAR chart, which was created due to the lack of a commercially available alternative (see section 2.4.2). Near word acuity, reading acuity, CPS (all in logMAR) and CPS reading speed (in wpm) were measured using the MNRead chart and were calculated as described in section 2.2.1. All VA and reading assessments were conducted binocularly and at a standard working distance of 40cm, under consistent illumination of 500 lux (chart luminance of 120cdm^{-2}), following the recommendations stipulated for measuring VA (BSI4274-1 1968, Pandit 1994, BSI4274-1 2003).

All subjects (see section 2.4.1) were instructed to read the optotypes on each chart as far down as possible, starting from the top-most line of acuity. When subjects stopped reading the optotypes, the phrase "*can you read any more letters on the line below*" was used to encourage subjects to continue. This was done until the subject did not wish to continue, as they could not correctly identify any more optotypes on the next line of acuity. The VA was then defined based on the total number of optotypes that had been identified correctly, each being assigned a value of 0.02 logMAR, and the total number of lines of acuity that had been attempted. For the MNRead chart, subjects were given the additional instruction of reading each sentence on the chart as quickly but as comfortably as possible so that their natural reading technique would be represented. Also, the time taken to read each sentence was measured using a stopwatch, and was recorded to the nearest hundredth of a second.

The order of testing between the charts was randomised to average any fatigue influences, although subjects were given a 2-5 minute break between each measure and were asked to look into the distance so that any potential eyestrain and after-image effects would be minimised. All subjects were assessed according to the best near vision achievable with their correction, which included best distance-corrected near vision for those implanted with 'accommodating' IOLs. The author performed subjective refractions for all subjects at distance (six metres) and near (40cm), monocularly and binocularly, to confirm that the best possible vision was obtained. These involved adjustment of the spherical refractive error, under the principle of maximum plus without a reduction in best VA, by presentation of positive and negative lenses, and cross-cylinder test and binocular balancing; contact lenses were fitted based on these refractions and were adjusted binocularly thereafter.

2.4.1 Subjects

Subject characteristics for all participants in this study are shown in Table 2.7 according to the types of presbyopic correction. In total, 77 subjects were recruited for this study, of which 36 subjects were male and 41 subjects were female; the mean age of all of the subjects was 64.4±11.8 years (range 30 to 88 years).

Type of Presbyopic Correction	Number of Subjects (n)	Mean Age ± SD & Range	Gender
Contact Lenses (*Monovision & Multifocal*)	20	55.0±5.1 years Range: 49-67 years	11 males 9 females
'Accommodating' IOL	19	67.1±15.8 years Range: 30-88 years	6 males 13 females
Varifocal Spectacles	38	68.0±9.3 years Range: 49-82 years	19 males 19 females
Total	**77**	**64.4±11.8 years** **Range: 30-88 years**	**36 males** **41 females**

Table 2.7 Subject characteristics for the comparison of near VA and reading metrics

All subjects were required to be able to read English and were screened by the author, or a consultant ophthalmologist (subjects implanted with 'accommodating' IOLs only), using slit lamp examination (anterior eye) and direct ophthalmoscopy (posterior eye) to ensure that there was an absence of ocular pathology, including cataract, glaucoma, AMD and diabetic retinopathy. Cover tests, and fixation disparity tests using the Mallett unit, were performed at distance (six metres) and near (40cm) to ensure the absence of binocular vision anomalies, including decompensated heterophoria, heterotropia, and amblyopia. These screening procedures ensured that no visual dysfunction, other than possibly due to the presbyopic correction itself, would affect the near visual measures.

Subjects wearing presbyopic contact lenses were fitted with either the PureVision® Multi-focal (Bausch & Lomb Corp., Rochester, NY., USA.) (n=10), which is a centre-near aspheric simultaneous vision design, or with monovision (n=10) using single vision PureVision® lenses and which was achieved by inducing an interocular power difference equal to the near spectacle addition. These subjects were participants of a clinical trial comparing visual function between the two lens types and to best binocular spectacle-corrected vision, and were recruited from the Optometry Clinic and staff of Aston University (see section 5.3, Chapter 5).

The inclusion and exclusion criteria of the clinical trial were also applied for this study, in addition to those described above, whilst the lenses were fitted as described in section 5.3 (see Chapter 5). All subjects had worn their respective contact lens corrections for at least one month to allow for adaptation. The mean age of these subjects was younger than the other groups due to issues of contact lens handling and dry eye associated with increasing age. However, since an absence of pathology was confirmed in all subjects, it was unlikely that this would have affected the near vision measures.

Subjects implanted with the 'accommodating' IOL were recruited from Solihull Hospital and from the Midland Eye Institute in Birmingham and had received a single-piece single optic design due to either cataract extraction or CLE. All operative procedures were conducted at least two years before the start of this study, which allowed time for subjects to adapt to the correction. This time period also allowed for complications such as PCO to be dealt with if they occurred (see Chapter 7).

Subjects wearing varifocal spectacles were recruited from the Optometry Clinic of Aston University. All subjects had received a full sight examination within the six months prior to initiation of this study, which ensured that the optimal refractive correction had been obtained and that there was no ocular pathology. Each subject had then been fitted, by an experienced Dispensing Optician, with either Varilux® Physio™ or Varilux® Panamic (Essilor Ltd., Thornbury, Bristol, UK.) varifocal spectacle lenses. Subjects had been wearing their spectacles for at least three months, which again allowed time for adaptation.

Informed consent was obtained from all of the subjects after explanation of the nature and possible consequences of the study, and ethical approval was obtained from the National Health Service (NHS) Local Research Ethics Committee of Solihull and the Ethical Committee of Aston University.

2.4.2 Design of the Single Lowercase Letter Logarithmic Near VA Chart

The single lowercase letter optotype logMAR chart (Figure 2.9) was created using CorelDRAW version 8.0 (Corel Corporation, Ottawa, Canada), following the logMAR design principles of Bailey and Lovie (1976) (see section 2.1.5). Since computer programs use the Point system for denoting letter sizes, these had to be calculated first for each of the logMAR values within the desired range of acuity sizes.

For a particular logMAR value, the MAR was calculated in radians using Equation 2.3.

$$\text{MAR (radians)} = \frac{[\,(10^{a} / 60) \times \pi\,]}{180} \qquad \textbf{Equation 2.3}$$

where 'a' is a particular logMAR value of interest

From trigonometry, the vertical size of an object (in this case the x-height of a letter) can be calculated from the tangent of the angle (in this case MAR) and the viewing distance used (in this case 40cm). However, since MAR refers to the *minimum* size of spatial detail that can just be resolved, i.e. one letter limb width, and since the VA measures were required to represent the ability to resolve a *whole* letter, i.e. five letter limb widths (Tunnacliffe 1993a), the MAR was multiplied by 5 and the letter x-height was then calculated using Equation 2.4.

$$\text{Letter x-height (cm)} = \text{Tan}\,[5 \times \text{MAR (in radians)}] \times 40 \qquad \textbf{Equation 2.4}$$

The Point size for various letter x-heights was then calculated for the Times New Roman font using Equation 2.5 (Tunnacliffe 1993a); the x-height of a 72 Point Times New Roman letter that is produced by CorelDRAW (13.5mm) was confirmed by measurement with a ruler.

$$\text{Point Size} = \frac{\text{'x'-height}}{13.5} \times 72 \qquad \textbf{Equation 2.5}$$

where 13.5 (mm) is the 'x' height of a 72 Point Times New Roman letter (Tunnacliffe 1993a)

This procedure was conducted for a range of acuities from 1.30 logMAR to -0.30 logMAR inclusive, in 0.10 logMAR steps, in accordance with the typical range of acuity sizes that are found on most VA charts. The resulting conversions are shown in Table 2.8.

The chart was produced using the Times New Roman font to match that used on the MNRead chart and due to its familiarity.

Figure 2.9 The purpose-designed single lowercase letter logMAR near VA chart

LogMAR	MAR (arc minutes)	Approximate Snellen Denominator (at 6-metres)	Times New Roman Letter x-height (at 40cm) (mm)	Approximate Point Size (N-Notation) (at 40cm)
1.30	19.95	120	11.6	62
1.20	15.85	95	9.2	49
1.10	12.59	75.5	7.3	39
1.00	10.00	60	5.8	31
0.90	7.94	48	4.6	24.5
0.80	6.31	38	3.6	19.5
0.70	5.01	30	2.9	15.5
0.60	3.98	24	2.3	12.5
0.50	3.16	19	1.8	10
0.40	2.51	15	1.4	8
0.30	2.00	12	1.1	6
0.20	1.58	9.5	0.9	5
0.10	1.26	7.5	0.7	4
0.00	1.00	6	0.6	3
-0.10	0.79	4.8	0.5	2.5
-0.20	0.63	3.8	0.4	2
-0.30	0.50	3	0.3	1.5

Table 2.8 LogMAR to Point size conversions for near VA at 40cm

To ensure minimal differences in letter legibility, only letters that do not possess ascenders or descenders, and those that are of approximately equal character width, were selected for this chart. As such, from the available group of ten letters (c, e, n, o, r, s, u, v, x and z), five letters were randomly selected and were placed in a random order on each line of acuity, with care taken to ensure that no words were inadvertently created and that all lines of acuity began and ended with a different letter. The letter 'a' however was not selected, in order to avoid the potential confusion that may arise due to the variation in form that this letter may present with (i.e. "a" compared to "*a*"). In order to ensure consistency of task difficulty across the chart, all of the letters appeared with approximately equal frequency.

Finally, the chart was printed using a high quality laser printer on matt white card, in order to ensure a similar, high, letter contrast to other near VA charts.

2.5 Statistical Analysis

Data were analysed for all subjects as a whole group and also for each type of presbyopic correction. Pair-wise comparisons were conducted between each and every other metric in turn by Pearson's Product Moment Correlation (PPMC) Coefficients, and associated significance was determined by linear regression, using SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.) (see Appendix for details of statistical test selection). Since the risk of rejecting a null hypothesis when it is in fact true (Type 1 statistical error) increases when several statistical tests are performed on one dataset, a Bonferroni adjustment was applied (significant $p=0.0033$, 15 pair-wise comparisons) in order to reduce this risk; this correction ensures that the risk of a Type 1 error remains constant and similar to that of a single statistical test, assessed at a significance level of $p=0.05$ (Bland and Altman 1995).

Agreement of the magnitudes of the near vision metrics were assessed for each pair-wise comparison by calculating two-way random effects Intraclass Correlation Coefficients (ICC) using Microsoft® Excel® (Microsoft® Corporation, Redmond, WA., USA.). The ICC is typically used to calculate the test-retest reliability of questionnaire scores (see Chapter 4 and Appendix). However, it can also be used to assess the absolute agreement of other measures, in this case near vision metrics, provided that they are conducted under the same conditions and measured on the same scale. This particular model of the ICC was selected as it accounts for two sources of variability, the type of presbyopic correction and the type of near vision metric, and so that the inferences made would be applicable to the general population and not just the population sampled in this study (Shrout and Fleiss 1979). The calculation is based on the statistical test of analysis of variance (ANOVA) (see Appendix for details) and in all cases the ICC has a value between -1 and +1 inclusive, with a higher positive value indicating greater agreement (Kramer and Feinstein 1981).

The Bland-Altman limits of agreement were calculated, using Microsoft® Excel®, to determine the 95% confidence intervals of agreement between each pair of near vision metrics in turn. In a Bland-Altman analysis, the mean of two methods is compared to the difference between the two methods, provided that they are measured on the same scale, to reveal any systematic bias. If this bias is deemed to be clinically acceptable, then the two methods (in this case a pair of near vision metrics) can be deemed to be suitable substitutes for each other (Bland and Altman 1986).

Pair-wise comparisons that yielded a strong correlation (>0.70), a high ICC (>0.70) and limits of agreement of less than ±0.20 logMAR were taken to be indicative of redundant metrics of near visual ability in presbyopes, due to their similarity. The size of the limits of agreement was selected based on that reported for natural variability in repeated VA measures, which ranges from ±0.15 logMAR (Siderov and Tiu 1999) to ±0.10-0.20 logMAR (Lovie-Kitchin and Brown 2000); the *mean* variability however is reportedly ±0.04 logMAR (Raasch *et al.* 1998).

In order to determine whether any of the optotypes possessed discrimination ability to detect differences between various presbyopic corrections, a single factor ANOVA was conducted for each of the metrics. If a significant difference was found (at p=0.05) pairwise comparisons were made, using a Bonferroni adjustment (significant p=0.0167, 3 pair-wise comparisons), and where significant pairwise comparisons were *different* for a particular metric compared to others, this was taken as evidence of discriminant validity.

2.5.1 Power Analysis

Previous studies that have investigated VA comparisons in various contexts have used differing subject sample sizes. For example, Liu and Arditi (2001) used four subjects in their study investigating the effects of crowding on VA measures whilst Arditi and Cho (2007) used nine subjects to determine the variation of letter legibility according to the case of letters. Morad et al. (1999) used 40 subjects in their study investigating differences in VA when a single optotype is presented compared to if a line of optotypes or the whole chart is presented. To determine the minimum sample size required for the present study, to achieve a statistical power of at least 80% (0.80), power analysis was conducted based on the PPMC coefficient. The effect size is taken to be the expected magnitude of the PPMC coefficient and according to published power tables (Table 2.9, produced based on a table in Cohen 1988), a minimum sample size of 16 subjects was required to achieve a power of 0.80 for a correlation coefficient of 0.7, at a significance level of p=0.01.

Significance Level (One-tailed)	Minimum Sample Size for Power of 80% (0.80) According to Effect Size (r)			
	r = 0.1	r = 0.3	r = 0.5	r = 0.7
p = 0.01	1000	108	36	16
p = 0.05	617	68	22	10

Table 2.9 Sample size determination for the correlation coefficient – *produced based on a table in Cohen (1988)*

Using G*Power version 3.0.5 (University of Kiel, Germany) (Faul *et al.* 2007), a minimum required sample size of 20 subjects was determined for this study, in order to achieve a power of 0.80 at a significance level of p=0.0033. *Post hoc* analysis using this program, and based on the actual total sample size in this study (n=77), indicated that a power of more than 0.99 was present for an effect size (magnitude of the PPMC coefficient) of 0.7 or more, at a significance level of p=0.0033.

2.6 Results

For the group as a whole and for each type of presbyopic correction, mean near VA measured with uppercase letters was better than that measured with word optotypes, which was in turn better than that measured with lowercase letters (Table 2.10). Mean reading acuity yielded the lowest mean magnitude of the VA measures, whilst CPS yielded the largest mean magnitude (Table 2.10). For the group as a whole, all of the near vision metrics were highly and significantly correlated to each other, although CPS reading speed did not correlate significantly to any of the other metrics (Table 2.11).

Near Visual Acuity / Reading Metric	Mean Acuity (± Standard Deviation) by Type of Presbyopic Correction			
	Contact Lenses *(Monovision & Multifocal)* (n=20)	'Accommodating' IOL (n=19)	Varifocal Spectacles (n=38)	All Subjects (Whole Group) (n=77)
Uppercase Letters (LogMAR)	0.17 ± 0.14	0.44 ± 0.12	0.09 ± 0.11	**0.20 ± 0.22**
Lowercase Letters (LogMAR)	0.26 ± 0.13	0.67 ± 0.16	0.14 ± 0.09	**0.30 ± 0.25**
Words (LogMAR)	0.24 ± 0.11	0.53 ± 0.19	0.15 ± 0.12	**0.27 ± 0.21**
Reading Acuity (LogMAR)	0.10 ± 0.11	0.45 ± 0.15	0.04 ± 0.11	**0.15 ± 0.21**
Critical Print Size (CPS) (LogMAR)	0.40 ± 0.12	0.72 ± 0.13	0.38 ± 0.16	**0.47 ± 0.20**
CPS Reading Speed (Words per minute - wpm)	155.0 ± 17.5	177.6 ± 29.5	175.0 ± 22.4	**170.4 ± 24.8**

Table 2.10 Mean (± standard deviation) near VA and reading metrics by type of presbyopic correction and for the group as a whole (n=77)

	Uppercase Letters	Lowercase Letters	Words	Reading Acuity	Critical Print Size (CPS)
Uppercase Letters	-	-	-	-	-
Lowercase Letters	*0.96* *p<0.001*	-	-	-	-
Words	*0.89* *p<0.001*	*0.91* *p<0.001*	-	-	-
Reading Acuity	*0.93* *p<0.001*	*0.95* *p<0.001*	*0.94* *p<0.001*	-	-
Critical Print Size (CPS)	*0.81* *p<0.001*	*0.79* *p<0.001*	*0.75* *p<0.001*	*0.81* *p<0.001*	-
CPS Reading Speed	0.05 p=0.64	0.12 p=0.32	0.11 p=0.33	0.09 p=0.44	0.12 p=0.30

Table 2.11 Pearson's Product Moment Correlation coefficients (r; top value) and associated significance values (p; bottom value) for each pair-wise comparison between near VA and reading metrics. Significant correlations (at p=0.0033) are highlighted in italic (n=77)

For the group as a whole, ICCs and limits of agreement are shown in Table 2.12. Near VA measured with uppercase letters had high ICCs to that measured with lowercase letters, words, and reading acuity, but CPS had only moderate ICCs with the other metrics. Limits of agreement were within ±0.20 logMAR for near VA measured with uppercase letters compared to lowercase letters and reading acuity whilst this was true for reading acuity compared to near VA measured with lowercase letters and words. Limits of agreement between CPS and all of the other metrics were larger than ±0.25 logMAR on all occasions.

	Uppercase Letters	Lowercase Letters	Words	Reading Acuity
Uppercase Letters	-	-	-	-
Lowercase Letters	0.88 ± 0.18	-	-	-
Words	0.84 ± 0.21	0.90 ± 0.22	-	-
Reading Acuity	0.86 ± 0.17	0.70 ± 0.16	0.71 ± 0.15	-
Critical Print Size (CPS)	0.34 ± 0.26	0.50 ± 0.30	0.43 ± 0.28	0.23 ± 0.26

Table 2.12 Intraclass Correlation Coefficients (ICCs) (top value) and Bland-Altman limits of agreement in logMAR (bottom value) for each pair-wise comparison between near VA and reading metrics (n=77)

For each individual type of presbyopic correction, PPMC coefficients for each comparison between the near vision metrics were similar to the "whole group" comparisons (Table 2.13), although ICC values were generally lower and limits of agreement were generally smaller (Tables 2.14, 2.15 and 2.16 for presbyopic contact lenses, 'accommodating' IOL and varifocal spectacle corrections, respectively). These differences would have been expected to some extent due to the smaller sample sizes involved, although statistical power was still adequate since the minimum required sample sizes were present in each group (see section 2.5.1).

	Uppercase Letters	Lowercase Letters	Words	Reading Acuity	Critical Print Size (CPS)
Uppercase Letters	-	-	-	-	-
Lowercase Letters	0.93 0.89 0.88	-	-	-	-
Words	0.83 0.71 0.71	0.85 0.75 0.75	-	-	-
Reading Acuity	0.79 0.81 0.84	0.87 0.91 0.79	0.83 0.87 0.86	-	-
Critical Print Size (CPS)	0.39 0.66 0.65	0.33 0.69 0.54	0.35 0.56 0.50	0.36 0.75 0.57	-
CPS Reading Speed	0.19 -0.22 -0.03	0.18 0.05 0.06	0.08 -0.03 0.20	-0.07 -0.04 0.05	0.43 -0.11 -0.04

Table 2.13 Pearson's Product Moment Correlation coefficients (r) for each pair-wise comparison between near VA and reading metrics, for presbyopic contact lens (red), 'accommodating' IOL (blue), and varifocal spectacle (green) corrections

Near Vision Metric	Intraclass Correlation Coefficients (ICCs) and Bland-Altman limits of agreement for pair-wise comparisons with:			
	Uppercase Letters	Lowercase Letters	Words	Reading Acuity
Uppercase Letters	-	-	-	-
Lowercase Letters	0.68 ± 0.10	-	-	-
Words	0.60 ± 0.16	0.85 ± 0.14	-	-
Reading Acuity	0.69 ± 0.17	0.38 ± 0.12	0.36 ± 0.13	-
Critical Print Size (CPS)	0.07 ± 0.27	0.16 ± 0.28	0.16 ± 0.25	0.03 ± 0.25

Table 2.14 Intraclass Correlation Coefficients (ICCs) (top value) and Bland-Altman limits of agreement in logMAR (bottom value) for each pair-wise comparison between near VA and reading metrics for subjects wearing presbyopic contact lenses (n=20)

Near Vision Metric	Intraclass Correlation Coefficients (ICCs) and Bland-Altman limits of agreement for pair-wise comparisons with:			
	Uppercase Letters	Lowercase Letters	Words	Reading Acuity
Uppercase Letters	-	-	-	-
Lowercase Letters	0.62 ± 0.18	-	-	-
Words	0.72 ± 0.21	0.54 ± 0.24	-	-
Reading Acuity	0.73 ± 0.21	0.43 ± 0.14	0.78 ± 0.18	-
Critical Print Size (CPS)	0.30 ± 0.23	0.63 ± 0.24	0.26 ± 0.31	0.22 ± 0.20

Table 2.15 Intraclass Correlation Coefficients (ICCs) (top value) and Bland-Altman limits of agreement in logMAR (bottom value) for each pair-wise comparison between near VA and reading metrics for subjects implanted with 'accommodating' IOLs (n=19)

Near Vision Metric	Intraclass Correlation Coefficients (ICCs) and Bland-Altman limits of agreement for pair-wise comparisons with:			
	Uppercase Letters	Lowercase Letters	Words	Reading Acuity
Uppercase Letters	-	-	-	-
Lowercase Letters	0.65 ± 0.10	-	-	-
Words	0.58 ± 0.17	0.75 ± 0.15	-	-
Reading Acuity	0.50 ± 0.12	0.17 ± 0.14	0.29 ± 0.12	-
Critical Print Size (CPS)	0.16 ± 0.24	0.21 ± 0.26	0.19 ± 0.27	0.06 ± 0.26

Table 2.16 Intraclass Correlation Coefficients (ICCs) (top value) and Bland-Altman limits of agreement in logMAR (bottom value) for each pair-wise comparison between near VA and reading metrics for subjects wearing varifocal spectacles (n=38)

2.6.1 Discriminant Validity

The discriminant validity results are summarised in Table 2.17. A significant difference in near VA/reading ability between the three types of presbyopic correction was found with all of the near VA and reading metrics (ANOVA, $p<0.001$ on all occasions). Pairwise comparisons revealed that a significant difference existed between the contact lens correction and the 'accommodating' IOL group and between the varifocal spectacle correction and the 'accommodating' IOL group, with each of the metrics. One exception to this however was the finding of no significant difference in CPS reading speed between the varifocal spectacle correction and the 'accommodating' IOL group ($p=0.70$).

Significant differences between the contact lens correction and the varifocal spectacle correction were *only* identified when assessed using lowercase letter optotypes ($p<0.005$) and CPS reading speed ($p<0.005$) (Table 2.17).

Near VA or Reading Metric	Overall Significance *(ANOVA P-Value)*	ANOVA F-Value	Pairwise Comparisons *(Significant p=0.0167)*		
			Correction Type	'Accommodating' IOL	Contact Lenses
Near VA with Uppercase Letters	*<0.001*	67.0	'Accommodating' IOL	-	-
			Contact Lenses	*<0.001*	-
			Varifocal Spectacles	*<0.001*	0.06
Near VA with Lowercase Letters	*<0.001*	121.3	'Accommodating' IOL	-	-
			Contact Lenses	*<0.001*	-
			Varifocal Spectacles	*<0.001*	*<0.005*
Near VA with Words	*<0.001*	50.6	'Accommodating' IOL	-	-
			Contact Lenses	*<0.001*	-
			Varifocal Spectacles	*<0.001*	0.02
Reading Acuity	*<0.001*	72.6	'Accommodating' IOL	-	-
			Contact Lenses	*<0.001*	-
			Varifocal Spectacles	*<0.001*	0.08
CPS	*<0.001*	39.3	'Accommodating' IOL	-	-
			Contact Lenses	*<0.001*	-
			Varifocal Spectacles	*<0.001*	0.69
CPS Reading Speed	*<0.005*	6.0	'Accommodating' IOL	-	-
			Contact Lenses	*<0.005*	-
			Varifocal Spectacles	0.70	*<0.005*

Table 2.17 Discriminant validity analysis for each of the near VA and reading metrics, to assess for the ability to detect for differences between various presbyopic corrections (n=77). Significant results are highlighted in italic.

2.7 Discussion

The increasing variety of techniques that are available to correct presbyopia, such as 'accommodating' and multifocal IOLs and presbyopic contact lenses, has increased the importance of conducting standardised comparisons of visual function with each, in order to obtain evidence of benefit. Near VA is perhaps the most common and well-known measure of near visual function although reading metrics such as reading acuity, CPS and CPS reading speed offer a more real world visual assessment. However, no previous study has investigated whether there are any differences in near VA when measured with different logMAR optotypes, or how these compare to reading metrics, in presbyopic subjects wearing different corrections. It is therefore unclear whether all of these metrics are necessarily required to assess near visual function in presbyopia.

Assessment of near visual function in presbyopes with near VA (measured with uppercase letter optotypes, lowercase letter optotypes, and word optotypes), reading acuity and CPS were all found in this study to be strongly and statistically significantly correlated to each other. CPS reading speed however did not correlate well to any other near vision metric nor was there a significant relationship with any of the other measures. This is not surprising since an assessment of reading speed is not solely an assessment of visual resolution but is heavily dependent on other non-visual processes such as comprehension and memory (see section 2.2). Consequently, an assessment of optimal reading speed provides additional information of near visual function in presbyopia and is therefore a useful measure that gives an indication of reading fluency. Indeed, reading is considered to be one of two fundamental aspects of visual ability (Massof *et al.* 2007) and therefore an assessment of this, in terms of reading speed, is of prime importance. Furthermore, comparisons of reading speed between two different presbyopic corrections, for example between two different types of contact lens corrections, can be made for an individual to determine the effect of, or difference in, the corrections, since this within-subject design will then cancel out the extraneous factors that influence reading speed measurements.

In this study, the mean magnitude of near VA measured with uppercase letters was approximately one line of logMAR acuity better than that measured with lowercase letters, with word optotypes in-between. The differences are likely to have arisen partly due to factors such as familiarity with the use of uppercase letters for VA assessments, or perhaps more likely due to disparity in font style and letter legibility between the different optotypes. The presence of ascenders or descenders on lowercase letters, as found on the MNRead chart but not on the single lowercase letter chart, improves the legibility of such letters whilst the absence of serifs on the ETDRS chart may also have given rise to differences (see sections 2.1.6 and 2.1.7). Word acuity should however be poorer than single lowercase letter acuity since word recognition is a more complex cortical task that may also be prone to greater contour interaction effects (Flom *et al.* 1963a). Indeed, in accordance with previous findings (Sheedy *et al.* 2005), this study found that near VA measured with single uppercase letters was better than that measured with words, with limits of agreement that were just greater than two lines of logMAR acuity. However, near VA measured with all three optotypes in this study was strongly correlated and had very close agreement suggesting redundancy of measuring near VA with more than one of these when assessing presbyopic corrections. Since uppercase letters had the highest correlations and closest agreement to all of the other optotypes, this ought to be the optotype of choice.

Considering that assessment of near visual function with word optotypes is more representative of real world tasks (see sections 2.1.6 and 2.2), there ought to be some value in measuring this. However, it has now been established that near VA measured with word optotypes is similar to that measured with both uppercase letters and lowercase letters. Similarly, it was found in this study that reading acuity, which also assesses the ability to resolve word optotypes, had high ICCs and small limits of agreement (approximately 1.5 lines of logMAR acuity) with near VA measured with uppercase letters, lowercase letters and word optotypes. In fact, of all the near vision metrics, reading acuity provided the lowest mean magnitude of near acuity, indicating the best near visual performance. It is possible that this is an over-estimate of true reading ability, since the design of the MNRead chart requires subjects to read print of high contrast, which is very unlike the type of materials that are encountered in real world reading tasks. Of importance is that the high agreement of reading acuity with the other near vision metrics again suggests redundancy of this metric. As such, a more useful assessment of the ability to resolve word optotypes is perhaps provided by measurement of the CPS instead.

CPS had moderate ICCs to near VA measured with uppercase letters, to reading acuity and to word acuity, with large limits of agreement also observed (approximately 2.5 to 3.0 lines of logMAR acuity). This disparity may be due to the fact that CPS is not measured to the same level of accuracy as the other metrics (0.10 logMAR as opposed to 0.02 logMAR) but, more importantly, it also represents the difference in the nature of the actual measurements. Whereas near VA, regardless of the optotype used, and reading acuity both assess near vision at the limits of resolution, CPS is representative of the most comfortable print size that can be read prior to an observed deterioration in reading speed. Based on the existence of this *acuity reserve* (see section 2.2) it would be intuitively expected that the magnitude of the CPS would be poorer than any other near VA measure, as is observed in this study. The importance of CPS is herein made obvious since people read most proficiently with letters sized at or above their most comfortable print size and therefore determination of this would certainly be of value for patient care and advice.

A similar comparison of near VA and reading metrics for each of the individual types of presbyopic corrections (Tables 2.13 to 2.16) revealed comparable findings to those of the overall group, although ICC values were generally lower and the limits of agreement were predominantly smaller, with the latter indicating greater agreement between measures.

Of interest however, was the finding that in subjects implanted with 'accommodating' IOLs, most of the reading metrics were inversely correlated to CPS reading speed, suggesting that these subjects need to read smaller print sizes in order to achieve a consistent and maximal reading speed. This may reflect a more accurate stabilisation of the 'accommodation' response with concentration on smaller print sizes and therefore this adds further support for the measurement of CPS when evaluating such corrections.

All of the near vision and reading metrics were found to detect significant differences between the 'accommodating' IOL correction and the contact lenses and varifocal spectacles corrections. However, only near VA measured with lowercase letters and CPS reading speed detected a significant difference between the contact lenses and varifocal spectacles corrections, suggesting that these metrics are the most sensitive for detecting differences between various presbyopic corrections. Further evidence for this could have been obtained if the reliability and validity (see sections 4.1.5.1 and 4.1.5.2, Chapter 4, respectively) of these metrics were assessed and this perhaps is a limitation of this study.

2.8 Conclusion

Standardised measurement of near visual ability is important to allow for accurate comparisons of presbyopic corrections to be made. Based on the correlation and agreement analysis in this study, measurement of near visual ability in terms of acuity and reading performance should include an assessment of:

(a) The smallest resolvable size of uppercase letter logMAR optotype.
(b) The smallest logMAR print size that maintains the maximal reading speed (CPS).
(c) The reading speed at this CPS.

The latter two metrics can be measured using, for example, the MNRead chart, whilst the first metric can be measured using, for example, the ETDRS logMAR chart. When comparing different presbyopic corrections, the CPS reading speed and smallest resolvable size of lowercase letter logMAR optotype should be measured for discrimination purposes.

Having now optimised the measurement of near VA and reading ability, the next Chapter investigates the measurement and quantification of the subjective AoA from defocus curves, which is another important assessment of near visual ability in presbyopia.

CHAPTER 3

Optimising Measurement of Subjective Amplitude of Accommodation with Defocus Curves

3. Introduction

The primary goal of all presbyopic corrections is to achieve a range of clear vision that is as similar as possible to pre-presbyopic levels. It is the AoA that primarily governs this range although one must also consider an element of blur tolerance if subjective methods of quantifying this are used. This refers to a lack of subjectively perceived blur, even with full accommodative effort, when an object is spatially displaced from its origin and the corresponding image is displaced from the retina; this is known as *depth of focus* (DoF) in the latter case, or *depth of field* in the former (Wang and Ciuffreda 2006). DoF may form part of the accommodation mechanism since its magnitude is similar to micro-fluctuations in steady-states of accommodation that have been recorded (Table 3.1); DoF may therefore prevent any consequential perception of blur from interfering with vision (Walsh and Charman 1988, Winn *et al.* 1989). It is the influence of this blur tolerance on the measurement of subjective AoA that forms the focus for this Chapter.

3.1 Quantification of the Amplitude of Accommodation

The AoA can be measured either objectively, where determination is solely by the investigator and ideally by automated means, or subjectively, where subject participation is required. Unlike the latter, objective techniques are independent of DoF and this is of importance when a measure of a change in optical focus *only* is desired, for example to ascertain true pseudophakic accommodation with 'accommodating' IOLs (Wold *et al.* 2003, Ostrin and Glasser 2004). However, such techniques cannot be used to assess the range of clear vision with, for example, monovision and simultaneous vision contact lenses, since these types of correction aim to enhance the natural DoF of the eye as opposed to creating a change in optical focus. Therefore, subjective techniques are required and although 'real-distance' tests such as the push-up/push-down test (see section 3.1.7.3) are most ideal (Charman 2003), variable DoF will be included in the measure since not all of the factors that influence DoF (see sections 3.1.1 to 3.1.6) can be controlled.

Study	Number of Subjects	Method Used	Depth of Focus
Vasudevan et al. (2006a)	35	Objective: dynamic changes in refraction	±0.26D to ±0.32D
Vasudevan et al. (2006b)	20	Objective: dynamic changes in refraction	±0.46D to ±0.81D
Ciuffreda et al. (2005)	10	Subjective: just detectable blur	±0.73D to ±1.15D
Wang & Ciuffreda (2004)	7	Subjective: just detectable blur	±0.45D to ±1.75D
Marcos et al. (1999)	3	Objective: variation in image quality Subjective: just detectable blur	Objective = ±0.10D to ±0.27D Subjective = ±0.21D to ±0.54D
Rosenfield & Abraham-Cohen (1999)	24	Subjective: just detectable blur	±0.11D to ±0.19D
Jiang & Morse (1999)	18	Subjective: just detectable blur	±0.17D to ±0.21D
Mordi & Ciuffreda (1998)	30	Objective: dynamic changes in refraction Subjective: just detectable blur	Objective = ±0.20D to ±0.64D Subjective = ±0.40D to ±0.90D
Wang et al. (1997)	3	Subjective: change in resolution & detection acuity	±3.00D for 20° to 40° of retinal eccentricity
Atchison et al. (1997)	5	Subjective: just detectable blur	±0.27D to ±0.43D
Winn et al. (1989)	3	Subjective: just detectable blur	±0.13D to ±0.19D
Jacobs et al. (1989)	5	Subjective: just detectable blur	±0.10D to ±0.18D
Walsh & Charman (1988)	18	Subjective: just detectable blur	±0.10D to ±0.12D
Legge et al. (1987b)	2	Subjective: just detectable blur	±0.27D to ±8.50D
Tucker & Charman (1986)	1	Subjective: just detectable blur	Not quantified in the study, only the trends are shown
Kotulak & Schor (1986)	3	Objective: dynamic changes in accommodation Subjective: just detectable blur	Objective = ±0.12D Subjective = ±0.18D
Green et al. (1980)	N/A	Theoretical, based on subjective detection of blur	±0.05D
Charman & Whitefoot (1977)	6	Subjective: just detectable blur	±0.15D to ±1.20D
Tucker & Charman (1975)	2	Subjective: just detectable blur	Not quantified in the study, only the trends are shown
Ronchi & Fontana (1975)	1	Subjective: just detectable blur	±0.04D
Ronchi & Molesini (1975)	2	Subjective: just detectable blur	±1.10D to ±2.30D
Ludlam et al. (1968)	4	Objective: dynamic changes in accommodation	±0.10D
Schwartz & Ogle (1959)	3	Subjective: just detectable blur	±0.19D to ±0.33D
Ogle & Schwartz (1959)	3	Subjective: just detectable blur	±0.32D to ±0.47D
Oshima (1958)	1	Subjective: just detectable blur	±0.004 to ± 0.052
Campbell & Westheimer (1958)	1	Subjective: just detectable blur	±0.10D
Campbell (1957)	1	Subjective: just detectable blur	±0.33D to ±0.54D
Miles (1953)	25 (50 eyes)	Subjective: just detectable blur	±0.13D to ±0.20D
Von Bahr (1952)	3	Subjective: just detectable blur	±0.50D to ±0.75D

Table 3.1 Depth of focus (DoF) of the human eye as ascertained by various studies – *produced based on a table in Wang & Ciuffreda (2006)*

3.1.1 Effect of Pupil Size & Spherical Aberration (SA)

Several studies have investigated the effect of pupil size on DoF (Campbell 1957, Oshima 1958, Ogle and Schwartz 1959, Schwartz and Ogle 1959, Tucker and Charman 1975, Charman and Whitefoot 1977, Green *et al.* 1980, Tucker and Charman 1986, Legge *et al.* 1987b, Atchison *et al.* 1997, Marcos *et al.* 1999). Most of these studies suggest that DoF may *increase* with larger pupil diameters due to an increase in SA, whereby peripheral rays of incident light are refracted more than central rays, which produces multiple foci that increase the range of clear vision akin to simultaneous vision contact lenses (see section 1.3.2, Chapter 1) (Charman and Whitefoot 1977, Marcos *et al.* 1999). However, this effect plateaus with pupil diameters of 4.0mm or more, as a consequence of the Stiles Crawford Effect (see section 1.3.2.1, Chapter 1) (Campbell 1957, Tucker and Charman 1975, Legge *et al.* 1987b, Marcos *et al.* 1999). It is more conceivable however that as pupil diameter increases, the presence of non-axial rays of incident light increases retinal blur circle size, which increases blur perception and decreases DoF (Oshima 1958, Green *et al.* 1980).

3.1.2 Effect of Chromatic Aberration (CA) & Wavelength

Chromatic aberration (CA) describes how the eye refracts different wavelengths of light to different foci. Shorter wavelengths are refracted more than longer wavelengths, which creates an extended image along the optic axis (*longitudinal CA*) and coloured fringes perpendicular to the axis (*transverse CA*) (Millodot 2004). If longitudinal CA is large then DoF will also be large since the range of clear foci increases analogous to SA (see section 3.1.1) (Campbell 1957, Oshima 1958, Green *et al.* 1980, Legge *et al.* 1987b, Marcos *et al.* 1999). However, when measured with monochromatic light, the DoF varies according to the wavelength, with this being larger as the wavelength reduces (Ronchi and Molesini 1975). This is most likely to reflect the fact that the number of cones that are sensitive to short-wavelengths of light in the fovea is lower than the number of cones that are sensitive to long-wavelengths, which biases visual resolution towards the latter (Campbell 1957).

3.1.3 Effect of Target Size & VA

Several studies have found that as target size (or SF) increases, DoF also increases (Miles 1953, Ogle and Schwartz 1959, Schwartz and Ogle 1959, Tucker and Charman 1975, Legge *et al.* 1987b, Jacobs *et al.* 1989, Marcos *et al.* 1999).

Atchison et al. (1997) reported a 60% increase in DoF for a 13.5-fold increase in target size and this is thought to occur due to variations in blur sensitivity. Blur sensitivity has been shown to be higher for small targets because these produce relatively larger retinal blur circles compared to large targets (Jacobs *et al.* 1989). A change in retinal image contrast is therefore more readily detected, which increases the perception of blur (Atchison *et al.* 1997). In a similar fashion, blur sensitivity is lower in those with poor VA since retinal image contrast is reduced (see section 3.1.4). Therefore as VA reduces, DoF increases (Green *et al.* 1980, Legge *et al.* 1987b, Sergienko and Tutchenko 2007).

3.1.4 Effect of Contrast & Luminance

Atchison et al. (1997) found that as contrast reduces from 99% to 21%, DoF increases by approximately 0.08±0.05D. This finding was supported by Oshima (1958) and Campbell (1957) and was thought to be due to a reduced ability of the visual system to detect edges or detail in the retinal image. The effects of luminance on DoF are somewhat inter-linked with the effects of contrast, i.e. DoF increases as luminance decreases, primarily because retinal image contrast is affected by luminance, which subsequently affects visual resolution and blur sensitivity (Campbell 1957, Oshima 1958, Tucker and Charman 1986).

3.1.5 Effect of Retinal Eccentricity

DoF has been shown to be larger in the peripheral retina than in the central retina (Ronchi and Molesini 1975, Wang *et al.* 1997, Marcos *et al.* 1999, Wang and Ciuffreda 2004, Ciuffreda *et al.* 2005), with this increasing at a rate of 0.05D (Ciuffreda *et al.* 2005) to 0.15D per degree of retinal eccentricity (Wang and Ciuffreda 2004). It is thought that this reflects the changing function of the retina, since wiring of retinal ganglion cells in the fovea makes the central retina suited for spatial resolution tasks, whilst the peripheral retina is instead suited for object detection and mobility; the latter is therefore less able to discriminate changes in clarity of visual detail (Wang *et al.* 1997, Ciuffreda *et al.* 2005).

3.1.6 Effect of Refractive Error & Age

Green et al. (1980) reported DoF to increase as axial length reduces (hypermetropes) but others found the DoF in myopic eyes to be larger than emmetropic (Jiang and Morse 1999, Rosenfield and Abraham-Cohen 1999) and hypermetropic eyes (Vasudevan *et al.* 2006a).

DoF may be larger in myopic eyes due to reduced blur sensitivity, conferred by genetic factors or by blur adaptation of the visual system (Vasudevan *et al.* 2006a, Wang *et al.* 2006, Cufflin *et al.* 2007). DoF has also been reported to increase with age, by 0.03D per year (Mordi and Ciuffreda 1998). This may be due to senile pupil miosis, which reduces retinal blur circle size, or perhaps due to ocular changes that also affect VA and reading ability (see section 2.2, Chapter 2). This relationship however was assessed by subjective means and it is known that evaluation of DoF, and the AoA, depends on the method used.

3.1.7 Methods of Evaluating the Amplitude of Accommodation

The objective AoA is usually assessed by dynamic retinoscopy (see section 3.1.7.1) or objective optometers (see section 3.1.7.2), whilst the subjective AoA is usually assessed by the push-up/push-down test (see section 3.1.7.3) or by defocus curves (see section 3.1.7.4).

3.1.7.1 Dynamic Retinoscopy

Introduced by Cross in 1902 (cited in Rabbetts 2007a), dynamic retinoscopy is a modification of the static technique traditionally used in routine refraction. However, whereas the latter requires a steady non-accommodative state to be maintained, the dynamic technique requires accommodation to be stimulated. The Cross method involves a well illuminated, near, accommodative target to be placed at the retinoscope plane, which the subject fixates binocularly. The target is typically a card printed with text and which has a hole in the centre through which the retinoscope is placed. Lenses of increasing positive power are then placed in front of both eyes, first until a neutral point is reached and then for the whole range for which a neutral reflex is maintained; the range of lenses that provides a neutral reflex then corresponds to the AoA (Rabbetts 2007a).

Instead of placing lenses in front of the eyes, the *Nott* method of dynamic retinoscopy requires the examiner to move back and forth with the retinoscope for the range for which a neutral reflex is observed. If however, the accommodative response is greater than (*lead of accommodation*) or less than (*lag of accommodation*) the stimulus demand, the neutral point will not coincide with the point of fixation. The fixation target must therefore be separated from the retinoscope (Leat and Gargon 1996), and the AoA is then quantified as the dioptric difference between the range of retinoscope movement for which a neutral reflex is observed and any accommodative lead or lag that may be present (Goss 1992).

Dynamic retinoscopy is repeatable in young adult subjects (Locke and Somers 1989) but it is not an entirely objective technique since the neutral point determination by the examiner is wholly subjective. Indeed, misalignment with the visual axis, even by as little as 5°, can lead to an inaccurate neutral point determination (Rabbetts 2007a). In addition, the retinoscope light shone onto the subject may cause changes in pupil size and target contrast that results in variation of target clarity and hence steadiness of fixation. As such, the technique is only suggested to be a valuable screening tool for detecting astigmatism, anisometropia and anomalies of accommodation (Guyton and O'Connor 1991).

3.1.7.2 Objective Optometers

Objective optometers are usually encountered as autorefractors and an open-field of view, or the incorporation of a Badal system, can allow the AoA to be evaluated. A Badal system is created when a positive lens is placed such that the anterior focal point is coincident with the nodal point of the eye whilst a fixation target is placed at the posterior focal point of the lens (Rabbetts 2007b). In this configuration the object vergence is zero i.e. an object at optical infinity is simulated, and as the target is brought closer to the eyes the object divergence increases, which increases the need to accommodate (Figure 3.1) (Gallagher and Citek 1995). The fixation target used is typically a high contrast Maltese cross (see Figure 3.1) since an accommodative stimulus is visible regardless of the individual's VA.

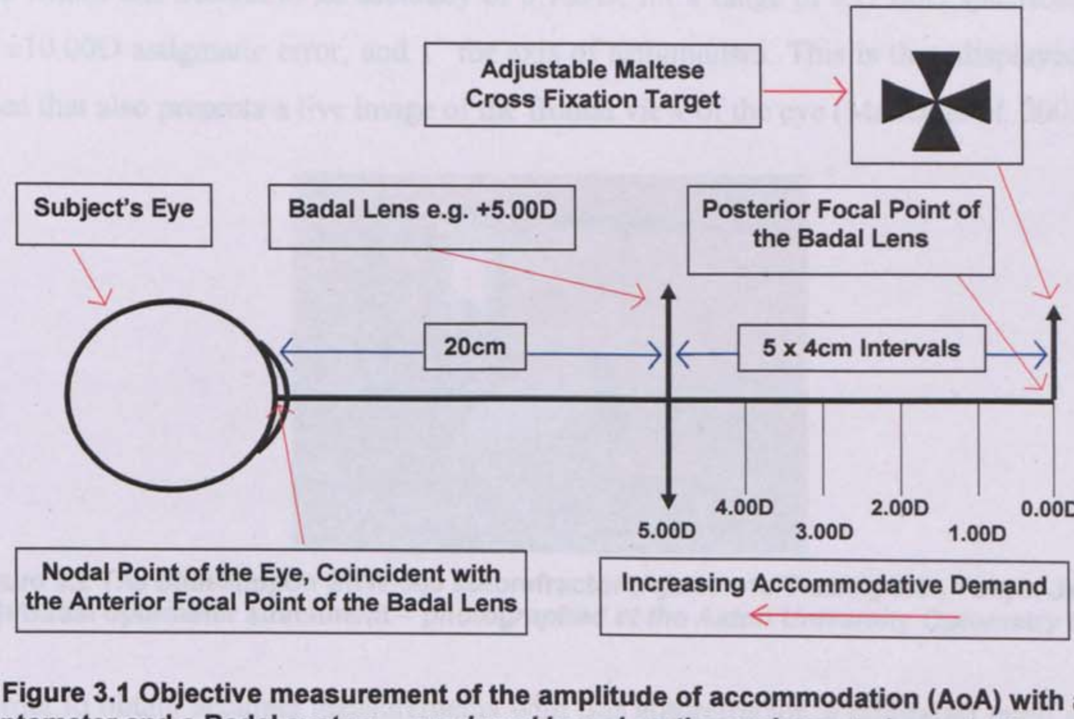


Figure 3.1 Objective measurement of the amplitude of accommodation (AoA) with an optometer and a Badal system – *produced based on the equipment shown in Figure 3.2*

The Badal system utilises a linear scale such that accommodative demand increases by 1.00D per $1000/F^2$ mm (where F is the power of the Badal lens) of target movement towards the eyes (Tunnacliffe 1993b). The AoA can then be determined by measuring the maximum change in refractive status with the change in object vergence, or from a stimulus-response curve (see section 3.1.7.2.2). A constant image size and luminance is maintained throughout the measurement, removing the implications of variable target size associated with the push-up/push-down test (see section 3.1.7.3), and although the range of measurable AoA is limited to the power of the Badal lens, a lens power of +5.00D is usually ample for presbyopic subjects (Tunnacliffe 1993b, Gallagher and Citek 1995).

3.1.7.2.1 Autorefractors

Open-field autorefractors are preferred for measurements of the objective AoA since these are minimally prone to changes in accommodation that occur due to an awareness of closeness i.e. *proximal accommodation* (Rosenfield and Ciuffreda 1991). One example is the Shin-Nippon SRW-500 autorefractor (Ajinomoto Trading Inc., Tokyo, Japan) (Figure 3.2), which is a validated, binocular, infrared, open-field objective optometer that calculates refractive error in two stages (Mallen *et al.* 2001). First, a rapid lens movement correctly focuses an image of a ring of dots after reflection from the retina. The image is then digitally analysed in multiple meridians to determine the refractive error, reporting these within one second to an accuracy of 0.125D, for a range of ±22.00D spherical error and ±10.00D astigmatic error, and 1° for axis of astigmatism. This is then displayed on a screen that also presents a live image of the frontal view of the eye (Mallen *et al.* 2001).

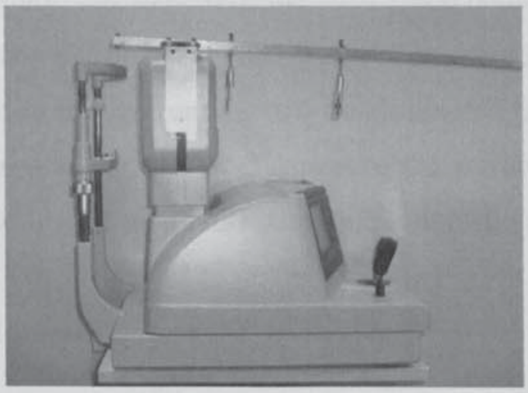


Figure 3.2 The Shin-Nippon SRW-500 autorefractor (Ajinomoto Trading Inc., Tokyo, Japan) with Badal optometer attachment – *photographed at the Aston University Optometry Clinic*

In order to obtain accurate measurements with this autorefractor, a minimum pupil size of 2.9mm is required so that the image of the ring of dots is not distorted (Mallen *et al.* 2001).

3.1.7.2.2 Stimulus-Response Curves

The accommodative response for a particular stimulus demand can be determined by measuring the mean spherical equivalent (MSE) refractive error for the stimulus demand in question. A plot of the measured responses to various stimulus demands then produces a *stimulus-response curve* (Figure 3.3). Perfect responses will produce a straight line that passes through the origin, but in reality, the curve plateaus as the limit to the AoA is reached. The AoA can then be determined either as the highest point on the curve or directly from the refractive error measures as the difference in MSE at a stimulus demand of zero and the most negative MSE that is obtained. With this method however, one must consider that once the maximum AoA has been reached, a blurred target does not stimulate accommodation well, and therefore the response may be reduced (Wolffsohn *et al.* 2006a).

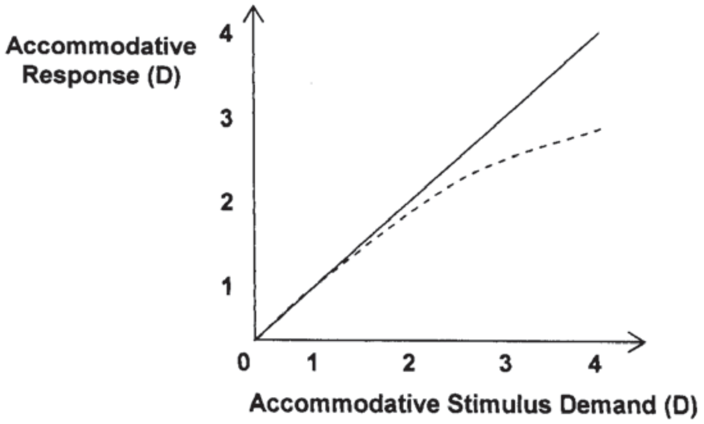


Figure 3.3 A stimulus-response curve. Perfect responses produce a straight-line passing through the origin (—) but as the limit to the amplitude of accommodation (AoA) is reached the response plateaus (---)

This method represents a static assessment of the AoA since both accommodative state and accommodative stimulus are stationary at each point of the measurement. Any systematic errors that may be present in the instrument will be eliminated through subtraction whilst the MSE is used as opposed to the spherical aspect of the refractive error since the eye's accommodation is accurate for the circle of least confusion if there is an astigmatic image.

3.1.7.2.3 Dynamic Accommodation

Dynamic measurement of the AoA can be obtained using the same set-up as the static approach (see section 3.1.7.2.2), provided that the autorefractor allows continuous measurement of refractive error to detect changes as a result of oscillation of the fixation target; the maximal refractive change is then taken as the AoA (Wolffsohn *et al.* 2001).

Small fluctuations in the refractive error are likely to occur during a dynamic measurement as a result of natural micro-fluctuations in accommodation. In fact, these can be used to evaluate the DoF of the eye, by determining the object range for which the magnitude of these oscillations remains constant (Vasudevan *et al.* 2006b). However, although the AoA can be reliably measured with the dynamic method, its accuracy is dependent upon the speed at which the autorefractor can obtain the data, as well as on the tolerance to fixation steadiness of the subject and the alignment of the eyes (Jainta *et al.* 2004).

3.1.7.3 Subjective Push-up/Push-down Test

The subjective push-up/push-down test is perhaps the simplest method of measuring the AoA. It is typically measured with a Royal Air Force (RAF) rule (Clement Clarke International Ltd., Harlow, Essex, UK.), although any accommodative target may be used. The subject is asked to report first sustained blurring of the smallest resolvable print size as it is gradually brought closer to the eyes. The print is then brought closer to the patient so that it is completely blurred, before it is gradually moved *away* from the subject to a point when it just becomes clear. The dioptric distance of the average of these two near points from the eyes is then taken as the AoA, provided that any uncorrected refractive error is accounted for (Goss 1992, Barrett and Elliott 2007). Presbyopic subjects may require a reading addition, usually +2.50DS, to be used for the measurement so that the print is resolvable within the physical target placement range; the difference between the average near point and the power of the reading addition is then the AoA.

Measurement of the AoA with the push-up/push-down test is dependent on the target size used, with larger targets shown to produce a larger AoA due to a greater blur tolerance (see section 3.1.3) (Rosenfield and Cohen 1995). There are also implications of variable DoF since the angular subtense of the target increases as it is brought closer to the eyes, which as described in section 3.1.3, results in an increase in DoF and therefore an increase in the AoA. This can however be overcome if variable target sizes are used, such that this reduces systematically as it is brought closer to the eyes, thus maintaining an approximately equal target size for the whole measurement range (Atchison *et al.* 1994). However, stimulation of the near triad will cause pupil miosis, which can potentially create an increase in DoF (see section 3.1.1) and therefore the AoA as well (Atchison *et al.* 1994). This technique also has poor repeatability since a difference in the AoA of ±1.50D is indicative of a clinically significant change in young adults (Rosenfield and Cohen 1996).

3.1.7.4 Defocus Curves

Defocus curves allow the AoA to be assessed by measuring the change in distance VA under varying focal demands, as an alternative to the physical approach of measuring VA at different distances, which can often be impractical. Defocus curves are a repeatable and reliable method for quantifying the AoA (Langenbucher *et al.* 2003b, 2003c) but may over-estimate the true AoA compared to the physical method (Pieh *et al.* 2002), due to an increase in DoF that arises from pupil miosis (see section 3.1.1). The technique is also susceptible to memory effects if letter sequences on acuity charts and/or the order of lens presentation are not randomised. In many cases, researchers do not report the methodology used and as such the measured AoA may be inaccurate (Tables 3.2 to 3.4). Furthermore, quantification of the AoA is dependent on the criterion definition used. A *relative* criterion refers to the range of object vergences that is associated with the best level of VA (Figure 3.4, *line A*), and may include an allowance for 'adequate vision'. An *absolute* criterion is independent of the individual's best VA and includes only the range of object vergences through which VA is considered to be 'adequate' (Figure 3.4, *line B*) (Tucker and Charman 1975). These criteria may also be applied to only negative levels of defocus (Figure 3.4, *lines C* (relative) *and D* (absolute)) since it should be expected that only negative lenses will stimulate accommodation if the eye is refracted to maximum plus.

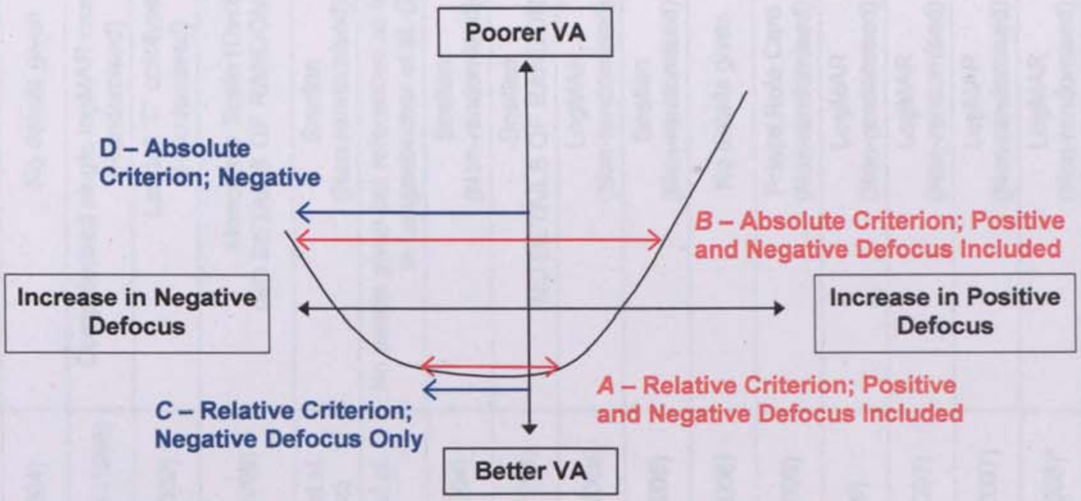


Figure 3.4 Defocus curve criteria can be relative (A) or absolute (B) and may include only negatively stimulated defocus (C and D for relative and absolute criteria, respectively)

There is however no consensus for the definition of 'adequate vision' (Tables 3.5 and 3.6), with many setting this arbitrarily, or not stating it at all (e.g. Auffarth *et al.* 1993, Elder *et al.* 1996, Weghaupt *et al.* 1996, Walkow *et al.* 1997, Vaquero-Ruano *et al.* 1998, Jacobi *et al.* 1999, Walkow and Klemen 2001, Leyland *et al.* 2002, Ostrin *et al.* 2004). Comparable quantification of the AoA, and hence the range of clear vision, is therefore prevented.

Type of Correction	Author(s)	Type of Acuity Chart	Lens Sequence & Range
Scleral Expansion Band	Ostrin et al. (2004)	No details given	No details given other than 'minus to blur'
Presbyopic Contact Lenses	Plakitsi & Charman (1995)	Computerised single logMAR crowded optotypes (Randomised)	+6.00DS to -10.00DS in 0.50DS steps (Non-randomised)
	Collins et al. (2002)	Landolt 'C' optotypes (Randomised)	+2.00DS to -2.00DS (Randomised)
Accommodating IOLs	Legeais et al. (1999)	Monoyer's Scale (Decimal) (NO DETAILS OF RANDOMISATION)	Increase in negative and then positive lens power from best correction in 0.50DS steps (Non-randomised)
	Langenbucher et al. (2003b, 2003c)	Snellen (Non-randomised)	+0.50DS to -3.00DS in 0.50DS steps (Non-randomised)
	Langenbucher et al. (2003a)	No details given but referenced as being the same as in Langenbucher et al. (2003c)	No details given but referenced as being the same as in Langenbucher et al. (2003c)
	Kuchle et al. (2004)	Snellen (Non-randomised)	Increase in negative lens power from best correction in 0.50DS steps (Non-randomised)
	Marchini et al. (2004)	Snellen (NO DETAILS OF RANDOMISATION)	Increase in negative lens power from best correction in 0.25DS steps (Non-randomised)
	Heatley et al. (2005a)	LogMAR (Non-randomised)	-2.50DS to +2.00DS in 0.50DS steps (Non-randomised)
	Sauder et al. (2005)	Snellen (Non-randomised)	+3.00DS to -3.00DS in 0.50DS steps (Non-randomised)
	Hancox et al. (2006)	No details given	Only negative spheres presented (NO DETAILS OF RANDOMISATION)
	Macsai et al. (2006)	Prince Rule Card (Non-randomised)	Increase in positive/negative lens power in 0.25DS steps (Non-randomised)
	McLeod (2006)	LogMAR (Non-randomised)	Increase in positive/negative lens power from best correction in 0.50DS steps (Non-randomised)
	Ossma et al. (2007)	LogMAR (Non-randomised)	Increase in positive/negative lens power from best correction in 0.50DS steps (Non-randomised)
	Marchini et al. (2007)	LogMAR (Non-randomised)	Increase in negative lens power from best correction in 0.25DS steps (Non-randomised)
	Harman et al. (2008)*	LogMAR (Non-randomised)	+3.00D to -5.00D in 1.00DS steps (Non-randomised)

Table 3.2 Summary of defocus curve methodology used for evaluating different presbyopic corrections

*This study also assessed a multifocal IOL. LogMAR = logarithm of the minimum angle of resolution

Type of Correction	Author(s)	Type of Acuity Chart	Lens Sequence & Range
Multifocal IOLs	Post (1992)	Snellen (Non-randomised)	+6.00DS to -6.00DS in 0.50DS steps (Non-randomised)
	Steinert et al. (1992)	Snellen (NO DETAILS OF RANDOMISATION)	+6.00DS to +1.00DS in 1.00DS steps, +1.00DS to -2.00DS in 0.50DS steps and -2.00DS to -6.00DS in 0.25DS steps (NO DETAILS OF RANDOMISATION)
	Knorz et al. (1993)	Snellen (NO DETAILS OF RANDOMISATION)	+1.00DS to -5.00DS in 0.50DS steps (NO DETAILS OF RANDOMISATION)
	Auffarth et al. (1993)	Decimal (NO DETAILS OF RANDOMISATION)	+1.00D to +5.00D and -1.00D to -5.00D (no details of steps) (NO DETAILS OF RANDOMISATION)
	Weghaupt et al. (1996)	Snellen (NO DETAILS OF RANDOMISATION)	-6.00DS to +3.00DS in 0.50DS steps (Non-randomised)
	Walkow et al. (1997)	Snellen (NO DETAILS OF RANDOMISATION)	+5.00DS to +2.00DS in 1.00DS steps and +2.00DS to -5.00DS in 0.50 steps (NO DETAILS OF RANDOMISATION)
	Weghaupt et al. (1998)	Snellen (NO DETAILS OF RANDOMISATION)	-6.00DS to +3.00DS In 0.50DS steps (Non-randomised)
	Vaquero-Ruano et al. (1998)	Decimal (NO DETAILS OF RANDOMISATION)	+3.00DS to -4.00DS In 1.00DS steps (NO DETAILS OF RANDOMISATION)
	Arens et al. (1999)	Decimal (NO DETAILS OF RANDOMISATION)	+3.00DS to -5.00DS in 1.00DS steps (NO DETAILS OF RANDOMISATION)
	Jacobi et al. (1999)	Snellen (NO DETAILS OF RANDOMISATION)	-5.00DS to +3.00DS in 0.50DS steps (NO DETAILS OF RANDOMISATION)
	Walkow & Klemen (2001)	Snellen (Randomised charts)	+5.00DS to -5.00DS in 0.50DS steps (Non-randomised)
	Kamlesh et al. (2001)	Snellen (NO DETAILS OF RANDOMISATION)	Increase in positive/negative lens power from best correction in 0.50DS steps (Non-randomised)
	Leyland et al. (2002)	LogMAR (NO DETAILS OF RANDOMISATION)	+3.00DS to -5.00DS In 1.00DS steps (NO DETAILS OF RANDOMISATION)
	Tsorbatzoglou et al. (2006)	LogMAR (Non-randomised)	Increase in negative lens power from best correction in 0.25DS steps (Non-randomised)
	Toto et al. (2007)	LogMAR (NO DETAILS OF RANDOMISATION)	+2.00DS to -5.00DS In 0.50DS steps (Non-randomised)

Table 3.3 Summary of defocus curve methodology used for evaluating multifocal intraocular lenses (IOLs)

LogMAR = logarithm of the minimum angle of resolution

Author(s)	Aim of Study	Type of Acuity Chart	Lens Sequence & Range
Powers & Dobson (1982)	To assess the effect of defocus on VA in adults compared to infants	Teller Acuity Cards (Random orientations)	±14.00DS, ±6.00DS, ±3.00DS and plano (Randomised)
Rabin (1994)	To determine which out of VA and contrast sensitivity is affected the most by defocus	Computerised LogMAR (Non-randomised)	0.00 to +1.25DS (NO DETAILS OF RANDOMISATION)
Rosenfield & Cohen (1996)	To determine the repeatability of AoA measures in pre-presbyopes	Single Optotype on a Near Card (Non-randomised)	Increase in negative lens power from best correction (no details of steps) (Non-randomised)
Elder et al. (1996)	To assess depth of field in phakic and pseudophakic eyes to determine why there is good uncorrected distance and near vision in pseudophakes	LogMAR (Randomised)	+1.50DS to -1.50DS in 0.50DS but also including ±0.75DS defocus levels (NO DETAILS OF RANDOMISATION)
Pieh et al. (2002)	To compare the measurement of defocus curves to the more physical method of assessing VA at different distances	LogMAR (Randomised)	-3.00DS to -0.50DS in 0.50DS steps (Non-randomised)
Altan-Yaycioglu et al. (2002)	To evaluate the AoA in subjects implanted with a single vision IOL	Snellen (Non-randomised)	Increase in negative lens power from best correction (no details of steps) (Non-randomised)
Wold et al. (2003)	Assessment of AoA in pre-presbyopic subjects by various techniques including defocus to negative lenses	Snellen (Non-randomised)	Increase in negative lens power from best correction in 0.50DS steps (Non-randomised)
Radhakrishnan et al. (2004)	To investigate the effect of blur on VA in myopes compared to non-myopes	LogMAR (Non-randomised)	+3.00DS to -3.00DS in 0.25DS steps (Randomised)
Ostrin & Glasser (2004)	To determine the most appropriate method of assessing AoA including defocus to negative lenses	Snellen (Non-randomised)	Increase in negative lens power from best correction in 0.25DS steps (Non-randomised)
Muftuoglu et al. (2005)	To determine the factors that influence movement of a single vision IOL and associated near VA	No details given	+0.25DS to -3.00DS in 0.25DS steps (Non-randomised)
Trager et al. (2005)	To propose a new mathematical model for evaluating accommodation with defocus curves	LogMAR (Non-randomised)	Increase in negative and then positive lens power from best correction in 0.50DS steps (Non-randomised)

Table 3.4 Summary of defocus curve methodology used in various studies not directly related, if at all, to presbyopia correction

LogMAR = logarithm of the minimum angle of resolution

Criterion Type	Criterion Definition	Studies Using This Criterion	Measured Amplitude of Accommodation (AoA) or Range of Clear Vision
Relative	Best VA	Rosenfield & Cohen (1996)	AoA in pre-presbyopic subjects Natural eye = 9.10±0.73D
		Altan-Yaycioglu et al. (2002)	AoA of a single vision IOL = 1.11±0.39D
		Wold (2003)	AoA in pre-presbyopic subjects Natural eye = 7.02±2.00D
		Ostrin & Glasser (2004)	AoA for various age ranges 31-35 year olds = 4.40±1.61D; 36-40 year olds = 3.13±1.00D 41-45 year olds = 1.45±0.45D; 46-50 year olds = 1.24±0.58D 51-55 year olds = 0.83±0.26D
		Marchini et al. (2004)	AT-45 'accommodating' IOL = 1.08±0.54D at 6 months post-operatively
		Macsai et al. (2006)	AT-45 'accommodating' IOL, monocular = 1.74±0.48D, binocular = 1.96±0.50D
		Marchini et al. (2007)	1CU 'accommodating' IOL at 1 month = 1.08±0.72D, at 12 months = 1.40±0.66 AT-45 'accommodating' IOL at 1 month = 1.19±0.60D, at 12 months = 0.96±0.44
	Best VA / Best VA + 0.10 LogMAR	Sauder et al. (2005)*	1CU 'accommodating' IOL = 1.01±0.40D (Range 0.50D to 1.70D)
	Best VA + 0.20 LogMAR	Collins et al. (2002)	Effect of aberrations on the AoA of aphakic infants corrected with contact lenses Natural eye = 1.46D, decreases to 0.99D with 8.14D of spherical aberration Spherical contact lens = 1.46D, increases to 3.06D with 6.80D of spherical aberration
		McLeod (2006)	Single vision IOL = 1.65±0.58D (range 1.00D to 2.50D) Dual optic 'accommodating' IOL = 3.22±0.88D (range 1.00 to 5.00D)
		Ossma et al. (2007)	Single vision IOL = 1.65±0.58D (range 1.00D to 2.50D) Dual optic 'accommodating' IOL = 3.22±0.88D (range 1.00 to 5.00D)
	Best VA + 0.30 LogMAR	Plakitsi & Charman (1995)	Natural eye = 2.64±0.49D Centre-near annular simultaneous vision contact lens = 4.51±1.20D Centre-distance aspheric simultaneous vision contact Lens = 4.17±1.04D Centre-near aspheric simultaneous vision contact lens = 4.70±1.29D
		Trager et al. (2005)	Pseudophakic patients = 1.04D Phakic patients = 0.09D to 2.62D

Table 3.5 Summary of relative defocus curve criteria used by various studies

All studies in the above table refer to presbyopic subjects unless otherwise stated. Standard deviations are only stated if they were given in original publications

*This study evaluated the AoA of an 'accommodating' IOL using five techniques, one of which was by defocus curve. Two criteria for quantifying the AoA were used: ' best VA' and 'best VA + 0.10 logMAR'. Individual evaluations for each method are not stated but only the mean and range of all methods is given by the paper

Criterion Type	Criterion Definition	Studies Using This Criterion	Measured Amplitude of Accommodation (AoA) or Range of Clear Vision
Absolute	0.15 LogMAR	Legeais et al. (1999)	BioComFold 'accommodating' IOL = 2.10±0.58D
	0.30 LogMAR	Post (1992)	Single vision IOL = 1.80D Multifocal IOL = 3.80D
		Knorz et al. (1993)	Single vision IOL = 2.50D for a 3.2 mm pupil Bifocal IOL = 2.50D, Diffractive IOL = 4.50D & Varifocal IOL = 3.00D for a 2.9mm pupil Bifocal IOL = 4.50D, Diffractive IOL = 4.50D & Varifocal IOL = 3.00D for a 2.3mm pupil
		Plakitsi & Charman (1995)	Natural eye = 3.18±0.59D Centre-near annular simultaneous vision contact lens = 4.52±1.28D Centre-distance aspheric simultaneous vision contact lens = 3.97±1.05D Centre-near aspheric simultaneous vision contact lens = 3.97±1.00D
		Weghaupt et al. (1998)	3M diffractive multifocal IOL = 5.00D Array refractive multifocal IOL = 4.50D
		Arens et al. (1999)	Multifocal IOL = 4.00D Single vision IOL = 2.00D
		Kamlesh et al. (2001)	Progress 3 multifocal IOL = 3.10D Single vision IOL = 1.65D
		Heatley et al. (2005a)	1CU 'accommodating' IOL = 1.73±0.56D
		Hancox et al. (2006)	1CU 'accommodating' IOL = 1.09±0.58D
		Toto et al. (2007)	Aspheric diffractive multifocal IOL = 4.50D Adopised diffractive multifocal IOL = 4.00D
		Harman et al. (2008)	1CU 'accommodating' IOL = 2.47±0.80D at 18 months Array multifocal IOL = 3.38±1.14D at 18 months
	0.40 LogMAR	Steinert et al. (1992)	Multifocal IOL = 4.75D Single vision IOL = 2.75D
		Langenbucher et al. (2003b, 2003c)	1CU 'accommodating' IOL at 1 month = 1.43±0.60D, at 6 months = 1.46±0.53D
		Langenbucher et al. (2003a)	1CU 'accommodating' IOL = 1.66±0.48D
		Kuchle et al. (2004)	1CU 'accommodating' IOL = 1.85±0.43D
		Muftuoglu et al. (2005)	Single vision IOL = 1.14±0.24D
		Tsorbatzoglou et al. (2006)	Single vision IOL type 1 = 0.82±0.18D, Single vision IOL type 2 = 1.00±0.35D Multifocal IOL = Not quantified

Table 3.6 Summary of absolute defocus curve criteria used by various studies

All studies in the above table refer to presbyopic subjects unless otherwise stated. Standard deviations are only stated if they were given in original publications

3.2 The Study Aim

Given the importance of DoF-free measurement of the AoA, subjective AoA ought to be evaluated in a standardised manner such that there is minimal influence of blur tolerance (DoF) from pupil size and target size variations. The measurement of a defocus curve is a desirable alternative method to the push-up/push-down test since target size variation can be accounted for by the use of a consistent and far testing distance, and by correcting all VA measures for lens magnification effects. However, the lack of randomisation of letter sequences on acuity charts and/or the order of lens presentation, together with the AoA quantification being dependent on the criterion used means that accurate description of the subjective AoA has not been achieved (see section 3.1.7.4). The purpose of this study therefore was to investigate the effect of non-randomisation when measuring defocus curves and to determine the most appropriate criterion for quantifying the subjective AoA.

3.3 Method

This study was conducted in two phases such that the effect of non-randomisation of letter sequences and/or lens presentation order when measuring defocus curves was investigated first, using both pre-presbyopic and presbyopic populations. The second phase of the study investigating the most appropriate criterion for quantifying the subjective AoA was conducted only on presbyopic subjects and included an objective measurement of the AoA.

3.3.1 Effect of Non-randomisation in the Measurement of Defocus Curves

Eighteen pre-presbyopic subjects (mean age 24.1±4.2 years, range 20 to 32 years) and 20 presbyopic subjects (mean age 54.3±4.7 years, range 46 to 63 years) were recruited from staff and students of Aston University. The author screened all subjects, using the methods described in section 2.4.1 (see Chapter 2), to ensure an absence of ocular pathology, including cataract, glaucoma, AMD, and diabetic retinopathy, and an absence of binocular vision and accommodative anomalies, including decompensated heterophoria, heterotropia and amblyopia. All presbyopic subjects were also required to have no more than 0.75DC of spectacle astigmatism for the purposes of measuring the objective AoA (see section 3.3.2). Subjects were then refracted monocularly at six metres to obtain the best VA and to eliminate any latent hypermetropia, under the principal of maximum plus without a reduction in best VA, using a phoropter at a back vertex distance (BVD) of 12.0mm.

Mean distance VA of the pre-presbyopic subjects was -0.12±0.06 logMAR (range -0.20 to 0.00 logMAR) whilst that of the presbyopic subjects was -0.10±0.08 logMAR (range -0.20 to 0.06 logMAR). Six defocus curves, each corresponding to the different combinations of randomised or non-randomised letter sequences and/or lens presentation order (including positive and negative progressions) (Table 3.7), were then measured in turn on one eye only of each subject. In the pre-presbyopic group, all of the defocus curves were measured for a range of +2.00DS to -2.00DS in 0.50DS steps, whilst subsequent measurements on presbyopic subjects were made for a range of +3.00DS to -3.00DS in 0.50 steps, primarily to ensure that a complete defocus curve would be measured for the expected AoA of this age group. Lenses were presented in the same phoropter and all VAs were measured using the computerised *Test Chart 2000 Pro* (Thomson Software Solutions, Hatfield, Herts., UK.) logMAR chart at six metres. Each VA was measured and defined as described in the context of near VA measurements in section 2.4 (see Chapter 2). The eye was occluded between each lens presentation so that the subject was not aware of which lens had been inserted or whether the letter sequences on the chart had been changed or not. No two combinations were implemented on the same chart whilst subjects were not informed of which combination was being measured or of any order of implementation of the six combinations. This randomisation therefore allowed any fatigue effects to be averaged across subjects. All measurements were made under the same conditions, with consistent illumination (500 lux) and chart luminance (120cdm^{-2}) used, in accordance with the required standards for VA testing (BSI4274-1 1968, Pandit 1994, BSI4274-1 2003).

Combination	Letters	Lens Sequence
1	Non-randomised	Plus to Minus
2	Non-randomised	Minus to Plus
3	Non-randomised	Randomised
4	Randomised	Plus to Minus
5	Randomised	Minus to Plus
6	Randomised	Randomised

Table 3.7 Six possible combinations of presenting letter sequences and the order of lenses when measuring defocus curves

The mean natural variability of repeated VA measures is reportedly ±0.04 logMAR (Raasch *et al.* 1998) whilst the 95% confidence intervals are ±0.10-0.20 logMAR, with no significant change with age (Lovie-Kitchin and Brown 2000). This variability was therefore accounted for in the next phase of the study investigating the most appropriate criterion for quantifying the subjective AoA from defocus curves (see section 3.3.2).

3.3.2 Investigation of Optimum Defocus Curve Criteria

After analysis to determine the most appropriate method of measuring a defocus curve from the first phase of the study (see sections 3.3.1 and 3.4), the subjective AoA was quantified according to various criteria (Table 3.8) for each of the 20 presbyopic subjects, using the curve-fitting method. For each individual, a best-fit regression curve was plotted against the measured defocus curve using SigmaPlot 2000 (SPSS Inc., Chicago, IL., USA.); the best-fit curve was defined as that which provided a coefficient of determination (R^2) as close as possible to a value of 1.0 but which passed through, or as close as possible to, all of the defocus curve points based on visual inspection. Using the equation provided by SigmaPlot for this best-fit curve and the corresponding table of x-values (in this case referring to the amount of defocus) and y-values (in this case referring to the VA), a 'trial-and-error' determination of the range of x-values for which the y-value matched a particular criterion (Table 3.8) was then performed to quantify the AoA. This method has been used previously to quantify the AoA from defocus curves and although a perfect match between the regression curve and the measured defocus curve may not always be obtained, the difference is unlikely to be clinically significant (Plakitsi and Charman 1995).

Criterion Type	Criterion Definition	Defocus Curve Calculation: *Range of 'x' values for which:*
Absolute	0.30 LogMAR (Snellen 6/12)	'y' ≤ 0.30
	Negative defocus only	'y' ≤0.30 (negative x-values only)
	0.40 LogMAR (Snellen 6/15)	'y' ≤ 0.40
	Negative defocus only	'y' ≤0.40 (negative x-values only)
Relative	Best VA*	'y' ≤ best VA
	*Negative defocus only**	'y' ≤Best VA (negative x-values only)
	Best VA + 0.10 LogMAR	'y' ≤ Best VA + 0.10
	Negative defocus only	'y' ≤ Best VA + 0.10 (negative x-values only)
	Best VA + 0.20 LogMAR	'y' ≤Best VA + 0.20
	Negative defocus only	'y' ≤ Best VA + 0.20 (negative x-values only)
	Best VA + 0.30 LogMAR	'y' ≤Best VA + 0.30
	Negative defocus only	'y' ≤ Best VA + 0.30 (negative x-values only)
	Best VA + 0.40 LogMAR	'y' ≤ Best VA + 0.40
	Negative defocus only	'y' ≤ Best VA + 0.40 (negative x-values only)

Table 3.8 List of defocus curve criteria investigated

*These criteria included allowances of 0.04 logMAR for natural variability in repeated VA measures whilst variability of 0.10 logMAR and 0.20 logMAR were assessed by the criteria *Best VA + 0.10 LogMAR* and *Best VA + 0.20 LogMAR*, respectively (see section 3.3.1)

The static objective AoA was measured on each of the 20 presbyopic subjects, to allow for calculation of the eye's DoF, using the theory and equipment described in section 3.1.7.2 and under the test conditions described in section 3.3.1. Subjects were seated with their chin on the rest of a Shin-Nippon SRW-500 autorefractor with one eye occluded using an eye patch. The non-occluded eye, which corresponded to the eye upon which the defocus curve was measured, was corrected for distance vision using a spherical contact lens (1-Day Acuvue®, Johnson & Johnson Vision Care Inc., Jacksonville, FL., USA.), the power of which was calculated as the MSE of the distance spectacle refraction, as per normal optometric procedure. Subjects were then instructed to fixate and maintain as much clarity as possible of a Maltese cross target that was part of a Badal optometer attachment, as visible through a +5.00DS Badal lens, and which was randomly placed at each of 0.00D, 1.00D, 2.00D, 3.00D, 4.00D and 5.00D of accommodative demand in turn (see Figures 3.1 and 3.2). At each of these locations, the autorefractor was aligned with the pupil centre, as visible on the autorefractor screen, and five readings of the refractive error were taken. As shown in Figure 3.5, a minimum of five autorefractor readings is required since the MSE calculation varies considerably for up to and including four readings in a presbyopic subject, and for up to and including three readings in a pre-presbyopic subject (Figure 3.6).

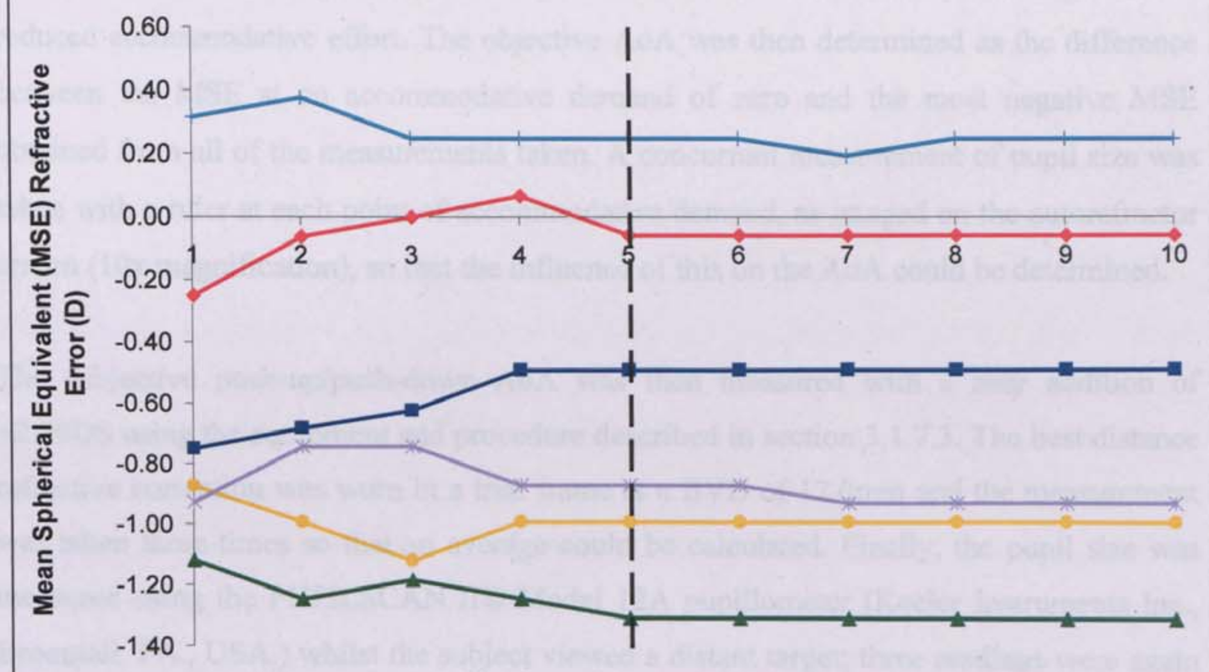


Figure 3.5 Variation of mean spherical equivalent (MSE) refractive error calculation according to the number of autorefractor readings taken (presbyope, GM, age 50 years)

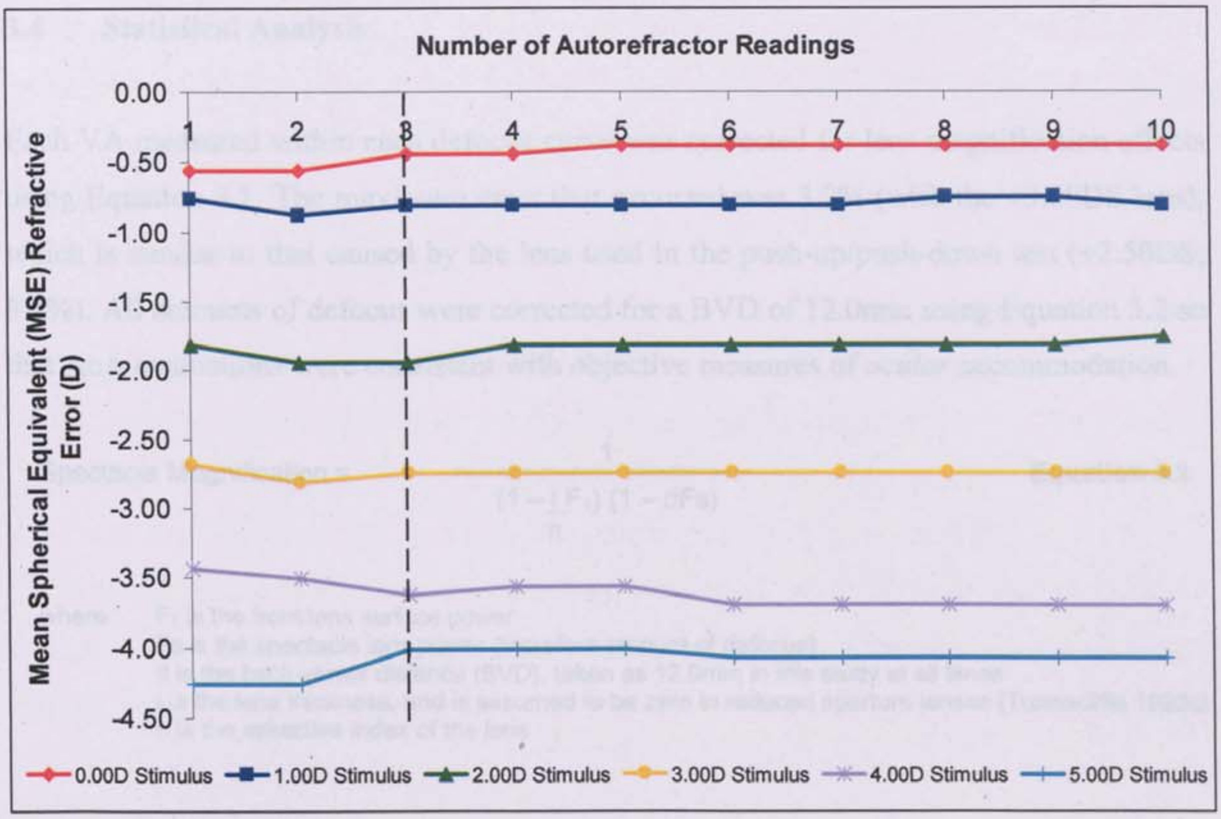


Figure 3.6 Variation of mean spherical equivalent (MSE) refractive error calculation according to the number of autorefractor readings taken (pre-presbyope, AW, age 26 years)

Throughout the measurement, subjects were not given any indication of the actual position of the Maltese cross target, in order to prevent them from consciously exerting extra or reduced accommodative effort. The objective AoA was then determined as the difference between the MSE at an accommodative demand of zero and the most negative MSE obtained from all of the measurements taken. A concurrent measurement of pupil size was taken with a ruler at each point of accommodative demand, as imaged on the autorefractor screen (10x magnification), so that the influence of this on the AoA could be determined.

The subjective push-up/push-down AoA was then measured with a near addition of +2.50DS using the equipment and procedure described in section 3.1.7.3. The best distance refractive correction was worn in a trial frame at a BVD of 12.0mm and the measurement was taken three times so that an average could be calculated. Finally, the pupil size was measured using the PUPILSCAN II® Model 12A pupillometer (Keeler Instruments Inc., Broomall, PA., USA.) whilst the subject viewed a distant target; three readings were again taken so that an average could be calculated. All of these measurements were made under the conditions described in section 3.3.1. Informed consent was obtained from all participants following explanation of the nature and possible consequences of the study and ethical approval was obtained from the Ethical Committee of Aston University.

3.4 Statistical Analysis

Each VA measured within each defocus curve was corrected for lens magnification effects using Equation 3.1. The maximum error that occurred was 3.7% (with the +3.00DS lens), which is similar to that caused by the lens used in the push-up/push-down test (+2.50DS; 3.1%). All amounts of defocus were corrected for a BVD of 12.0mm using Equation 3.2 so that AoA evaluations were consistent with objective measures of *ocular* accommodation.

$$\text{Spectacle Magnification} = \frac{1}{\left(1 - \frac{t}{n}F_1\right)(1 - dFs)} \qquad \textbf{Equation 3.1}$$

where F_1 is the front lens surface power
Fs is the spectacle lens power (therefore amount of defocus)
d is the back vertex distance (BVD), taken as 12.0mm in this study at all times
t is the lens thickness, and is assumed to be zero in reduced aperture lenses (Tunnacliffe 1993c)
n is the refractive index of the lens

$$\text{Ocular Defocus} = \frac{Fs}{(1 - dFs)} \qquad \textbf{Equation 3.2}$$

where Fs is the spectacle lens power (therefore amount of defocus)
d is the back vertex distance (BVD), taken as 12.0mm in this study at all times

A single factor ANOVA was first conducted for each defocus curve combination in turn, to determine whether any of the 18 pre-presbyopic subjects and any of the 20 presbyopic subjects produced significantly different defocus curves to other subjects within their respective groups. This analysis allowed subjects that themselves could have been the cause of any significant differences between combinations to be identified and eliminated. A two-factor repeated measures ANOVA was then used to determine whether there was an overall significant difference between the mean defocus curves obtained from each of the six combinations, for each of the study populations; this ANOVA model was selected to account for the additional variable of 'amount of defocus' (see Appendix for details of statistical test selection). Pair-wise comparisons between each and every other combination in turn were then conducted, again using the two-factor repeated measures ANOVA, to determine if any single defocus curve combination was significantly different to any other combination. Differences were considered to be significant at p=0.05 at all times other than the pair-wise comparisons, where a Bonferroni adjustment for multiple comparisons was made (significant p=0.0033, 15 pair-wise comparisons) in order to reduce the risk of making a Type 1 statistical error (see section 2.5, Chapter 2).

In the second phase of the study, the defocus curve AoA for each criterion (see Table 3.8) was compared to the push-up/push-down test AoA using PPMC (correlation) coefficients, whilst linear regression was used to determine the statistical significance as assessed at $p=0.05$. The two-way random effects ICC (see Appendix for details) and Bland-Altman limits of agreement (see section 2.5, Chapter 2) were then calculated to determine the agreement between the AoA measures. Blur thresholds (DoF), calculated as the difference between the subjective AoA (for each defocus curve criterion and the push-up/push-down test) and the objective AoA, were then correlated to pupil size to determine the effect of this on the AoA measure. The most suitable defocus curve criterion for quantifying the AoA was then defined as that which had the highest correlation and ICC and smallest limits of agreement to the push-up/push-down test, with a minimal correlation to DoF. All analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.) and all graphs were produced using Microsoft® Excel® (Microsoft® Corporation, Redmond, WA., USA.).

3.4.1 Power Analysis

No previous study has investigated the need for randomisation when measuring defocus curves and therefore statistical power analysis and sample size calculations were conducted *a priori* for this study based on the PPMC coefficient. According to Table 2.9 (see section 2.5.1, Chapter 2), a sample size of 16 subjects was required to achieve a power of 80% (0.80), for a magnitude of the correlation coefficient of 0.7, at a significance level of $p=0.01$. *Post hoc* analysis based on the two-factor repeated measures ANOVA revealed that a power of 0.64 was present for the pre-presbyopic subjects whilst a power of 0.70 was present for the presbyopic subjects (see Appendix for full calculations).

3.5 Results

None of the subjects recruited for this study produced significantly different defocus curves to other subjects within their respective groups for each of the combinations (single factor ANOVA, $p>0.05$ on all occasions). As such no subjects were eliminated from the analysis. Figure 3.7 displays the mean defocus curves obtained for pre-presbyopic subjects with each combination. There was no significant difference between the six combinations overall (two-factor repeated measures ANOVA, $F=2.1$, $p=0.07$), and there was also no significant difference between any pairs of combinations (Table 3.9).

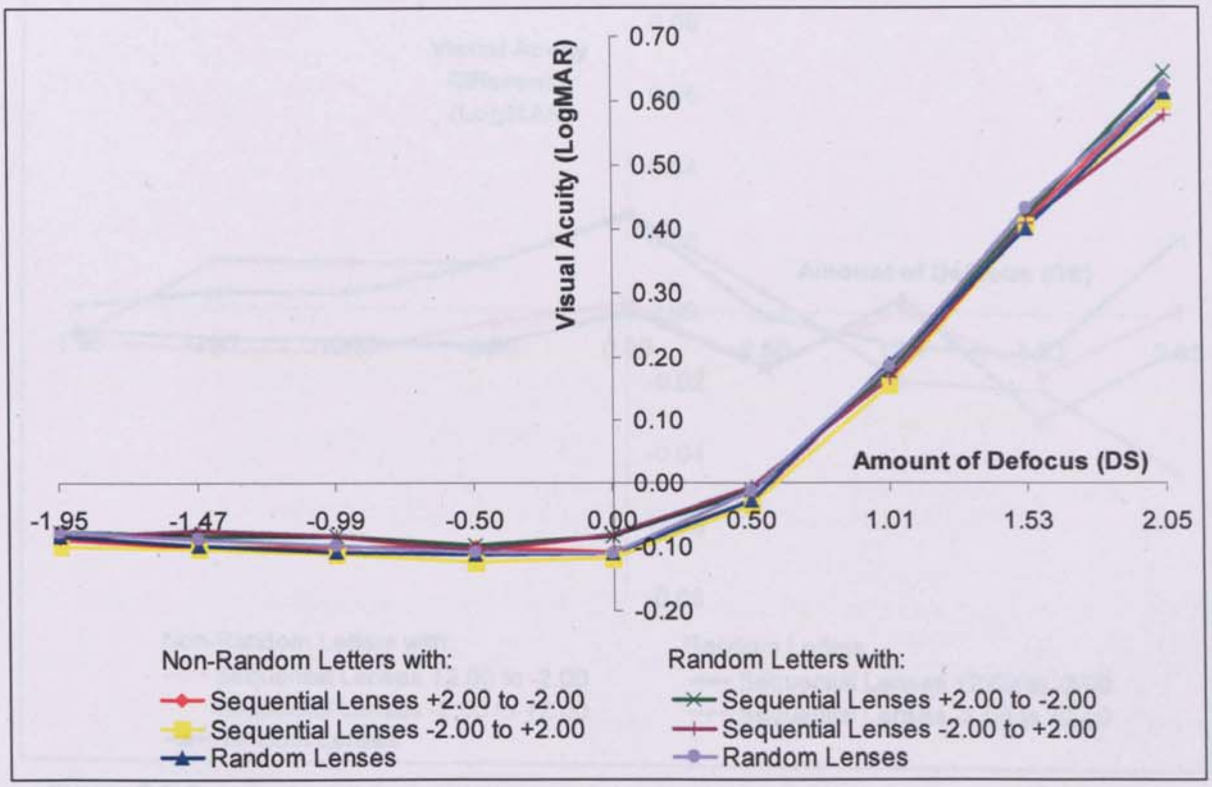


Figure 3.7 Mean defocus curves for each combination in pre-presbyopic subjects (n=18)

			P-value for Pair-wise Comparisons with each Combination				
Combination	**Letters**	**Lens Sequence**	**1**	**2**	**3**	**4**	**5**
1	Non-randomised	Plus to Minus	-	-	-	-	-
2	Non-randomised	Minus to Plus	0.11	-	-	-	-
3	Non-randomised	Randomised	0.70	0.19	-	-	-
4	Randomised	Plus to Minus	0.09	0.005	0.08	-	-
5	Randomised	Minus to Plus	0.88	0.06	0.51	0.27	-
6	Randomised	Randomised	0.57	0.03	0.37	0.47	0.74

Table 3.9 Pair-wise comparisons of each defocus curve combination to all other combinations for pre-presbyopic subjects (significant p=0.0033) (n=18)

Due to the lack of a significant difference, the difference between the mean defocus curve measured by combination 6 (maximal randomisation) and that measured by each and every other combination was calculated in turn (Figure 3.8). On all occasions, mean VA was disparate by one or two letters (0.02 to 0.04 logMAR) at each level of defocus, which is consistent with the natural variation of repeated VA measures expected in pre-presbyopes (Raasch *et al.* 1998). However, combinations 1, 2 and 3, in which the letter sequences were not randomised, consistently yielded better VA at each level of defocus compared to combination 6, since all differences were negative; this was not significantly different to the other comparisons though (two factor repeated measures ANOVA, F=2.5, p=0.051).

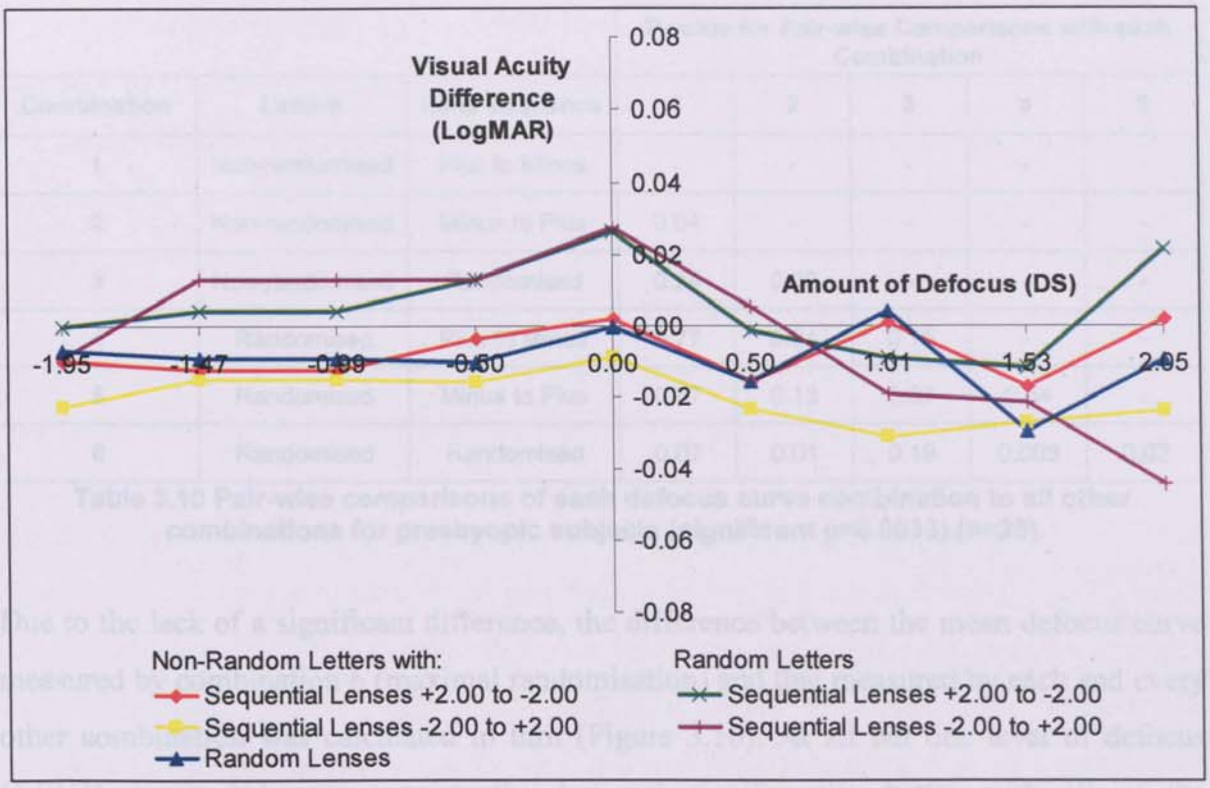


Figure 3.8 Comparison of mean VA at each level of defocus between combination 6 and each of combinations 1 to 5 in turn, for pre-presbyopic subjects (n=18)

Figure 3.9 displays the mean defocus curves obtained for presbyopic subjects with each combination. There was no significant difference between the six combinations overall (two-factor repeated measures ANOVA, F=4.5, p=0.07) and there was also no significant difference between any pairs of combinations (Table 3.10).

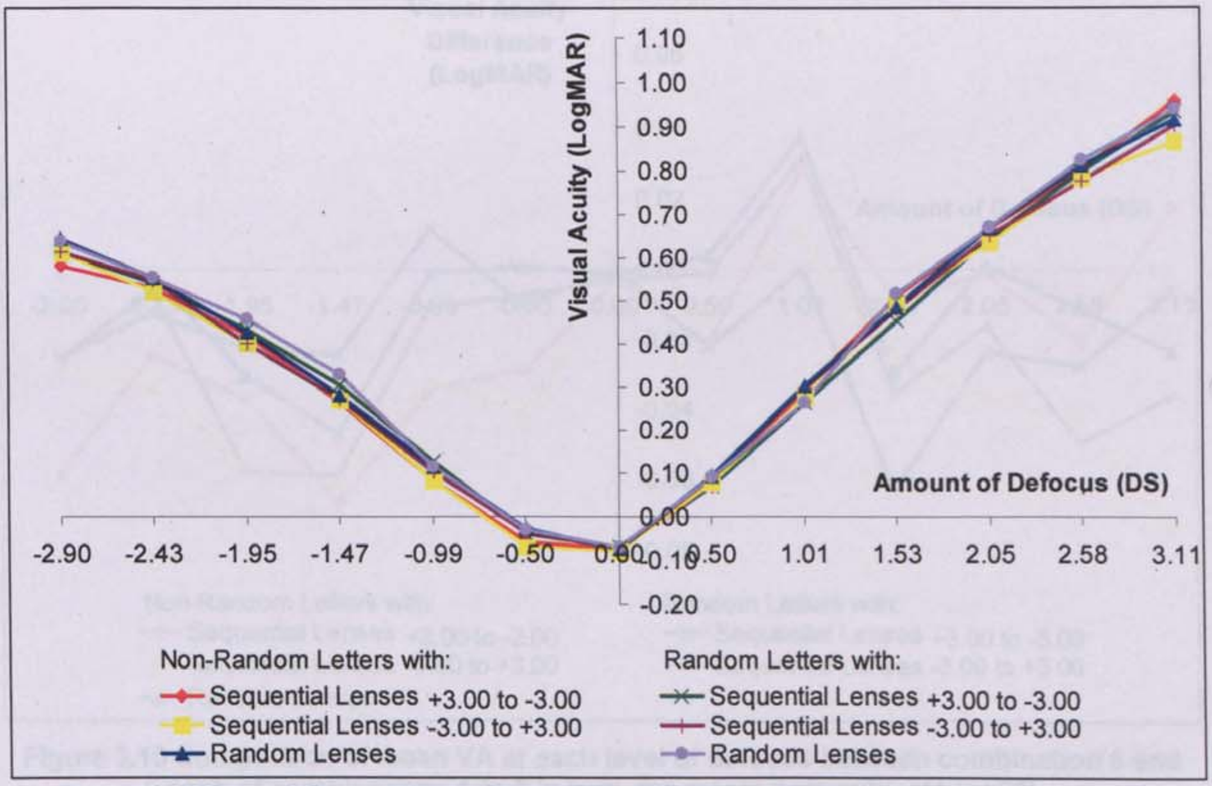


Figure 3.9 Mean defocus curves for each combination in presbyopic subjects (n=20)

Combination	Letters	Lens Sequence	P-value for Pair-wise Comparisons with each Combination				
			1	2	3	4	5
1	Non-randomised	Plus to Minus	-	-	-	-	-
2	Non-randomised	Minus to Plus	0.04	-	-	-	-
3	Non-randomised	Randomised	0.24	0.02	-	-	-
4	Randomised	Plus to Minus	0.77	0.04	0.16	-	-
5	Randomised	Minus to Plus	0.87	0.13	0.07	0.54	-
6	Randomised	Randomised	0.07	0.01	0.19	0.005	0.02

Table 3.10 Pair-wise comparisons of each defocus curve combination to all other combinations for presbyopic subjects (significant p=0.0033) (n=20)

Due to the lack of a significant difference, the difference between the mean defocus curve measured by combination 6 (maximal randomisation) and that measured by each and every other combination was calculated in turn (Figure 3.10). At all but one level of defocus (1.01D), mean VA was consistently, but not significantly, *better* with all of the combinations compared to combination 6, by up to four letters of acuity (0.08 logMAR) (two factor repeated measures ANOVA, F=2.9, p=0.052). Although this variability was greater than that expected in pre-presbyopic subjects (Raasch *et al.* 1998), it was within the maximum limit expected of subjects in this age group (Lovie-Kitchin and Brown 2000).

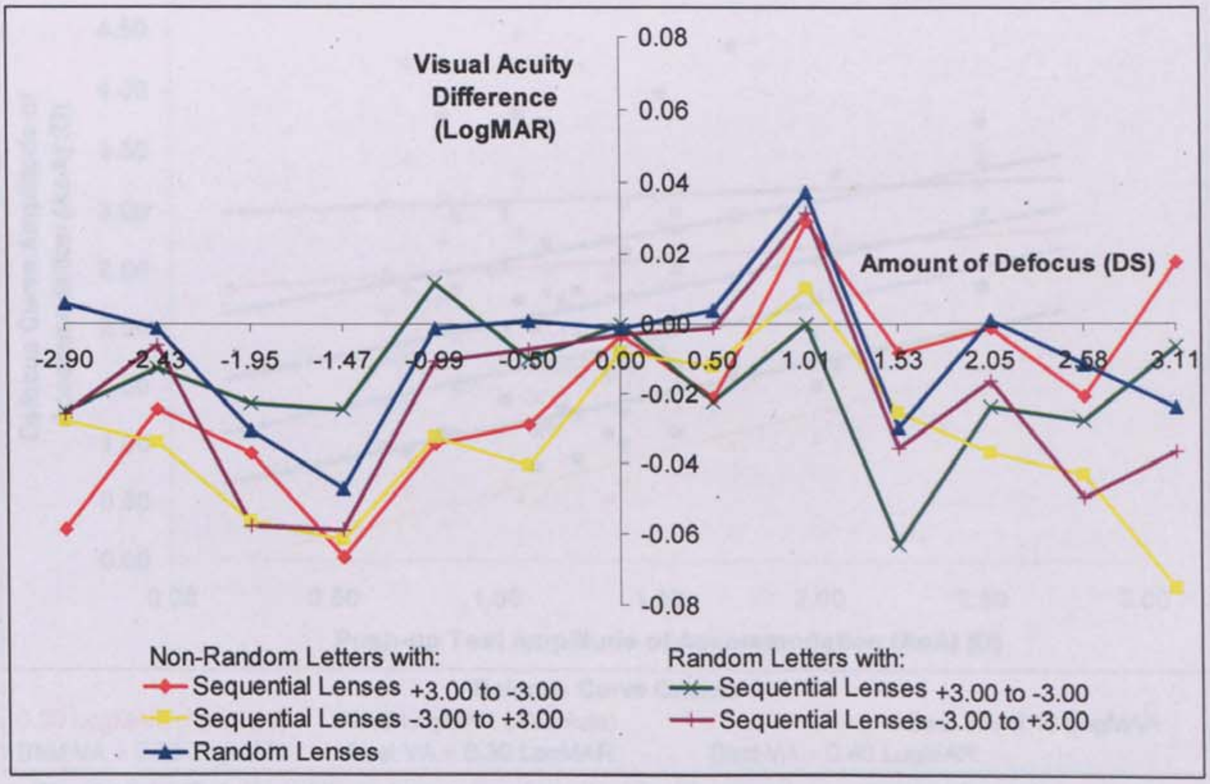


Figure 3.10 Comparison of mean VA at each level of defocus between combination 6 and each of combinations 1 to 5 in turn, for presbyopic subjects (n=20)

A similar analysis in which only negative defocus or only positive defocus was included, and with each of the individual defocus curves adjusted to a common VA of 0.00 logMAR at a defocus level of zero, failed to reveal any significant differences between any of the combinations in both pre-presbyopic and presbyopic subjects. As a result, in order to determine the most appropriate criterion to quantify the subjective AoA from defocus curves, curve-fitting was conducted for each of the 20 presbyopic subjects for the defocus curve measured by combination 6; through maximal randomisation this combination represents best clinical practice (Altman and Bland 1999).

For all of the 20 presbyopic subjects, the best-fit regression curves from the curve-fitting procedure matched the measured defocus curves to a high level of accuracy ($R^2>0.98$ on all occasions), with curves varying from 6th-order to 10th-order functions (see Appendix for curve-fitting results). Figures 3.11 and 3.12 reveal the correlations between the subjective AoA as evaluated from the defocus curves to subjective AoA as measured by the push-up/push-down test, for each of the absolute and relative criteria listed in Table 3.8. Corresponding means, standard deviations, PPMC coefficients, significance, ICCs and Bland-Altman limits of agreement are shown in Table 3.11. Mean push-up/push-down AoA of all subjects was 1.35±0.47D (range 0.66D to 2.50D).

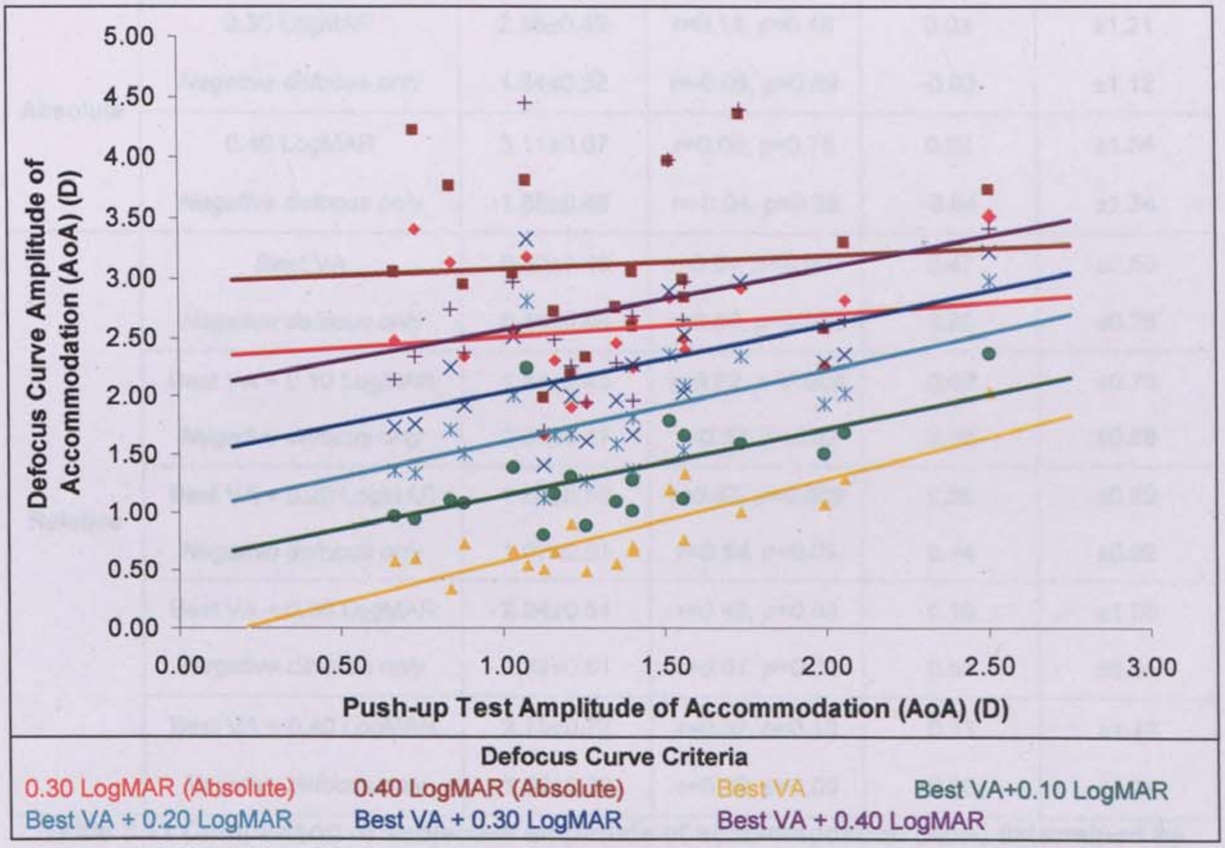


Figure 3.11 Relationship between push-up/push-down test amplitude of accommodation (AoA) and defocus curve AoA with various criteria (n=20)

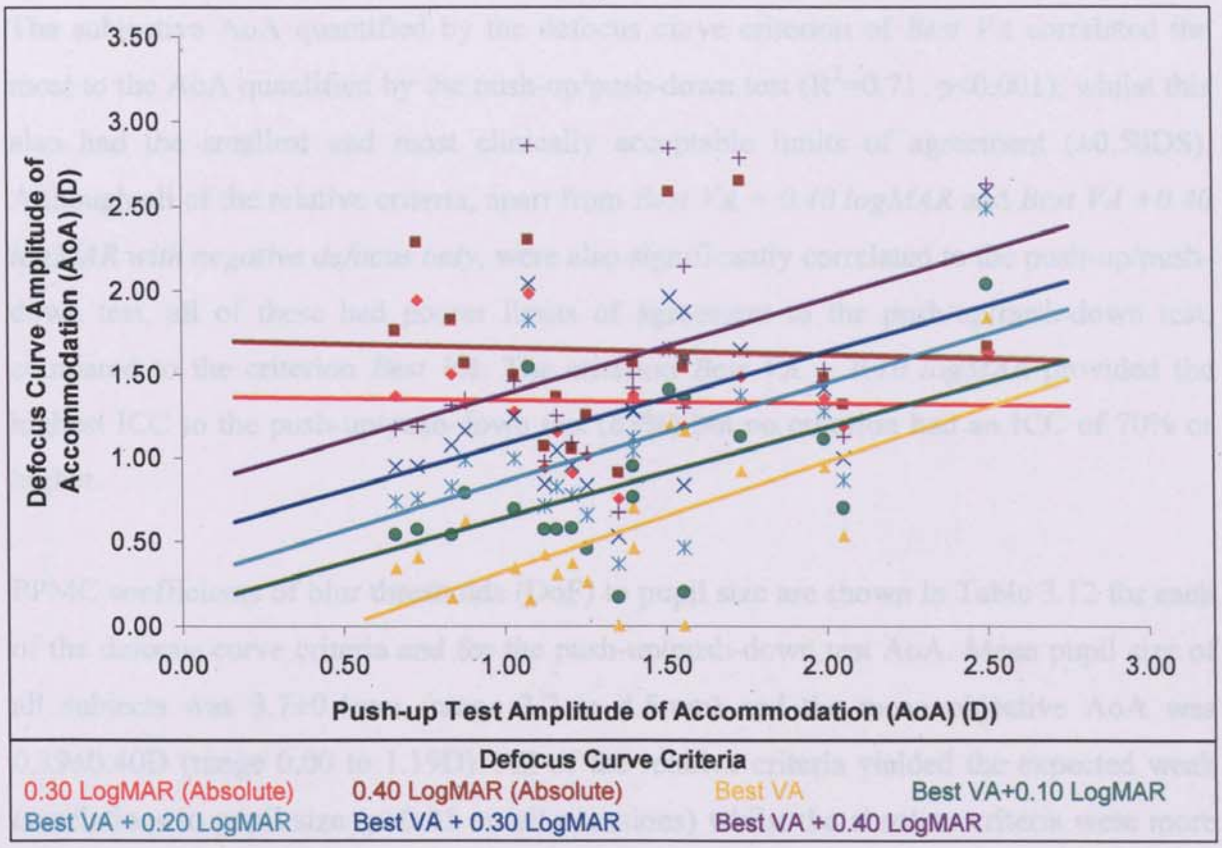


Figure 3.12 Relationship between push-up/push-down test amplitude of accommodation (AoA) and defocus curve AoA with various criteria, for negative defocus only (n=20)

Criterion Type	Criterion Definition	Mean Defocus Curve AoA (D)	Correlation (r) to push-up AoA & Significance	Intraclass Correlation Coefficient	Limits of Agreement (D)
Absolute	0.30 LogMAR	2.58±0.49	r=0.18, p=0.46	0.03	±1.21
	Negative defocus only	1.34±0.32	r=-0.03, p=0.89	-0.03	±1.12
	0.40 LogMAR	3.11±0.67	r=0.08, p=0.75	0.02	±1.54
	Negative defocus only	1.65±0.48	r=-0.04, p=0.86	-0.04	±1.34
Relative	Best VA	0.82±0.40	*r=0.84, p<0.001*	0.47	±0.50
	Negative defocus only	0.56±0.46	*r=0.66, p<0.002*	0.20	±0.75
	Best VA + 0.10 LogMAR	1.34±0.43	*r=0.62, p<0.004*	0.63	±0.76
	Negative defocus only	0.84±0.47	*r=0.53, p=0.02*	0.30	±0.88
	Best VA + 0.20 LogMAR	1.83±0.50	*r=0.57, p=0.009*	0.38	±0.89
	Negative defocus only	1.07±0.51	*r=0.54, p=0.01*	0.44	±0.92
	Best VA + 0.30 LogMAR	2.24±0.54	*r=0.49, p=0.03*	0.19	±1.00
	Negative defocus only	1.28±0.51	*r=0.51, p=0.02*	0.51	±0.95
	Best VA + 0.40 LogMAR	2.75±0.77	r=0.32, p=0.18	0.11	±1.49
	Negative defocus only	1.59±0.68	r=0.39, p=0.09	0.38	±1.24

Table 3.11 Comparison of subjective amplitude of accommodation (AoA) determined by various defocus curve criteria to subjective AoA measured by the push-up/push-down test. Significant relationships (at p=0.05) are highlighted in italic (n=20)

The subjective AoA quantified by the defocus curve criterion of *Best VA* correlated the most to the AoA quantified by the push-up/push-down test (R^2=0.71, p<0.001), whilst this also had the smallest and most clinically acceptable limits of agreement (±0.50DS). Although all of the relative criteria, apart from *Best VA + 0.40 logMAR* and *Best VA +0.40 logMAR with negative defocus only*, were also significantly correlated to the push-up/push-down test, all of these had poorer limits of agreement to the push-up/push-down test, compared to the criterion *Best VA*. The criterion *Best VA + 0.10 logMAR* provided the highest ICC to the push-up/push-down test (63%) but no criterion had an ICC of 70% or higher.

PPMC coefficients of blur thresholds (DoF) to pupil size are shown in Table 3.12 for each of the defocus curve criteria and for the push-up/push-down test AoA. Mean pupil size of all subjects was 3.7±0.4mm (range 3.2 to 4.5mm) and the mean objective AoA was 0.39±0.40D (range 0.00 to 1.19D). All of the relative criteria yielded the expected weak correlations to pupil size (p>0.05 on all occasions) whilst the absolute criteria were more inversely correlated.

Criterion Type	Criterion Definition	Mean Blur Threshold (DoF) ±Standard deviation (D)	Correlation (r) to Pupil Size & Significance
Absolute	0.30 LogMAR	2.19±0.51	r=-0.29, p=0.22
	Negative defocus only	0.96±0.45	r=-0.31, p=0.19
	0.40 LogMAR	2.73±0.66	r=-0.24, p=0.31
	Negative defocus only	1.26±0.56	r=-0.20, p=0.39
Relative	Best VA	0.44±0.30	r=-0.19, p=0.41
	Negative defocus only	0.17±0.37	r=-0.14, p=0.55
	Best VA + 0.10 LogMAR	0.96±0.35	r=-0.12, p=0.61
	Negative defocus only	0.45±0.41	r=-0.16, p=0.49
	Best VA + 0.20 LogMAR	1.44±0.41	r=-0.03, p=0.91
	Negative defocus only	0.54±0.38	r=-0.13, p=0.59
	Best VA + 0.30 LogMAR	1.86±0.47	r=-0.03, p=0.90
	Negative defocus only	0.90±0.47	r=-0.13, p=0.58
	Best VA + 0.40 LogMAR	2.37±0.70	r=-0.01, p=0.95
	Negative defocus only	1.20±0.62	r=-0.07, p=0.75
Subjective Push-up/Push-down Test		0.97±0.28	r=0.02, p=0.93

Table 3.12. Correlations, and associated significance (at p=0.05), between blur threshold (depth of focus - DoF) and pupil size for subjective amplitude of accommodation (AoA) as determined by each defocus curve criterion and the push-up/push-down test (n=20)

The mean change (decrease) in pupil size during measurement of the objective AoA, determined as the difference in pupil sizes between an accommodative demand of zero and the maximum accommodative response observed, was 0.42±0.24mm. Figure 3.13 reveals that a greater decrease in pupil size was expectedly associated with a larger AoA, due to stimulation of the near triad, but since the correlation was not significant (R^2=0.23, p=0.73) it was confirmed that the change in AoA was not significantly associated with pupil miosis and therefore was not due to a corresponding increase in DoF.

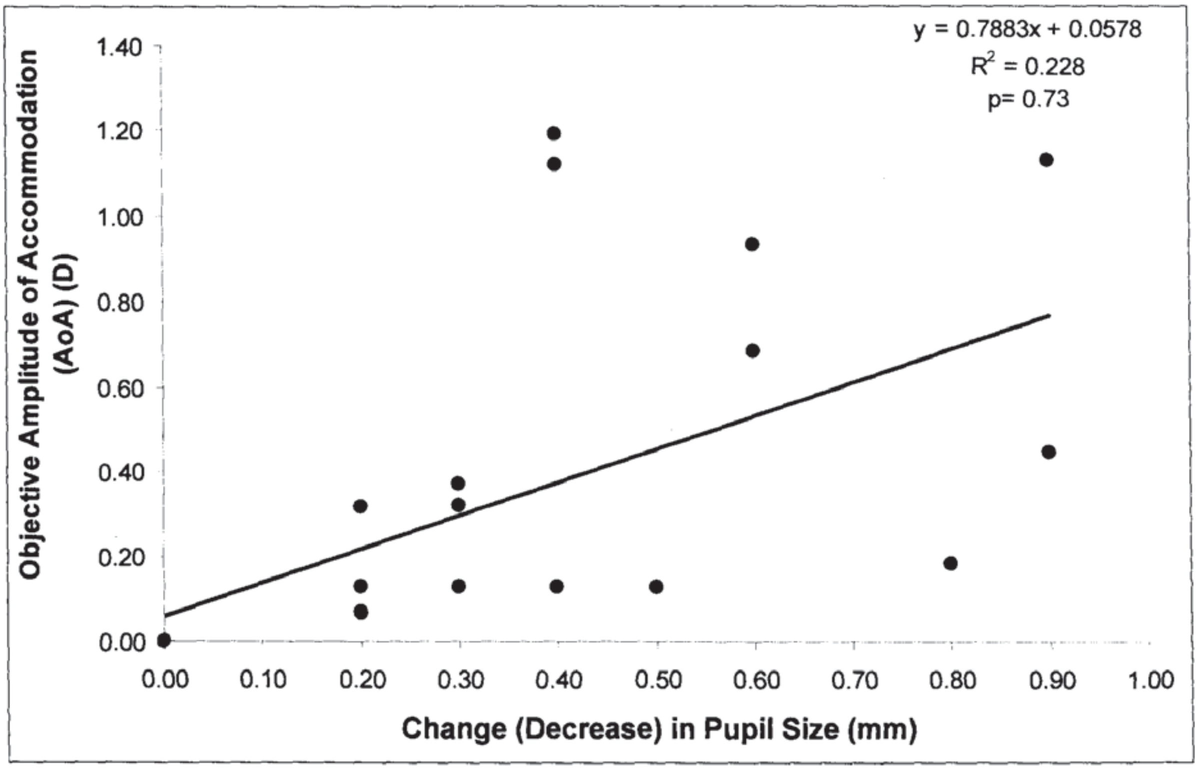


Figure 3.13 The effect of pupil size changes on measurement of the objective amplitude of accommodation (AoA) (n=20)

3.6 Discussion

All of the defocus curves measured in this study demonstrated the expected shapes according to the expected levels of accommodation for the respective cohorts. Defocus induced by negative lenses is overcome by accommodation in pre-presbyopic subjects, maintaining the highest level of VA, whilst positive lenses induce defocus that cannot be overcome by adjusting accommodative state, resulting in a gradual decline in VA. For presbyopic subjects, negative defocus is overcome by accommodation for a smaller range than in pre-presbyopic subjects due to a lower expected accommodative ability. As such, VA declines when the amount of negative defocus exceeds the maximum AoA. Positive defocus has a similar effect on presbyopic eyes as it does on pre-presbyopic eyes.

There was no significant difference between the six possible combinations of presenting letter sequences and the order of the lenses when measuring defocus curves, in both pre-presbyopic and presbyopic subjects. There were also no significant differences between any pairs of combinations. In pre-presbyopic subjects however, defocus curves measured without the randomisation of letter sequences, regardless of whether the order of lens presentation was randomised or not, consistently yielded lower magnitudes of mean VA at each level of defocus, compared to if both of these factors were randomised (combination 6). Although these were not significantly different to similar comparisons conducted for the combinations involving the randomisation of letter sequences (combinations 4 and 5), this may have occurred due to memory effects. Without the randomisation of letter sequences, subjects are essentially required to repeatedly read the same lines of acuity, which includes the highest achievable VA with all negative amounts of defocus since this can be overcome with adjustment of accommodative state. This is likely to lead to memorisation of the letter sequences and consequently the suggestion of a high (good) VA, regardless of whether the letters are actually resolvable or not. Indeed, when the letter sequences are randomised (combinations 4 and 5), the memory effect is reduced, as displayed by the more variable comparison to combination 6 (see Figure 3.8).

In presbyopic subjects one may expect similar effects to occur, especially with the presentation of further defocus *after* the apex (best achievable VA) has been reached with combinations 1 and 2. In fact, it was found that *all* of the defocus curve combinations consistently yielded lower magnitudes of mean VA at each level of defocus compared to if both letter sequences and the lens presentation order were randomised (combination 6). Although not significant, this suggests that all but combination 6 may be susceptible to memory effects, either through subjects memorising the letter sequences or perhaps pre-empting the sequence of lens presentation order and therefore responding accordingly.

It is possible that the lack of significant differences between each of the defocus curve measurements merely represents variation of memory effects from person to person, with some subjects having a poorer short-term memory than others. There may also be variations in the level of honesty of subjects, with some being more honest in what letters they can actually read, when they have not been randomised, even if letters on better lines of acuity can be remembered. Indeed, in this particular study subjects may have made a subconscious effort of trying not to memorise letter sequences since they were aware of the repetitive nature of the measurements through the process of obtaining informed consent.

Attempts were made in this study to keep the influence of prior knowledge to a minimum by not informing subjects of the combination that was being implemented at any point in time. However, the clear susceptibility of defocus curve measurements to individual over-estimations in this manner suggests that at least the use of non-randomised letter sequences should be avoided. Since there was no significant difference between defocus curves measured by randomising letter sequences only compared to randomising both this and the order of lens presentation, in both pre-presbyopic and presbyopic subjects, it would appear sufficient to randomise just the letter sequences to remove any memory effects. However, in view of the over-estimations that are still possible with randomisation of letter sequences alone in presbyopic subjects (see Figure 3.10) and in the interests of best clinical practice, it is advisable to achieve maximal randomisation (Altman and Bland 1999) and therefore both letter sequences and lens presentation order ought to be randomised.

As discussed in section 3.1 it is desirable to quantify the AoA independently of DoF. Subjective techniques require a report of perceived blur and are therefore dependent on DoF, the influence of which can vary if pupil size and target size alter during the measure (see sections 3.1.1 and 3.1.3). In this study, pupil size did not correlate to DoF (blur thresholds) for the push-up/push-down test (R^2=0.0005) or the relative defocus curve criteria (R^2=0.04 to 0.0002), suggesting no influence of this on the quantified AoA. This is likely to represent the counteractive effects of SA and the Stiles Crawford Effect, which maintains a consistent pupil size for the measurement range (see section 3.1.1). In contrast, DoF derived from absolute criteria was *more* inversely correlated to pupil size (Table 3.12), albeit insignificantly, indicating greater dependency of the AoA on DoF. The greater variation in pupil size may occur due to a larger defocus range that is measured to include letter sizes that are above the acuity threshold, compared to relative criteria. As a result, the AoA is poorly correlated to and has larger limits of agreement with the push-up/push-down test. Absolute criteria therefore should not be used to quantify AoA from defocus curves.

The AoA measured by the push-up/push-down test is dependent on DoF that arises from variations in target size (see section 3.1.7.3). With relative defocus curve criteria a similar effect can be artificially induced by the definition of the criterion limit i.e. the inclusion of letter sizes that are increasingly larger than the acuity threshold. This increases the range of tolerable blur (DoF) and subsequently increases the likelihood of producing a measure of the AoA that is considerably larger compared to objective measurements or to relative defocus curve criteria that are restricted to the limits of resolution only (Table 3.12).

Of all the relative criteria, only one, *the range of defocus for which the best VA can be maintained*, quantified the AoA with a high correlation, acceptable ICC and clinically acceptable limits of agreement with the push-up/push-down test. This criterion should therefore be used to quantify the subjective AoA from a defocus curve. An allowance of 0.04 logMAR ought to be included to account for natural variability in repeated VA measures, with little need to amend this for increasing age as there is no significant age-dependent change (Lovie-Kitchin and Brown 2000). In fact, including allowances of 0.10 logMAR (*Best VA + 0.10 logMAR*) or 0.20 logMAR (*Best VA + 0.20 logMAR*) produced poorer comparisons of the AoA to the push-up/push-down test and therefore should not be used. The criterion *Best VA* provides a measure of the AoA that is intuitive to the definition of *range of clear vision* since the inclusion of artificial blur tolerance from variable target size is minimised by the use of a consistent (far) test distance and by correcting all VA measures for lens magnification effects (Equation 3.1). The defocus curve can be implemented quickly since measurements need only be made at the limits of visual resolution, although the inclusion of positive defocus in the measurement is recommended since this helps with the curve-fitting procedure and also allows the end-point of the refraction to be confirmed. Also, a logMAR chart ought to be used so that VA can be recorded to an accuracy of 0.02 logMAR units (see section 2.1.5.3, Chapter 2).

The findings of this study have potential implications on the evaluations of the AoA/range of clear vision reviewed in Tables 3.5 and 3.6. For example, Heatley et al. (2005a) measured defocus curves for the 1CU 'accommodating' IOL (HumanOptics AG, Erlangen, Germany) without randomising letter sequences and by presenting lenses in sequential order from negative to positive. This methodology may have over-estimated the AoA of this IOL through memory effects, although it is not certain whether randomisation of both letter sequences and the order of lens presentation may instead produce an *under*-estimate due to the fatigue of irregularly alternately presenting positive and negative lenses. Errors in quantifying the AoA may also have been made according to the criteria used. The criterion of *Best VA* has only been used in a few studies, whilst the majority have used a criterion that extends beyond the resolution limit, potentially over-estimating the AoA. For example, Sauder et al. (2005) quantified the AoA of the 1CU 'accommodating' IOL as 1.01±0.40D six months after implantation, using the relative criterion of *Best VA*, whilst Kuchle et al. (2004) found the AoA of the same IOL after the same period of time after implantation to be 1.85±0.43D, using an absolute criterion of *0.40 logMAR*. Differences in study design could also be accountable, but the varying criterion is perhaps the main cause.

3.6.1 Limitations

The push-up/push-down technique used for subjective AoA measurements in this study differs to the method that may be used, for example, in USA, where only the push-up element is assessed. It may therefore have been useful to compare the defocus curve outcomes to push-up AoA, to see if there are any differences in the findings. However, the push-up/push-down method used here minimises the influence of variable target size, and therefore DoF, since the target size increases in the direction towards the eyes (push-up) whilst the target size decreases in the opposite direction (push-down), thus averaging out. The problem of variable target size could in fact have been overcome if the method described by Atchison et al. (1994) had been used, whereby the letter size is progressively reduced as they are brought closer to the eyes, thus maintaining an approximately equal size throughout the measurement. This would therefore minimise DoF effects.

The accuracy of the defocus curve measurements in this study may have been influenced by fatigue effects, due to the large number of measurements made i.e. six defocus curves with thirteen points each (+3.00DS to –3.00DS in 0.50DS steps). Also, quantification of the AoA may have been influenced by the use of a best-fit curve-fitting method. However, there is no satisfactory alternative, especially since scale drawing is more time consuming whilst calculating the area under the curve instead, as described by Trager et al. (2005), has not been validated against other techniques. Using the lens power interval that corresponds to the criterion definition, or extending this between two defocus points by linear fitting until the VA falls below the criterion definition is also not feasible since correlations, ICCs and limits of agreement with the push-up/push-down test were poorer (see Appendix for details of the comparison). In view of this, one may choose to measure the defocus curve in steps of 0.12DS instead, but the accuracy and validity of this has not been examined.

The accuracy of the objective AoA measures also may not have been optimal if a subject's maximum AoA lay between two measurement points, especially since blurred targets are poor stimulators of accommodation, and may therefore have produced reduced responses if an individual's maximum AoA had been exceeded (Wolffsohn *et al.* 2006a).

Finally, measurement of SA may have been advantageous in the present study to confirm the effects of pupil size on the DoF and AoA. However, sufficient information was obtained from the measurements made to allow definitive conclusions to be drawn.

3.7 Conclusion

This study has shown that the method for measuring defocus curves should be carefully considered to prevent biased evaluations of the subjective AoA. Measurements should be standardised by randomising both letter sequences on acuity charts and the order in which lenses are presented, primarily because there are individual subject implications of over-estimating the true AoA due to memory effects if neither of these is randomised. Also, the AoA should be quantified from defocus curves as the range of defocus for which only the level of best VA can be maintained, as assessed by curve-fitting, with an allowance of 0.04 logMAR included to account for natural variation in repeated VA measures. The use of this criterion includes minimal DoF influences and therefore whilst an AoA of zero may not be measurable with the push-up/push-down test, this ought to be possible with the defocus curves technique.

Having now standardised the measurement and quantification of the subjective AoA from defocus curves, the next Chapter uses this and the findings of Chapter 2 to aid in the development of a new questionnaire to evaluate subjective perceptions of near visual ability and satisfaction with various presbyopic corrections.

CHAPTER 4

Development of the Near Activity Visual Questionnaire (NAVQ) For Presbyopia

4. Introduction

The measurement of psychological or *latent* traits such as vision-related QoL (VRQoL), perceptions of ability, and satisfaction, cannot be performed by any mechanical devices and must instead be determined through the use of questionnaires (Vitale and Schein 2003). Questionnaires can be categorised into *generic* measures, which aim to assess a variety of conditions, or *specific* measures, which target particular aspects of a disease. The latter are often favoured since generic measures may not be sensitive to issues that are specific to a particular visual condition (Walline et al. 2000). There are a large number of specific questionnaires that can be used to measure VRQoL (see Appendix for details), but none of these may be suitable for use in a particular situation of interest. For example, local cultural differences in Asia compared to western countries were cited as the reason for the need to develop a new questionnaire to assess the outcomes of cataract extraction in Hong Kong (Chan *et al.* 2003). In other cases a relevant questionnaire simply might not exist, requiring a new one to be developed (Streiner and Norman 1995).

4.1 The Process for Developing a New Questionnaire

The first step in new questionnaire development requires the type of questions or *items* to be decided upon. The majority of VRQoL questionnaires use a *closed-ended* approach, which requires responses to be given from a pre-defined set of options. This allows quicker implementation than an *open-ended* approach, since that encourages open thought and can increase the time taken to elicit the response, which in turn may not be quantifiable (Oppenheim 1992). Once this choice has been made, the items must then be produced.

4.1.1 <u>Generating Items</u>

Items for a new questionnaire can be sourced from existing questionnaires, since these can be trusted to have been put through vigorous testing to ensure optimal phrasing and comprehension (Streiner and Norman 1995).

Where items need to be devised wholly originally, patient interviews are the most desirable approach since the problems to be investigated can be ascertained based on first-hand experience (Frost *et al.* 1998, Mangione *et al.* 1998b). Indeed, focus groups are ideal here since exact terminology, relevance and level of language can be gauged (Stewart and Shamdasani 1990, Lundstrom *et al.* 1997), which is important to ensure that items do not create multiple interpretations and/or responses, resulting in respondents giving inaccurate answers if they do not understand the question(s) (Streiner and Norman 1995). However, one must ensure that the focus group discussion is not influenced by the facilitator based on any preconceived ideas (Mangione *et al.* 1998b), whilst the participants must be representative of the target questionnaire audience in terms of gender, race, age, and socio-economic background (Berry *et al.* 2003). Murthy et al. (2005) for example, held 46 separate focus groups to determine the relevant content for a questionnaire to evaluate VRQoL for a variety of ocular conditions in India.

Where patient interviews cannot be carried out, the items for a questionnaire can be ascertained from professionals in the field. Steinberg et al. (1994) for example developed a questionnaire to assess the outcomes of cataract extraction based on the typical symptoms that ophthalmologists enquire about when considering patients for cataract extraction. The *Delphi Technique* can be used here since this allows expert opinion to be gathered from a variety of different locations and sources. It is an anonymous process that involves a series of discussions taking place on a topic of interest, which continues until a consensus is reached; the responses are analysed by an independent group and these are then relayed back to the participants at each stage (Linstone and Turoff 1975). The benefit of this technique is that an informed group judgement can be made as opposed to an individual judgement that may be based on little or no information (Dalkey 1975).

Items can also be generated using previously published research. For example, Lundstrom et al. (1994) used published reports of difficulties that patients experience due to cataract, to generate items for a questionnaire to compare changes in visual ability before and after cataract surgery. In contrast, Brenner et al. (1993) used cataract referral criteria to develop a similar questionnaire. Theoretical models aimed at explaining the cause and impact of diseases may also be useful since items can then be devised with the aim of verifying or disproving these (Putnam 2002). In many cases, a combination of all of these approaches can be used for item generation, and those taken by researchers for the development of existing VRQoL questionnaires are summarised in Table 4.1.

Questionnaire & Reference(s)	Existing Questions	Patient Interviews	Professionals	Research and Theory
Visual Functioning Index (VFI) (Bernth-Petersen 1981)		✓		
Prospective Evaluation of Radial Keratotomy (PERK) Study Questionnaire (Waring *et al.* 1983, Bourque *et al.* 1984, 1986)	✓	✓	✓	
Activity Level of the Blind (ALB) (Becker *et al.* 1985)			✓	
Visual Status Inventory (VSI) (Coren and Hakstian 1987)		✓		
Perceived Visual Disability (PVD) (Elliott *et al.* 1990a)	✓			
Nottingham Adjustment Scale (NAS) (Dodds *et al.* 1991, 1993)	✓			
Visual Activities Questionnaire (VAQ) (Sloane *et al.* 1992)				✓
Activities of Daily Vision Scale (ADVS) (Mangione *et al.* 1992)		✓	✓	
Visual Function-related Quality of Life (VFQOL) (Brenner *et al.* 1993)		✓	✓	✓
Visual Function -14 (VF-14) & -7 (VF-7) Item (Steinberg *et al.* 1994, Uusitalo *et al.* 1999)	✓	✓	✓	
Cataract Questionnaire (Catquest) (Lundstrom *et al.* 1994, 1997)	✓		✓	✓
Activity Breakdown Structure (ABS) (Massof 1995, 1998)				✓
Studies of Ocular Complications of Aids (SOCA) (Wu *et al.* 1996, Martin *et al.* 2001)	✓	✓		
Cataract Type Specification (TyPE) (Javitt *et al.* 1997, Lawrence *et al.* 1999, 2003)	✓		✓	
Madurai Intraocular Lens Study (MIOLS) (Fletcher et al. 1997, 1998)		✓		
National Eye Institute Visual Functioning Questionnaire (NEI-VFQ) (1998a, Mangione *et al.* 1998b, 2001)		✓		
Vision-related Quality of Life (VQOL) & Vision Quality of Life Core Measure (VCM1) (Frost *et al.* 1998, 2001)	✓	✓		
Visual Disability Assessment (VDA) (Pesudovs and Coster 1998)	✓	✓		
Adaptation to Age-related Vision Loss (AVL) (Horowitz and Reinhardt 1998)	✓		✓	
Graves' Ophthalmopathy Quality of Life (GO-QOL) (Terwee *et al.* 1998, 1999)	✓	✓		
Independent Mobility Questionnaire (IMQ) (Turano *et al.* 1999)	✓		✓	
Visual Disability Questionnaire (VDQ) (Nelson *et al.* 1999)	✓		✓	✓
Cataract Symptom Score (CSS) (Crabtree *et al.* 1999)		✓		

Table 4.1 Summary of methods used for item generation by existing vision-related quality of life (VRQoL) questionnaires

Questionnaire & Reference(s)	Existing Questions	Patient Interviews	Professionals	Research and Theory
Daily Living Tasks Dependent on Vision (DLTV) (Hart *et al.* 1999, Denny *et al.* 2007)		✓	✓	
Low Vision Quality of Life (LVQOL) (Wolffsohn and Cochrane 2000a)	✓	✓		
Measure of Outcome in Ocular Disease (MOOD) (Foss *et al.* 2000)	✓	✓		
Refractive Status and Vision Profile (RSVP) (Vitale *et al.* 2000)	✓	✓		
Houston Vision Assessment Test (HVAT) (Prager *et al.* 2000)		✓		
Impact of Vision Impairment (IVI) (Hassell *et al.* 2000, Weih *et al.* 2002, Lamoureux *et al.* 2007)	✓	✓		
Canadian Refractive Surgery Research Group Questionnaire (Brunette *et al.* 2000)	✓		✓	
Melbourne Low Vision Activities of Daily Living Index (MLVAI) (Haymes *et al.* 2001)	✓			
National Eye Institute Refractive Error Quality of Life Questionnaire (NEI-RQL) (Berry *et al.* 2003, Hays *et al.* 2003)		✓		
Quality of Life Questionnaire (QoLQ) (Chan *et al.* 2003)	✓		✓	
Low Vision Prasad Functional Vision Questionnaire (LVP-FVQ) (Gothwal *et al.* 2003)	✓	✓	✓	
Veterans Affairs Low Vision Functioning Questionnaire (VA LV-VFQ-48) (Stelmack *et al.* 2004b, Szlyk *et al.* 2004)	✓		✓	
Quality of Life Impact of Refractive Correction (QIRC) (Pesudovs et al. 2004a)	✓	✓	✓	
Pseudophakic Visual Quality Questionnaire (PVQQ) (Aslam et al. 2004)	✓		✓	
Andhra Pradesh Eye Disease Study Visual Function Questionnaire (APEDS-VFQ) (Nutheti *et al.* 2004)			✓	
Focus Quality of Life Questionnaire (Focus-QOL) (Fylan *et al.* 2005)	✓	✓		
Vision Quality of Life Index (VisQoL) (Misajon *et al.* 2005)		✓		
Activity Inventory (AI) (Massof *et al.* 2005, 2007)	✓	✓		
Indian Vision Function Questionnaire (INDVFQ) (Gupta et al. 2005, Murthy et al. 2005)		✓		
Spatial Localisation Questionnaire (SLQ) (Subramanian and Dickinson 2006)	✓		✓	
Assessment of Function Related to Vision (AFREV) (Altangerel *et al.* 2006)	✓		✓	
Contact Lens Impact on Quality of Life (CLIQ) (Pesudovs *et al.* 2006)	✓	✓	✓	

Table 4.1 cont. Summary of methods used for item generation by existing vision-related quality of life (VRQoL) questionnaires

4.1.2 Selection of a Response Scale

Response scales for closed-ended items can be classified into *categorical scales*, which require an answer to be given from a limited set of options, and *continuous scales*, which aim to describe a continuum of a trait or *attribute*. The latter type of response scaling is the most widely used for VRQoL questionnaires, although some may employ the structure of a categorical scale to a continuous scale for ease of data collection. Continuous response scales are most commonly encountered as *visual analogue scales* (see section 4.1.2.1) and *Likert scales* (see section 4.1.2.2) (Streiner and Norman 1995).

4.1.2.1 Visual Analogue Scales (VAS)

Visual analogue scales (VAS) require the respondent to mark a line, usually 10cm in length with stops on either end, which represents a continuum of the attribute in question; the amount of attribute usually increases from left to right on the line, whilst the stops on either end indicate the extremes of attribute amount. VAS may be accompanied by descriptors along the scale, which aid the decision-making process. However, although this type of response scaling is simple to use and easily understood, they can be difficult to score as their interpretation is dependent on the level of measurement accuracy employed. For the responses displayed in Figure 4.1 for example, subjects Y and Z may be interpreted as being somewhat neutral with a slight tendency to agree or disagree, respectively, if a high level of measurement accuracy is used, e.g. 1.0mm. If however, a lower level of measurement accuracy is used, e.g. 1cm, then both subjects could be interpreted as being neutral (Streiner and Norman 1995).

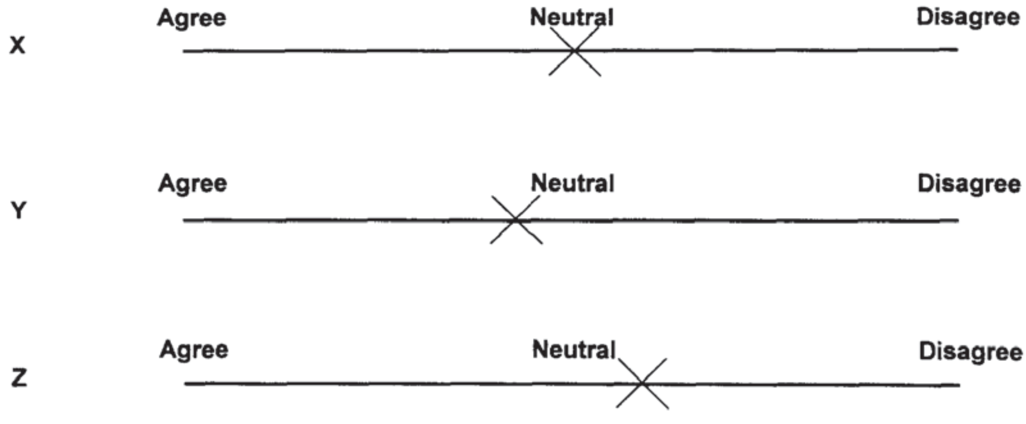


Figure 4.1 Scoring of visual analogue scales is dependent on the measurement accuracy – *produced based on a description in Streiner & Norman (1995)*

4.1.2.2 Likert Scales

Likert scales present a list of categorised response options in an ordered fashion, with the aim of reflecting an underlying continuum of an attribute (Likert 1932). For example, one may be required to indicate the amount of agreement with a presented statement, on a scale of 1, 2, 3, 4, and 5, where '5' indicates strong agreement and '1' indicates strong disagreement. This is a simple approach to obtaining questionnaire responses, which are in turn easily interpretable if the numbers corresponding to the responses on the scale are used to describe the attribute in question, either in the form of a mean score of all items or by the total questionnaire score (Likert 1932, Massof 2002). This however, presents the biggest problem with Likert scales, since these are typical of an *ordinal rating scale*, in which responses are placed in a ranked order but no inference is made as to the true difference between each of the options. In order to achieve this, one must instead use an *interval rating scale* since these not only order observations but also ensure equal and known differences between each (Massof and Rubin 2001). The relative simplicity of Likert scales however, means that VRQoL questionnaires still employ this methodology to obtain responses. As such, the responses must instead be analysed using statistical methods that allow an interval scale to be estimated from ordinal scales, so that an actual measure of the true attribute can be obtained (see section 4.1.4) (Massof and Rubin 2001). Before questionnaires are analysed however, they must first be administered.

4.1.3 Administering Questionnaires

Self-administration is perhaps the simplest method of administering a questionnaire since the individual completes this in person whilst in attendance or it is sent to an address to be completed (Streiner and Norman 1995). The benefit of this approach, particularly if completed in person, is that the influence of external bias can be kept to a minimum (Wolffsohn *et al.* 2000). Self-administration is also inexpensive as there are no considerable costs of staff employment, training, travel and time (O'Toole *et al.* 1986). If administered in person, there is also ample opportunity for any issues of confusion or lack of understanding to be clarified. If a postal approach is used however, this cannot be done and this perhaps is a cause for poor questionnaire return rates. Also, a postal approach does not ensure that all of the items will be completed or that the required individual completed the questionnaire instead of a friend or relative (Streiner and Norman 1995).

The telephone or in-person interview approach to administering questionnaires overcomes the disadvantages of self-administration, as it can be ensured that all items are completed whilst a high return rate can be achieved through repeated visits or telephone calls, if there is no answer (Streiner and Norman 1995). Frost et al. (2001) however, reported that implementation time can increase if the interviewer cannot rapidly match the elicited responses to a response on the scale. Indeed, if the interviewer is forced into a 'best match' choice or misinterprets the elicited response, a source of bias arises. Respondents also tend to remember only the first and last few options of a response scale when described verbally and this will in turn reduce the accuracy of the response scale (Streiner and Norman 1995). When dealing with individuals that are hearing impaired, unwell, or have language difficulties, personal contact by telephone is recommended, although this may then lead to the psychological phenomenon of *satisficing* whereby a positive impression is intentionally created by individuals when they are dealing with those involved, or perceived to be involved, with their care or management (Brewer *et al.* 2004).

Questionnaire responses may also be obtained through the use of computers. This may require an interviewer to input responses directly into a computer as they conduct an interview in person or on the telephone, or it may involve self-administration of a questionnaire that is presented on the Internet. The latter provides advantages of accessibility and anonymity, along with reduced staff expense, whilst inbuilt programming can be used to check for errors and to ensure completion of all of the items (Rhodes *et al.* 2003). The decreasing cost of computers and the increased use of the Internet are certainly driving the popularity of this approach, although one must bear in mind that socio-demographic differences may occur if only the wealthy and computer-literate are able to access and use this method (Link and Mokdad 2005).

It has been suggested that a combination of implementation methods can be used to maximise questionnaire return rates, without affecting reliability and validity (Hawthorne 2003). However, differences may occur in terms of the quality of data, completeness of responses and socio-economic factors, whilst there may also be an over-reporting of symptoms (Weinberger *et al.* 1996). For VRQoL questionnaires, there appears to be a greater preference for the self-administration method (Mangione *et al.* 1992, Wolffsohn *et al.* 2000), since telephone and in person interviews may produce an under-reporting of problems (Frost *et al.* 2001).

4.1.4 Questionnaire Analysis

Questionnaires must be analysed not only to estimate interval scales from ordinal scales (see section 4.1.2.2), but also to ensure that the content is optimal and to eliminate any items that do not provide any additional information. In turn, this optimises questionnaire length and minimises respondent burden. Several approaches can be used for this purpose, including those used for item generation (see section 4.1.1), but statistical analysis will ensure that the questionnaire is able to *measure* an attribute (Mallinson 2007). Classical Test Theory (CTT) has long been the method of choice for item elimination but due to limitations of Likert scales (see section 4.1.2.2), it has often been applied incorrectly (Coste *et al.* 1997). There are also greater advantages of newer statistical methods such as Item Response Theory (IRT) (see section 4.1.4.2), which make this the method of choice.

4.1.4.1 Classical Test Theory (CTT)

CTT is based upon the assumption that the amount of an attribute is characterised by the questionnaire 'raw' score. This comprises the true score, which represents the actual attribute amount, plus an error that arises from the measurement, for example due to a lack of attention (Lord and Novick 1968). The raw scores are then used to calculate reliability statistics (see section 4.1.5.1) so that it can be confirmed that all of the items contain minimal error. In this respect, the raw score more reliably reflects the true score and therefore the attribute amount (Streiner and Norman 1995). In the majority of cases, the raw score is derived from ordinal scales, for example Likert scales, and it therefore follows that the difference between subjects is simply the difference in ordinal scores of each (Massof 2002). CTT also assumes that the attribute is normally distributed in the population and therefore all raw scores can be standardised to allow comparisons between individuals to be made (Lord and Novick 1968).

CTT requires that the reliability statistics be calculated from questionnaire scores that are derived from a sample that is representative of the target population. This is primarily because there are several sources of measurement error, all of which are impossible to quantify practically, and therefore these must be generalised as a 'best estimate'; this is known as *Generalizability Theory* (Shavelson *et al.* 1989). It is evident from this however, that the reliability statistics will then reflect a population characteristic rather than a questionnaire feature, since these statistics will vary according to the population sampled.

It is known that raw scores derived from ordinal data cannot be used as a measurement of an attribute since the interval between different respondents cannot be determined (see section 4.1.2.2). In addition, it cannot be assumed that an attribute is normally distributed within a population. Also, it cannot be assumed that all of the tasks in a questionnaire are of equal difficulty. For example, it is known that the visual requirements for reading small print such as newspaper text, is greater compared to that required to read larger print such as newspaper headlines (Whittaker and Lovie-Kitchin 1993). As a result of these limitations, there is increasing support for the use of IRT, which avoids these assumptions.

4.1.4.2 Item Response Theory (IRT)

IRT is also known as *latent trait theory* as it is primarily used to analyse non-manifest variables or attributes. The primary advantage of IRT is that it separates the attribute in question from the population sampled such that characteristics of the *questionnaire* are displayed as opposed to the population. Furthermore, it is able to estimate an interval scale from raw scores derived from an ordinal scale so that a true measure of the attribute can be obtained, allowing for fair comparisons between individuals. IRT is also able to account for the varying difficulty of different tasks and whilst tasks must be related to a single attribute, they need not be related to each other (Lord and Novick 1968).

Unlike CTT, which compares individuals to each other, IRT compares individuals to an independent standard (Embretson 2006). This standard is derived from a mathematical model that describes the relationship between the level of a latent trait 'θ' for a particular person 'n' and the probability of that person selecting a particular response to an item 'i'. This probability $P(\theta_{ni})$ is governed by the latent trait threshold 'b_i', which will lead to a person giving a particular response to an item 50% of the time, and can be modelled by Birnbaum's logistic (Equation 4.1) (Lord and Novick 1968, Massof and Fletcher 2001).

$$P(\theta_{ni}) = c + \frac{d - c}{1 + e^{-a_i(\theta_n - b_i)}}$$ **Equation 4.1**

where c = lower performance asymptote ($0 \leq c < 1$) i.e. chance performance

d = upper performance asymptote ($0 \leq d < 1$) i.e. rate of carelessness of responses

a_i = controls the slope of the item response function i.e. item discrimination ability

b_i = the latent trait threshold for item 'i'

This relationship can also be displayed as an *item characteristic curve* (Figure 4.2), which indicates an increasing probability for positive endorsement of an item with increasing amount of attribute, before reaching a plateau. The shape of the curve however may change to display variations in item discrimination ability, in which case the gradient of the slope will alter, or to display variations in item difficulty, in which case the curve will be displaced along the x-axis. In the former case, a steeper gradient indicates greater discrimination ability, since small changes in attribute amount will cause greater increases in the probability of endorsement, whilst in the latter case, a curve displaced to the right indicates a more difficult item, since a larger amount of attribute is required to increase the probability of endorsement (Streiner and Norman 1995, Hays *et al.* 2000).

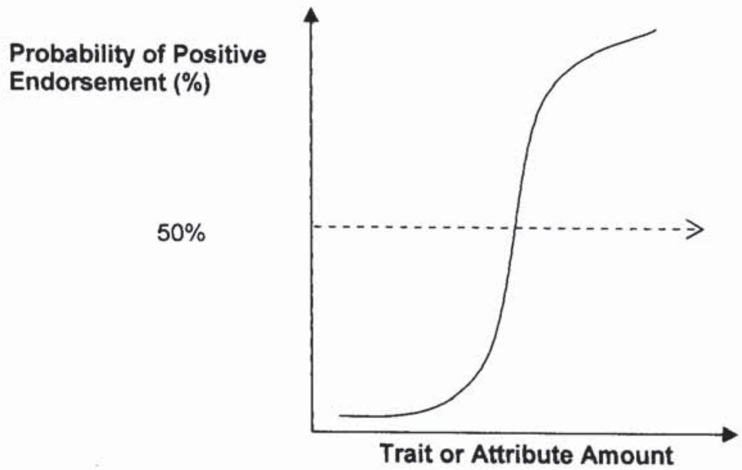


Figure 4.2 An item characteristic curve. The curve gradient indicates discrimination ability whilst the position along the x-axis indicates item difficulty – *reproduced and modified from Streiner & Norman (1995)*

4.1.4.2.1 Rasch Analysis

Originating from the work of the Danish mathematician and statistician Georg Rasch in the late 1950s, Rasch Analysis is a form of IRT that is based on Poisson models and was adopted for use in vision research in the late 1980s (Tennant *et al.* 2004). The Rasch model is derived from Equation 4.1 such that the constants 'c' and 'd' are given values of '0' and '1' respectively, as there are no 'correct' answers and little chance of careless errors, respectively, when VRQoL questionnaires are completed by individuals. However, a constant 'a' is added and given a value of '1' to account for natural variability of responses and to increase the precision of the measurement. The Rasch model is therefore given as shown in Equation 4.2 and can be further simplified to Equation 4.3 if there is a rating scale option of *unable to do the activity* (Massof 1998, Massof and Fletcher 2001).

$$P(\theta_{ni}) = \frac{1}{1 + e^{-(\theta_n - b_i)}} \equiv \frac{e^{(\theta_n - b_i)}}{1 + e^{(\theta_n - b_i)}} \quad \textbf{Equation 4.2}$$

$$P(\theta_{ni}) = 1 - \left[\frac{e^{(\theta_n - b_i)}}{1 + e^{(\theta_n - b_i)}} \right] = \frac{1}{1 + e^{(\theta_n - b_i)}} \quad \textbf{Equation 4.3}$$

The primary objective of Rasch Analysis is to enhance the objectivity of questionnaires and this is achieved through three concepts. The first of these, *order*, reflects the manner whereby scores are arranged to indicate an increasing amount of attribute (or decreasing depending on the direction in which the questionnaire is scored). The second concept is that of *additivity*, which reflects the manner whereby scores are estimated onto an interval scale. In doing this, Rasch Analysis confers that the raw score of a questionnaire can be used for the measurement of an attribute. The third concept is that of *unidimensionality*, which reflects the manner whereby the questionnaire only measures a single attribute. Questionnaires that are developed using Rasch Analysis are therefore independent of the sample used to obtain the initial responses, allowing subsequent use with any population without variation of the psychometric properties (see section 4.1.5) (Tennant *et al.* 2004).

The Rasch model described here is known as a *one-parameter model* since it is assumed that only one variable, item difficulty, affects the item characteristic curves. Since discrimination ability of all items is then deemed equal, the item characteristic curves for different items will be as shown in Figure 4.3 (Streiner and Norman 1995).

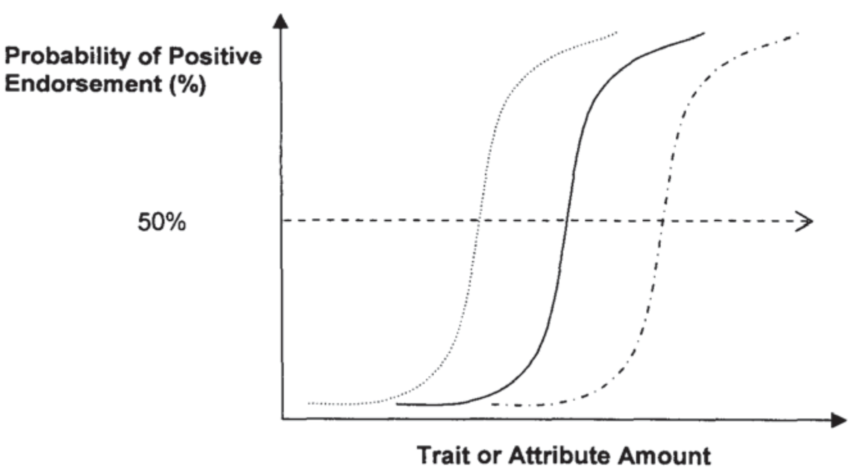


Figure 4.3 Item characteristic curves for the one parameter Rasch Model - *reproduced and modified from Streiner & Norman (1995)*

4.1.4.2.2 *Other IRT Models*

The one parameter Rasch model is the simplest of all IRT models. There are however, other IRT models that can be applied to various measurement purposes. The *two-parameter* IRT model introduced by Andrich (1982) for example, extends upon the one-parameter model by estimating variations in item discrimination as well as item difficulty. This therefore provides additional information about the respondents and increases questionnaire sensitivity. Unfortunately however, a larger population sample is required whilst it is insufficient to provide only a raw score to compute a measure of the attribute. The *three-parameter* IRT model is typically used where there are correct or incorrect answers since this model takes into account the probability of *correct guessing* (Streiner and Norman 1995). Although this is not likely to occur with VRQoL questionnaires, this model may be used if one wishes to account for random responses given through a lack of attention (Hays *et al.* 2000). Unfortunately, both the two- and three-parameter IRT models will result in crossing-over of the item characteristic curves (Figure 4.4) and as a consequence, some amount of questionnaire objectivity is lost since the items are no longer independent of each other (Streiner and Norman 1995).

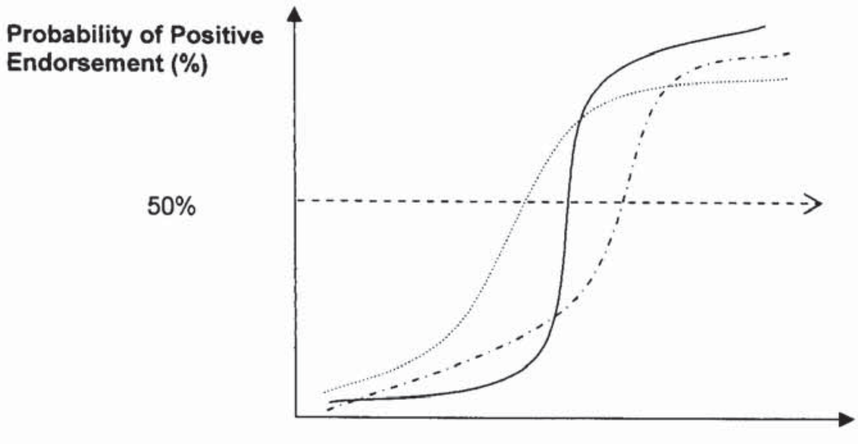


Figure 4.4 Item characteristic curves for two and three-parameter Rasch models – *produced based on a description in Streiner & Norman (1995)*

IRT models also exist for analysis of questionnaires that are rated using polytomous response scales, as is often the case with VRQoL questionnaires. The *graded response model* (GRM), for example, estimates the probability of endorsement for each of the response options and then converts these into an amount of attribute that is required for endorsement. The GRM may account for variations in item difficulty only or in item discrimination ability also (Uttaro and Lehman 1999).

The *partial credit model* (PCM) differs from the GRM in that each item has a unique response scale (Masters 1982). In contrast, the *rating scale model* (RSM) assumes that all items are rated on the same ordered response scale and this therefore allows an assessment of the appropriateness and functionality of the rating scale (Andrich 1978). Regardless of the model used, the mathematical demand of IRT is great and it is therefore necessary to use computer programs for the purposes of item reduction and questionnaire analysis.

4.1.4.3 Item Reduction by Rasch Analysis

The process for item reduction of QoL questionnaires is based upon a comparison of observed questionnaire scores to an independently derived standard i.e. the Rasch model. Mathematically this equates to the ratio of Equation 4.2 to Equation 4.3 and is known as the *odds ratio*, the natural logarithm of which is known as the *log odds ratio* or *logits*. These are the units of the interval scale estimated in Rasch Analysis (Massof and Fletcher 2001, Massof 2002) and conceptually this comparison represents the probability of selecting a particular response option on a scale over an adjacent option, where all options are equidistant by a factor of 2.718 (the base of the natural logarithm) i.e. 1 logit (Tennant *et al.* 2004). A great deal of statistical information is produced in Rasch Analysis but it is up to the individual to select the most appropriate outputs for item reduction. The approach described here is similar to that used in the development of the ABS (Massof 1998), IMQ (Turano *et al.* 1999) and QIRC (Pesudovs *et al.* 2004a) questionnaires, and has also been used to re-analyse existing questionnaires, including the VF-14 (Velozo *et al.* 2000), the NEI-VFQ (Massof and Fletcher 2001), the ADVS (Pesudovs *et al.* 2003) and the RSVP (Garamendi *et al.* 2006).

Before any items are eliminated from a questionnaire, it is first important to ensure that the response scale employed is appropriate and functions as intended. Provided that all of the response scales are scored in the same direction i.e. a larger number reflects an increasing amount of attribute, or vice versa, and that there are at least ten observations in each category, one can ascertain this through the *structure calibration* and *category measure* columns of the *category function* table (Table 4.2) (Linacre 2002). These columns should display increasing values for each response option, to indicate increasing amounts of attribute, whilst the *outfit mean square* should be within the range of 0.6 to 1.4 (see section 4.1.4.3.1). Where these criteria are not met, unused or rarely used options should be removed from the scale or combined with adjacent options, respectively (Linacre 2002).

Category		Observed		Observed	Sample	Infit	Outfit	Structure	Category
Label	Score	Count	%	Average	Expected	Mean SQ	Mean SQ	Calibration	Measure
0	0	667	33	-1.30	-1.30	0.96	0.95	NONE	(-2.04)
1	1	757	37	-0.08	-0.09	0.90	0.78	-0.82	0.00
2	2	609	30	1.40	1.41	1.09	1.33	0.82	(2.04)

Table 4.2 Category function of a response scale – *produced from a table in (Linacre 2006a)*

Once the response scale function has been optimised, the procedure for item reduction can begin. This process centres on the assessment of four criteria for each item in the questionnaire. These criteria, *item fit statistics* (see section 4.1.4.3.1), *item targeting* (see section 4.1.4.3.2), *frequency of endorsement* (see section 4.1.4.3.3), and *tests of normality* (skew and kurtosis) (see section 4.1.4.3.3), have specific requirements that need to be met in order to indicate conformance with the Rasch model; a criterion table (Table 4.3) can be generated to indicate the total number of criteria that each item fails, if any.

Item Number	Decreasing Priority →				No. of Criteria NOT Met
	Item Fit Statistics	Item Targeting	Frequency of Endorsement	Normality	
1					
2					
3					
4					
5					
Etc.					

Table 4.3 Criterion table for the Rasch Analysis procedure

If any items do not meet all of the criteria, the item that fails the most number of criteria is eliminated from the questionnaire and all of the statistics and criteria are re-calculated and re-assessed. If any items still fail to meet any criteria, another item is eliminated and this iterative process continues until all of the remaining items meet all of the criteria or until the removal of an item causes the separation index (see section 4.1.4.3.4) to fall below a value of '2', which indicates a loss in questionnaire precision (Pesudovs *et al.* 2003, Garamendi *et al.* 2006). For the purposes of item reduction, the four criteria are arranged in a hierarchy such that if two or more items fail the *same* number of criteria, then the item fit statistics must be met in priority to item targeting, which in turn must be met in priority to frequency of endorsement; this in turn must be met in priority to the tests of normality (Pesudovs *et al.* 2004a, 2007). The item selected for elimination therefore is that which fails the more important criteria by a greater degree.

4.1.4.3.1 Item Fit Statistics

The comparison of observed item scores to the Rasch model is typically described in the form of residuals known as *item fit statistics.* For a single item and a single person, this can be calculated using Equation 4.4 and if found not to be too large, the observed data are said to 'fit' the Rasch model. For groups of data, there are two forms of item fit statistics, both of which have a range of negative infinity to positive infinity and can be calculated using Equation 4.4. *Outfit mean square* (outfit MNSQ) (Equation 4.5) is sensitive to outliers in the data whereas *infit mean square* (infit MNSQ) (Equation 4.6) is weighted by the variance of scores and is therefore less susceptible to outlier responses (Karabatsos 2000).

$$Z_{ni} = \frac{y_{ni}}{\sqrt{W_{ni}}}$$ **Equation 4.4**

where $y_{ni} = (X_{ni} - P_{ni})$ and P_{ni} is the probability of a person 'n' giving a response X_{ni} to an item 'I', and y_{ni} is the residual

$W_{ni} = P_{ni}(1-P_{ni})$ and W_{ni} is the variance of P_{ni} (between 0 and 0.25)

$$\text{Outfit MNSQ} = \left[\sum_{i=1}^{L} Z_{ni}^{2}\right] L^{-1}$$ **Equation 4.5**

where 'L' is the number of items

$$\text{Infit MNSQ} = \sum_{i=1}^{L} y_{ni} \left[\sum_{i=1}^{L} W_{ni}\right]^{-1}$$ **Equation 4.6**

When infit and outfit statistics have a value of '1' the observed data are shown to perfectly fit the Rasch model. A value of more than '1' suggests that observed data are too random and variable compared to that which was expected, whilst values of less than '1' indicate that the observed data are too predictable. In either case, the data are said to be *misfitting*. It is however, very unlikely that the observed data will perfectly fit the Rasch model and therefore acceptable limits for these statistics have been suggested (Table 4.4) (Wright and Linacre 1994, Pesudovs *et al.* 2007). Standardised residuals (ZSTD) can also be calculated from these statistics and these should not exceed a value of '2' (Karabatsos 2000).

Type of test	Acceptable Infit and Outfit Value Range
Multiple Choice Questions (MCQ) (high stakes)	0.8 – 1.2
Multiple Choice Questions (MCQ) (run of the mill)	0.7 – 1.3
Rating Scale (survey)	*0.6 – 1.4*
Clinical Observation	0.5 – 1.7
Judged (agreement encouraged)	0.4 – 1.2

Table 4.4 Acceptable limits for item fit statistics – *reproduced from a table in Wright & Linacre (1994)*

4.1.4.3.2 Item Targeting

Item targeting is a description of whether the difficulty of items matches the difficulty experienced by individuals. This is displayed by a *person (or subject)-item map* in which a vertical ruler represents the amount of an attribute and all of the subjects are plotted against this on left, whilst all of the items are plotted on the right (Figure 4.5). Where a high questionnaire score indicates greater difficulty, individuals experiencing the least amount of difficulty will be located at the bottom of the map whilst those experiencing the most difficulty will be located at the top. Accordingly, easier items will be located at the top of the map and more difficult items will be located at the bottom (Stelmack *et al.* 2004a).

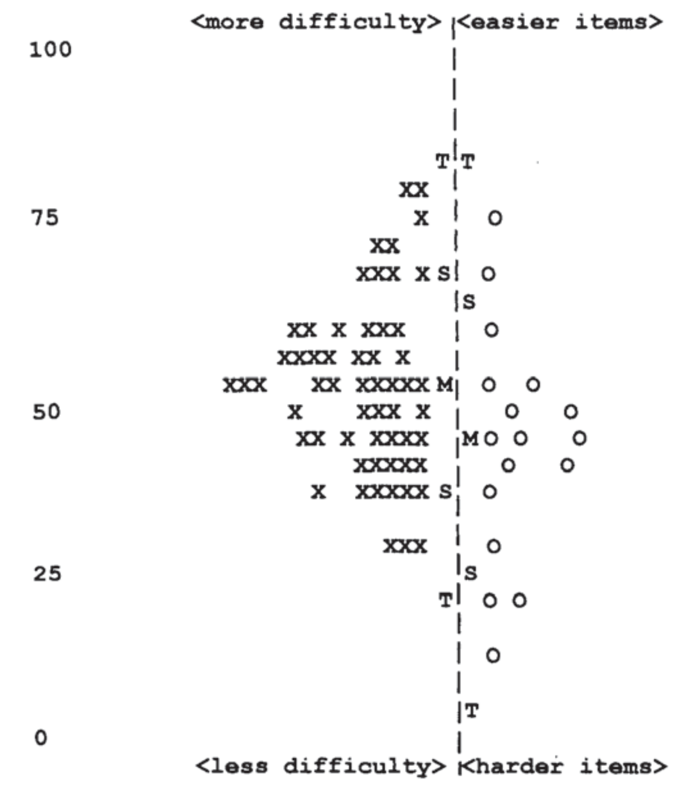


Figure 4.5 Example person-item map scored on a 0-100 logit scale. 'X' indicates an individual and 'O' indicates an item. 'M' is the mean score, 'S' is one standard deviation from the mean and 'T' is two standard deviations from the mean

The appropriateness of item targeting is indicated by the difference in mean score between items and subjects, with a small difference (e.g. 0.50 logits) indicating better targeting; items located furthest from the subject mean represent greatest disparity in difficulty and this is indicative of a need for elimination (Pesudovs *et al.* 2004a, 2007). In order to capture a wide range of subject abilities however, items ought to be located at all positions on the map, whilst gaps indicate the need to add further items and multiple items at one location indicate a need for redundancy (Stelmack *et al.* 2004a).

4.1.4.3.3 Frequency of Endorsement & Tests of Normality

Calculation of the proportion of subjects that respond to each response option on a scale is an assessment of the frequency of endorsement. This is a particularly useful assessment to make as it describes the relative difficulty of the task in question and therefore indicates whether an item is too predictable. For example if 80% of subjects endorse the 'extreme difficulty' option, it is likely that the general population will similarly endorse the item and it can therefore be selected for elimination (Streiner and Norman 1995). However, there is no consensus on the criterion that should be used to indicate excessive endorsement. Streiner and Norman (1995) suggested a value of 80%, whilst Wolffsohn and Cochrane (2000a) used a value of 65% and Hassell et al. (2000) used a value of 70%. Assessments of *skew* and *kurtosis* can help here since these describe the distribution of responses across the scale. Skew describes the horizontal displacement of the peak such that relocation towards lower values is known as a *negative skew* and relocation towards higher values is known as a *positive skew*. The horizontal spread of the peak itself is described by kurtosis, with a steep peak indicating clustering of data whilst a shallow peak indicates that data are widely spread. In both cases, a value of '2' should not be exceeded (Streiner and Norman 1995).

4.1.4.3.4 Separation Index

The separation index is similar to an assessment of reliability but is calculated in Rasch terms as the ratio between the variance in observed responses, after adjustment for measurement error, to the variance due to error, which is derived from the model as the mean square standard error of subject's scores after adjustment for misfit. The separation index can take any value from zero to infinity and a value of at least '2' is required since, conceptually, the index is a measure of precision and describes the number of performance levels that can be discriminated by the questionnaire (Wright 1996, Mallinson *et al.* 2004).

4.1.4.4 Limitations of Rasch Analysis

Although Rasch Analysis takes into account randomness and variability in a more realistic fashion than other methods of questionnaire analysis such as CTT, there are certain issues that may hinder its usefulness. For example, Rasch Analysis requires a large sample size to be used but there is no consensus on an acceptable minimum population. There is also a need to be familiar with the mathematical concepts of IRT, in addition to requiring a computer program capable of carrying out the complex evaluations, which can often be costly. Despite this debate however, it is increasingly evident that Rasch Analysis and IRT provide many advantages over CTT and therefore this statistical methodology is fast becoming the method of choice for questionnaire development (Andiel 1995).

4.1.5 Psychometric Properties

Psychometric properties of a questionnaire refer to its *reliability* and *validity*, which are important assessments that need to be made to ensure that the questionnaire performs as intended. Reliability has been defined as *the extent to which measurements are repeatable, stable and free from error* (Nunnally and Bernstein 1994). Errors can arise from several sources, including the items themselves, the respondents, the implementers and a period of time if measurements are made on several occasions. If the error is consistent such that all measurements are always and equally affected, this is referred to as a *systematic error*. If however the error affects only certain observations, this acts as a source of bias and is referred to as *random error*. Although the latter typically occurs through the respondent, for example in misreading information or holding prejudicial views, both types of error are present in questionnaires and since neither can be completely eradicated, there is a need to assess their influence on the observed measurements (Nunnally and Bernstein 1994).

Validity is a measure of how well a questionnaire is able to measure what it is supposed to measure. It is therefore a description of how well the questionnaire has met the standards by which it is judged. Such investigations are usually made empirically and are not 'all-or-nothing' i.e. correlations between the questionnaire and a standard do not have to be strong but should at least display the expected relationship to suggest that validity is achieved. In fact, strong relationships with objective measures could indicate that the questionnaire is actually redundant. Validation is therefore an on-going process that typically requires re-evaluation as new developments occur (Nunnally and Bernstein 1994).

4.1.5.1 Assessment of Reliability

Reliability is usually expressed as a ratio of the variability in observed questionnaire scores to the total variability including error, and in essence represents a measure of precision that is akin to the separation index of Rasch Analysis (see section 4.1.4.3.4). Coefficients used to express reliability usually yield a value of between 0 and 1, with a value closer to '1' indicating higher reliability (Streiner and Norman 1995). The most common reliability assessments that are usually made in questionnaire development are *internal consistency* (see section 4.1.5.1.1) and calculation of the *test-retest reliability* (see section 4.1.5.1.2).

4.1.5.1.1 Internal Consistency

Internal consistency is a measure of the inter-relationship between items in a questionnaire. Several coefficients can be used to express internal consistency, with *item-total correlations* being one of the oldest (Osburn 2000). This requires the observed scores for each item in a questionnaire to be correlated in turn to the total questionnaire scores excluding that particular item. High correlations indicate high internal consistency since the total questionnaire scores are similar to the individual item scores; if however the correlation was only moderate or low, this would indicate that the excluded item is not well related to the other items of the questionnaire since the total questionnaire scores are considerably different (Streiner and Norman 1995). The most common assessment of internal consistency that is made however, is known as *Cronbach's alpha coefficient* (Cronbach 1951). This represents the mean of all *split-half reliabilities* i.e. all items of a questionnaire are split into two halves and the scores of each half are correlated to each other, for all the possible ways of splitting the questionnaire. In essence, this is an alternative method of revealing that all items in a questionnaire are related to each other and the coefficient can be calculated from Equation 4.7 (Cronbach 1951).

$$\alpha = \frac{k}{k-1}\left[1 - \frac{\Sigma s^2_i}{s^2_T}\right] \qquad \textbf{Equation 4.7}$$

where k is the number of items

s^2_i is the variance of item 'i'

s^2_T is the variance of the total score

Since calculation of Cronbach's alpha depends on the variance of each item (see Equation 4.7), internal consistency will be high if all items have a similar variance, which would occur if there is minimal error (Cortina 1993). However, despite the widespread use of this coefficient, its true worth has been questioned since the calculation is also dependent on the total number of items. Therefore, if there are a large number of items, the likelihood of a high coefficient will increase since the likelihood of similar items being present increases. Furthermore, Cronbach's alpha reflects a population characteristic rather than a questionnaire feature since the value will vary according to the responses of the population sampled. For this reason, it is instead recommended that the separation index of Rasch Analysis is used to provide evidence of precision (Mallinson *et al.* 2004).

4.1.5.1.2 Test-retest Reliability

The calculation of test-retest reliability is an assessment of the ability of a questionnaire to produce repeatable responses, when separated by a period of time (Pesudovs *et al.* 2007). Although correlations such as the PPMC coefficient can be used for this purpose, these only indicate the trend between two variables i.e. the association between repeated questionnaire scores; they do not account for any systematic variation or bias that might be present. As such, a high correlation may indicate that a high score on one implementation is likely to produce a high score on a second implementation, but there is no indication as to whether the scores would be systematically different by a certain amount. For this reason, it is important to assess the absolute agreement of the values of the variables instead (Kramer and Feinstein 1981).

Where variables are measured on nominal scales, absolute agreement can be assessed by *coefficient kappa* (κ), which assumes that the variance is equal between the two variables or weighted kappa (κw) if the variance is unequal. Unfortunately however, where data are obtained from ordinal or interval rating scales, as evidently would be the case for VRQoL questionnaires, several generalisations must be made for these coefficients to be used, which can affect the overall measurement of agreement (Fleiss 1971). For this reason, the test-retest reliability of questionnaire scores can instead be determined by the ICC, which is a calculation based on the statistical test of ANOVA (see Appendix for full details of the calculation). An ICC value of 0.8 is typically desired to be indicative of good questionnaire test-retest reliability, although a value of at least 0.6 is deemed to be acceptable (Pesudovs *et al.* 2007).

4.1.5.2 Assessment of Validity

A questionnaire can only be considered to be valid if an attribute exists for it to be measured by the questionnaire, and if variations in the attribute amount causally produce changes in the questionnaire scores (Borsboom *et al.* 2004). In order to determine whether a new questionnaire is valid, it is necessary to assess five specific areas that together encompass the meaning of validity. Indeed, these assessments can actually be made during the process of questionnaire development. For example, *face validity* is an assessment of whether the questionnaire looks right or appropriate on the face of it. This typically requires subjective judgement by experts and is a form of validity assessment that does not require any formal calculations (Streiner and Norman 1995). Similarly, *content validity* requires a judgement on whether the coverage and content of the items is appropriate, in terms of being applicable to all subjects within the intended target audience (Nunnally and Bernstein 1994). Both face validity and content validity are usually determined at the design stage of questionnaire development, when items are being generated (see section 4.1.1). The other three assessments of validity that can be made are *construct validity* (see section 4.1.5.2.1), *criterion validity* (see section 4.1.5.2.2), and *factorial validity* (see section 4.1.5.2.3), all of which are typically made after the questionnaire has been statistically analysed.

4.1.5.2.1 Construct Validity

Construct validity is an assessment of whether questionnaire scores are related to other measures of the attribute in question, as would be expected in theory. The relationships may not be physical entities but can be hypothetically constructed from theory. As such, construct validity requires some proof that the questionnaire is actually 'tapping' the attribute of interest (Nunnally and Bernstein 1994). Cronbach & Meehl (1955) who coined the concept of construct validity, recommended that it should be determined by a three stage process. First, a set of theoretical concepts ought to be generated and the expected inter-relations hypothesised. Second, the method(s) of assessing these hypothetical relationships must be determined and then finally, the hypotheses must be tested empirically. A more modern approach to evaluating construct validity however sees the process adapted into a two-phased methodology of first evaluating *representational validity* and then evaluating *elaborative validity*.

Representational validity requires comparisons to be made between questionnaire scores and other similar measures of the attribute of interest (*convergent validity*) or for comparisons to be made with measures that are known *not* to tap the attribute of interest (*divergent validity*); this latter approach will therefore at least confirm that the questionnaire does not measure what it isn't supposed to measure (Nunnally and Bernstein 1994, Pesudovs *et al.* 2007). Elaborative validity on the other hand confirms the need for the existence of the questionnaire, by showing that it can be used in some way, for example to predict or to monitor change. In questionnaire development, this is often encountered as an evaluation of *discriminative validity*, which assesses the ability of the test to distinguish between different groups of subjects. In fact, this then leads to more criterion-based assessments of validity (see section 4.1.5.2.2).

Construct validity requires a series of investigations to be conducted, as it is insufficient to decide upon the utility of a questionnaire simply on the testing of a single hypothesis. If however a hypothesis is disproved, one cannot be certain of where the fault lies since it may be within the new questionnaire, the measure against which it is being compared, or within the theory itself. Only repeated evidence in support of a hypothesis can gradually increase the confidence in validity and as such construct validity is an ongoing process that must adapt as theory changes (Streiner and Norman 1995).

4.1.5.2.2 Criterion Validity

Criterion validity aids elaborative validity as it can be ascertained as to whether the questionnaire can provide a measure that is of some usefulness. For VRQoL questionnaires, criterion validity typically involves determination of whether the questionnaire can categorise respondents into groups, for example by varying ability, and this is conferred if the questionnaire possesses sufficient discriminative ability. One method of determining this is through the use of a *Receiver Operating Characteristic (ROC) curve* (Figure 4.6), which is a plot of the *sensitivity* of the questionnaire against *100 minus the specificity* of the questionnaire. Sensitivity is the true positive rate i.e. the proportion of respondents correctly diagnosed by the questionnaire, whilst specificity is the true negative rate i.e. the proportion of 'normal' respondents correctly identified as being 'normal'. Both are dependent on the criteria used to define 'normal' but the area under the ROC curve is then an index of discriminative ability (Massof and Emmel 1987).

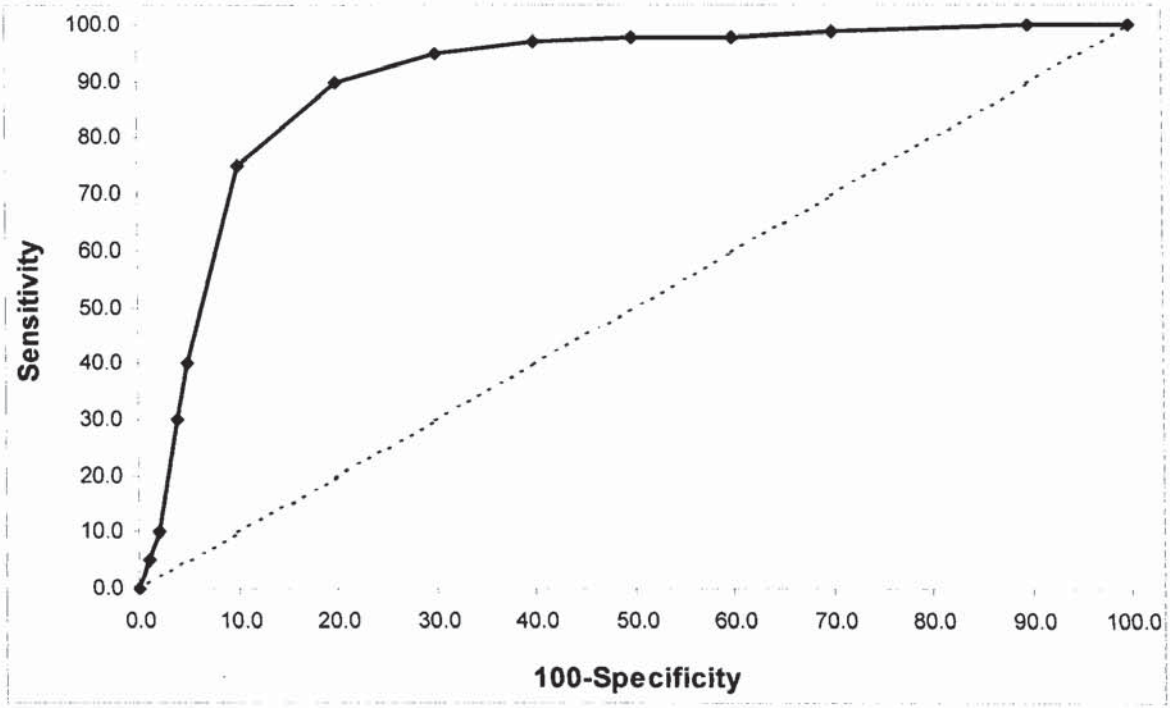


Figure 4.6 Example receiver operating characteristic (ROC) curve – *produced using Microsoft® Excel® based on a description in Massof and Emmel (1987)*

The area under the ROC curve represents the probability that a person will be correctly discriminated as 'normal' or otherwise (Hanley and McNeil 1982). An area of 0.5 (Figure 4.6, diagonal line) indicates that a test has no discriminative ability and the closer the curve is to the top left corner of the plot, the greater the area and therefore the greater the discriminative ability; an area of 1.0 indicates perfect discriminative ability (Hanley and McNeil 1982). Ideally the ROC curve should compare the questionnaire against an existing 'gold standard' but often one is not available and it can then be difficult to determine the criterion that should be used for discrimination.

4.1.5.2.3 Factorial Validity

All of the items in a questionnaire can potentially measure a large number of possibly unrelated attributes or variables. It is therefore necessary to assess this statistically and *Factor Analysis* is one such tool that can be used for this purpose. Factor Analysis is used to compute the proportion of the observed variability that an increasing number of *core* or *principal factors* can be accountable for. The result is described by *eigenvalues* or in the form of a *Scree Plot* (Figure 4.7) and a factor is only considered to be significant if it has an eigenvalue of 1.0 or more since it accounts for more than 10% of the observed variation; it is typical that as the number of factors increases, each accounts for progressively smaller amounts of the observed variation (Dancey and Reidy 2007).

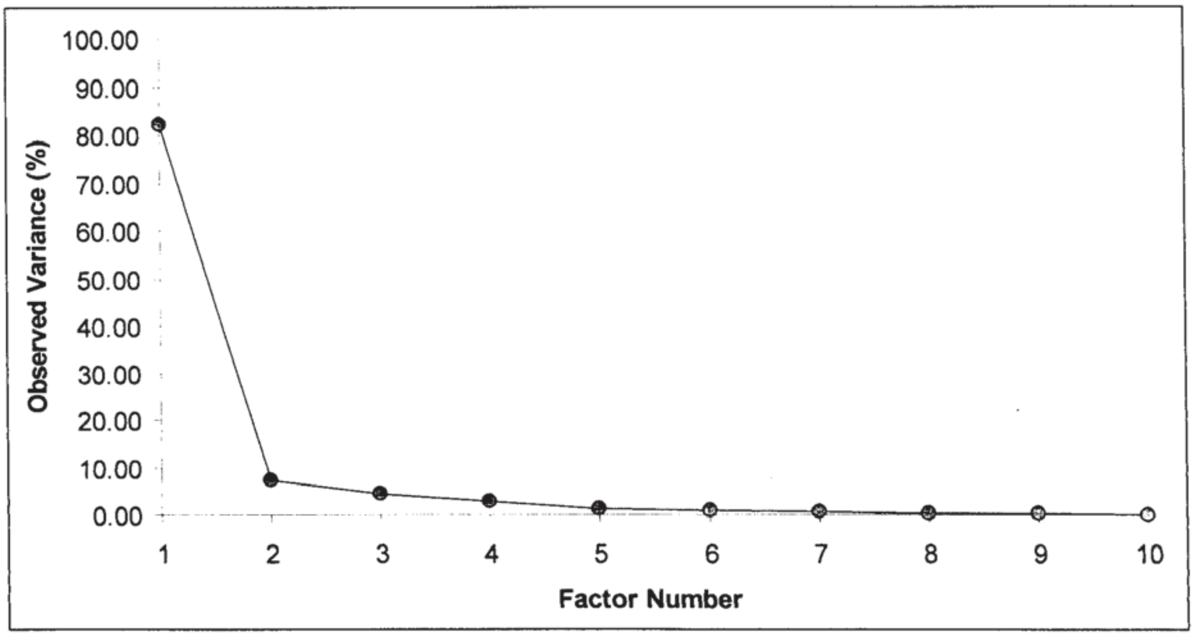


Figure 4.7 Example Scree Plot displaying the variation of each questionnaire factor – *produced using Microsoft® Excel® based on a description in Dancey and Reidy (2007)*

If Factor Analysis indicates only one principal factor to be present then this can be taken as evidence of a questionnaire's unidimensionality, which is important where Rasch Analysis has been employed for questionnaire development (Pesudovs *et al.* 2007). However, where more than one principal factor is identified, i.e. more than one factor accounts for more than 10% of the observed variation each, then an *exploratory Factor Analysis* ought to be conducted to determine how each of the items relate to each of the factors (Dancey and Reidy 2007). In this, each item is correlated to each identified factor and the results are described as *factor loadings*. Where items load onto each factor distinctly differently, then the questionnaire is likely to be measuring more than one attribute. If however, the loadings are similar for each of the factors, then the additional factors may be considered to be subscales of the primary factor; these decisions however depend on a minimum loading criterion (Dancey and Reidy 2007), with a value of 40% suggested (Pesudovs *et al.* 2007).

4.2 The Study Aim

It has been suggested that QoL in presbyopic subjects corrected with spectacles is only slightly reduced compared to the average presbyope (Luo *et al.* 2008). However, validated questionnaires have shown that VRQoL is poorer in presbyopia compared to pre-presbyopic emmetropes, and although this can be improved upon with monovision correction, this is not restored to comparable levels (McDonnell *et al.* 2003).

Whilst evaluations of near VA and the AoA are the primary descriptors of near visual ability conferred by presbyopic corrections, the subjective assessment of perceived effects is equally important to determine whether visual outcomes are acceptable for a person's needs and therefore whether VRQoL may be improved. However, questionnaires that have been used previously for this purpose contain too few items to assess near vision (e.g. Wang *et al.* 2005) or concentrate on spectacle dependence only (e.g. Jacobi *et al.* 1999, Claoue 2004). In many cases, questionnaires that are not appropriately validated have been used to assess outcomes of presbyopic corrections (Walkow and Klemen 2001, Alio *et al.* 2004, Alio and Mulet 2005). The VF-14 questionnaire (Steinberg *et al.* 1994), for example, has been used to assess the effectiveness of multifocal IOL implantation after cataract extraction (Nijkamp *et al.* 2004) but this questionnaire was not originally validated for this type of correction and was instead designed to assess functional impairment caused by cataract. Similarly, the ADVS (Mangione *et al.* 1992) assesses visual function in patients with cataract and was validated using only patients aged 65 or over. As such this questionnaire would not be suitable for younger presbyopes, for example those undergoing CLE procedures or those wearing contact lens corrections.

The PVQQ (Aslam *et al.* 2004) concentrates on aspects of visual dysfunction caused by PCO only, whilst the QIRC questionnaire (Pesudovs *et al.* 2004a) was validated in a pre-presbyopic population and is therefore not valid for those aged 45 and over. Furthermore, this questionnaire does not deal directly with issues of visual function but instead assesses matters relating to costs, cosmetics, convenience, and personality (see Appendix for a full description of existing VRQoL questionnaires). It was apparent from this review that a questionnaire was required that could be used to evaluate individual's perceptions of near visual ability, and their satisfaction with this, as conferred by a variety of presbyopic corrections. This therefore formed the purpose of the proceeding study.

4.3 Method

A pilot study conducted by the author, which aimed to develop a questionnaire to assess the near visual outcomes of 'accommodating' IOL implantation, has been reported previously (Gupta *et al.* 2007). The purpose of the pilot study was to assess the potential success of, and to determine any possible difficulties with, the development of a validated questionnaire that would be applicable to a variety of presbyopic corrections; this larger scale study to develop the *Near Activity Visual Questionnaire (NAVQ)* is reported here.

4.3.1 Questionnaire Design

An extensive review of existing VRQoL questionnaires was first conducted to identify all items relating to near vision tasks and activities. Review papers focussing predominantly on questionnaires that assess visual impairment and rehabilitation were used as a starting point (Massof and Rubin 2001, de Boer *et al.* 2004), but other questionnaires that assess visual outcomes, ability and satisfaction after cataract and/or CLE surgery with multifocal and 'accommodating' IOL implantation were also included. Items were not limited to those appearing in final questionnaires only but also included those in initial item banks so that their relevance could also be assessed. A total of 374 items were identified but these were reduced to a smaller list since many of the items appeared in multiple questionnaires. This reduced list of items was then presented to a group of eight ophthalmic professionals and then to a group of ten lay presbyopes to ensure that content was appropriate and that the items were relevant, especially in terms of expected difficulty. In order to ensure adequate comprehension of each item, each individual in the group of lay presbyopes was also asked to describe their understanding of what each item was questioning. Once a consensus had been reached within the focus groups, a final list of 26 items was produced, including one item (Item 26) to rate overall satisfaction, and this then formed the initial NAVQ. This is shown in Table 4.5, which includes details of the source(s) of the items.

It has been shown that a 5-option rating scale is the most optimal for VRQoL questionnaires (Nagata *et al.* 1996). Indeed, this was supported by the pilot study and therefore a 5-option Likert scale was designed for Items 1 to 23 inclusive, with responses and scores shown in Table 4.6. A *not applicable* response option was also included for subjects that did not do the activity at all or for those who had stopped doing that activity for non-visual reasons. These responses are treated as 'missing data' by the Rasch Analysis model and are assigned a mathematically calculated value, for each individual, according to the responses given to other items. For Items 24 and 25, a 6-option Likert scale was designed with descriptors varying according to the type of question (see Table 4.6). A longer response scale was selected for these items by the group of ophthalmic professionals since these items differed to all of the preceding ones, and therefore it was not certain whether the 5-option scale would be optimal for these or not. Indeed, response options cannot be added to a questionnaire after implementation whilst a larger number of response options at the start can allow for later scale reduction. Finally, Item 26 was assigned a 6-option Likert scale with responses and scores as shown in Table 4.6.

Item	*'How much difficulty do you have ...' (for Items 1-23 only)*	**Original Source(s)** *(Questionnaire names are listed in most cases)*
1	Reading small print, e.g. newspaper articles, books, magazine articles, menu at a restaurant, telephone directories, etc.?	VFI, PERK, ALB, VSI, PVD, VAQ, ADVS, VFQOL, VF-14, SOCA, MIOLS, NEI-VFQ, VQOL, VDA, GO-QoL, VDQ, TyPE, Catquest, CSS, DLTV, LVQOL, MOOD, HVAT, IVI, MLVAI, NEI-RQL, QoLQ, LVP-FVQ, VA LV-VFQ-48, PVQQ, APEDS-VFQ, Focus-QoL, AI, INDVFQ, AFREV, Kohnen et al. (2006)
2	Reading labels / instructions / ingredients / prices on, e.g. medicine bottles, food packaging, etc.?	ALB, ADVS, VFQOL, VF-14, Catquest, VQOL, TyPE, LVQOL, MOOD, HVAT, IVI, MLVAI, QoLQ, VA LV-VFQ-48, PVQQ, AI
3	Reading your post / mail, e.g. electric bills, greetings cards, bank statements, letters, etc.?	Catquest, NEI-VFQ, VQOL, DLTV, LVQOL, MLVAI, QoLQ, VA LV-VFQ-48, Focus-QoL, AI
4	Reading large print, e.g. newspaper headlines, large print books, etc.?	VF-14, VQOL, DLTV, LVQOL, IVI, MLVAI, VA LV-VFQ-48, AI
5	Writing & reading your own hand writing, e.g. greetings cards, notes, letters, filling-in forms, cheques, signing your name, etc.?	ALB, VF-14, SOCA, Catquest, VQOL, CSS, DLTV, LVQOL, HVAT, MLVAI, LVP-FVQ, VA LV-VFQ-48, AI, SLQ
6	Seeing the screen & keyboard when using a computer?	ALB, NEI-RQL, AI, AFREV
7	Seeing the display & keypad on a mobile or fixed telephone, or calculator?	ALB, Catquest, MLVAI, QoLQ, AI, SLQ, AFREV
8	Seeing the display / face of your wristwatch?	PVD, VQOL, MLVAI, AI
9	Handling money and identifying different coins and notes by appearance?	ALB, Catquest, CSS, DTLV, MLVAI, LVP-FVQ, VA LV-VFQ-48, AI, INDVFQ, SLQ, AFREV
10	Seeing objects close to you to engage in your hobbies, e.g. playing games such as cards, bingo and dominoes, gardening, seeing photographs and pictures, etc.?	VFI, ALB, VF-14, MIOLS, NEI-VFQ, VQOL, VDA, GO-QoL, TyPE, LVQOL, HVAT, IVI, NEI-RQL, QoLQ, VA LV-VFQ-48, Focus-QoL, AI, VisQoL, AFREV
11	Doing fine handwork, e.g. threading a needle, sewing, knitting, crochet, etc.?	ADVS, VF-14, VF-7, VDQ, TyPE, MLVAI, NEI-RQL, QoLQ, LVP-FVQ, PVQQ, APEDS-VFQ, Focus-QoL, AI, SLQ, Catquest
12	Using tools, e.g. a hammer, screwdriver, power tools, rulers, tape measures, inserting a key into a lock etc.?	ALB, ADVS, VQOL, LVQOL, NEI-RQL, AI, SLQ, AFREV
13	Cooking, preparing and eating meals, e.g. reading recipes, seeing food on the plate, pouring drinks / judging the level of a liquid, etc.?	ALB, VAQ, ADVS, VF-14, VF-7, VQOL, TyPE, VDQ, Catquest, CSS, DLTV, HVAT, IVI, MLVAI, NEI-RQL, QoLQ, LVP-FVQ, VA LV-VFQ-48, AI, INDVFQ, SLQ, AFREV

Table 4.5 List of items and their sources for the initial Near Activity Visual Questionnaire (NAVQ)

Item	*'How much difficulty do you have …' (for Items 1-23 only)*	**Original Source(s)** *(Questionnaire names are listed in most cases)*
14	Using kitchen utensils, e.g. knives, forks, spoons, scissors, etc.?	MIOLS, VQOL, AI, SLQ
15	Using kitchen appliances and reading the dials on, e.g. a washing machine, a dishwasher, a cooker, an oven, a microwave, etc.?	ALB, VQOL, DLTV, IVI, AI, SLQ
16	Seeing yourself (in the mirror) for grooming, e.g. shaving, styling your hair, applying make-up, trimming your nails, pasting your toothbrush, etc.?	VFI, ALB, NEI-VFQ, VQOL, VDQ, TyPE, DLTV, IVI, MLVAI, LVP-FVQ, VA LV-VFQ-48, Focus-QoL, AI, INDVFQ, SLQ
17	Seeing to dress yourself, e.g. matching clothes, seeing your buttons, lacing your shoes, etc.?	VFI, ALB, MIOLS, NEI-VFQ, VQOL, VDQ, TyPE, DLTV, IVI, MLVAI, LVP-FVQ, VA LV-VFQ-48, Focus-QoL, AI, SLQ
18	Finding objects on a crowded shelf, e.g. in a cupboard, a supermarket shelf, etc.?	VAQ, NEI-VFQ, VA LV-VFQ-48, Focus-QoL
19	Distinguishing between colours?	VAQ, Catquest, MIOLS, NEI-VFQ, VQOL, VDA, VDQ, LVP-FVQ, PVQQ, APEDS-VFQ, AI
20	Recognising people's faces when they are close to you?	VQOL, VDQ, DLTV, MOOD, MLVAI, VA LV-VFQ-48, PVQQ, APEDS-VFQ, AI
21	Seeing objects near to you in poor or dim light?	VQOL, VDA, IMQ, RSVP, PVQQ, APEDS-VFQ, AFREV, CLIQ
22	Seeing objects near to you if there is glare or haloes from lights and shiny surfaces?	VAQ, Catquest, MIOLS, NEI-VFQ, VQOL, VDA, VDQ, LVP-FVQ, PVQQ, APEDS-VFQ, AI, INDVFQ, Gimbel et al. (1991), Gray & Lyall (1992), Walkow et al. (1997), Walkow & Klemen (2001), Shoji & Shimizu (2002), Vingolo et al. (2007)
23	Maintaining focus for prolonged near work?	Sasaki (2000)
24	How quickly does your focus change from distance vision to near vision?	OPHTHALMIC PROFESSIONALS
25	How often do you have to rely on reading or magnifying aids to do near tasks?	Gimbel et al. (1991), Steinert et al. (1992), Lindstrom (1993), Allen et al. (1996), Sasaki (2000), Jacobi et al. (1999), Slagsvold (2000), Walkow & Klemen (2001), Shoji & Shimizu (2002), Claoue (2004), Nijkamp et al. (2004), Alio et al. (2004), Pineda-Fernandez et al. (2004), Alio & Mulet (2005), Wang et al. (2005), Kohnen et al. (2006), Chiam et al. (2006), Vingolo et al. (2007), Fernandez-Vega et al. (2007b)
26	Overall, how satisfied are you with the near visual ability that you have?	OPHTHALMIC PROFESSIONALS, Gimbel et al. (1991), Lindstrom et al. (1993), Avitabile et al. (1999), Souza et al. (2006)

*Items were predominantly derived from non-validated general satisfaction and spectacle dependency measures that were used to assess the success of multifocal IOL implantations

Table 4.5 cont. List of items and their sources for the initial Near Activity Visual Questionnaire (NAVQ)

Item No.	Response Category Scores	Response Category Descriptors
1 to 23 (Inclusive)	N/A (Missing Data)	Not applicable *or* Stopped for Non-visual Reasons
	0	No Difficulty
	1	A Little Difficulty
	2	Moderate Difficulty
	3	Extreme Difficulty
	4	Stopped for Visual Reasons
24	0	Instantly
	1	Very Quickly
	2	Moderate to Quickly
	3	Moderate to Slowly
	4	Very Slowly
	5	Never Changes
25	0	Never
	1	Rarely
	2	Occasionally
	3	More than Occasionally
	4	Most of the Time
	5	Always
26 (Overall Satisfaction)	0	Completely Satisfied
	1	Very Satisfied
	2	Very to Moderately Satisfied
	3	Moderately to A Little Satisfied
	4	A Little Satisfied
	5	Completely Unsatisfied

Table 4.6 List of response scale descriptors used for each item of the initial NAVQ

4.3.2 Subjects & Implementation

Subject characteristics for all participants in this study are shown in Table 4.7, for each type of presbyopic correction. All subjects were required to be able to read English and in order to ensure that no visual dysfunction would influence questionnaire responses, other than perhaps due to the type of correction itself, further inclusion criteria were applied including an achievable best-corrected distance VA of at least 0.30 logMAR in both eyes, an absence of binocular vision anomalies (e.g. decompensated heterophoria, heterotropia, or amblyopia), and an absence of ocular pathology (e.g. glaucoma, AMD and diabetic retinopathy). Since some of the subjects in this study were also participants of other clinical trials assessing visual function, the eligibility criteria of the respective trials were also adhered to, as indicated below. In all cases, the author or a consultant ophthalmologist (subjects implanted with 'accommodating' IOLs only) conducted all of these screenings using the procedures and techniques described previously (see section 2.4.1, Chapter 2).

Type of Presbyopic Correction	Number of Subjects (n)	Mean Age ± SD & Range	Gender	First NAVQ Implementation At:
Contact Lenses *(Monovision & Multifocal)*	20	55.0±5.1 years Range: 49-67 years	11 males 9 females	1 month post-fitting
'Accommodating' IOL	29	68.0±13.9 years Range: 30-91 years	11 males 18 females	24 to 36 months post-operative
Varifocal Spectacles	38	68.0±9.4 years Range: 46-82 years	19 males 19 females	3-6 months post-fitting
Totals	**87**	**65.0±11.7 years Range: 30-91 years**	**41 males 46 females**	

Table 4.7 Characteristics of the subjects recruited for development of the NAVQ

Subjects wearing contact lenses were fitted with either the PureVision® Multi-focal (Bausch & Lomb Corp., Rochester, NY., USA.) (n=10), which is a centre-near aspheric simultaneous vision design, or with monovision (n=10) using single vision PureVision® lenses and which was achieved by inducing an interocular power difference equal to the near spectacle addition. These subjects were participants of a clinical trial comparing visual function between the two correction types and to best binocular spectacle-corrected vision, and were recruited from the Optometry Clinic and staff of Aston University (see Chapter 5). Subjects completed the NAVQ for their respective lens type after at least one month of wear, which allowed time for adaptation to the correction. The mean age of these subjects was lower than that of the other groups due to issues of contact lens handling and dry eye associated with increasing age. Since an absence of pathology was confirmed in all subjects however, it was unlikely that this would have affected the questionnaire responses.

Subjects implanted with 'accommodating' IOLs were recruited from Solihull Hospital and from the Midland Eye Institute in Birmingham and had received a single-piece single optic design due to either cataract extraction or CLE. Nineteen subjects in this group received bilateral IOL implants whilst the remaining subjects did not require treatment of the second eye; based on their age however (all presbyopic), no accommodative ability was expected in this eye. All operative procedures, including second eye implants for those that required them, were successful and without complication, and had taken place approximately two to three years prior to the start of this study (see Chapter 7). It has been shown that subjective reports of visual function and satisfaction are typically better after second eye cataract extraction compared to after the first eye (Javitt *et al.* 1993, 1995), whilst issues of anisometropia are also minimised, thus removing any implications of this on near visual ability (Elliott *et al.* 1997). Therefore, this study was accordingly designed for NAVQ responses to be obtained after second eye treatment in those subjects that required this.

Additional time after 'accommodating' IOL implantation was allowed so that subjects could adapt to the correction. Indeed, adaptation is important for all types of corrections, to ensure that issues relating to the *use* of a correction do not confound any issues relating to visual function and ability. This additional time also meant that complications such as PCO could be dealt with. Indeed, 23 subjects experienced PCO in the time between IOL implantation and the start of this study, for which they received Nd:YAG laser treatment. All subjects had received this treatment without complications at least four weeks before completing the NAVQ, whilst any recurrence, or newly forming PCO in previously untreated subjects, was not considered to be significant enough to affect questionnaire responses, as examined by slit-lamp biomicroscopy (see Chapter 7).

Subjects wearing varifocal spectacles were recruited from the Optometry Clinic of Aston University. All subjects received a full sight examination about six months prior to the start of this study, which ensured that the optimal refraction had been obtained. Subjects had then been fitted by an experienced Dispensing Optician with either Varilux® Physio™ or Varilux® Panamic varifocal spectacle lenses (Essilor Ltd., Thornbury, Bristol, UK.). The subjects had been wearing these lenses for at least three months, allowing for adaptation.

The initial 26-item NAVQ was self-administered to all subjects whilst in attendance for an appointment at which the clinical measures required for validation were also made (see section 4.4). This ensured a 100% completion rate. Implementation time was 10-15 minutes and all subjects (apart from those wearing varifocal spectacles) were instructed to answer the items as though the described activities were performed *without* near-focussed spectacles or other magnifying aids. All subjects were also asked to complete the questionnaire on their own to eliminate interviewer and third-person bias. For the purposes of calculating test-retest reliability, a further implementation of the questionnaire was conducted by post (mail), two weeks after the first implementation. Subjects who failed to return the questionnaire received a follow-up telephone call or email correspondence as a reminder two weeks after the original questionnaires had been posted, and then again after a further two weeks if there was still no response. Non-return of questionnaires two weeks after this time point resulted in exclusion for the calculation of test-retest reliability.

Informed consent was obtained from all subjects after explanation of the nature and possible consequences of the study, and ethical approval was obtained from the NHS Local Research Ethics Committee of Solihull and the Ethical Committee of Aston University.

4.4 Statistical Analysis

Rasch Analysis was performed with all subjects (n=87) and for 25 of the initial 26 items of the questionnaire, using Winsteps® Rasch Measurement Program version 3.63.1 (Linacre 2006b), following the procedure detailed in section 4.1.4.3. Item 26 (overall satisfaction) was not considered to be a near activity-related item and was therefore omitted from the Rasch Analysis and was instead reserved for use in a later analysis. The Winsteps® program (Figures 4.8 and 4.9) uses the *rating scale model* of Andrich (1978) (see section 4.1.4.2.2) and was used for optimising category function, calculating the item fit statistics, assessing item targeting, calculating the separation index and investigating Differential Item Functioning (DIF). Frequency of endorsement (set at >70%), skew and kurtosis were calculated using Microsoft® Excel® (Microsoft® Corporation, Redmond, WA., USA.).

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Figure 4.8 Screenshot of the control and data file set-up screen of Winsteps® Rasch Measurement Program into which all of the raw data are input (Linacre 2006b)

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Figure 4.9 Screenshot of the iteration screen of Winsteps® Rasch Measurement Program from which all of the Rasch Analysis outputs can be obtained (Linacre 2006b)

On completion of Rasch Analysis, the reduced NAVQ was assessed for its psychometric properties following the descriptions in section 4.1.5. Reliability was assessed from the Rasch separation index and Cronbach's alpha coefficient, the latter of which was calculated using SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.). The item-total correlations were also calculated using Microsoft® Excel®, to provide further evidence of internal consistency, whilst the test-retest reliability was assessed by calculation of the two-way random effects ICC, again using Microsoft® Excel®. Content validity was achieved at the design stage by using a multi-disciplinary approach to item generation (see section 4.3.1), whilst construct validity was tested according to the following hypotheses: *With the best vision offered by their respective presbyopic corrections (best distance-corrected vision for those with 'accommodating' IOLs), subjects with higher NAVQ scores will, compared to subjects with lower NAVQ scores, have:*

(a) A poorer near VA, as measured with the ETDRS Near logMAR Chart (Precision Vision™, La Salle, IL., USA.) (see section 2.1.5.2, Chapter 2).
(b) A poorer CPS in logMAR, as measured with the MNRead chart (Lighthouse Low Vision Products, Long Island City, NY., USA.) (see section 2.2.1, Chapter 2).
(c) A slower CPS reading speed (in wpm), as measured with the MNRead chart.
(d) A smaller subjective AoA/range of clear vision, as quantified from a defocus curve.

The near vision assessments in points "a", "b" and "c" above were selected based on the findings of Chapter 2 and each was conducted following the methods described in section 2.4 (see Chapter 2). All of the defocus curves (assessment "d" above) were measured for a range of +3.00DS to -3.00DS in 0.50DS steps, with randomised letter sequences and a randomised lens presentation order, using the equipment and methods described in section 3.3.1 (see Chapter 3). The subjective AoA/range of clear vision was quantified from each defocus curve by the curve-fitting method, using the criterion *the range of defocus that provides the best VA (plus 0.04 logMAR, which was included to account for natural variability in repeated VA measures)*, as described in section 3.3.2 (see Chapter 3).

All of the near vision assessments were conducted binocularly in all of the subjects, and refractive corrections were worn as optical lenses placed in a trial frame at a BVD of 12.0mm if required. PPMC (correlation) coefficients were used to assess the strength of these construct validity hypotheses whilst statistical significance (assessed at p=0.05) was determined by linear regression.

As there is no known 'gold standard' for assessing near visual ability, criterion validity was obtained by ROC curve analysis, using SPSS, with Item 26 used to diagnostically differentiate those with near vision difficulties (a score of 3, 4 or 5) from those without (a score of 0, 1 or 2). Factor Analysis was then conducted using SPSS to assess the dimensionality of the NAVQ. All graphs were produced using Microsoft® Excel®.

4.4.1 Power Analysis

No precedents have been set to define a minimum sample size required for Rasch Analysis and all that is clear is that a *large sample* ought to be used (see section 4.1.4.4). Previous studies that have conducted Rasch Analyses have used sample sizes ranging from 43 subjects (Pesudovs *et al.* 2003) to 386 subjects (Denny *et al.* 2007). Accordingly, in order to determine the minimum sample size required for the present study to achieve a statistical power of 80% (0.80), power analysis was conducted *a priori* based on the PPMC coefficients used for construct validity. Based on the pilot study (Gupta *et al.* 2007), the magnitudes of the PPMC coefficient were expected to be low (0.3) and according to Table 2.9 (see section 2.5.1, Chapter 2), to achieve a power of 0.80 at a significance level of p=0.05 for a PPMC coefficient of 0.3, a minimum sample size of 68 subjects is required. *Post hoc* analysis using G*Power version 3.0.5 (University of Kiel, Germany) (Faul *et al.* 2007) revealed that power ranged from 0.20 (PPMC coefficient of 0.09) to 0.99 (PPMC coefficient of 0.42), for the actual sample size of 87 subjects in this study.

4.5 Results

All of the subjects in this study achieved the minimum best-corrected distance VA required by the inclusion criterion, as shown for each type of presbyopic correction in Table 4.8.

Type of Presbyopic Correction	Mean & Range of Best-corrected Distance VA (LogMAR)	
	RE	LE
Contact Lenses (n=20)	-0.10±0.07 (range: -0.20 to 0.06)	-0.10±0.07 (range: -0.20 to 0.10)
'Accommodating' IOL (n=29)	0.04±0.25 (range -0.20 to 0.30)	0.00±0.16 (range -0.20 to 0.30)
Varifocal Spectacles (n=38)	0.03±0.12 (range: -0.18 to 0.20)	0.04±0.15 (range: -0.18 to 0.20)
Overall (n=87)	*-0.02±0.16 (range: -0.20 to 0.30)*	*-0.02±0.20 (range: -0.20 to 0.30)*

Table 4.8 Mean and range of best-corrected distance VA for each eye of all subjects, by type of presbyopic correction

4.5.1 Category Function

Prior to item reduction, the categories of the NAVQ response scales were analysed and optimised to ensure that the categories were used in a sequential order as intended, and to remove or combine any redundant response options. The initial category function statistics are shown in Table 4.9 for Items 1 to 23 inclusive, and in Table 4.10 for Items 24 and 25.

Category Label / Score	Observed Count	Observed Average	Expected Average	Infit MNSQ	Outfit MNSQ	Structure Calibration	Category Measure
N/A	77	-19.91	-	-	-	-	-
0	1295	-32.38	-32.1	0.97	0.98	NONE	-22.44
1	351	-15.03	-15.5	0.90	0.69	-15.12	-10.67
2	152	-5.32	-5.95	0.86	0.95	-5.49	0.07
3	43	1.30	2.44	1.08	1.07	5.68	10.68
4	14	17.30	15.47	0.53	0.57	14.93	22.29

Table 4.9 Category function of the response scale for Items 1 to 23 of the initial 26-Item NAVQ (n=87)

Category Label / Score	Observed Count	Observed Average	Expected Average	Infit MNSQ	Outfit MNSQ	Structure Calibration	Category Measure
0	35	-17.90	-20.8	2.38	1.82	NONE	-27.08
1	56	-14.45	-13.2	0.82	1.00	-19.97	-14.40
2	45	-5.84	-5.69	1.20	1.21	-8.14	-3.36
3	20	2.53	0.49	1.18	2.04	2.39	5.06
4	9	2.71	5.71	1.63	1.75	7.77	13.67
5	3	4.73	19.99	6.03	7.40	17.95	25.22

Table 4.10 Category function of the response scale for Items 24 & 25 of the initial 26-Item NAVQ (n=87)

The corresponding category function probability curves for each response option are shown in Figure 4.10 for Items 1 to 23 inclusive, and in Figure 4.11 for Items 24 and 25. It can be seen that each response category in the response scale for Items 1 to 23 inclusive had a peak of probability along the attribute scale, indicating that as the amount of attribute (difficulty with near vision) increases, the probability of selecting a higher response option also increases. However, this was not true for response option "3" on the response scale for Items 24 and 25 (Figure 4.11), since this had a peak probability of less than 50%. Since several response options for these items also had poor fit statistics, response scale reduction was conducted, which was then confirmed after the item reduction procedure.

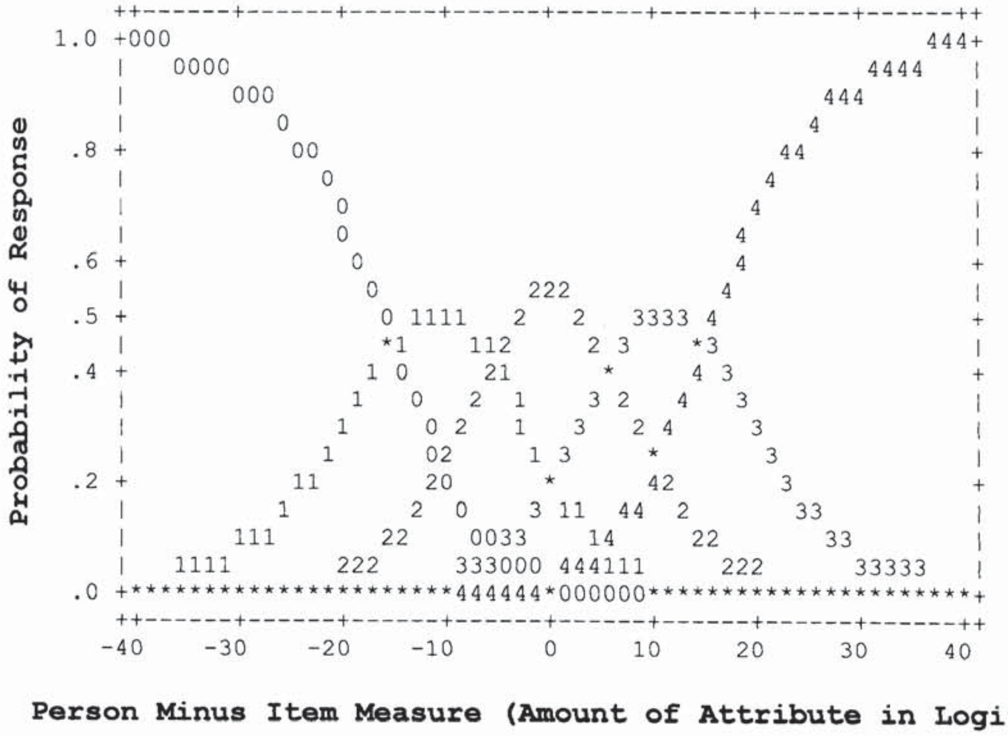

Figure 4.10 Category probability curves for Items 1 to 23 of the initial 26-Item NAVQ response scale, indicating an increasing probability of endorsement of a higher response option with increasing amount of attribute (difficulty with near vision) for all options (n=87)

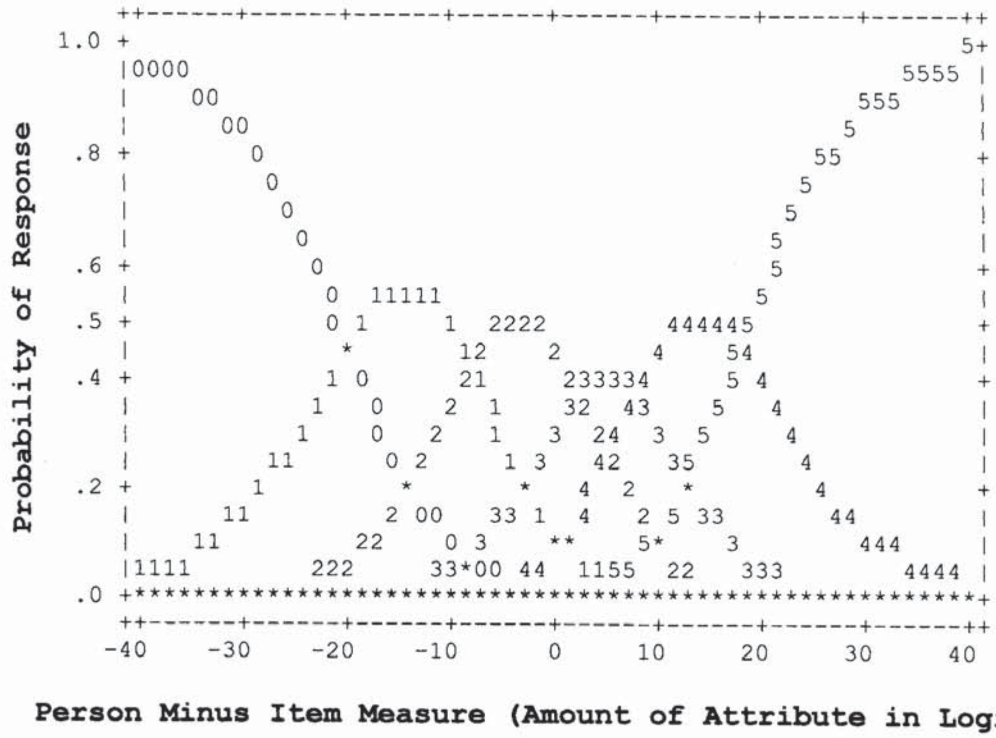

Figure 4.11 Category probability curves for Items 24 and 25 of the initial 26-Item NAVQ response scale, indicating an increasing probability of endorsement of a higher response option with increasing amount of attribute (difficulty with near vision) for all options apart from option "3" (n=87)

The response category function *after* scale and item reduction is shown in Table 4.11 for Items 1 to 23 inclusive and in Table 4.12 for Items 24 and 25. A 4-option response scale was indicated for Items 1 to 23 inclusive, plus a *not applicable* response option, whilst a 3-option response scale was indicated for Items 24 and 25. The response scale descriptors are shown in Table 4.13, which also indicates which options were combined in scale reduction.

Category Label / Score	Observed Count	Observed Average	Expected Average	Infit MNSQ	Outfit MNSQ	Structure Calibration	Category Measure
N/A	39	-19.14	-	-	-	-	-
0	241	-27.06	-26.8	1.07	1.05	NONE	-28.31
1	199	-11.84	-11.8	0.97	0.88	-17.55	-8.87
2	101	1.33	0.87	0.76	0.64	0.82	9.22
3	36	15.01	14.63	1.07	1.12	16.73	27.71

Table 4.11 Category function of the response scale for Items 1 to 23 of the final NAVQ (n=87)

Category Label / Score	Observed Count	Observed Average	Expected Average	Infit MNSQ	Outfit MNSQ	Structure Calibration	Category Measure
0	76	-16.72	-17.9	1.23	1.21	NONE	-17.60
1	46	-4.78	-3.51	1.11	1.17	-6.25	0.00
2	32	8.41	9.37	1.20	1.29	6.25	17.60

Table 4.12 Category function of the response scale for Items 24 & 25 of the final NAVQ (n=87)

Item No.	Response Category Scores	Response Category Descriptors
1 to 23 (Inclusive)	N/A (Missing Data)	Not Applicable *or* Stopped for Non-visual Reasons
	0	No Difficulty
	1	A Little Difficulty
	2	Moderate Difficulty
	3	Extreme Difficulty *or* Stopped for Visual Reasons
24	0	Instantly *or* Very Quickly
	1	Moderately
	2	Very Slowly *or* Never Changes
25	0	Never *or* Rarely
	1	Occasionally
	2	Most of the Time *or* Always
26 (Overall Satisfaction)	0	Completely Satisfied
	1	Very Satisfied
	2	Very to Moderately Satisfied
	3	Moderately to A Little Satisfied
	4	A Little Satisfied
	5	Completely Unsatisfied

Table 4.13 Descriptors for each of the response options of the scales in the final NAVQ

The corresponding category probability curves (Figure 4.12 for Items 1 to 23 inclusive and Figure 4.13 for Items 24 and 25) revealed that each response option had a peak of probability of at least 0.5, indicating the desired increase in probability of selecting a higher response option with an increase in the amount of near vision difficulty.

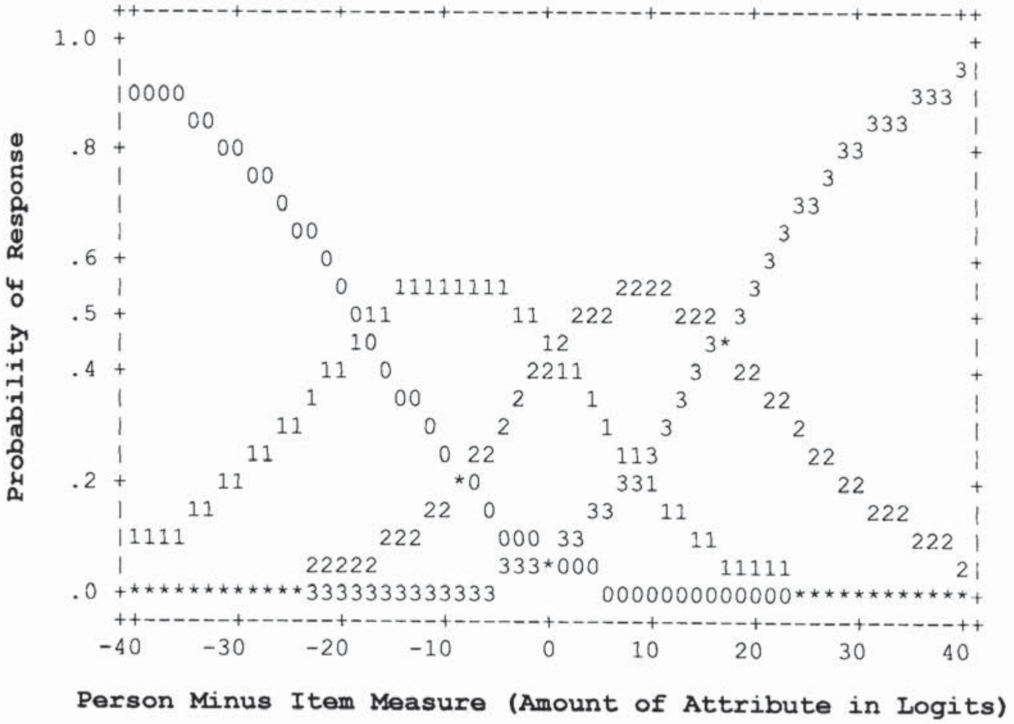

Figure 4.12 Category probability curves for the response scale for Items 1 to 23 of the final NAVQ (n=87)

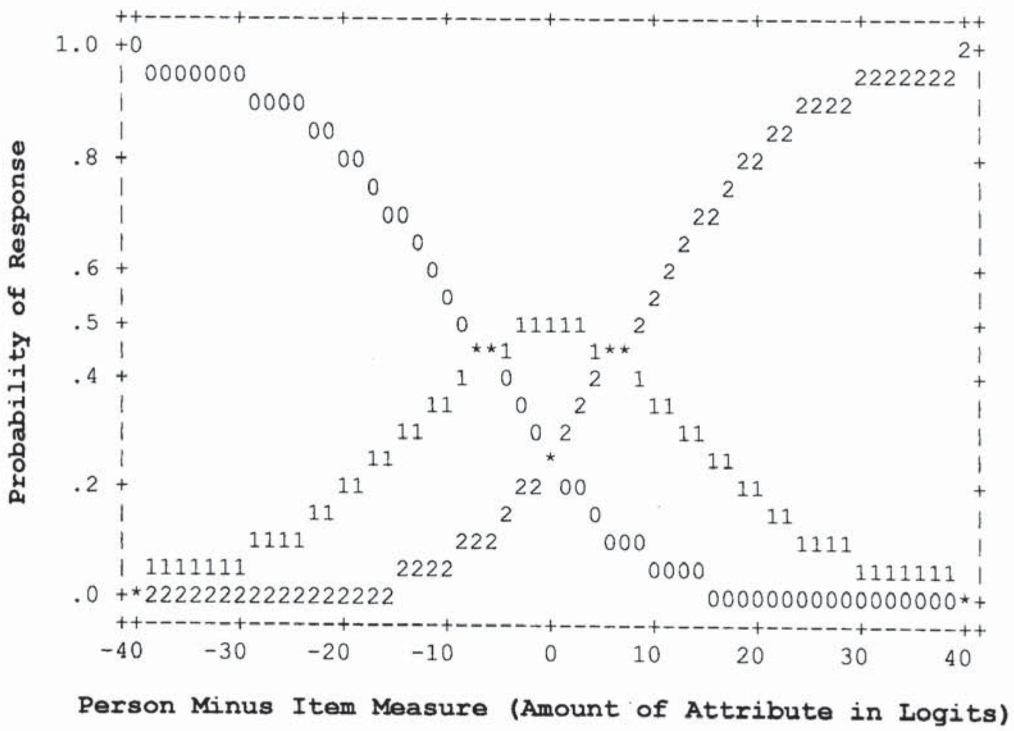

Figure 4.13 Category probability curves of the response scale for Items 24 and 25 of the final NAVQ (n=87)

4.5.2 Item Reduction

After response scale reduction, the initial targeting of the items before item reduction was as shown in Figure 4.14, which has been re-scaled to report scores on a scale of 0-100 logits (USCALE = 6.686, UMEAN = 26.615). The item fit statistics, skew, and kurtosis for these items is shown in Table 4.14, whilst the frequency of endorsement is shown in Table 4.15. The Rasch separation index was 2.95, whilst the Rasch reliability index was 0.90.

```
             <more>|<rare>
                   |T Q17 Dressing
                X  |
 70                +
                   |  Q14 Utensils       Q20 Faces
                   |
                   |  Q9 Money
                   |
                   |S Q19 Colours
 60                +  Q4 Large Print
                   |  Q18 Shelf
                   |  Q15 Appliances
                   |
                   |  Q13 Meals          Q16 Grooming
                X T|
 50                +  Q12 Tools          Q5 Own Writing      Q8 Watch
              XXX  |M
                   |
              XXX  |  Q10 Hobbies        Q3 Mail
                   |  Q6 Computer        Q7 Telephone
                   |
 40          XXXX S+  Q21 Poor Light
           XXXXXX  |  Q22 Haloes Glare
               XX  |S Q23 Focus
            XXXXX  |  Q1 Small Print     Q24 Change
              XXX  |  Q25 Use Aids
                X  |  Q2 Labels
 30             X  +
          XXXXXXX  |
               XX M|  Q11 Handwork
              XXX  |
      XXXXXXXXXXX  |T
             XXXX  |
 20          XXXX  +
                X  |
              XXX  |
                X S|
             XXXX  |
                   |
 10             X  +
         XXXXXXXX  |
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                  T|
                   |
  0      XXXXXXXX  +
             <less>|<frequ>
```

Figure 4.14 Person-item map revealing the targeting of the items in the initial 26-Item NAVQ before item reduction (n=87)

Item Number	Infit MNSQ	Infit ZSTD	Outfit MNSQ	Outfit ZSTD	Skew	Kurtosis
1	0.68	-2.20	0.62	-2.20	0.61	-0.80
2	0.75	-1.70	0.69	-1.70	0.61	-0.64
3	0.89	-0.50	0.62	-1.30	1.48	1.08
4	1.26	0.80	0.36	-0.60	4.64	24.18
5	0.83	-0.80	0.57	-0.90	2.08	3.34
6	0.96	-0.10	1.33	0.90	1.36	0.85
7	0.83	-0.90	0.60	-1.60	1.29	0.58
8	0.92	-0.30	0.51	-1.10	2.27	4.81
9	0.80	-0.40	0.38	-0.50	4.20	18.86
10	0.86	-0.70	1.32	1.00	1.62	2.06
11	0.67	-2.20	0.67	-1.50	0.27	-1.09
12	0.72	-1.20	0.65	-0.50	2.15	5.20
13	0.99	0.10	0.56	-0.70	2.15	3.47
14	0.64	-0.70	0.16	-0.90	5.30	30.10
15	0.70	-1.10	0.45	-0.60	3.46	15.62
16	1.13	0.60	1.73	1.20	2.57	6.64
17	2.18	1.60	0.36	-0.30	5.19	25.55
18	1.06	0.30	0.55	-0.30	3.86	18.99
19	1.48	1.40	3.50	2.00	4.67	24.49
20	1.05	0.30	0.53	-0.20	7.35	58.40
21	1.65	3.20	1.60	2.20	1.00	0.41
22	1.32	1.80	1.58	2.40	0.75	0.36
23	1.21	1.30	1.29	1.40	0.70	-0.24
24	1.14	0.90	1.18	0.70	0.81	-0.72
25	1.36	2.00	1.58	1.80	0.69	-1.15

Table 4.14 Item fit statistics, skew and kurtosis of the initial 26-Item NAVQ before item reduction (n=87)

Option	Frequency of Endorsement (%) for Item Number:																								
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
N/A	0.0	0.0	1.1	1.1	0.0	36.8	0.0	2.3	1.1	2.3	11.5	26.4	2.3	2.3	1.1	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.0	-	-
0	42.5	34.5	67.8	90.8	79.3	40.2	63.2	77.0	92.0	65.5	21.8	54.0	79.3	93.1	83.9	81.6	96.6	85.1	92.0	96.6	50.6	39.1	39.1	23.5	42.6
1	27.6	36.8	16.1	5.7	10.3	12.6	19.5	13.8	5.7	21.8	31.0	16.1	11.5	3.4	13.8	12.6	3.4	11.5	5.7	2.3	35.6	47.1	39.1	51.0	29.4
2	21.8	17.2	12.6	1.1	9.2	8.0	13.8	5.7	1.1	8.0	19.5	2.3	6.9	1.1	0.0	4.6	0.0	0.0	1.1	0.0	11.5	11.5	17.2	25.5	27.9
3	8.0	11.5	2.3	1.1	1.1	2.3	3.4	1.1	0.0	2.3	16.1	1.1	0.0	0.0	1.1	1.1	0.0	1.1	1.1	1.1	2.3	2.3	4.6	-	-
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Table 4.15 Frequency of endorsement data for the 26-Item initial NAVQ before item reduction (n=87)

The Rasch item reduction procedure resulted in elimination of 15 items (Items 2, 4, 5, 8, 9, 10, 12, 13, 14, 15, 16, 17, 18, 19, and 20; see Appendix for the final NAVQ). The targeting of the remaining 10 items is shown in Figure 4.15 (USCALE = 9.057, UMEAN = 36.642).

```
               <more>|<rare>
80                   +
                 X   |
                     |
                     |
                     |
                 X   |
                     |
                     |
70                   +
                     |
                 X T |
                     |
                     |
                     |T
                     |
                     |
60               X   +  Q3 Mail
                     |  Q6 Computer
                XX   |S
                 X   |  Q7 Telephone
                 X   |
                XX   |  Q21 Poor Light
             XXXXX S |
                     |  Q22 Haloes Glare
50            XXXX   +M
                XX   |
                XX   |  Q23 Focus
              XXXX   |  Q1 Small Print    Q24 Change
                     |
                     |  Q25 Use Aids
                 X   |S
                     |
40          XXXXXX   +
                XX   |
                XX   |
                   M |T Q11 Handwork
                 X   |
                     |
                 X   |
       XXXXXXXXXXX   |
30                   +
                XX   |
                XX   |
                     |
             XXXXX   |
               XXX   |
                     |
                   S |
20           XXXXX   +
                     |
                     |
                 X   |
                     |
                     |
          XXXXXXXX   |
                     |
10      XXXXXXXXXX   +
               <less>|<frequ>
```

Figure 4.15 Person-item map revealing the targeting of the items in the final 10-Item NAVQ (n=87)

The item fit statistics, skew, and kurtosis for the 10-Item NAVQ is shown in Table 4.16.

Item Number	Infit MNSQ	Infit ZSTD	Outfit MNSQ	Outfit ZSTD	Skew	Kurtosis
1	0.73	-1.80	0.68	-2.10	0.61	-0.80
3	0.89	-0.50	0.65	-1.30	1.48	1.08
6	1.05	0.30	1.26	0.80	1.36	0.85
7	0.93	-0.30	0.71	-1.30	1.29	0.58
11	0.66	-2.30	0.65	-2.20	0.27	-1.09
21	1.42	2.20	1.27	1.20	1.00	0.41
22	1.09	0.60	1.07	0.40	0.75	0.36
23	1.03	0.30	1.03	0.30	0.70	-0.24
24	1.16	0.90	1.25	1.00	0.81	-0.72
25	1.22	1.30	1.49	1.90	0.69	-1.15

Table 4.16 Item fit statistics, skew and kurtosis of the final 10-Item NAVQ (n=87)

Not all of the items in the 10-Item NAVQ met all of the criteria of Rasch Analysis. However, further item reduction from this list resulted in a decrease in the Rasch separation index, which indicated a loss in questionnaire precision. The item reduction procedure was therefore halted at this point, with the least number of misfitting items remaining. Indeed, it can be seen from Table 4.16 that the degree of misfit in the final item list was not large.

Table 4.17 reveals how raw (ordinal) NAVQ scores can be converted into Rasch scores in logits; intuitively a raw score of '0' equates to a Rasch score of '0' logits and a maximum raw score of '28' equates to a Rasch score of '100' logits.

Raw Score	Rasch Score (Logits)	Raw Score	Rasch Score (Logits)	Raw Score	Rasch Score (Logits)
0	0.00	10	42.47	20	62.18
1	11.85	11	44.43	21	64.49
2	19.38	12	46.34	22	66.98
3	24.21	13	48.24	23	69.70
4	27.91	14	50.12	24	72.78
5	30.99	15	52.02	25	76.43
6	33.68	16	53.94	26	81.12
7	36.10	17	55.90	27	88.41
8	38.34	18	57.92	28	100.00
9	40.45	19	60.00	-	-

Table 4.17 Conversion of raw total NAVQ scores into Rasch total NAVQ scores in logits.

The item characteristic curves for each of the final 10 items in the NAVQ are shown in Figure 4.16 for Items 1 to 11 inclusive, and in Figure 4.17 for Items 21 to 25 inclusive. Although the curves do not reveal a sequential increase in the response scale category endorsed for every increase in attribute amount (difficulty with near vision), a *general* increase is at least observable in each of these curves, as desired.

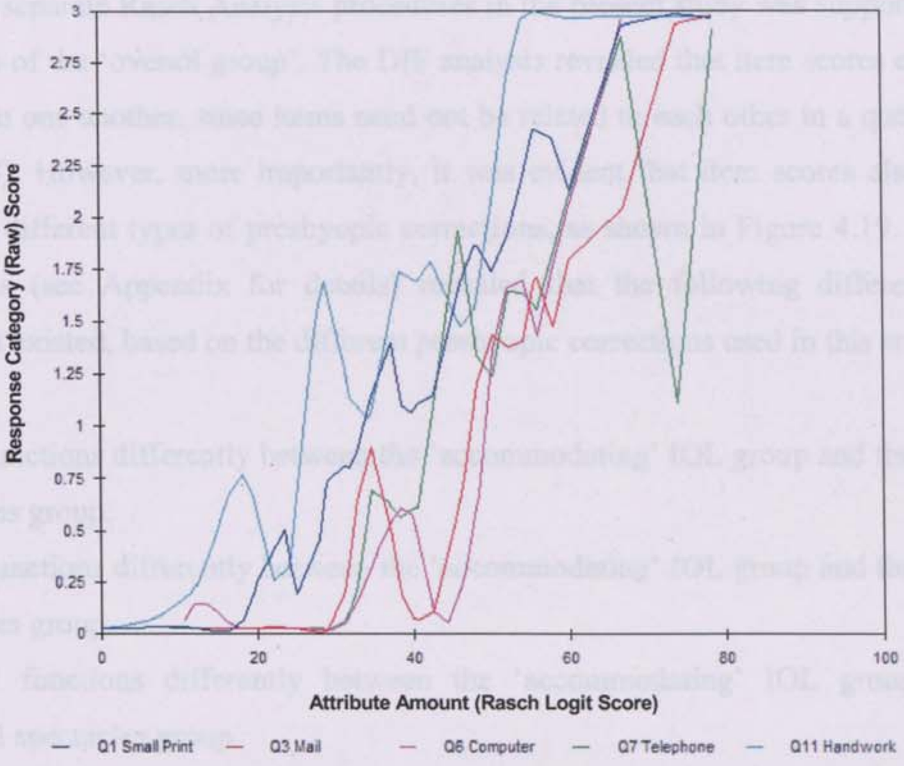

Figure 4.16 Item characteristic curves for the first five Items of the final 10-Item NAVQ (n=87)

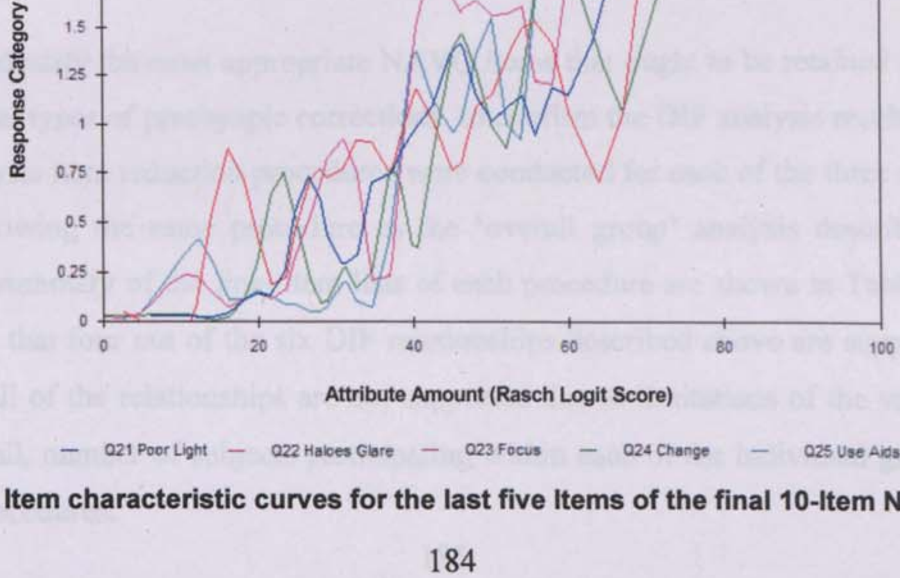

Figure 4.17 Item characteristic curves for the last five Items of the final 10-Item NAVQ (n=87)

4.5.3 Differential Item Functioning (DIF)

It has been suggested that where questionnaire responses have been obtained from several constituent groups, Rasch Analysis ought to be conducted on each separate group as well as collectively so that all common items can be identified (Chang and Chan 1995). Indeed, the need for separate Rasch Analysis procedures in the present study was supported by the DIF analysis of the 'overall group'. The DIF analysis revealed that item scores expectedly differed from one another, since items need not be related to each other in a questionnaire (Figure 4.18). However, more importantly, it was evident that item scores also differed *between* the different types of presbyopic corrections, as shown in Figure 4.19. Statistical DIF analysis (see Appendix for details) revealed that the following differential item relationships existed, based on the different presbyopic corrections used in this study:

- Item 1 functions differently between the 'accommodating' IOL group and the varifocal spectacles group.
- Item 3 functions differently between the 'accommodating' IOL group and the varifocal spectacles group.
- Item 21 functions differently between the 'accommodating' IOL group and the varifocal spectacles group.
- Item 22 functions differently between the 'accommodating' IOL group and the varifocal spectacled group.
- Item 23 functions differently between the 'accommodating' IOL group and the varifocal spectacles group.
- Item 25 functions differently between the contact lenses group and both the 'accommodating' IOL group and the varifocal spectacle group.

In order to identify the most appropriate NAVQ items that ought to be retained for each of the individual types of presbyopic corrections, to confirm the DIF analysis results, separate Rasch Analysis item reduction procedures were conducted for each of the three constituent groups, following the same procedure as the 'overall group' analysis described in this Chapter. A summary of the final item lists of each procedure are shown in Table 4.18 and it is evident that four out of the six DIF relationships described above are supported. It is likely that all of the relationships are not supported due to limitations of the varying, and perhaps small, number of subjects participating within each of the individual group Rasch Analysis procedures.

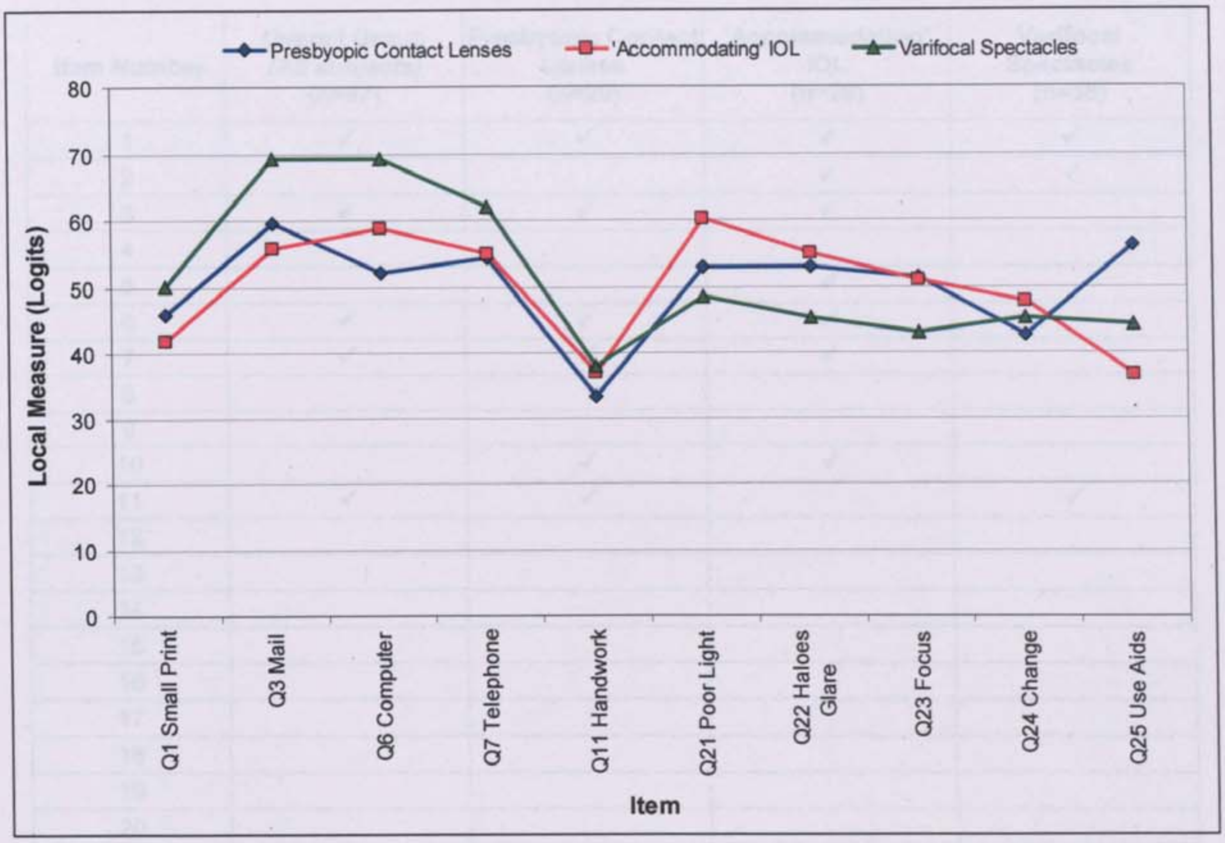

Figure 4.18 Differential Item Functioning (DIF) of the 10-Item NAVQ reveals expected differences in scores between different items (n=87)

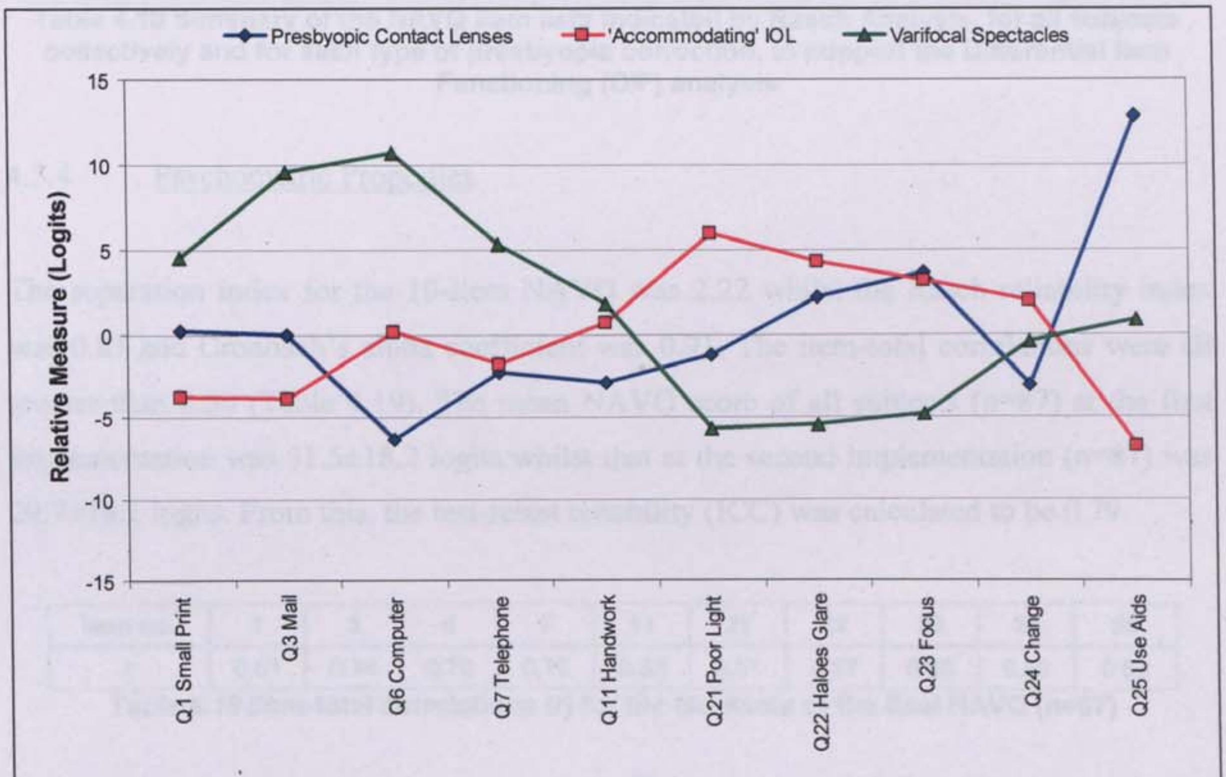

Figure 4.19 Differential Item Functioning (DIF) of the 10-Item NAVQ reveals differences in individual item scores between different types of presbyopic corrections (n=87)

Item Number	Overall Group *(All subjects)* (n=87)	Presbyopic Contact Lenses (n=20)	'Accommodating' IOL (n=29)	Varifocal Spectacles (n=38)
1	✓	✓	✓	✓
2			✓	✓
3	✓	✓	✓	
4				
5			✓	
6	✓	✓	✓	
7	✓	✓	✓	
8				
9				
10		✓	✓	
11	✓	✓		✓
12				
13				
14				
15				
16				
17				
18				
19				
20				
21	✓	✓		✓
22	✓	✓		✓
23	✓	✓	✓	✓
24	✓	✓	✓	✓
25	✓		✓	✓

Table 4.18 Summary of the NAVQ item lists indicated by Rasch Analysis, for all subjects collectively and for each type of presbyopic correction, to support the Differential Item Functioning (DIF) analysis

4.5.4 Psychometric Properties

The separation index for the 10-Item NAVQ was 2.22 whilst the Rasch reliability index was 0.83 and Cronbach's alpha coefficient was 0.91. The item-total correlations were all greater than 0.50 (Table 4.19). The mean NAVQ score of all subjects (n=87) at the first implementation was 31.5±18.2 logits whilst that at the second implementation (n=87) was 29.7±18.1 logits. From this, the test-retest reliability (ICC) was calculated to be 0.79.

Item no.	1	3	6	7	11	21	22	23	24	25
r	0.81	0.74	0.70	0.76	0.83	0.51	0.57	0.66	0.59	0.63

Table 4.19 Item-total correlations (r) for the ten items of the final NAVQ (n=87)

For construct validity, the mean best (distance)-corrected near VA was 0.27±0.26 logMAR and the PPMC coefficient between this and NAVQ scores was 0.42 (R^2=0.18, $p<0.001$) (Figure 4.20).

The mean best (distance)-corrected CPS was 0.51±0.23 logMAR and the PPMC coefficient between this and NAVQ scores was 0.39 (R^2=0.15, p<0.001) (Figure 4.20). The mean best (distance)-corrected CPS reading speed was 166.6±27.4 wpm and the PPMC coefficient between this and NAVQ scores was -0.09 (R^2=0.008, p=0.41) (Figure 4.21).

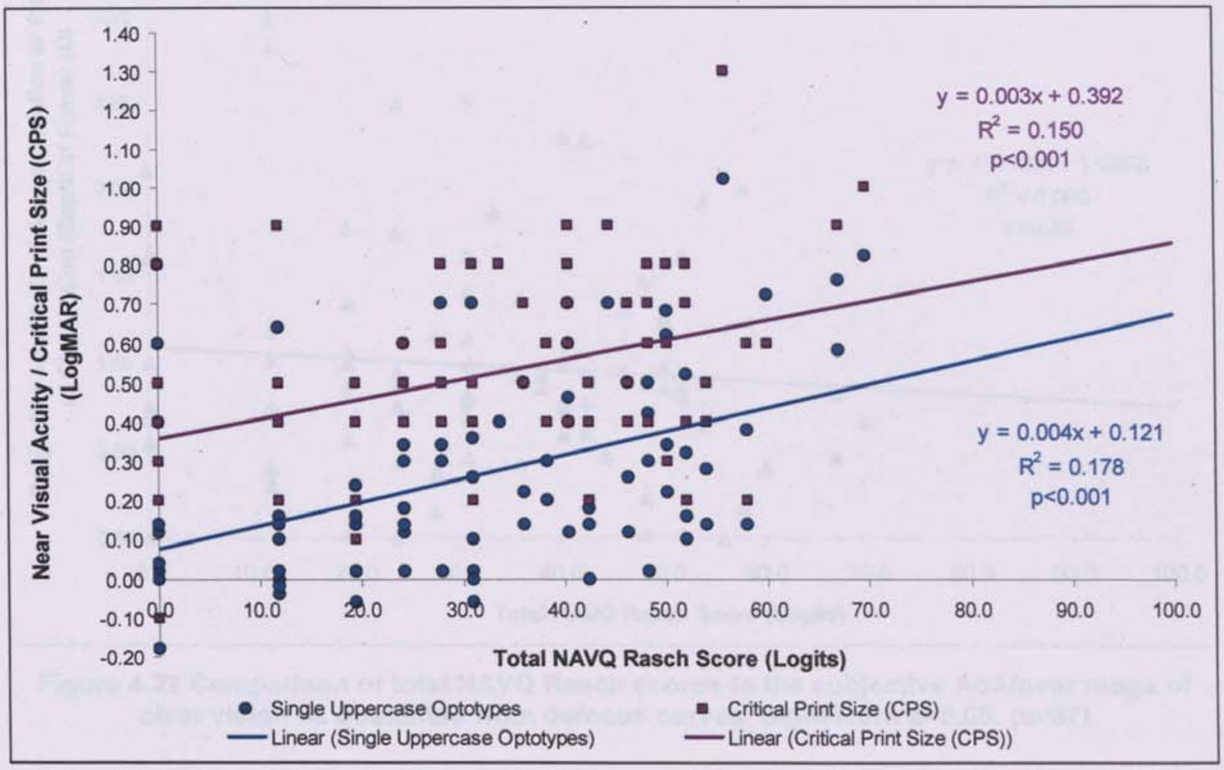

Figure 4.20 Comparison of total NAVQ Rasch scores to best (distance)-corrected near VA and critical print size (CPS). Significant p=0.05. (n=87)

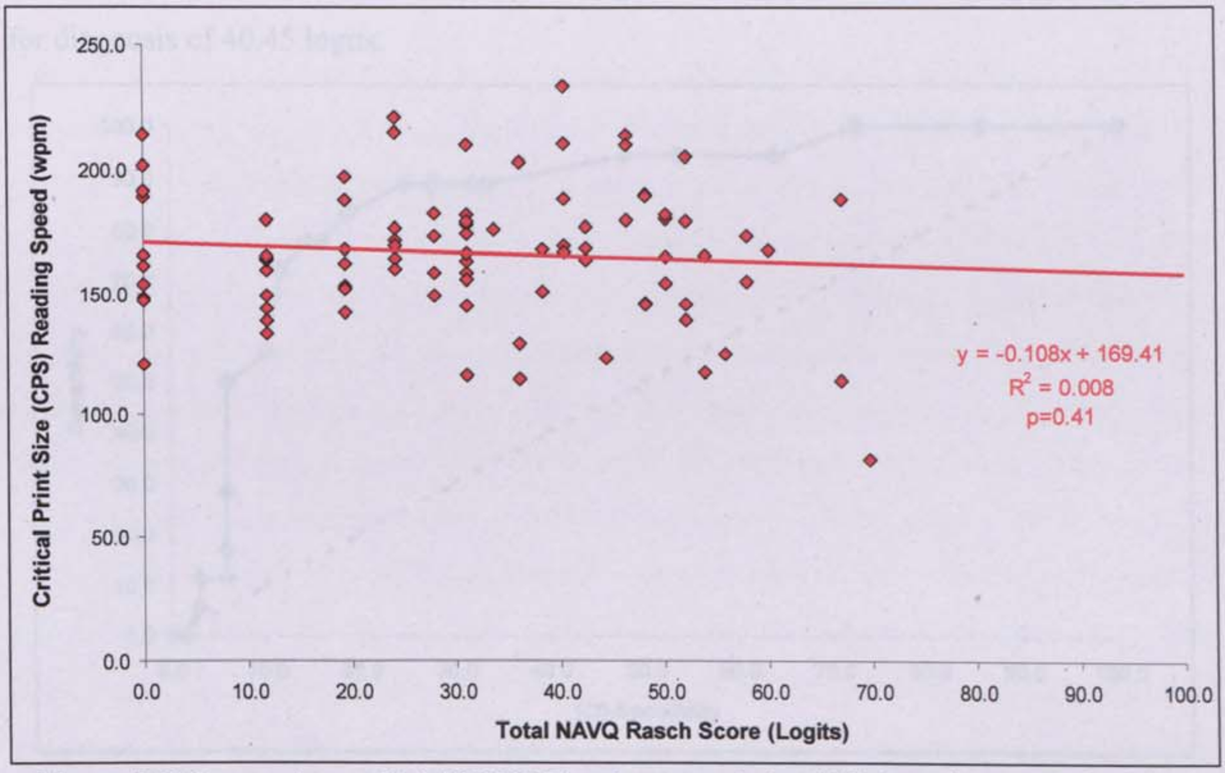

Figure 4.21 Comparison of total NAVQ Rasch scores to best (distance)-corrected critical print size (CPS) reading speed in words per minute (wpm). Significant p=0.05. (n=87)

The mean subjective AoA/range of clear vision was 0.98±0.64D and the PPMC coefficient between this and NAVQ scores was -0.09 (R^2=0.009, p=0.39) (Figure 4.22).

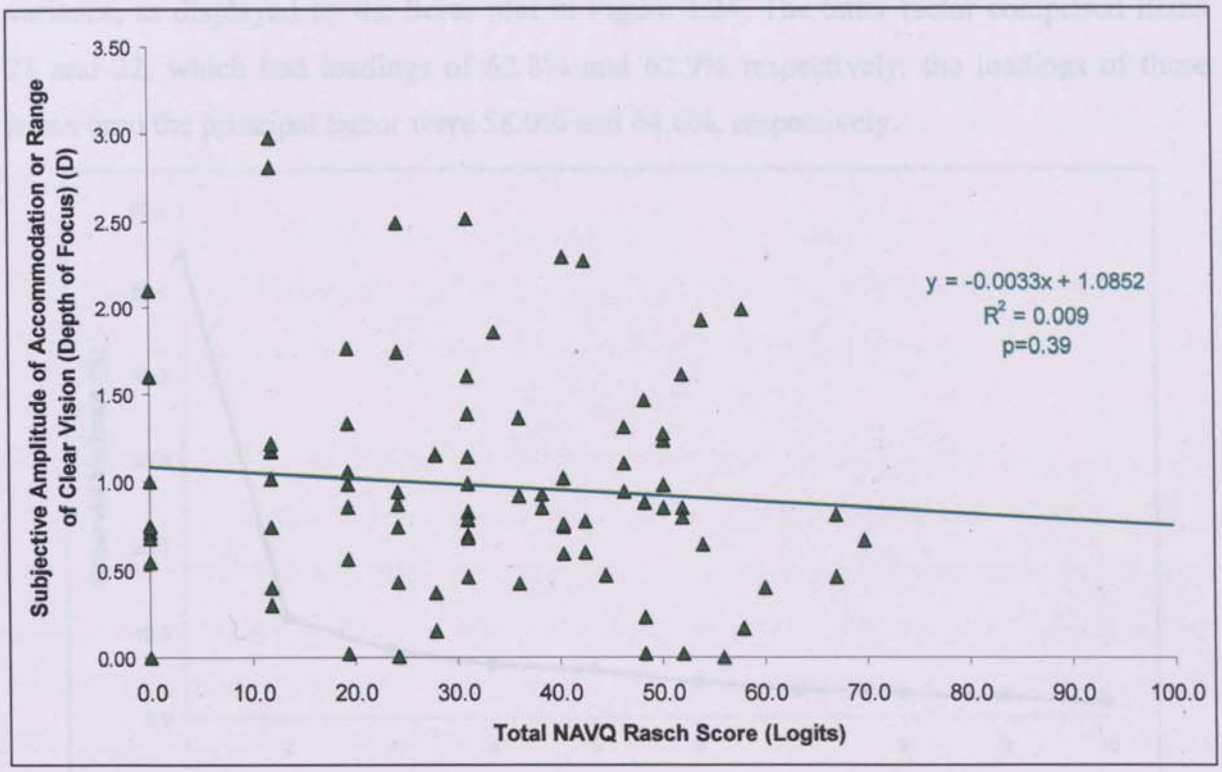

Figure 4.22 Comparison of total NAVQ Rasch scores to the subjective AoA/near range of clear vision as quantified from defocus curves. Significant p=0.05. (n=87)

The ROC curve for criterion validity is shown in Figure 4.23. The area under the curve was 0.86 and 18 subjects were classified as having near vision difficulties, at a criterion score for diagnosis of 40.45 logits.

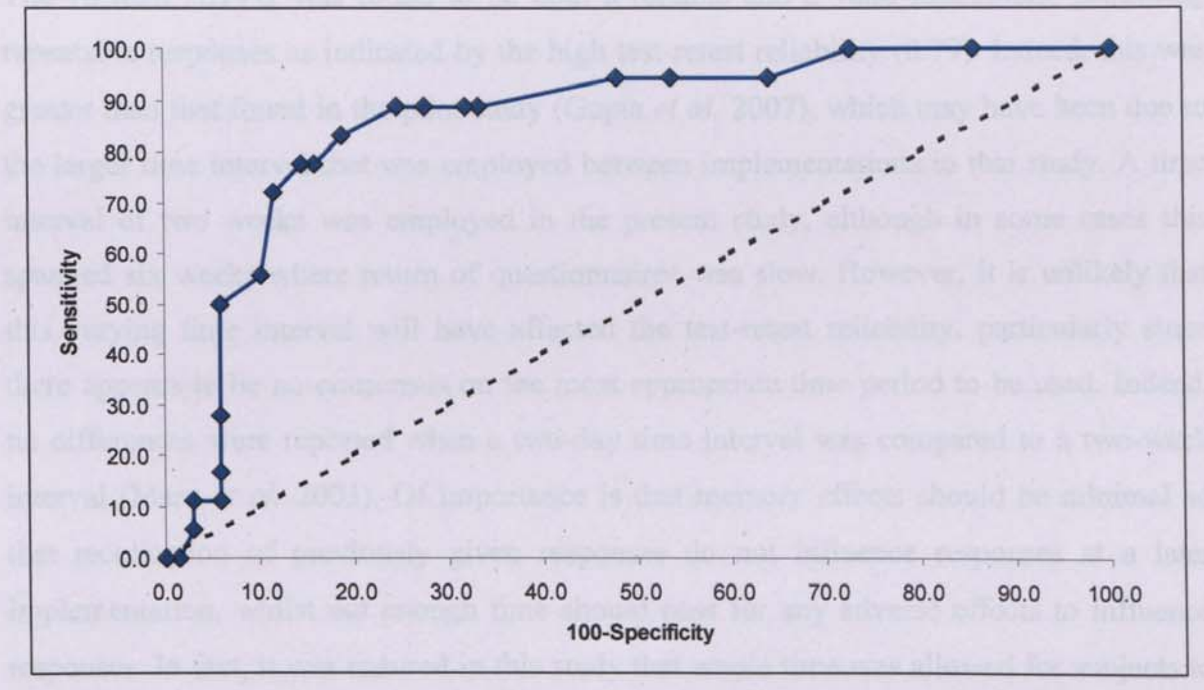

Figure 4.23 Receiver operating characteristic (ROC) curve for the 10-Item NAVQ revealing criterion validity (n=87)

Factor Analysis revealed that the NAVQ comprised one principal factor accounting for 54.3% of the observed variance and a further factor accounting for 11.8% of the observed variance, as displayed by the Scree plot in Figure 4.24. The latter factor comprised Items 21 and 22, which had loadings of 62.8% and 62.9% respectively; the loadings of these items onto the principal factor were 58.0% and 64.6%, respectively.

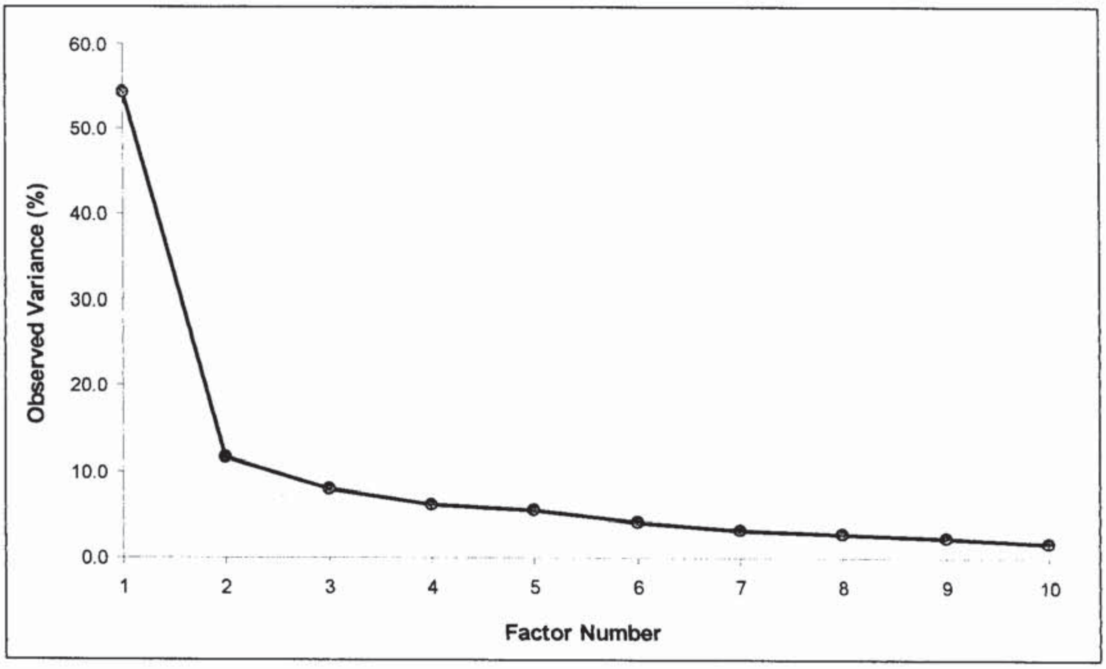

Figure 4.24 Factor Analysis Scree plot displaying two principal factors in the NAVQ (n=87)

4.6 Discussion

The 10-Item NAVQ was found to be both a reliable and a valid instrument, producing repeatable responses as indicated by the high test-retest reliability (0.79). Indeed, this was greater than that found in the pilot study (Gupta *et al.* 2007), which may have been due to the larger time interval that was employed between implementations in that study. A time interval of two weeks was employed in the present study, although in some cases this spanned six weeks where return of questionnaires was slow. However, it is unlikely that this varying time interval will have affected the test-retest reliability, particularly since there appears to be no consensus on the most appropriate time period to be used. Indeed, no differences were reported when a two-day time interval was compared to a two-week interval (Marx *et al.* 2003). Of importance is that memory effects should be minimal so that recollection of previously given responses do not influence responses at a later implementation, whilst not enough time should pass for any adverse effects to influence responses. In fact, it was ensured in this study that ample time was allowed for subjects to adapt to their correction type and for any visual deterioration to have been dealt with.

The high internal reliability of the NAVQ is reflected by the item-total correlations, which were above the recommended minimum of 0.3 (Ramos *et al.* 2003) and even 0.5 (Streiner and Norman 1995). Cronbach's alpha coefficient (0.91) was *just* above the recommended range of 0.7 to 0.9 (Cortina 1993) but indicates that all of the items were well correlated to each other and were therefore relevant to the purpose of assessing near visual ability with presbyopic corrections. Indeed, Cronbach's alpha compared well to that of previously validated near vision questions, including the near vision domain of the NEI-VFQ (0.94) (Mangione *et al.* 1998a), the near vision questions within the VF-QoL (0.89) (Brenner *et al.* 1993), and the near vision domain of the NEI-RQL (0.85) (Hays *et al.* 2003).

The person-item map of the NAVQ revealed that item targeting was generally too easy relative to the ability of the subjects. This could be interpreted as a lack of scope of the items to cater for more capable subjects. Conversely, one should not expect presbyopic corrections to cause a level of difficulty that could be expected of, for example, low vision patients. In fact, subjects in this study were known to have 'normal' vision, with no ocular pathology, and therefore would have been fairly able. Of importance is that the NAVQ was able to discriminate between those subjects with near vision difficulties and those without. The separation index (2.22) provided evidence of this, suggesting enough precision to detect two levels of difficulty, and further support was provided by the ROC curve analysis, where the area under the curve (0.86) was well above the minimum required (0.50). The criterion Rasch score for discrimination is 40.45 logits (range 0-100 logits).

For construct validity NAVQ scores were weakly correlated to near VA, CPS, CPS reading speed and the subjective AoA/range of clear vision. These correlations were expected to some extent based on the findings of the pilot study (Gupta *et al.* 2007). In particular, it was not surprising that CPS reading speed did not correlate well to NAVQ scores since the former is influenced by non-visual factors (see section 2.2, Chapter 2). It could also reflect the manner whereby the high contrast nature of the MNRead chart poorly represents reading materials that are typically encountered in daily life. In addition, correlation of NAVQ scores to the AoA/range of clear vision is dependent on one's preferred working distances, and the type and frequency of work. If these are not sufficiently achieved within the provisions of the correction, then a subject's ratings of near visual ability will reduce. For example, subjects with a low AoA may be fully satisfied (low NAVQ score) if they typically work at long distances or rarely do near work whilst those with a large AoA may feel aggrieved (high NAVQ score) if near work cannot be sustained for long periods.

The weak correlations of near VA and CPS to NAVQ scores may be explained by the finding that less than 33% of the items related specifically to reading tasks. Two items in the NAVQ relate to the use of computers and mobile phones/calculators, which is understandable given the technological state of the world we live in today. Furthermore, one item relates to more practical tasks such as sewing and knitting, which are also important, for example, for relaxation and building social contacts. Naturally the inclusion of such activities where reading may not be a major feature will reduce correlations with reading metrics such as near VA and CPS. In fact, even though reading is of great value to society in general, the subjects in this particular cohort may not have regarded reading as such an important task, thus reducing the correlations with NAVQ scores. Correlation of NAVQ scores to *low contrast* near VA may have been beneficial instead, for further construct validity, since contrast sensitivity better reflects real world visual function (Amesbury and Schallhorn 2003). However, this would not have affected the final questionnaire design. Also, of importance is that the correlations to near VA and CPS in this study were found to be significant and were also within the required range for such questionnaires (Pesudovs *et al.* 2007), thus providing support of validity for the NAVQ.

Factor Analysis revealed that there were two principal factors to the NAVQ. Although this suggests that the questionnaire is not unidimensional, the items within the second factor (Items 21 and 22) had similar (high) loadings to the principal factor. These items investigate the effects of lighting and glare on near visual ability and can therefore be considered to be a subscale of the NAVQ, which in turn is still actually unidimensional.

4.6.1 Limitations

It is possible in this study that the inclusion of subjects that had received only monocular 'accommodating' IOL implants may have produced lower NAVQ scores in this particular group of subjects, especially if sufficient near visual ability was present in the unoperated eye. However, NAVQ scores of these subjects (mean of 31.4±22.9 logits) were not significantly different to subjects who received bilateral implants (mean of 46.9±10.4 logits) (independent Student's T-Test, t=-2.0, p=0.07; calculated using SPSS) and therefore this is unlikely to have been a major cause of error. Furthermore, these subjects represented only a small proportion of the overall group (10 out of 87; 11.5%), whilst the resulting *modified monovision* correction in fact represents a valid correction type for analysis.

The number of participants in this study may have limited the Rasch Analysis results since a large sample size is required for its statistical inferences to be accepted with confidence. However, a minimum sample size requirement has not been indicated in the literature. In fact, the subject numbers in this study were limited by the nature of the corrections themselves. Indeed, it is not very common for large numbers of subjects to receive corrections such as 'accommodating' IOLs, primarily since these are as yet largely experimental. Consequently, although corrections such as varifocal spectacles are more prevalent, the inclusion of a large cohort of these subjects would have induced a bias towards their perceptions. Therefore, the sample sizes of this and the contact lens group were limited according to the number of subjects that could be recruited for the 'accommodating' IOL group. It is perhaps for this reason that the DIF results were also not fully supported by the individual group Rasch Analyses, and therefore further research is required with larger sample sizes of each. The overall sample size did at least provide adequate statistical power based on the magnitudes of the correlation coefficients observed for construct validity (see section 4.4.1). In turn, these weak correlations indicate the existence of a definite difference between objective clinical evaluations and subjective perceptions of near visual ability, necessitating the questionnaire developed. Indeed, if these metrics were more cost effective and less time consuming to assess, then the purpose of developing this questionnaire would be defeated (Streiner and Norman 1995).

Of greatest importance from this study is that this questionnaire now provides the basis for the evaluation of other presbyopic corrections not included in this study, for example multifocal IOLs, as well as new or improved techniques as and when these are developed. Furthermore, the validity of the NAVQ can then be expanded, whilst the confidence in the statistical inferences made by Rasch Analysis will also be improved.

The use of questionnaires to evaluate subjective outcomes and ability in healthcare have been criticised for failing to account for realistic help subjects may seek in order to overcome a difficulty (for example, one may exert extra effort or seek external support and/or encouragement from a friend or relative), and for failing to recognise the varying importance patients may place on a task or activity (for example, one may be happy to refrain from performing a particular task if it means that they can do another instead) (Feinstein *et al.* 1986). However, despite these issues, questionnaires are an increasingly important means of assessing outcomes in many health-related fields, and should at least be considered to ensure that the results of any intervention are adequate for the individual.

4.7 Conclusion

This study has shown that the NAVQ is a reliable and a valid measure of subjective perceptions of near visual ability, and the level of satisfaction with this, as conferred by a variety of presbyopic corrections. The questionnaire should therefore be incorporated into any evaluation of visual function with techniques such as 'accommodating' and multifocal IOLs, and presbyopic (multifocal and monovision) contact lenses. Indeed, the clinical usefulness of the NAVQ, along with the findings of Chapters 2 and 3, is in the next Chapter demonstrated as part of the evaluation of visual function with a new centre-near aspheric design, simultaneous vision multifocal contact lens.

CHAPTER 5

Clinical Comparison of Visual Function with a Simultaneous Vision Multifocal Contact Lens to Monovision and Best Binocular Spectacle Correction

5. Introduction

There are many methods of vision correction available to the presbyope who does not wish to use spectacles, as described in Chapter 1. Of these, a contact lens correction is perhaps the most common choice. Indeed, the average age of contact lens wearers in the UK has steadily increased over the last ten years (Morgan *et al.* 2007) and as a result, 36% of all fittings during this period were for people aged 40 years or over (Morgan and Efron 2006). The binocular correction of distance vision with contact lenses, and the use of spectacles for near vision, is the simplest option available for presbyopes, but does not leave them completely spectacle-free (Stein 1990). The relative simplicity of fitting monovision and simultaneous vision contact lenses means that these are the most preferred choices, as opposed to alternating vision designs. Monovision however only slightly improves VRQoL in presbyopes compared to pre-presbyopic emmetropes (McDonnell *et al.* 2003), and therefore better contact lens designs are continually sought in order to improve this.

5.1 Visual Performance of Presbyopic Contact Lenses

The performance of monovision and simultaneous vision contact lenses is dependent on the factors described in sections 1.3.1 and 1.3.2 (see Chapter 1), respectively. The effects of monovision on the CSF, which better describes real world visual function than VA (Amesbury and Schallhorn 2003), have already been described (see section 1.3.1.1, Chapter 1) and the effects of simultaneous vision contact lenses are similar, owing to a reduction in retinal image contrast from the presence of superimposed images (McGill *et al.* 1987, Charman and Saunders 1990, Zandvoort *et al.* 1993, Bierly *et al.* 1995, Soni *et al.* 2003). However, the reduction may not be *clinically* significant since Van Meter et al. (1990) reported the distance and near CSF to be within 'normal' limits as defined by the Vision Contrast Test System (VCTS) (Vistech Consultants Inc., Dayton, OH., USA.) (Ginsburg 1984), whilst the CSF may be superior at intermediate distances, especially with aspheric lenses, due to the additional visual foci (Collins *et al.* 1989a, Bradley *et al.* 1993).

It is possible that the performance of presbyopic contact lenses is also dependent on the material used, with RGP simultaneous vision lenses shown to provide a comparable CSF to best binocular vision where soft materials of a similar design do not (Rajagopalan *et al.* 2006). This may be due to the superior surface optics of the RGP material (Rajagopalan *et al.* 2007). However, in addition to assessing the CSF, it is also important to consider other elements of visual function including VA (see section 5.1.1), the range of clear vision (see section 5.1.2), stereoacuity (see section 5.1.3), fusional vergence range (see section 5.1.4), and task performance (see section 5.1.5).

5.1.1 Visual Acuity

Unlike the CSF, which is measured using sine-wave gratings (Figure 5.1), VA is usually measured with letter optotypes (see Chapter 2) and therefore may not be affected by presbyopic contact lens wear in the same way. Binocular distance VA with monovision correction is better than best monocular VA, but it is poorer than the best binocular VA, regardless of the amount of anisometropia (Collins *et al.* 1993). This primarily reflects the role of interocular blur suppression (see section 1.3.1.2, Chapter 1), which can reduce VA by 0.08-0.10 logMAR (Jain *et al.* 1996). In contrast, interocular blur suppression is not possible with simultaneous vision contact lenses, since out-of-focus contours are present in both eyes, and VA is therefore reduced by 0.80 to 1.40 lines of acuity (about 0.10-0.15 logMAR) (Sheedy *et al.* 1991). However, the magnitude of this reduction may vary depending on the lens design, with distance VA reportedly better with centre-distance designs and near VA reportedly better with centre-near designs (McGill *et al.* 1987, McGill and Erickson 1988, Hutnik and O'Hagan 1997).

Figure 5.1 The Contrast Sensitivity Function – *reproduced and modified with permission from Mather (2006) ©2006, from the website: http://www.psypress.com/mather/resources/topic.asp?topic=ch08-tp-01, accessed 10:40, 19/10/2007*

Binocular VA with monovision and simultaneous vision contact lenses will also be impacted upon by the presence of any uncorrected astigmatism. With best binocular vision, astigmatic blur in one eye may be compensated by interocular suppression in favour of the other clearer eye, without great detriment to binocular VA (Collins *et al.* 1993). However, this process is not possible with monovision or simultaneous vision since the alternative eye is already substantially more blurred. VA may then be reduced by 0.31 logMAR for up to 1.00DC of uncorrected astigmatism in monovision (Collins *et al.* 1993), and possibly more with simultaneous vision contact lenses and for near vision.

Although assessment of VA with high contrast optotypes is well correlated to subjective reports of visual performance (Zandvoort *et al.* 1993), assessment of VA with low contrast optotypes and differing levels of illumination provides greater sensitivity to detecting the effects of blur, and this is therefore advised where the CSF is not measured (Shah and Gundel 2000). Compared to monovision and best binocular vision, VA measured in low contrast and low illumination conditions with simultaneous vision contact lenses is poorer, primarily due to the lack of interocular blur suppression (Back *et al.* 1992a) and due to pupil size dependency (see section 1.3.2.2, Chapter 1) (Guillon *et al.* 2002), respectively.

In addition to evaluation of central VA it is also important to consider peripheral VA, as this reflects any adverse affect on the ability to carry out tasks such as object detection and mobility. However, Collins et al. (1989b) reported that the natural reduction in VA of the eye, from 0.00 logMAR centrally to 1.30 logMAR peripherally, was not compounded by monovision correction regardless of the amount of anisometropia. They suggested that this may reflect the manner whereby 50% of the primary visual cortex is disproportionately assigned to process the central 10° of the visual field, making visual perception less sensitive to the detection of peripheral blur (Azzopardi and Cowey 1993, Horton 2006).

5.1.2 Binocular Range of Clear Vision

The binocular range of clear vision achievable with presbyopic contact lenses depends on the AoA, DoF (see Chapter 3) and the lens power of each eye. With monovision, the far point or *distal extent* of this range corresponds to optical infinity, as conferred by the 'distance eye', whilst the near point, referred to as the *proximal extent*, is dependent on the maximum AoA and the DoF of the 'near eye' (Figure 5.2) (Erickson 1988).

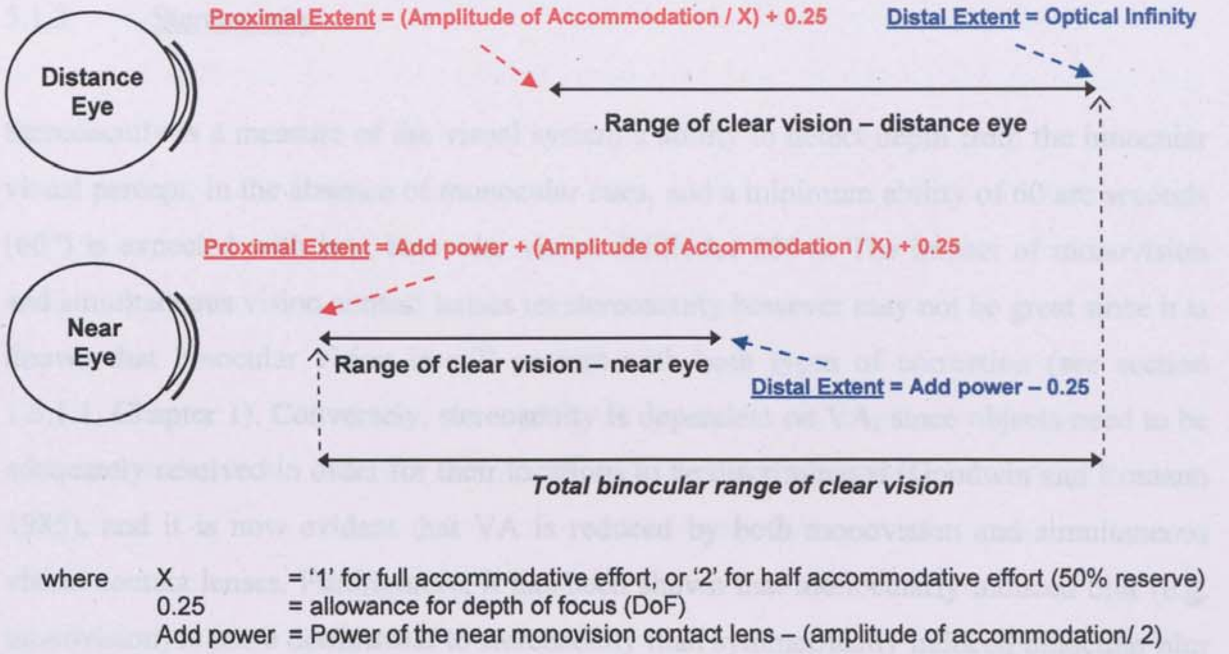

Figure 5.2 The binocular range of clear vision in monovision is governed by the amplitude of accommodation (AoA), depth of focus (DoF) and the contact lens power of the 'near eye'– *produced based on a description in Erickson (1988)*

Erickson (1988) suggested that the range of clear vision with monovision extends from optical infinity to 36cm, for near additions of up to +1.50DS, whilst additions of +2.00DS or higher reduce the distal extent of the near eye, adversely affecting visual function at intermediate distances. This finding was supported by Legras et al. (2001) and reflects the mechanism of alternate interocular blur suppression such that fixation can change from one eye to the other as objects transition from the clear range of one eye to the clear range of the other. However, this process can be adversely impacted upon by the presence of strong ocular dominance since alternate interocular blur suppression becomes more difficult (Schor and Erickson 1988). Furthermore, since the dominant eye governs the accommodation response, if this is corrected for distance vision the reduced ability to alternately suppress will result in a reduced range of clear vision that is similar to that of the monocular distance eye. These effects however, are more likely to hinder the younger presbyope owing to the better accommodative ability (Schor and Erickson 1988).

The binocular range of clear vision conferred by simultaneous vision contact lenses is reportedly better than best binocular vision by as much as 4.40D (Plakitsi and Charman 1995). Fisher et al. (1999) reported no differences between monovision and two different simultaneous vision contact lenses, although Situ et al. (2003) reported the range to be smaller with monovision. As discussed in Chapter 3 however, evaluation of the range of clear vision depends upon the method of measurement and definition of clear vision used.

5.1.3 Stereoacuity

Stereoacuity is a measure of the visual system's ability to detect depth from the binocular visual percept, in the absence of monocular cues, and a minimum ability of 60 arc seconds (60") is expected with best binocular vision (Millodot 2004). The impact of monovision and simultaneous vision contact lenses on stereoacuity however may not be great since it is known that binocular vision is still present with both types of correction (see section 1.3.1.1, Chapter 1). Conversely, stereoacuity is dependent on VA, since objects need to be adequately resolved in order for their locations to be discriminated (Goodwin and Romano 1985), and it is now evident that VA is reduced by both monovision and simultaneous vision contact lenses. Furthermore, it has been shown that monocularly induced blur (e.g. monovision) is more detrimental to stereoacuity than symmetrically induced binocular blur (e.g. simultaneous vision) (Larson and Lachance 1983). Consequently, stereoacuity with monovision is reportedly reduced to 87.5" (Jain *et al.* 1996), whilst that with simultaneous vision varies from 60" (Sheedy *et al.* 1991) to 126" (Richdale *et al.* 2006) depending on the contact lens design. However, reports of stereoacuity also vary greatly from one study to another because of differences in the type of stereotest used (Garnham and Sloper 2006).

Differences in stereoacuity between various stereotests primarily arise from the presence of monocular depth cues that can overestimate true stereoacuity. Practical methods of measurement that require the physical alignment of objects typically yield the largest over-estimates, since they are the most liable to monocular depth cues such as *perspective* and *overlapping contours*. Stereoacuity evaluations for monovision correction therefore range from 19" to 55" (Ong and Burley 1972, Back 1995). The Stereo Fly (also known as Titmus Fly) test (Stereo Optical, Chicago, IL., USA.) on the other hand uses polarised filters to present different but real contoured stimuli to each eye. However, these stimuli are also visible when viewed monocularly and therefore stereoacuity can be over-estimated, with estimates for monovision ranging from 50" (Kastl 1983) to 96" (Koetting 1970), or more variably to 384" (Gutkowski and Cassin 1991). Random dot stereograms such as the TNO stereotest (Laméris Ootech B.V., NC Nieuwegein, Holland) are perhaps the most ideal test of stereoacuity since these are not susceptible to monocular cues. However, these tests are considered to be more difficult since the manner in which the contours must be cortically generated from monocular stimuli is considered to be a more complex task than perceiving real stimuli. Furthermore, complete dissociation of the eyes is required (using red-green lenses), which is more difficult to achieve for older persons (Garnham and Sloper 2006).

Of importance is that despite measurable reductions in stereoacuity with both monovision and simultaneous vision contact lenses, subjective reports of the effect of this on near vision activities that are dependent on this function, e.g. reading and knitting, have actually been fairly minimal (Gutkowski and Cassin 1991, Richdale *et al.* 2006, Evans 2007).

5.1.4 Fusional Vergence Range

Whilst diplopia cannot be avoided with simultaneous vision, owing to the presence of superimposed retinal images, interocular blur suppression works to prevent this in monovision and it is therefore important to assess this ability. Measuring the fusional vergence range, which represents the amount of retinal disparity or 'visual stress' that can be absorbed before binocular fusion is disrupted, can allow this and typically requires the placement of increasing amounts of prism in front of one eye, under binocular conditions, until diplopia is reported ('break' point). This can be measured at distance and near, with typical values for best binocular vision shown in Table 5.1 (Evans 2002).

	Divergent Reserve (Base In)	Convergent Reserve (Base Out)
Distance	7 ± 3Δ	19 ± 8Δ
Near	21 ± 4Δ	21 ± 6Δ

Table 5.1 Normal distance and near fusional vergence ranges. Values specified are those needed to induce diplopia ('break' point) – *reproduced from Evans (2002)*

A small but significant esophoric change, in the order of 1-3Δ, may be observed in the distance fusional range with monovision correction, if the dominant eye is corrected for distance vision (McGill and Erickson 1991a). However, a larger change may be observed if the non-dominant eye is instead corrected for distance vision, which can increase visual stress and therefore produce unwanted asthenopic symptoms (McGill and Erickson 1991b).

5.1.5 Task Performance

In order to better understand the effect of presbyopic contact lens wear on near visual ability, Sheedy et al. (1988) devised a set of occupational tasks, with each having different stereoacuity demands. The tasks involved placing wooden rods into straws that were fixed at different orientations in a box, filing cards alphabetically within a drawer, and counting the frequency of appearance of a particular letter of the alphabet in a paragraph of text.

It was found that task performance with monovision correction was 2-6% poorer compared to best binocular vision, although monovision performance was significantly better than best monocular vision in the task that required the greatest stereoscopic demand, highlighting the importance of the retaining some binocularity (Sheedy *et al.* 1988). There is however no considerable dependency of task performance on the strength of interocular blur suppression, since Schor et al. (1989) reported a high correlation only for the card-filing task, which has moderate stereoacuity demand, and not for the other two tasks.

Sheedy et al. (1991) found task performance with a centre-near annular design simultaneous vision contact lens to be poorer compared to best binocular vision, despite good stereoacuity. Similarly, Fisher et al. (1999) found that the ability to thread a needle was impaired with simultaneous vision compared to best binocular vision, which they believed may be due to the reduced VA. However, Rajagopalan et al. (2006) found no difference in task performance between best binocular vision, simultaneous vision and monovision, but suggested that soft materials under-perform for an unknown reason.

5.2 Study Aim

The PureVision® Multi-focal contact lens (Bausch & Lomb Corp., Rochester, NY., USA.) (Figure 5.3) is a centre-near simultaneous vision design that has an aspheric front surface and a spherical rear surface. It has a back optic zone diameter of 8.0mm, a back optic zone radius of 8.6mm and a total diameter of 14.0mm. The lens is manufactured from a silicone hydrogel material and was introduced for the UK presbyopic market in July 2006.

Figure 5.3 The Bausch & Lomb PureVision® Multi-focal contact lens is available as a 'low addition' lens (left in picture) and a 'high addition' lens (right in picture) – *photographed at the Aston University Optometry Clinic*

The PureVision® Multi-focal contact lens is available as a 'low addition' lens and as a 'high addition' lens, to cater for two ranges of near spectacle reading addition powers.

The 'low addition' lens has a central aspheric region carrying the near refractive power and a peripheral spherical region carrying the distance refractive power; this lens is used where the near spectacle addition is +1.50DS or less (Figure 5.4a). The 'high addition' lens has a central spherical region carrying the near refractive power, whilst an aspheric intermediate surface links this to a peripheral spherical region carrying the distance refractive power; this lens is used where the near spectacle addition is +1.75DS or more (Figure 5.4b).

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Illustration removed for copyright restrictions

Figure 5.4 **(a) Theoretical power profile of the 'low addition' PureVision® Multi-focal**
(b) Theoretical power profile of the 'high addition' PureVision® Multi-focal
(Images courtesy of Bausch & Lomb Corp., Rochester, NY., USA.)

The purpose of this study was to clinically compare visual function with the PureVision® Multi-focal contact lens to monovision correction with PureVision® single vision lenses, and to best binocular vision with spectacle correction, based on the standardised near vision metrics described in Chapters 2, 3 and 4.

5.3 Method

Twenty subjects (11 males, 9 females) of mean age 55.0±5.1 years (range 49 to 67 years) were recruited from the Optometry Clinic of Aston University and from staff of the university who responded to information leaflets and emails advertising this clinical trial. All subjects were required to meet the following eligibility criteria:

(a) Maximum spectacle astigmatism of 1.00DC in each eye.
(b) A best-corrected distance VA of at least 0.00 logMAR in each eye.
(c) An absence of binocular vision anomalies, including decompensated heterophoria, heterotropia and amblyopia, as confirmed by cover tests and fixation disparity tests, using the Mallett unit at distance (six metres) and near (40cm).
(d) An absence of ocular pathology, including glaucoma, AMD, diabetic retinopathy, cataract, and dry eye.
(e) An absence of systemic health problems or medication that would contraindicate contact lens wear, including diabetes or immunosuppressive conditions or medication.

Previous contact lens wear was not a requirement of subjects and only those who expressed a desire to wear contact lenses were selected to ensure adequate motivation. This was confirmed during a detailed history and symptoms discussion at the initial visit for the study. At this visit, the author also examined all of the subjects to ensure that the eligibility criteria were met. This included slit lamp examination of the anterior eyes and tear film, direct ophthalmoscopy, keratometry using the Bausch & Lomb one-position keratometer and a full subjective refraction with cross-cylinder and binocular balancing. The following clinical tests of visual function were then conducted on all eligible subjects, binocularly and under consistent room illumination of 500 lux (chart luminance of 120cdm^{-2}), whilst subjects wore the best binocular spectacle correction; subjects wore their own spectacles if the refraction was optimal or optical trial lenses placed in a trial frame if this was adjusted:

(a) Distance VA at 6m using the computerised *Test Chart 2000 Pro* (Thomson Software Solutions, Hatfield, Herts., UK.) logMAR chart.

(b) Distance CSF at 3m using the VCTS 6500 chart (Vistech Consultants, Dayton, OH., USA.) and a 4-alternate forced choice method (Ginsburg 1984, Ginsburg *et al.* 1984).

(c) Intermediate VA at 80cm (selected as a typical working distance to view a computer screen) using the ETDRS Near LogMAR Chart (Precision Vision™, La Salle, IL., USA.) (only the distance refraction was worn whilst varifocal spectacle wearers – see section 5.5 – were instructed to use only the distance portion of their lenses).

(d) Near VA at 40cm using the ETDRS logMAR chart, in accordance with the findings of Chapter 2 and measured as described in section 2.4 (see Chapter 2).

(e) CPS in logMAR and CPS reading speed in wpm at 40cm using the MNRead chart (Lighthouse Low Vision Products, Long Island City, NY., USA.), in accordance with the findings of Chapter 2 and measured as described in section 2.4 (see Chapter 2).

(f) Near CSF at 40cm using the VCTS 6000 chart (Vistech Consultants, Dayton, OH., USA.) and a 4-alternate forced choice method (Ginsburg 1984, Ginsburg *et al.* 1984).

(g) Stereoacuity at 40cm using the TNO random dot stereogram test (Laméris Ootech B.V., NC Nieuwegein, Holland), which was selected due to the lack of monocular cues for depth (see section 5.1.3).

(h) Subjective AoA/range of clear vision by curve-fitting of a defocus curve (range of +3.00DS to -3.00DS in 0.50DS steps) measured and quantified in accordance with the methods and findings of Chapter 3, with only the distance spectacle refraction worn.

(i) Subjective evaluation of near vision using the NAVQ, which also assesses satisfaction on a scale of 0 (completely satisfied) to 5 (completely unsatisfied) (see Chapter 4).

All subjects were given the opportunity to rest when necessary. Subjects were then randomly assigned to be fitted with either the PureVision® Multi-focal contact lens (n=10) or with monovision using PureVision® single vision contact lenses (n=10). With the former, the initial lens power selection for distance vision was equal to the MSE refractive error of the distance spectacle refraction, corrected for BVD as and when needed, with a 'low addition' lens selected where the near spectacle addition was +1.50DS or less (11 subjects), and a 'high addition' lens selected were the near spectacle addition was +1.75DS or more (9 subjects). For monovision correction, the dominant eye was fitted with a lens power corresponding to the MSE refractive error of the distance spectacle refraction whilst the non-dominant eye was fitted with a lens power corresponding to the MSE refractive error of the near spectacle refraction. The dominant eye was identified using the sighting method and this was confirmed using the acuity test (see section 1.3.1.3.1, Chapter 1). Where the two tests yielded conflicting results, the lenses were fitted according to how the subject felt that their general vision was most comfortable.

Fifteen minutes after insertion, the on-eye fitting characteristics of each contact lens was evaluated using a slit lamp, to ensure adequate centration, coverage, movement on blink ($\geq$0.3mm) and horizontal excursion lag ($\geq$0.3mm). Optimal distance and near VA and lens powers were ensured by presentation of positive and negative optical trial lenses to each eye, monocularly and binocularly, using standard optometric techniques. Where over-refractions were indicated from this, new contact lenses were inserted and the vision and fitting characteristics were re-assessed. Once the lens fit and power had been finalised for each eye, subjects were instructed on insertion, removal and cleaning techniques and all appropriate advice for contact lens wear was given; all subjects were provided with a supply of ReNu™ Multipurpose solution (Bausch & Lomb Corp., Rochester, NY., USA.).

Once the fitting procedure was complete, subjects were asked to trial the contact lenses for one month to allow for adaptation (Sheedy *et al.* 1993). All subjects who were new to contact lens wear were required to build-up their daily wearing time from 2 hours on the first day, increasing this by two hours each day thereafter to a maximum of 12 hours per day. A follow-up email was sent to all subjects one week after fitting to ensure that they were managing well. All subjects who reported any difficulties (5 occasions out of the 40 contact lens fittings conducted) were immediately reviewed (unscheduled visit) and all of the necessary modifications to the lens parameters were made and appropriate advice provided (a change in multifocal lens power, but not addition, was required in all cases).

Once the first month of contact lens wear was completed, subjects returned for aftercare and evaluation of visual function. The former involved confirmation of history and symptoms, including enquiry about any changes, slit lamp examination of the anterior eyes, and assessment of contact lens fit for each eye. The latter involved evaluation of the clinical measurements listed previously whilst subjects wore their contact lens correction. Subjects were then refitted with the alternative contact lens type, i.e. monovision subjects were refitted to the multifocal contact lens correction, whilst multifocal subjects were refitted to the monovision correction, using the same techniques described above. Previous studies have shown that monovision patients can be successfully refitted with simultaneous vision contact lenses, and vice versa (Josephson and Caffery 1987, Situ *et al.* 2003), supporting the cross-over design of this study. All of the procedures described were then repeated for the second lens type. Upon completion of the trial, subjects were asked about their contact lens preference so that a written specification could be provided.

The same practitioner (the author) conducted all procedures including contact lens fitting. The Ethical Committee of Aston University approved the study, informed consent was obtained from each subject after explanation of the nature and possible consequences of the study, and subjects were free to withdraw at any time without obligation.

5.4 Statistical Analysis

Visual function was compared between best binocular spectacle-corrected vision, monovision with contact lenses, and the multifocal contact lens by performing a single factor repeated measures ANOVA for each clinical measurement. For the distance and near CSFs however, the two-factor repeated measures ANOVA was used, after data were converted into logarithmic contrast sensitivity units (log CS units), in order to account for the additional variable of SF. For comparisons of stereoacuity and for satisfaction with near visual ability, Friedman's ANOVA was used since these metrics were assessed with arithmetical, and not interval, scales (see Appendix for details of statistical test selection). Where significant differences were indicated, as assessed at $p=0.05$, pair-wise comparisons were performed using a Bonferroni adjustment for multiple pair-wise comparisons (significant $p=0.0167$, 3 pair-wise comparisons), which reduces the risk of making a Type 1 statistical error (see section 2.5, Chapter 2), in order to determine which correction(s) performed better or worse. Where pair-wise comparisons of stereoacuity and/or satisfaction were required, the Wilcoxon Signed Ranks Test was used.

In order to assess the effect of the magnitude of the near spectacle addition on visual function with the multifocal contact lens, paired comparisons of each clinical measurement were conducted between the 'low addition' (n=11) and 'high addition' (n=9) multifocal lenses. In essence, this analysis amounted to a comparison between those subjects with a near spectacle addition of +1.50DS or less to those subjects with a near spectacle addition of +1.75DS or more. Whilst the groups were matched for gender (7 males and 4 females received the 'low addition' lens and 4 males and 5 females received the 'high addition' lens; Fisher's Exact Test, $p=0.65$), they were expectedly unmatched for age, since older subjects naturally require a stronger near addition power (the mean age of 'low addition' lens wearers was 52.9±3.9 years and the mean age of 'high addition' lens wearers was 57.6±5.3 years; independent samples Student's T-Test, $t=-2.2$, $p<0.05$). The independent samples Student's T-Test was used for all of these comparisons apart from the distance and near CSFs, where the two-factor ANOVA was used; for stereoacuity and satisfaction, the Mann-Whitney U Test was used. Finally, preference of contact lens type was compared using the Chi-square (χ^2) test whilst this was also used to determine whether there was a preference bias towards the "second lens" trialled in the study. All analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.) and all graphs were produced using Microsoft® Excel® (Microsoft® Corporation, Redmond, WA., USA.).

5.4.1 Power Analysis

Previous studies that have evaluated and compared visual function with presbyopic contact lenses have used sample sizes ranging from 10 subjects (McGill *et al.* 1987, McGill and Erickson 1988, Cagnolati 1993, Zandvoort *et al.* 1993) to 100 subjects (Key and Yee 1999). A study by Richdale et al. (2006) compared the SofLens® Multi-focal contact lens (Bausch & Lomb Corp., Rochester, NY., USA.), which is similar in design to and manufactured by the same company as the PureVision® Multi-focal, to monovision in a crossover manner, and used a sample size of 38 subjects. For the present study, statistical power analysis was conducted in order to determine the sample size required to ensure a power of at least 80% (0.80). Calculations were performed *a priori* based on the pair-wise comparisons that would be conducted by SPSS if overall differences in distance VA and near VA were found. The two-tailed paired-samples Student's T-Test would be used for this, and the comparison between monovision correction and the multifocal contact lens was selected as this was expected to display the smallest effect size. This analysis revealed that a minimum sample size of 32 subjects was required (see Appendix for calculations).

Post hoc analysis based on the actual observations and sample size in this study revealed that power ranged from 0.59 to 0.65 for the pair-wise comparisons of distance and near VA, whilst this was at least 0.99 for the two-factor repeated measures ANOVA (distance and near CSFs). For the comparisons between the 'low addition' and 'high addition' multifocal lenses, power ranged from 0.26 to 1.00 (see Appendix for all calculations).

5.5 Results

Of the 20 subjects recruited for this study, 9 subjects habitually wore varifocal spectacles whilst the remainder wore a combination of single vision distance and near spectacles. The spectacle refraction was found to be optimal in 12 subjects and therefore best binocular spectacle-corrected vision was assessed in these subjects with their own spectacles worn at a BVD of 12.0mm (5 varifocal spectacles and 7 single vision spectacles). The remaining subjects required some adjustment to their spectacle refraction and therefore best binocular spectacle-corrected vision was assessed using optical trial lenses placed in a trial frame at a BVD of 12.0mm. Hypermetropic and myopic refractive errors were equally prevalent, with the MSE refractive error being -1.42±2.87D in the right eye and -1.09±2.80D in the left eye. The mean near spectacle addition was 1.61±0.36D (range 0.75 to 2.25D). Three subjects had previously worn contact lenses but none had any experience with presbyopic contact lenses. No subjects chose to withdraw from the study and no subjects failed to attend any of the appointments for aftercare and visual function assessment.

5.5.1 Comparison of Visual Function Between Each Type of Correction

There was a significant difference in the mean distance VA between the three types of correction (single factor repeated measures ANOVA, $F=25.1$, $p<0.001$), with that provided by best binocular spectacle-correction (-0.10±0.07 logMAR) being significantly better than monovision correction (-0.01±0.07 logMAR) ($p<0.001$), which in turn was significantly better than the multifocal contact lens (0.05±0.08 logMAR) ($p<0.0167$).

The mean CSF curves for distance vision are shown for each of the three types of correction in Figure 5.5. Error bars are not displayed, since they overlap at each data point, but the standard deviation was consistent between each correction and ranged from approximately ±0.20 log CS units for SFs of 1.5, 3 and 6 cycles per degree (cpd), to approximately ±0.35 log CS units for SFs of 12 and 18 cpd.

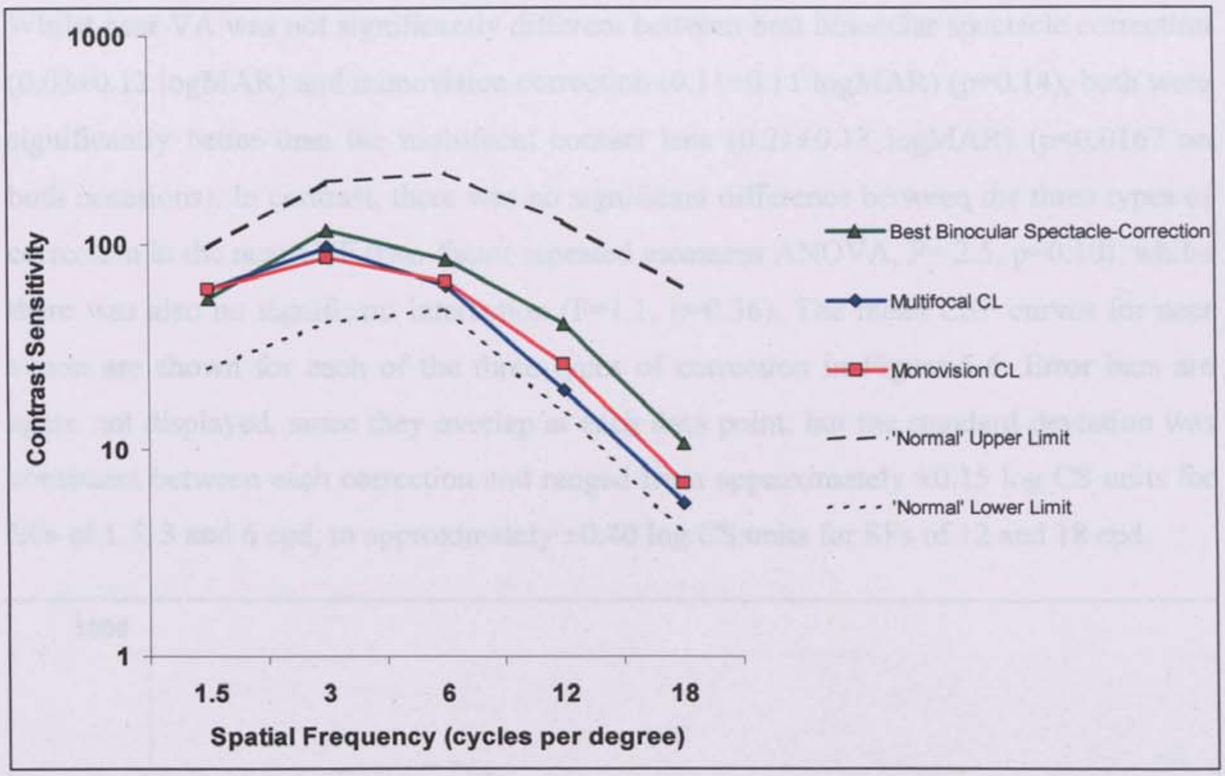

Figure 5.5 The mean contrast sensitivity functions (CSFs) for distance vision with best binocular spectacle-corrected vision, the PureVision® Multi-focal contact lens and monovision with contact lenses (n=20 per sample)

The distance CSF was significantly different between the three types of correction (two-factor repeated measures ANOVA, F=11.7, p<0.001) whilst there was also a significant interaction (F=6.5, p<0.001), indicating differential effects of the type of correction on SF. The two contact lens corrections were not found to be significantly different to each other (p=0.29), but each of these was significantly poorer than best binocular spectacle correction (p<0.005 on both occasions). The source of the interaction was determined by conducting paired comparisons of each SF between best binocular spectacle correction and each contact lens correction in turn, using two-tailed paired-samples Student's T-Tests (significant p=0.05). This analysis revealed that compared to best binocular spectacle correction, contrast sensitivity was significantly poorer with the multifocal contact lens at SFs of 6, 12 and 18 cpd (p<0.005 on all occasions), whilst this was true for monovision correction at SFs of 3, 6, 12 and 18 cpd (p<0.05 on all occasions).

There was no significant difference in intermediate VA between best binocular spectacle correction (0.28±0.10 logMAR), monovision correction (0.35±0.10 logMAR) and the multifocal contact lens (0.30±0.10 logMAR) (single factor repeated measures ANOVA, F=2.8, p=0.07). There was however a significant difference in mean near VA between the three types of correction (single factor repeated measures ANOVA, F=10.4, p<0.001).

Whilst near VA was not significantly different between best binocular spectacle correction (0.03±0.12 logMAR) and monovision correction (0.11±0.11 logMAR) ($p=0.14$), both were significantly better than the multifocal contact lens (0.21±0.13 logMAR) ($p<0.0167$ on both occasions). In contrast, there was no significant difference between the three types of correction in the near CSF (two-factor repeated measures ANOVA, $F= 2.5$, $p=0.10$), whilst there was also no significant interaction ($F=1.1$, $p=0.36$). The mean CSF curves for near vision are shown for each of the three types of correction in Figure 5.6. Error bars are again not displayed, since they overlap at each data point, but the standard deviation was consistent between each correction and ranged from approximately ±0.15 log CS units for SFs of 1.5, 3 and 6 cpd, to approximately ±0.40 log CS units for SFs of 12 and 18 cpd.

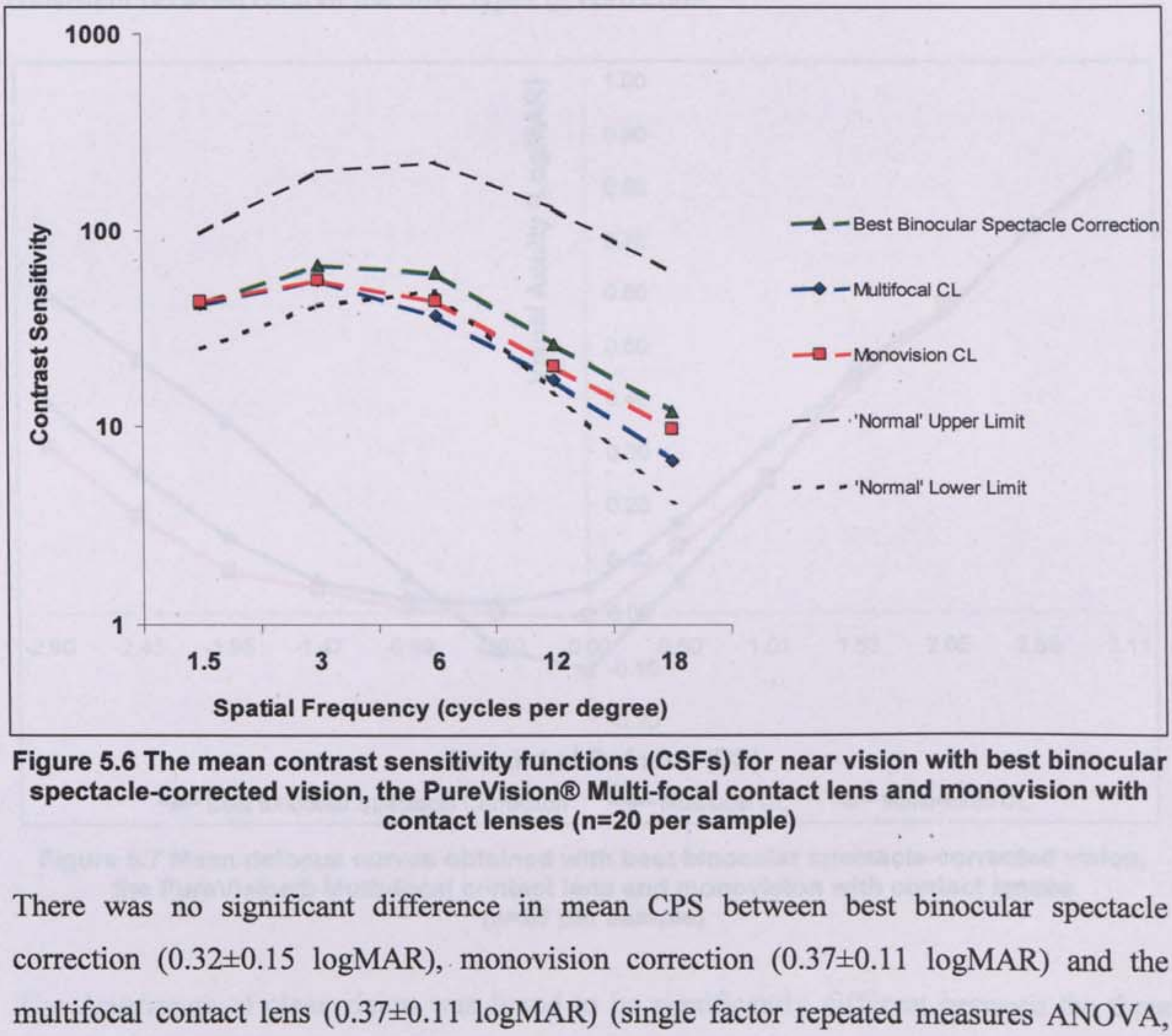

Figure 5.6 The mean contrast sensitivity functions (CSFs) for near vision with best binocular spectacle-corrected vision, the PureVision® Multi-focal contact lens and monovision with contact lenses (n=20 per sample)

There was no significant difference in mean CPS between best binocular spectacle correction (0.32±0.15 logMAR), monovision correction (0.37±0.11 logMAR) and the multifocal contact lens (0.37±0.11 logMAR) (single factor repeated measures ANOVA, $F=0.8$, $p=0.45$). There was however a significant difference in CPS reading speed (single factor repeated measures ANOVA, $F=0.8$, $p<0.01$), with best binocular spectacle correction (173.4±24.1 wpm) being significantly faster than both monovision (158.0±19.5 wpm) and the multifocal contact lens (154.9±17.9 wpm) ($p<0.0167$ on both occasions). There was however no significant difference between the two contact lens types ($p=0.48$).

A significant difference in stereoacuity was found between the three types of correction (Friedman's ANOVA, χ^2 = 26.0, p<0.001), with best binocular spectacle correction (77.3±48.0"; median of 60.0") being significantly better than the multifocal contact lens (174.0±95.2"; median of 120.0") (Z=-2.8, p<0.005), which in turn was significantly better than the monovision correction (273.0±102.0"; median of 300.0") (Z=-2.6, p<0.0167).

The mean defocus curves for evaluation of the AoA/range of clear vision with each of the three types of correction are shown in Figure 5.7, after correction for BVD (see 3.4, Chapter 3). Error bars are again not displayed, since they overlap at each data point, but the standard deviation at each level of defocus was approximately ±0.12 logMAR and was consistent between each of the three types of correction.

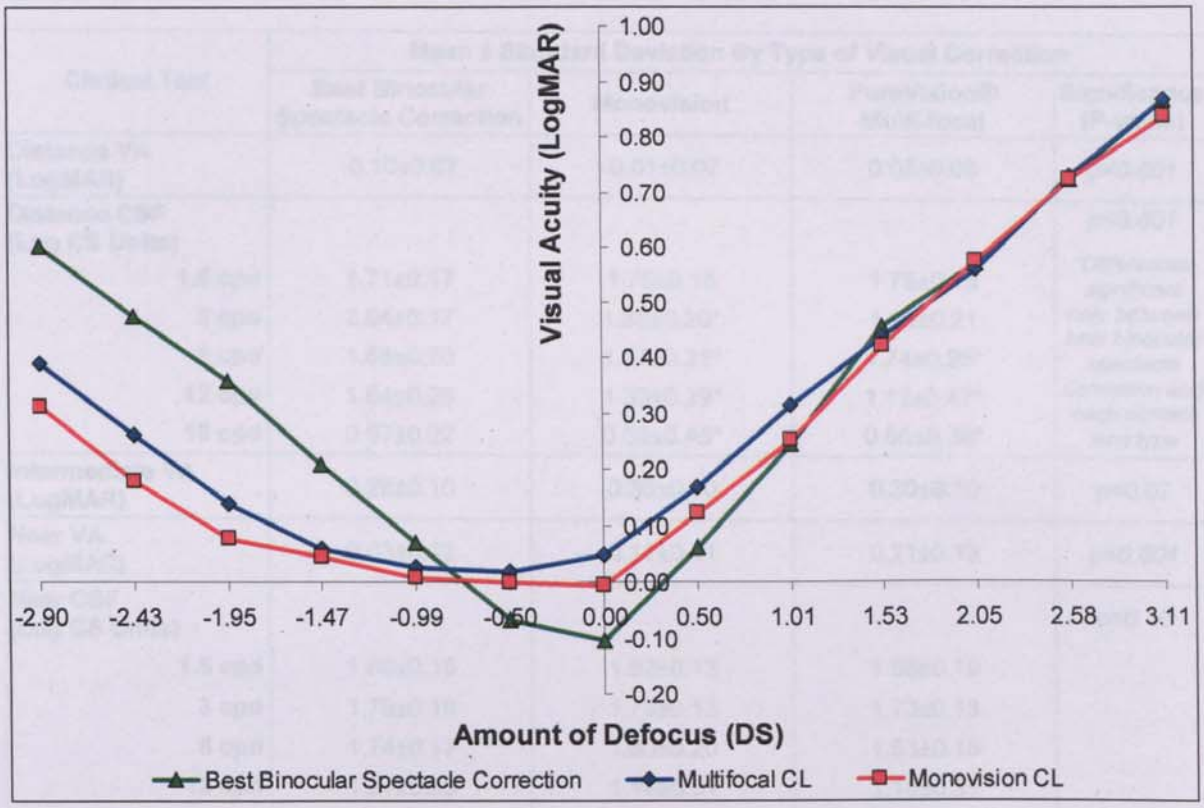

Figure 5.7 Mean defocus curves obtained with best binocular spectacle-corrected vision, the PureVision® Multi-focal contact lens and monovision with contact lenses (n=20 per sample)

The AoA/range of clear vision was found to be significantly different between the three types of correction (single factor repeated measures ANOVA, F=19.7, p<0.001). The AoA measured with best binocular distance-corrected spectacle vision (0.46±0.23D) was significantly lower than the range of clear vision offered by both monovision correction (1.21±0.77D) (p<0.001) and the multifocal contact lens (1.59±0.70D) (p<0.005), but there was no significant difference between the two contact lens options (p=0.04).

Subjective evaluation of near visual ability (NAVQ score) was not significantly different between best binocular spectacle correction (26.5±14.3 logits), monovision (34.8±19.2 logits), and the multifocal contact lens (34.1±17.4 logits) (single factor repeated measures ANOVA, F=2.2, p=0.13), whilst there was also no significant difference in overall satisfaction (Friedman's ANOVA, $\chi^2 = 2.0$, p=0.37). The mean satisfaction rating with best binocular spectacle correction was 1.6±1.5 (median of 1.0), whilst that with monovision was 2.3±1.4 (median of 2.5) and that with the multifocal contact lens was 2.4±1.8 (median of 2.0). With best binocular spectacle correction, 4 subjects were classified as having near vision difficulties (NAVQ score of 40.45 or more; see section 4.6, Chapter 4), whilst this was true of 10 subjects with monovision correction and 8 subjects with the multifocal contact lens ($\chi^2 = 2.5$, p=0.28). All of the comparisons are summarised in Table 5.2.

Clinical Test	Mean ± Standard Deviation By Type of Visual Correction			
	Best Binocular Spectacle Correction	Monovision	PureVision® Multi-focal	Significance (P-value)
Distance VA (LogMAR)	-0.10±0.07	-0.01±0.07	0.05±0.08	*p<0.001*
Distance CSF (Log CS Units)				*p<0.001*
1.5 cpd	1.71±0.17	1.75±0.16	1.75±0.16	**Differences significant only between best binocular spectacle correction and each contact lens type*
3 cpd	2.04±0.17	1.89±0.20*	1.93±0.21	
6 cpd	1.88±0.20	1.77±0.21*	1.74±0.25*	
12 cpd	1.54±0.28	1.33±0.29*	1.12±0.47*	
18 cpd	0.97±0.22	0.68±0.45*	0.65±0.36*	
Intermediate VA (LogMAR)	0.28±0.10	0.35±0.10	0.30±0.10	p=0.07
Near VA (LogMAR)	0.03±0.12	0.11±0.11	0.21±0.13	*p<0.001*
Near CSF (Log CS Units)				p=0.10
1.5 cpd	1.60±0.15	1.62±0.13	1.58±0.19	
3 cpd	1.79±0.18	1.73±0.13	1.73±0.13	
6 cpd	1.74±0.17	1.60±0.20	1.53±0.18	
12 cpd	1.27±0.35	1.19±0.31	1.10±0.31	
18 cpd	0.87±0.48	0.80±0.48	0.70±0.38	
Critical Print Size (CPS) (LogMAR)	0.32±0.15	0.37±0.11	0.37±0.11	p=0.45
CPS Reading Speed (wpm)	173.4±24.1	158.0±19.5	154.9±17.9	*p<0.01*
Stereoacuity (Seconds of arc)	77.3±48.0	273.0±102.0	174.0±95.2	*p<0.001*
Subjective AoA / range of vision (D)	0.46±0.23	1.21±0.77	1.59±0.70	*p<0.001*
NAVQ Score (logits) & Satisfaction	26.5±14.3 1.6±1.5	34.8±19.2 2.3±1.4	34.1±17.4 2.4±1.8	p=0.13 p=0.37

Table 5.2 Comparison of visual function with best binocular spectacle correction, monovision with contact lenses and the PureVision® Multi-focal contact lens. Overall significant differences (at p=0.05) between the three correction types are highlighted in italic (n=20 in each group)

5.5.2 Multifocal Lens Performance: Effect of Spectacle Addition Magnitude

The comparison of visual function between the 'low addition' lens and the 'high addition' lens is shown in Table 5.3. There was no significant difference in distance VA between the two lenses (t=1.0, p=0.34) but the distance CSF was generally poorer at all SFs with the 'high addition' lens than with the 'low addition' lens (two-factor ANOVA, F=7.8, p<0.01). There was no significant difference in intermediate VA (t=-1.1, p=0.30), but both near VA (t=-2.2, p<0.05) and CPS (t=-2.4, p<0.05) were significantly better with the 'low addition' lens than with the 'high addition' lens. The near CSF was also significantly better with the 'low addition' lens (two-factor ANOVA, F=29.0, p<0.001) at all SFs apart from 18 cpd (p=0.06). There were no significant differences in the CPS reading speed (t=-0.7, p=0.50), stereoacuity (U=32.5, Z=-1.4, p=0.20), the range of clear vision (t=0.4, p=0.73), NAVQ scores (t=-2.0, p=0.06), and rating of near vision satisfaction (U=36.5, Z=-1.0, p=0.33).

Clinical Test	Mean ± Standard Deviation By Magnitude of Near Addition		
	'Low Addition' PureVision® Multi-focal	'High Addition' PureVision® Multi-focal	Significance (P-value)
Distance VA (LogMAR)	0.02±0.06	0.08±0.10	p=0.34
Distance CSF (Log CS Units)			*p<0.01*
1.5 cpd	1.79±0.17	1.71±0.16	*No significant differences found at each SF*
3 cpd	1.97±0.22	1.87±0.20	
6 cpd	1.80±0.24	1.67±0.25	
12 cpd	1.26±0.49	0.96±0.42	
18 cpd	0.76±0.27	0.52±0.43	
Intermediate VA (LogMAR)	0.28±0.08	0.32±0.11	p=0.30
Near VA (LogMAR)	0.16±0.14	0.27±0.09	*p<0.05*
Near CSF (Log CS Units)			*p<0.001*
1.5 cpd	1.67±0.20	1.46±0.12	*p<0.001*
3 cpd	1.80±0.15	1.64±0.00	*p<0.01*
6 cpd	1.61±0.15	1.43±0.17	*p<0.05*
12 cpd	1.26±0.33	0.91±0.12	*p<0.01*
18 cpd	0.84±0.38	0.52±0.31	p=0.06
Critical Print Size (CPS) (LogMAR)	0.32±0.11	0.42±0.08	*p<0.05*
CPS Reading Speed (wpm)	152.4±16.6	158.0±20.0	p=0.50
Stereoacuity (Seconds of arc)	152.7±101.7	200.0±84.9	p=0.20
Subjective AoA / range of vision (D)	1.64±0.68	1.52±0.77	p=0.73
NAVQ Score (logits) & Satisfaction	27.7±18.8 2.7±1.8	42.1±12.1 1.9±1.7	p=0.06 p=0.33

Table 5.3 Comparison of visual function between the 'low addition' and 'high addition' PureVision® Multi-focal contact lenses. Significant differences (at p=0.05) are highlighted in italic (n=11 in the 'low addition' group and n=9 in the 'high addition' group)

5.5.3 Presbyopic Contact Lens Preference

At the end of the study, 10 out of the 20 subjects (50%) expressed an overall preference for the monovision correction but this was not significantly more than the number of subjects that preferred the multifocal contact lens correction (8 subjects; 40%) (χ^2 = 5.2, p=0.07). Two subjects (10%) were undecided between the two contact lens options. Although the majority of subjects in this study (17 subjects; 85%) had no previous experience of wearing contact lenses, there was no significant preference bias for subjects selecting the "second lens" type trialled in the study, indicating that adaptation or improved familiarity from the experiences of the first lens worn did not significantly influence the lens choice; 8 subjects (44.4%) preferred the "first lens" trialled and 10 subjects (55.6%) preferred the "second lens" trialled (χ^2 = 0.2, p=0.64).

5.6 Discussion

The PureVision® Multi-focal contact lens is one of the latest additions to the growing market of contact lens designs aimed at providing spectacle-free vision correction for the presbyopic patient. Given the success and popularity of monovision techniques, the purpose of this study was to compare visual function with the new multifocal contact lens to this and to best binocular spectacle-corrected vision.

Both distance VA and near VA measured with single letter high contrast optotypes in this study were found to be significantly better with monovision correction than with the centre-near aspheric simultaneous vision multifocal contact lens. This finding can be explained by the knowledge that interocular blur suppression in monovision allows the clearer eye to dominate perception and therefore results in a better VA (see section 1.3.1.2, Chapter 1, and section 5.1.1). In contrast, the creation of superimposed retinal images by the multifocal contact lens reduces retinal image contrast and quality in *both* eyes, preventing any similar compensation (see section 5.1.1). Although the average difference in VA between the two types of contact lenses was only three letters of logMAR acuity for distance vision, the average difference of five letters (one line of logMAR acuity) for near vision may be clinically significant. The optometric practitioner should therefore consider an individual's needs and demands for visual clarity, especially for near vision, when deciding upon which of the two types of contact lens corrections should be fitted.

These results however do not agree with the findings of Richdale et al. (2006), who instead found that distance VA and near VA with the similarly designed SofLens® Multi-focal contact lens were similar to monovision. In part, this may reflect differences in subject sample composition since the Richdale et al. study comprised mostly female subjects (87%), which is unlikely to be representative of presbyopic contact lens wearers in general. It is more likely however that this reflects differences in the manner that the multifocal contact lens was fitted, since some subjects in the Richdale et al. study received a 'low addition' lens in one eye and a 'high addition' lens in the other. This type of *modified multifocal* correction may have artificially led to greater similarity in distance VA and near VA to the monovision correction if one eye was rendered distance vision dominant and the other eye near vision dominant. As such, this fitting philosophy for the multifocal contact lens was intentionally avoided in the present study and subjects were fitted with the same multifocal contact lens addition bilaterally. Furthermore, the potentially large range of modified multifocal and monovision corrections that can be produced would have made the task of generally comparing the two contact lens corrections all the more difficult.

Compared to best binocular spectacle-corrected vision, both types of contact lens corrections produced significantly poorer distance VA, whilst at near this was only true of the multifocal contact lens. It is possible that the latter reflects the impact of using varifocal spectacles to measure best binocular spectacle-corrected near VA with some subjects in this study. As described in section 1.2.2 (see Chapter 1), varifocal spectacle lenses suffer from inherent blur and distortion effects in peripheral aspects of the lens, especially in the near region of the lens, whilst *near vision effectivity* can reduce the actual power of the near prescription due to variation in BVD. Consequently, best binocular near VA in varifocal spectacle wearers in this study may have been poorer, resulting in greater overall similarity to the monovision correction and therefore a lack of a significant difference.

In order to better gauge real-world visual function with the three types of visual correction, the distance and near CSFs were measured in this study. Whilst there was no significant difference between the two types of contact lenses for the distance CSF, each was found to be significantly poorer compared to best binocular spectacle-correction. This is likely to represent the effects of increased retinal blur and reduced retinal image contrast that occurs at medium and high SFs, as a consequence of superimposed images in simultaneous vision contact lenses or due to the presence of a resultant central blur suppression scotoma in monovision (see section 1.3.2.2, Chapter 1).

These findings are in accordance with those of other studies (Erickson and Schor 1990, Van Meter *et al.* 1990, Cagnolati 1993, Zandvoort *et al.* 1993, Rajagopalan *et al.* 2007). However, the multifocal contact lens was only found to cause a significant reduction in the CSF at SFs of 6, 12 and 18 cpd whereas the monovision correction was found to be more detrimental, causing a significant reduction at a SF of 3 cpd also. These findings are likely to reflect the knowledge that binocular summation is greater with multifocal contact lenses than with monovision correction, with binocular blur being less detrimental to binocular fusion (see section 1.3.1.1, Chapter 1).

The similarity in distance CSF between monovision correction and the multifocal contact lens may be explained by the presence of aspheric surfaces on the latter lens type, which creates additional foci to aid visual clarity. Indeed, a greater difference would have been expected if, for example, a *concentric* multifocal design approach had been used, since this produces more defined retinal images that interfere with retinal image contrast to a greater extent (McGill *et al.* 1987). This effect may also explain the observed lack of a significant difference in the near CSF between the two contact lens types in this study. Indeed, this is in agreement with other studies (Erickson and Schor 1990, Rajagopalan *et al.* 2007). However, unlike the distance CSF, neither contact lens correction produced a significantly different near CSF compared to best binocular spectacle correction. This is again likely to reflect the impact of measurements made with varifocal spectacles in some subjects.

When considering the effect of presbyopic contact lenses on the CSF, one must also consider the possibility that soft contact lens wear itself may reduce the CSF, compared to spectacle correction and hard/RGP lenses (Applegate and Massof 1975). Grey (1987) reported temporary reductions in the CSF during the first two weeks of soft contact lens wear and postulated that corneal oedema was the primary reason for this since the reduction and recovery was gradual, indicating a corneal response to reduced oxygen rather than a lens effect (Grey 1986). This is very unlikely to have been a significant issue in the present study since all subjects wore contact lenses manufactured from a silicone hydrogel material, which has known hyper-oxygen properties (Bruce 2003, Efron *et al.* 2007). It is possible however, that the CSF may have been reduced through other causes, including residual astigmatism, SA, and contact lens spoliation (Briggs 1998), although there is no great support for these possibilities, irrespective of the contact lens material (Bernstein and Brodrick 1981, Collins *et al.* 1989a, Ng *et al.* 1997).

In this study, the CPS was found to be similar between the three types of visual correction, suggesting that only the acuity threshold, and not the comfortable reading print size, is affected by retinal blur. In contrast, the CPS reading speed was significantly and equally slower with both contact lens corrections compared to best binocular spectacle correction. It therefore appears that any compromise to binocularity and visual clarity can reduce one's maximal reading speed, and this presents an important consideration for the optometric practitioner when fitting these types of contact lenses.

All three modalities of vision correction in this study provided similar levels of intermediate VA, suggesting equal benefit of alternate interocular blur suppression in monovision, to the function of the near addition and aspheric surfaces on the multifocal contact lens, and, most likely, to DoF of the best binocular distance-corrected eyes; the latter could however be better if varifocal spectacles are worn. Indeed, the *range* of clear vision assessed by defocus curves was found to be significantly and equally greater with both monovision and the multifocal contact lens compared to the AoA of the best binocular distance-corrected eyes, which may reflect the influence of improved blur tolerance that occurs due to the reduction in distance VA with each contact lens correction (see section 3.1.3, Chapter 3). However it is also likely to reflect the ability of interocular blur suppression in monovision to allow the individual range of clear vision of each eye to be summed (Schor and Erickson 1988), whilst the aspheric surfaces and near addition on the multifocal contact lens create a 'varifocal' effect that enhances this range. In contrast, the AoA of the best binocular distance-corrected eyes is expectedly limited, but would be greater if this was measured with a near spectacle addition (e.g. varifocal spectacles); the practical benefits of the contact lenses however would then be lost.

Stereoacuity in this study was found to be significantly poorer with monovision correction than with the multifocal contact lens, in agreement with other studies (Back *et al.* 1992a, Richdale *et al.* 2006). This reflects the greater impact that monocular blur (monovision) has on binocular fusion compared to binocular blur (multifocal contact lens) (see section 5.1.3). Furthermore, stereoacuity would expectedly be at it's best with the best binocular spectacle correction since it is only with this that the best possible VA and CSF are present (see section 5.1.3). However, the observed differences in stereoacuity in this study were greater than that reported in other studies investigating lenses of similar design (McGill and Erickson 1988, Sheedy *et al.* 1991, Hutnik and O'Hagan 1997). This is most likely to be due to differences in the type of stereotest used (see section 5.1.3).

Although some aspects of visual function were observed to be different between the three types of vision correction in this study, there was no significant difference in subjective perception of near visual ability (NAVQ score) or satisfaction. This may reflect the lack of a significant difference in the near CSF, which indicates similarity in general visual function at near. More likely, each correction type has its own relative advantages and disadvantages which when considered collectively, including varifocal spectacles, might average out to produce an overall similar perception of visual ability with each.

Comparison of visual function between the 'low addition' and the 'high addition' multifocal contact lenses revealed that the 'low addition' lens provided significantly better distance CSF, near CSF, near VA and CPS. In essence, these findings suggest that whilst binocularity is not adversely affected by the presence of a stronger near addition (+1.75DS or more), overall visual clarity is likely to be affected. However, this does not produce significant differences in subjective perceptions of near visual ability and satisfaction, perhaps because subjects requiring stronger near additions have lower expectations or demands of multifocal contact lens corrections. Indeed, this warrants further investigation.

5.6.1 Limitations

The performance of simultaneous vision contact lenses is known to be dependent on pupil size and centration (see sections 1.3.2.2 and 1.3.2.3, Chapter 1) and perhaps objective evaluation of these features in this study would have helped to better understand the performance of the PureVision® Multi-focal contact lens. However, it has been suggested that subjective findings are more important to judge the success of such lenses (Brenner 1994), whilst contact lens preference is supposedly rated largely on the quality of reading vision rather than on the quality of distance vision (Hutnik and O'Hagan 1997). In view of this, subjective evaluation of near visual function is perhaps of greatest importance.

It is likely that the use of varifocal spectacles for measurements of best binocular spectacle-corrected vision for five subjects in this study may have limited the near visual function measurements for this correction, especially if peripheral lens distortion effects interfered with near vision. The use of single vision spectacle lenses would have avoided this and therefore best binocular vision may actually perform better than indicated in this study, compared to monovision and the multifocal contact lens. Single vision spectacle lenses should therefore have been used for all subjects in this study to confirm this.

It is also possible that the lack of significant differences in the near CSF in this study relates to flaws in the test that was used. The VCTS was used in this study as it provides a quick assessment of the whole CSF, with different contrasts and SFs tested at once. Indeed, this also allowed the differential effects of the type of contact lens correction on SF to be investigated, without producing too onerous a task for subjects to perform. However, the VCTS has been shown to suffer from "floor" and "ceiling" effects, i.e. too many subjects correctly view the lowest and highest, respectively, contrasts and SFs, whilst it also has poor reproducibility, particularly in refractive surgery patients (Pesudovs *et al.* 2004b). This may be due to the large step changes in contrast and SF that are employed in this test and it has therefore been suggested that *letter* contrast sensitivity tests, such as the Pelli Robson chart (Pelli *et al.* 1988), ought to be used instead, as these are more sensitive to detecting even subtle differences (Pesudovs *et al.* 2004b).

The lack of significant differences in NAVQ scores between the three types of correction in this study may have been due to the responses relating to best binocular spectacle-corrected vision being obtained according to subjects' habitual correction, which was *not optimal* in eight subjects since some adjustment was required to the refraction before their vision was clinically assessed. NAVQ scores of these subjects may therefore have been higher (i.e. poorer ability) compared to if they had been wearing their optimal correction. The lack of significant differences, including between the 'low addition' and 'high addition' multifocal contact lenses, may also suggest that the NAVQ lacks sensitivity. Indeed, it is clear that further development of the NAVQ is required to include larger sample sizes and perhaps different types of presbyopic contact lenses (see Chapter 4).

It is also possible in this study that the aspheric surfaces of the PureVision® single vision lenses produced better near visual function with monovision correction than would have been expected of conventional methods with spherical lenses. However, Michaud et al. (1995) revealed that monovision with aspheric lenses is not notably different to compared to spherical lenses, and hence this is not likely to have been a major cause of error.

Finally, it may have been useful to measure the fusional vergence range with monovision correction in this study, in order to provide evidence of success for this correction in terms of the strength of interocular blur suppression. However, no comparative data to the multifocal lens would have been obtained since simultaneous vision inherently induces diplopia through superimposed retinal images.

5.7 Conclusion

This study has shown that the application of standardised near vision metrics can be used to successfully detect differences in visual function between best binocular spectacle-corrected vision, a centre-near aspheric simultaneous vision contact lens and monovision with contact lenses, in presbyopic subjects. As expected, best binocular spectacle-corrected vision provides the best possible visual function at distance and near, since visual clarity and binocular fusion are optimal. Monovision with PureVision® single vision contact lenses only provided better distance and near VA compared to the PureVision® Multi-focal contact lens, which may explain the greater, albeit insignificant, overall preference for this lens type. The multifocal contact lens however, provided better stereoacuity and produced insignificant differences in the CSF at both distance and near, along with insignificant differences in the near range of clear vision and subjective perceptions of near visual ability, compared to monovision. As such, the PureVision® Multi-focal contact lens can potentially provide a better balance of real world visual function due to minimal binocular disruption. Presbyopic patients wishing to achieve spectacle-free correction of their vision with contact lenses should therefore be given the opportunity to try both monovision and multifocal contact lens options and practitioners ought to consider the aspects of visual function that are most important to patients in their own environment.

Having applied standardised/optimised near vision metrics to the evaluation of visual performance of presbyopic contact lenses in this Chapter, these metrics are in the next Chapter applied to the evaluation of visual performance of a prototype single optic 'accommodating' IOL design, which is a method of presbyopia correction that is receiving increasing interest.

CHAPTER 6

Clinical Evaluation of Visual Function with a Prototype Single Optic 'Accommodating' Intraocular Lens

6. Introduction

There is currently a great amount of interest in 'accommodating' IOLs, primarily because they can potentially restore the AoA of presbyopic eyes to similar levels as pre-presbyopic eyes. The optics of these IOLs also means that visual function is not susceptible to the compromises that are typically associated with multifocal contact lenses and IOL alternatives (see sections 1.3 and 1.4.2, Chapter 1, and Chapter 5). Only a few single optic 'accommodating' IOL designs have been described, perhaps because their initial performance appears to be limited (see section 1.4.3.1, Chapter 1). Consequently, new or modified designs are being sought, in order to obtain improvements, and one such prototype design forms the focus for this Chapter.

6.1 Study Aim

Due to confidentiality agreements the single-piece single optic prototype 'accommodating' IOL cannot be identified. However, this acrylic IOL has an 'A' constant of 118.1, a single optic with a round edge and a diameter of 5.5mm, an overall diameter of 9.7mm and three flexible haptics that produce an accommodative effect by enabling anterior optic movement upon compression of the capsular bag with contraction of the ciliary muscle. The purpose of this study was to assess the feasibility this IOL by clinically evaluating the visual function that it confers during the first six months after implantation, with particular reference to the standardised near vision metrics described in Chapters 2, 3 and 4.

6.2 Method

Twenty-two subjects (11 males, 11 females) of mean age 70.4±11.2 years (range 41 to 84 years) were recruited from Solihull Hospital and from the Midland Eye Institute in Birmingham, as requiring cataract extraction or CLE in at least one eye. All subjects were required to meet the following eligibility criteria:

(a) A likely post-operative best-corrected distance VA of at least 0.18 logMAR, to meet the required vision standard for driving (Drasdo and Haggerty 1981, Westlake 2000).
(b) Clear ocular media (other than presence of cataract), and absence of ocular pathology including microphthalmos, keratitis, keratoconus (or other irregular astigmatism), corneal dystrophy, uveitis, glaucoma, optic atrophy, AMD and diabetic retinopathy.
(c) Absence of binocular vision and accommodative anomalies including decompensated heterophoria, heterotropia, and amblyopia as confirmed by cover tests and fixation disparity tests using the Mallett unit, at distance (six metres) and near (40cm).
(d) Absence of immunosuppressant conditions and/or medication.

A consultant ophthalmologist ensured that all of the eligibility criteria were met by each subject, after which the following tests of visual function were conducted, monocularly on the study eye, under consistent illumination of 500 lux (chart luminance of $120cdm^{-2}$):

(a) Uncorrected and best-corrected distance VA at 6m using the computerised *Test Chart 2000 Pro* (Thomson Software Solutions, Hatfield, Herts., UK.) logMAR chart.
(b) Uncorrected and best-corrected contrast sensitivity, measured in logarithmic contrast sensitivity (log CS) units at 3m with the Pelli Robson chart, and scored as the last triplet in which two out of the three letters were correctly identified and allowing for interchanged misreads of "C", "O" and "D" to be treated as correct; this scoring rule reduces the bias in test scores if suprathreshold letters are misread (Pelli *et al.* 1988).
(c) Retinoscopy at 66cm followed by a full subjective refraction.
(d) Best distance-corrected and best-corrected near VA at 40cm using the ETDRS Near LogMAR Chart (Precision Vision™, La Salle, IL., USA.), according to the findings of Chapter 2 and measured as described in section 2.4 (see Chapter 2).
(e) Best distance-corrected and best-corrected CPS in logMAR, and CPS reading speed in wpm, at 40cm using the MNRead chart (Lighthouse Low Vision Products, Long Island City, NY., USA.), in accordance with the findings of Chapter 2 and measured as described in section 2.4 (see Chapter 2).
(f) Subjective AoA by curve-fitting of a defocus curve (range of +3.00DS to -3.00DS in 0.50DS steps) measured and quantified in accordance with the methods and findings of Chapter 3, with only the best distance refractive correction worn.
(g) Subjective AoA by the push-up/push-down test using the equipment and procedure described in section 3.1.7.3 (see Chapter 3), which included the use of a near addition of +2.50DS, and was taken as the mean of three readings.

All clinical assessments that required a refraction to be worn were conducted with optical trial lenses placed in a trial frame at a BVD of 12.0mm, whilst a near addition of +2.50DS was included when necessary. Phacoemulsification followed by implantation of the prototype 'accommodating' IOL was then conducted for the right eye of 12 subjects and for the left eye of 10 subjects one week after the initial visit. Mean IOL power was 21.9±1.9D (range 19.0 to 26.5D) and mean pupil size was 4.8±0.9mm (range 3.0 to 6.5mm), as measured using the PUPILSCAN II® Model 12A pupillometer (Keeler Instruments Inc., Broomall, PA., USA.). The same consultant ophthalmologist performed all surgical procedures, using standard techniques and under standard hospital conditions.

All of the subjects returned for aftercare and assessment of visual function, at one month, three months and six months after IOL implantation. The former involved full examination of the operated eye to ensure that no complications had arisen, whilst the latter involved evaluation of the clinical tests of visual function listed previously. At each of these visits, the following additional clinical measurements were also assessed:

(a) Best distance-corrected intermediate VA at 80cm (selected as a typical working distance to view a computer screen) using the ETDRS logMAR chart.
(b) Objective AoA using the equipment and procedure described in sections 3.1.7.2 and 3.3.2 (see Chapter 3), respectively.
(c) Subjective evaluation of near vision using a pilot near activity visual questionnaire (Gupta *et al.* 2007), which also assesses satisfaction on a scale of 0 (completely satisfied) to 4 (completely unsatisfied). The NAVQ was not used since it had not yet been developed when this study was conducted. However, the questionnaires were similar since five questions (items) were common to both.

These additional measurements were not implemented at the pre-operative visit since it was expected that their accuracy would be negatively impacted upon by the presence of lenticular opacities. Furthermore, the various other measurements that were made at that stage of the study provided all of the clinical information that was required. No subjects failed to attend any of the post-operative aftercare and assessment visits and no complications were reported in any subjects at any stage during the six-month period of this study. The NHS Local Research Ethics Committee of Solihull approved this feasibility study and informed consent was obtained from each subject following explanation of the nature, possible risks and consequences of the study.

6.3 Statistical Analysis

In order to determine whether there was a significant change in visual function during the first six months after implantation of the prototype 'accommodating' IOL, each of the clinical measurements were assessed for overall significant differences between the one-month, three-months and six-months post-operative visits by performing a single factor repeated measures ANOVA. For comparisons of satisfaction with near visual ability (from the pilot near activity visual questionnaire), Friedman's ANOVA was used instead since this metric was assessed using an arithmetical, and not an interval, scale (see Appendix for details of statistical test selection). Where significant differences were indicated, as assessed at p=0.05, pair-wise comparisons were performed between each time point to determine when the difference(s) occurred; a Bonferroni adjustment for multiple pair-wise comparisons was applied in order to reduce the risk of making a Type 1 statistical error (significant p=0.0167, 3 pair-wise comparisons) (see section 2.5, Chapter 2). Where significant differences in satisfaction with near visual ability were indicated, the Wilcoxon Signed Ranks Test was used. Also, the number of subjects classified as having near visual problems by the pilot questionnaire (a score of 27.55 logits or more) at each post-operative visit was compared using the Chi-square (χ^2) test.

To assess the effect of the clearer ocular media on visual function, a comparison of each clinical measurement from pre-operatively to post-operatively was conducted using the two-tailed paired-samples Student's T-Test (significant p=0.05); only data from the one-month post-operative visit was used since this time point was expected to represent the point at which any post-operative adverse effects would be minimal. All analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.) and all graphs were produced using Microsoft® Excel® (Microsoft® Corporation, Redmond, WA., USA.).

6.3.1 Power Analysis

Previous studies that have investigated the visual function of single-optic 'accommodating' IOLs over a period of six-months after implantation have used sample sizes ranging from 20 subjects (Kuchle *et al.* 2004, Marchini *et al.* 2004) to 112 subjects (Macsai *et al.* 2006). The performance of the 'accommodating' IOL in the present study has not been previously investigated and therefore statistical power analysis was conducted in order to determine the minimum required sample size to ensure a power of at least 80% (0.80).

Power calculations were performed *a priori* based on the single factor repeated measures ANOVA and the pair-wise comparisons that would be conducted by SPSS if there were significant differences in distance VA, near VA and objective AoA. The two-tailed paired-samples Student's T-Test would be used for this and the comparison between the one-month and three-month post-operative visits was selected as this was expected to display the smallest effect size. This analysis revealed that a minimum sample size of between 60 and 250 subjects was required, based on the single factor repeated measures ANOVA. For the pair-wise comparisons, a minimum sample size of between 32 and 46 subjects was indicated (see Appendix for calculations). *Post hoc* analysis based on the actual sample size and observations in this study revealed that power ranged from 0.11 to 0.34 for the single factor repeated measures ANOVA, whilst this ranged from 0.05 to 0.25 for the pair-wise comparisons (see Appendix for calculations). As this was a feasibility study however, a small sample size was expected and therefore a low level of power could not be avoided.

6.4 Results: Pre-operative Data

The mean uncorrected distance VA was 0.87±0.49 logMAR whilst the mean uncorrected contrast sensitivity was 0.94±0.46 log CS units. The MSE refractive error was 0.40±2.51D and this gave a mean best-corrected distance VA of 0.47±0.48 logMAR and a mean best-corrected contrast sensitivity of 1.12±0.45 log CS units. Mean best distance-corrected near VA was 0.74±0.39 logMAR and this improved to 0.52±0.43 logMAR with a near addition of +2.50DS. Mean best distance-corrected CPS was 0.97±0.32 logMAR and this improved to 0.79±0.39 logMAR with a near addition of +2.50DS. Mean CPS reading speed with best distance-corrected vision was 189.6±38.1 wpm and this improved to 210.3±33.6 wpm with a near addition of +2.50DS. The mean subjective AoA as quantified from the defocus curves was 0.62±0.70D whilst that quantified with the subjective push-up/push-down test was 2.48±1.59D.

6.5 Results: Post-operative Data

There was no significant change in mean uncorrected distance VA from one month (0.36±0.23 logMAR) to three months (0.36±0.24 logMAR) or six months (0.33±0.26 logMAR) after surgery (repeated measures ANOVA, $F=0.40$, $p=0.67$). There was however a significant difference in mean uncorrected contrast sensitivity during the first six months after surgery (repeated measures ANOVA, $F=5.5$, $p<0.05$).

Pair-wise comparisons revealed that compared to one month after surgery (1.40±0.21 log CS units), the uncorrected contrast sensitivity was significantly poorer at six months after surgery (1.32±0.22 log CS units) ($p<0.005$), but there was no significant change from one month to three months (1.39±0.21 log CS units) after surgery ($p=0.55$), or from three months to six months after surgery ($p=0.06$).

There was no significant change in the MSE refractive error from one month (1.05±0.95D) to three months (0.98±1.19D) or six months (0.21±1.63D) after surgery (repeated measures ANOVA, $F=4.0$, $p=0.052$). As a result, there was also no significant change in mean best-corrected distance VA from one month (0.09±0.18 logMAR) to three months (0.06±0.15 logMAR) or six months (0.06±0.19 logMAR) after surgery (repeated measures ANOVA, $F=2.2$, $p=0.13$). There was however a significant change in mean best-corrected contrast sensitivity (repeated measures ANOVA, $F=7.5$, $p<0.005$). Pair-wise comparisons revealed that compared to one month (1.45±0.16 log CS units) after surgery, the best-corrected contrast sensitivity was significantly poorer at six months (1.35±0.20 log CS units) after surgery ($p<0.005$) but there was no significant change from one month to three months (1.43±0.19 log CS units) after surgery ($p=0.51$) or from three months to six months after surgery ($p=0.02$).

Mean best distance-corrected intermediate VA did not change significantly from one month (0.54±0.19 logMAR) to three months (0.58±0.20 logMAR) or six months (0.57±0.24 logMAR) after surgery (repeated measures ANOVA, $F=0.7$, $p=0.50$). Similarly, there was no significant change in mean best distance-corrected near VA from one month (0.48±0.20 logMAR) to three months (0.53±0.23 logMAR) or six months (0.53±0.22 logMAR) after surgery (repeated measures ANOVA, $F=1.9$, $p=0.17$). There was also no significant change in mean best-corrected near VA from one month (0.22±20 logMAR) to three months (0.21±0.23 logMAR) or six months (0.23±0.25 logMAR) after surgery (repeated measures ANOVA, $F=0.2$, $p=0.81$).

There was no significant change in mean best distance-corrected CPS from one month (0.75±0.19 logMAR) to three months (0.77±0.20 logMAR) or six months (0.77±0.23 logMAR) after surgery (repeated measures ANOVA, $F=0.2$, $p=0.86$). There was also no significant change in mean best-corrected CPS, with this being 0.52±0.22 logMAR at one month, 0.52±0.25 logMAR at three months, and 0.54±0.28 logMAR at six months after surgery (repeated measures ANOVA, $F=0.2$, $p=0.82$).

A significant change in mean best distance-corrected CPS reading speed was observed in this study (repeated measures ANOVA, F=4.5, p<0.05). Compared to one month after surgery (215.5±40.9 wpm), the best distance-corrected CPS reading speed was significantly slower at six months after surgery (195.7±33.3 wpm) (p<0.0167) but there was no significant change from one month to three months (202.9±46.3 wpm) after surgery (p=0.07) or from three months to six months after surgery (p=0.26). There was also a similar significant change in mean best-corrected CPS reading speed (repeated measures ANOVA, F=3.7, p<0.05), with that at one month after surgery (219.5±41.2 wpm) being significantly faster compared to six months after surgery (203.9±26.5 wpm) (p<0.0167). There was however no significant change from one month to three months (213.4±38.7 wpm) after surgery (p=0.17), or from three months to six months after surgery (p=0.15).

The mean defocus curves measured pre-operatively and at each post-operative visit are shown in Figure 6.1, after correction for BVD. Error bars are not displayed, since they overlap at each data point, but the standard deviation was approximately ±0.19 logMAR at each level of defocus and was consistent between each time point. The mean post-operative subjective AoA quantified from these changed significantly (repeated measures ANOVA, F=4.3, p<0.05) and although there was no significant difference between one month (0.89±0.42D) and three months (0.87±0.48D) after surgery (p=0.89), both were significantly larger than at six months (0.57±0.45D) after surgery (both p<0.0167).

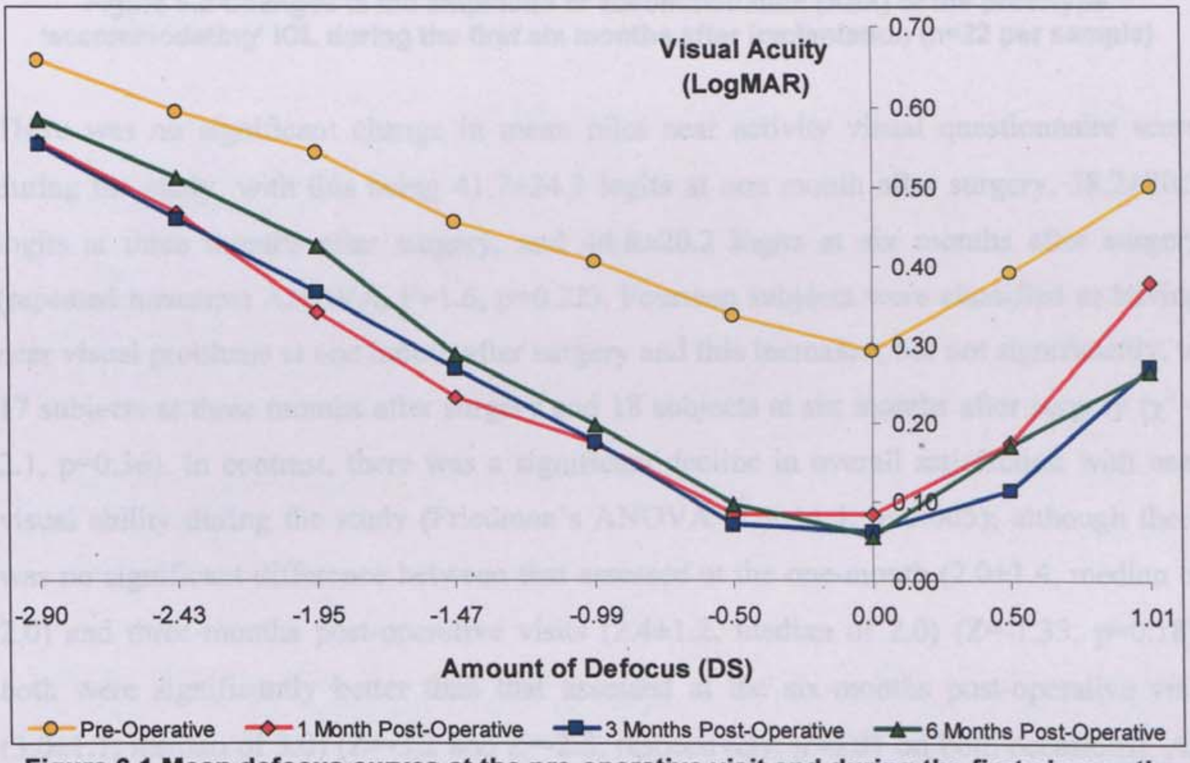

Figure 6.1 Mean defocus curves at the pre-operative visit and during the first six months after prototype 'accommodating' IOL implantation (n=22 per sample)

In contrast, when measured by the push-up/push-down technique, there was no significant change in the subjective AoA from one month (2.22±1.11D) to three months (2.41±1.57D) or six months (2.09±0.91D) after surgery (repeated measures ANOVA, F=0.8, p=0.47). This was corroborated by the objective measurements, with the AoA being 0.39±0.25D at one month after surgery, 0.35±0.27D at three months after surgery, and 0.49±0.43D at six months after surgery (repeated measures ANOVA, F=2.2, p=0.12) (Figure 6.2).

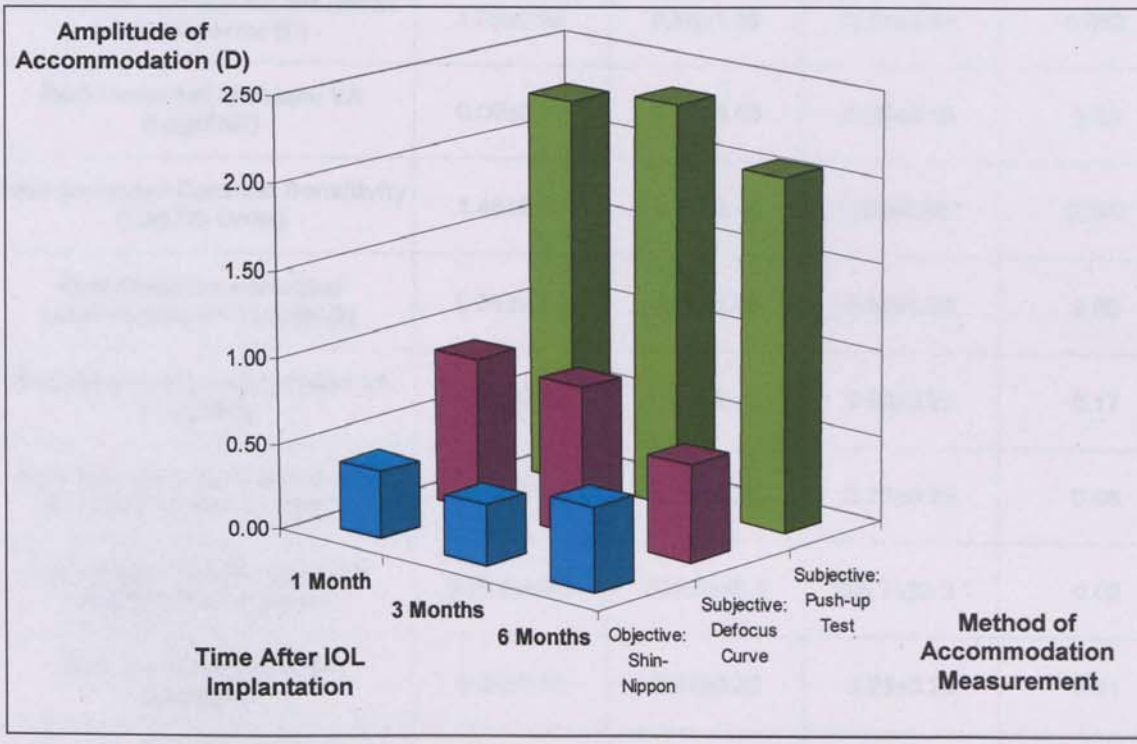

Figure 6.2 Changes in the amplitude of accommodation (AoA) of the prototype 'accommodating' IOL during the first six months after implantation (n=22 per sample)

There was no significant change in mean pilot near activity visual questionnaire score during the study, with this being 41.7±24.3 logits at one month after surgery, 38.2±20.5 logits at three months after surgery, and 44.8±20.2 logits at six months after surgery (repeated measures ANOVA, F=1.6, p=0.22). Fourteen subjects were classified as having near visual problems at one month after surgery and this increased, but not significantly, to 17 subjects at three months after surgery and 18 subjects at six months after surgery (χ^2 = 2.1, p=0.36). In contrast, there was a significant decline in overall satisfaction with near visual ability during the study (Friedman's ANOVA χ^2 = 14.4, p<0.005); although there was no significant difference between that assessed at the one-month (2.0±1.4, median of 2.0) and three-months post-operative visits (2.4±1.2, median of 2.0) (Z=-1.33, p=0.18), both were significantly better than that assessed at the six-months post-operative visit (3.0±1.1, median of 3.0) (Z=-3.2 and Z=-2.8, respectively, p<0.01 on both occasions). All of these results are summarised in Table 6.1.

Clinical Measurement	Post-operative Mean at:			Significance (P-value)
	1 Month	3 Months	6 Months	
Uncorrected Distance VA (LogMAR)	0.36±0.23	0.36±0.24	0.33±0.26	0.67
Uncorrected Contrast Sensitivity (Log CS Units)	1.40±0.21	1.39±0.21	1.32±0.22 *	*0.02*
Mean Spherical Equivalent (MSE) refractive error (D)	1.05±0.95	0.98±1.19	0.21±1.63	0.052
Best-corrected Distance VA (LogMAR)	0.09±0.18	0.06±0.15	0.06±0.19	0.13
Best-corrected Contrast Sensitivity (Log CS Units)	1.45±0.16	1.43±0.19	1.35±0.20 *	*0.002*
Best Distance-corrected Intermediate VA (LogMAR)	0.54±0.19	0.58±0.20	0.57±0.24	0.50
Best Distance-corrected Near VA (LogMAR)	0.48±0.20	0.53±0.23	0.53±0.22	0.17
Best Distance-corrected Critical Print Size (CPS) (LogMAR)	0.75±0.19	0.77±0.20	0.77±0.23	0.86
Best Distance-corrected CPS Reading Speed (wpm)	215.5±40.1	202.9±46.3	195.7±33.3 *	*0.02*
Best-corrected Near VA (LogMAR)	0.22±0.20	0.21±0.23	0.23±0.25	0.81
Best-corrected Critical Print Size (CPS) (LogMAR)	0.52±0.22	0.52±0.25	0.54±0.28	0.82
Best-corrected CPS Reading Speed (wpm)	219.5±41.2	213.4±38.7	203.9±26.5 *	*0.03*
Subjective Amplitude of Accommodation (AoA) (D) (Defocus curve)	0.89±0.42	0.87±0.48	0.57±0.45 *	*0.02*
Subjective Amplitude of Accommodation (AoA) (D) (Push-up/Push-down test)	2.22±1.16	2.41±1.57	2.09±0.91	0.47
Objective Amplitude of Accommodation (AoA) (D)	0.39±0.25	0.35±0.27	0.49±0.43	0.12
Pilot Near Activity Visual Questionnaire Score (logits) & Satisfaotion rating (0 to 4)	41.7±24.3 2.0±1.4	38.24±20.5 2.4±1.2 *	44.8±20.2 3.0±1.1 *	0.22 *0.001*

Table 6.1 Visual function of a prototype single optic 'accommodating' IOL during the first six months after implantation. Overall significant differences (assessed at p=0.05) are highlighted in italic whilst an asterisk (*) indicates the time point(s) at which the difference(s) occurred, according to pair-wise comparisons (n=22 per sample)

Compared to the pre-operative assessments, visual function was expectedly significantly better post-operatively (when compared to one month after surgery), although there was no significant difference in MSE refractive error, best-corrected CPS reading speed and subjective AoA, as quantified by both the defocus curve technique and the push-up/push-down test (p>0.05 on all occasions). These results are summarised in Table 6.2.

Clinical Measurement	Pre-operative Mean	Post-operative Mean at 1 Month	Significance
Uncorrected Distance VA (LogMAR)	0.87±0.49	0.36±0.23	*t=-4.2, p<0.001*
Uncorrected Contrast Sensitivity (Log CS Units)	0.94±0.46	1.40±0.21	*t=4.8, p<0.001*
Mean Spherical Equivalent (MSE) refractive error (D)	0.40±2.51	1.05±0.95	t=1.3, p=0.23
Best-corrected Distance VA (LogMAR)	0.47±0.48	0.09±0.18	*t=-3.5, p<0.005*
Best-corrected Contrast Sensitivity (Log CS Units)	1.12±0.45	1.45±0.16	*t=3.3, p<0.005*
Best Distance-corrected Near VA (LogMAR)	0.74±0.39	0.48±0.20	*t=-3.8, p<0.005*
Best Distance-corrected Critical Print Size (CPS) (LogMAR)	0.97±0.32	0.75±0.19	*t=-3.3, p<0.005*
Best Distance-corrected CPS Reading Speed (wpm)	189.6±38.1	215.5±40.1	*t=3.3, p<0.005*
Best-corrected Near VA (LogMAR)	0.52±0.43	0.22±0.20	*t=-3.1, p<0.01*
Best-corrected Critical Print Size (CPS) (LogMAR)	0.79±0.39	0.52±0.22	*t=-3.1, p<0.01*
Best-corrected CPS Reading Speed (wpm)	210.3±33.6	219.5±41.2	t=1.3, p=0.20
Subjective Amplitude of Accommodation (AoA) (D) (Defocus curve)	0.62±0.70	0.89±0.42	t=1.4, p=0.18
Subjective Amplitude of Accommodation (AoA) (D) (Push-up/Push-down test)	2.48±1.59	2.22±1.16	t=-0.6, p=0.59

Table 6.2 Comparison of visual function pre-operatively to post-operatively (one month) after implantation of a prototype single optic 'accommodating' IOL. Significant differences (assessed at p=0.05) are highlighted in italic (n=22 per sample)

6.6 Discussion

The feasibility of a prototype single piece single optic 'accommodating' IOL was assessed in this study by monitoring the visual function that it confers during the first six months after implantation. Several studies have previously reported on the initial outcomes of single optic 'accommodating' IOL implantation, namely the 1CU IOL (HumanOptics AG, Erlangen, Germany) and the AT-45 IOL (Bausch & Lomb Corp., Rochester, NY., USA.) (see section 1.4.3.1, Chapter 1) and the results of the current study appear to be similar.

The uncorrected and best-corrected distance VA with this prototype 'accommodating' IOL was maintainable throughout the six-month duration of this study. Indeed, the nature of the optics of this IOL expectedly produces little impact on distance visual quality compared to that expected of multifocal IOLs, which are known to cause adverse effects upon visual clarity through simultaneous vision (see sections 1.3.2 and 1.4.2, Chapter 1, and Chapter 5). Furthermore, these findings were comparable to those previously reported for the 1CU and AT-45 'accommodating' IOLs (see section 1.4.3.1, Chapter 1).

Implantation of this prototype 'accommodating' IOL however, was associated with a significant decline in contrast sensitivity from one month to six months after surgery, when measured both with and without the optimal refractive correction. This may reflect the influence of early PCO that is expected to occur after cataract surgery (Milauskas 1987, Douglas and Slack 2006), especially in IOLs that have round-edged optics (Nishi *et al.* 2000, Hayashi and Hayashi 2005). Furthermore, PCO is reportedly more prevalent with 'accommodating' IOLs due to the lack of an adequate barrier at the haptic-optic junction (Hancox *et al.* 2007) (see section 1.4.3.1, Chapter 1). Indeed, PCO is known to cause a reduction in contrast sensitivity due to an increase in light scatter (Meacock *et al.* 2003). However, at the completion of this study, no subjects were deemed to have clinically significant PCO by the consultant ophthalmologist. It is therefore possible that any effect the presence of early PCO had on contrast sensitivity may have been compounded by the consequential adverse effect of increased refractive error.

The MSE refractive error did not change significantly during this study, although the variation in refractive error was seen to increase, as indicated by the larger standard deviation. This suggests that progressively larger refractive errors were present in some subjects, which may have caused visual deterioration.

As an example, the astigmatic refractive error increased from 2.25DC at one month after surgery to 6.75DC at six months after surgery in one particular subject; the astigmatic image is therefore likely to have reduced the quality of uncorrected vision, whilst the best-corrected visual quality may have been adversely impacted upon by spectacle lens magnification and distortion effects.

There was no significant change in the best distance-corrected intermediate VA after implantation of the prototype 'accommodating' IOL. Similarly, there was no significant change in the best distance-corrected near VA throughout the six-month duration of this study. Of surprise however, was the finding that the magnitude of the latter was similar to that of the former, and was in fact poorer than that previously reported for the 1CU 'accommodating' IOL (Kuchle *et al.* 2003, Langenbucher *et al.* 2003b, 2003c, Kuchle *et al.* 2004, Dogru *et al.* 2005) and the AT-45 'accommodating' IOL (Macsai *et al.* 2006). This finding primarily reflects a poor ability of the prototype IOL to 'accommodate', whilst any accommodative ability that was present was observed to deteriorate significantly during the first six-months after implantation, as measured by the defocus curve method. Indeed, although there was no significant change in the objective measurements of the AoA, the magnitude of objective accommodation was always less than 0.50D throughout the study, suggesting that a high level of best distance-corrected near vision would not have been achievable. Furthermore, one must also consider that the subjective measurements of the AoA conducted with the push-up/push-down test are prone to variable DoF effects, due to pupil size and target size variation, and this is likely to explain the larger estimates of the AoA that were obtained compared to the defocus curve method (see sections 3.1.7.3 and 3.6, Chapter 3).

It is evident that the AoA of the prototype 'accommodating' IOL is not as great as the 1CU counterpart, which can reportedly provide 0.72D (Wolffsohn *et al.* 2006a) to 1.00D (Langenbucher *et al.* 2003c) of 'accommodation' (measured objectively) at similar times after implantation. In fact, the poor accommodative ability of the prototype IOL is further confirmed by the finding in this study that the AoA was not significantly better compared to pre-operatively, as measured by both of the subjective techniques. In addition, the best distance-corrected measures of near VA and CPS improved by two to three lines of logMAR acuity when measured with a near addition of +2.50DS, post-operatively, which would not have been expected if this IOL were truly 'accommodating'.

During the first six months after implantation of the prototype IOL, there was a significant deterioration in the CPS reading speed, as measured with both the best distance correction and with a near addition. It is likely that this reflects the reduction in contrast sensitivity observed, since reading ability is known to be greatly dependent on this function (Legge *et al.* 1987a). Indeed, this is supported further by the finding that the CPS reading speed was not significantly different compared to pre-operatively, whilst the CPS itself also did not change significantly, both of which should have improved due to the clearer ocular media.

Subjective perceptions of near visual ability conferred by the prototype 'accommodating' IOL did not change significantly during the first six months after implantation. This suggests that subjects either rapidly adapted to the near ability conferred by the correction, or did not have substantial demands for being able to do near visual tasks. It is not likely that pseudoaccommodation effects were present since near visual performance, in terms of reading speed, was evidently impacted upon even with best refractive correction. It is more likely that near visual ability was never altogether sufficient with this IOL, since the mean questionnaire score was always higher than the criterion score that is diagnostic of near visual problems. Consequently, the majority of subjects were classified as experiencing significant difficulties at each of the time points in the study (63.6% at one month, 77.3% at three months and 81.1% at six months after surgery). This in turn is reflected well by the observation of a significant reduction in the rating of overall satisfaction with near vision.

6.6.1 Limitations

It is likely that subjective perceptions of near visual ability observed in this study were not entirely accurate, since the optimal NAVQ developed in Chapter 4 was not used. However, the NAVQ had not yet been developed when this study was conducted and therefore this could not have been used. Indeed, the NAVQ may have better discriminated near visual problems that are experienced by individuals, compared to the pilot questionnaire, particularly since it was noted that questionnaire scores did not change significantly despite significant reductions in contrast sensitivity, reading speed and satisfaction. Further support for the subjective findings may have been obtained if each subject was asked about his or her spectacle usage/dependency. Development of the pilot questionnaire using Rasch Analysis (Gupta *et al.* 2007) however suggested redundancy of this item. In contrast, development of the NAVQ suggested retention of this item (see sections 4.5 and 4.6, Chapter 4), and therefore the NAVQ would have provided this information.

It is not certain in these monocularly implanted subjects, whether the near visual ability of the unoperated eye influenced the questionnaire responses or not. If this was substantially better or poorer, for example due to developing/existing cataract or the presence of a hypermetropic refractive error, the questionnaire scores are likely to have been biased.

The observation of only a few statistically significant differences in this study suggests that visual outcomes with this 'accommodating' IOL are likely to be stable in the short-term. Conversely, the presence of only a few significant differences may have been due to a low level of statistical power. The low statistical power may have arisen due to the small effect sizes observed but also due to the small sample size used in this study (see section 6.3.1). However, it is not common for feasibility studies of this kind to recruit large subject numbers, primarily due to reasons relating to managing costs, ensuring and assessing safety, and potentially needing to alter the design of a *prototype* IOL. In fact, after completion of this study with the cohort of 22 subjects, further recruitment of subjects and implantation of this IOL was terminated since five subjects (five eyes) required Laser-assisted Epithelial Keratomileusis (LASEK) corneal refractive surgery to correct induced refractive error, whilst the IOL in one subject (one eye) was explanted due to tilting, which induced a considerable astigmatic refractive error.

6.7 Conclusion

Implantation of this prototype single piece single optic 'accommodating' IOL was associated with a significant reduction in contrast sensitivity during the first six months after surgery, most likely due to the early influences of PCO that are associated with all cataract extractions. Although this had a significant impact on reading speed, as assessed by standardised near vision techniques, the lack of other significant differences suggests stability of visual function in the short term. However, there does not appear to be any substantial benefit conferred by this IOL over alternative single optic 'accommodating' designs, especially in terms of the amplitude of 'accommodation' that is present. Furthermore, subjective perceptions of near visual ability and satisfaction suggest that the performance was never entirely adequate for the needs of this particular cohort.

It is of great interest as to whether these visual outcomes would continue in the long-term. Indeed, few studies have assessed the long-term sustainability and feasibility of single optic 'accommodating' IOL performance, and this forms the focus for the next Chapter.

CHAPTER 7

Long-term Visual Outcomes of a Single Optic 'Accommodating' Intraocular Lens

7. Introduction

Current interest in single optic 'accommodating' IOLs predominantly surrounds the 1CU IOL (HumanOptics AG, Erlangen, Germany) and AT-45 IOL (Bausch & Lomb Corp., Rochester, NY., USA.). Both of these IOLs purportedly produce their 'accommodative' effect as a result of hinged-optic designs, which allow the optic to move anteriorly upon ciliary muscle contraction (see section 1.4.3.1, Chapter 1). In contrast, few studies have investigated the outcomes associated with *single-piece* designs (Wolffsohn *et al.* 2006b, Sanders and Sanders 2007) whilst few have considered whether any short-term benefits are maintained in the longer-term, beyond the first year after implantation (Claoue 2004, Koeppl *et al.* 2005, Kriechbaum *et al.* 2005, Hancox *et al.* 2006, Wolffsohn *et al.* 2006a, Hancox *et al.* 2007, Harman *et al.* 2008). In addition, only one study has considered if there is any benefit of bilateral IOL implantation compared to unilateral implantation (Sanders and Sanders 2007). These points therefore form the focus for this Chapter.

7.1 Study Aim

The Tetraflex™ KH3500 'accommodating' IOL (Lenstec, Inc., St. Petersburg, FL., USA.) (Figure 7.1) is a single-piece design that is manufactured from hydroxyethylmethacrylate (HEMA). This IOL has a single square-edged optic with a diameter of 5.75mm, a total diameter of 12.0mm, an 'A' constant of 118.0 (Wolffsohn *et al.* 2006b), and two angulated (5° anteriorly) flexible haptics that confer 'accommodation' by enabling the entire IOL to move anteriorly upon ciliary muscle contraction (Beiko 2007, Doane and Jackson 2007).

Figure 7.1 The Tetraflex™ KH3500 'accommodating' IOL (Lenstec, Inc., St. Petersburg, FL., USA.) – ©2008 *reproduced with permission from the website: http://www.lenstec.com/lenstec/menu_tf.html, accessed 15:20, 14/04/2008*

Two previous studies have investigated the visual outcomes six months after Tetraflex™ KH3500 'accommodating' IOL implantation, but these have produced conflicting results. The first study suggested that although distance VA was maintainable, the objectively and subjectively measured AoA reduced, resulting in a decrease in the best distance-corrected near VA (Wolffsohn *et al.* 2006b). The second study concurred with the finding of a reduction in the AoA but instead reported an improvement in the best distance-corrected near VA; it was also found that bilateral IOL implantation improved visual outcomes, in terms of the uncorrected distance and near VA, best distance-corrected near VA and the AoA, compared to unilateral implantation (Sanders and Sanders 2007). Further to these results, the purpose of the present study was to assess the long-term monocular and binocular visual outcomes after implantation of the Tetraflex™ KH3500 'accommodating' IOL, with reference to the near vision metrics standardised in Chapters 2, 3 and 4.

7.2 Method

Twenty-nine subjects (11 males, 18 females) of mean age 68.5±14.0 years (range 30 to 91 years) were recruited from Solihull Hospital and from the Midland Eye Institute in Birmingham, having received unilateral or bilateral Tetraflex™ KH3500 'accommodating' IOL implants due to cataract extraction or CLE approximately two to three years prior to the start of this study. These subjects included those that had also participated in the six-month post-operative evaluation study of Wolffsohn et al. (2006b). Since this was a retrospective study not requiring any treatments to be administered, only the following eligibility criteria were applied, which were ensured by a consultant ophthalmologist:

(a) The absence of ocular pathology, including AMD, glaucoma and diabetic retinopathy, in the operated eye(s).
(b) The absence of binocular vision and accommodative anomalies including decompensated heterophoria, heterotropia, and amblyopia, as confirmed by cover tests and fixation disparity tests using the Mallett unit at distance (six metres) and near (40cm).
(c) The absence of immunosuppressant conditions and/or medication.

All subjects were required to attend a single post-operative aftercare appointment at which the following measurements of visual function were conducted, monocularly on the operated eye(s), under consistent illumination of 500 lux and chart luminance of $120cdm^{-2}$:

(a) Uncorrected and best-corrected distance VA at 6m using the computerised *Test Chart 2000 Pro* (Thomson Software Solutions, Hatfield, Herts., UK.) logMAR chart.

(b) Best-corrected contrast sensitivity, measured in logarithmic contrast sensitivity (log CS) units at 3m with the Pelli Robson chart, and scored as the last triplet in which two out of the three letters were correctly identified and allowing for interchanged misreads of "C", "O" and "D" to be treated as correct; this scoring rule reduces the bias in test scores if suprathreshold letters are misread (Pelli *et al.* 1988).

(c) Retinoscopy at 66cm followed by a full subjective refraction.

(d) Uncorrected, best distance-corrected and best-corrected near VA at 40cm using the ETDRS Near LogMAR Chart (Precision Vision™, La Salle, IL., USA.), according to the findings of Chapter 2 and measured as described in section 2.4 (see Chapter 2).

(e) Best distance-corrected CPS in logMAR, and CPS reading speed in wpm, at 40cm using the MNRead chart (Lighthouse Low Vision Products, Long Island City, NY., USA.), in accordance with the findings of Chapter 2 and measured as described in section 2.4 (see Chapter 2).

(f) Objective AoA using the equipment and procedure described in sections 3.1.7.2 and 3.3.2 (see Chapter 3), respectively.

(g) Subjective AoA by curve-fitting of a defocus curve (range of +2.00DS to -2.00DS in 0.50DS steps) measured and quantified in accordance with the methods and findings of Chapter 3, with only the best distance refractive correction worn.

(h) Subjective AoA by the push-up/push-down test using the equipment and procedure described in section 3.1.7.3 (see Chapter 3), which included the use of a near addition of +2.50DS, and was taken as the mean of three readings.

(i) Subjective evaluation of near vision using the NAVQ, which also assesses satisfaction on a scale of 0 (completely satisfied) to 5 (completely unsatisfied) (see Chapter 4).

Of the 29 subjects recruited for this study, 19 subjects had received bilateral 'accommodating' IOL implants and therefore in order to assess for any visual benefit of bilateral IOL implantation over unilateral IOL implantation, the following measurements were repeated binocularly, using the equipment and methods described above:

(a) Best-corrected distance VA at 6m using the *Test Chart 2000 Pro* logMAR chart.

(b) Best-corrected contrast sensitivity at 3m using the Pelli Robson chart.

(c) Best distance-corrected near VA at 40cm using the ETDRS logMAR chart.

(d) Subjective AoA by the push-up/push-down test.

All of the clinical assessments that required a refraction to be worn were conducted with optical trial lenses placed in a trial frame at a BVD of 12.0mm; a near addition of +2.50DS was included when necessary. A consultant ophthalmologist also examined all of the subjects at the time of the clinical measurements to determine if any ocular complications, such as IOL dislocation or PCO, were present. Furthermore, the previous medical records of all of the subjects were examined to determine if any such complications had occurred in the time between surgery and the post-operative aftercare visit for this study.

The NHS Local Research Ethics Committee of Solihull approved this study and informed consent was obtained from each subject after explanation of the nature, possible risks and consequences of the study.

7.3 Statistical Analysis

For the NAVQ, the number of subjects classified as having near visual problems (NAVQ score of 40.45 logits or more; see section 4.6, Chapter 4) was compared to the number of subjects classified as *not* having near visual problems using the Chi-square (χ^2) test.

To assess for any benefit of bilateral Tetraflex™ KH3500 'accommodating' IOL implantation over unilateral implantation, all of the clinical measurements that were conducted binocularly on the 19 bilaterally implanted subjects were compared to the corresponding *average measure of the monocular eyes* and to the *best monocular eye measure* (defined as the eye that gave the better visual function in three or more out of the four assessments made) using the two-tailed paired-samples Student's T-Test (see Appendix for details of statistical test selection). The *predictive* benefit of bilateral IOL implantation over unilateral implantation, if any, was determined by assessing the PPMC (correlation) coefficients, and associated significance by linear regression, for the comparison between the 'best eye monocular measure' to the '*change* to binocular measure' (calculated as the difference between the binocular measure and the best monocular eye measure), for each of the four binocularly conducted clinical measurements. Differences and correlation relationships were considered to be significant at p=0.05 at all times. All analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.) and all graphs were produced using Microsoft® Excel® (Microsoft® Corporation, Redmond, WA., USA.).

7.3.1 Power Analysis

The two previous studies that have investigated the visual outcomes of the Tetraflex™ KH3500 'accommodating' IOL used sample sizes of 28 eyes (Wolffsohn *et al.* 2006b) and 85 eyes (Sanders and Sanders 2007), although the latter study only used a sample of 27 eyes for the comparison between monocular and binocular visual outcomes. In order to determine the minimum required sample size to ensure a statistical power of at least 80% (0.80) in the present study, power analysis was conducted *a priori* based on the two-tailed paired-samples Student's T-Test, for the comparisons between monocular and binocular measures of best distance-corrected near VA and subjective AoA. Based on this, a minimum sample size of between 24 and 49 subjects was indicated, whilst *post hoc* analysis based on the actual sample size and observations in this study revealed that power ranged from 0.63 (subjective AoA) to 0.98 (near VA) (see Appendix for all calculations).

7.4 Results: Monocular Data

The mean time between implantation of the Tetraflex™ KH3500 'accommodating' IOL and clinical evaluation for this study was 2.6±0.4 years (range 1.9 to 3.2 years). The mean IOL power was 21.4±4.7D (range 10.0 to 32.0D). Mean uncorrected distance VA was 0.17±0.23 logMAR whilst mean uncorrected near VA was 0.61±0.25 logMAR. The MSE refractive error was 0.15±0.89D and this gave a mean best-corrected distance VA of 0.02±0.20 logMAR and a mean best-corrected contrast sensitivity of 1.39±0.19 log CS units. Mean best distance-corrected near VA was 0.58±0.17 logMAR and this improved to a mean best-corrected near VA of 0.21±0.19 logMAR with a near addition of +2.50DS. The mean best distance-corrected CPS was 0.80±0.16 logMAR and the associated mean CPS reading speed was 168.2±32.3 wpm.

The mean stimulus-response curve is shown in Figure 7.2. Individual stimulus-response curves revealed no notable change in refractive power in 23 eyes, a linear increase in 5 eyes, an initial increase followed by a plateau in 13 eyes, an initial increase followed by a decrease in 6 eyes, and a decreasing response in one eye, in response to increased accommodative demand. The mean objective AoA evaluated from these was 0.25±0.24D.

The mean defocus curve is shown in Figure 7.3, after correction for BVD, and the mean subjective AoA quantified from these by the curve-fitting method was 0.83±0.42D.

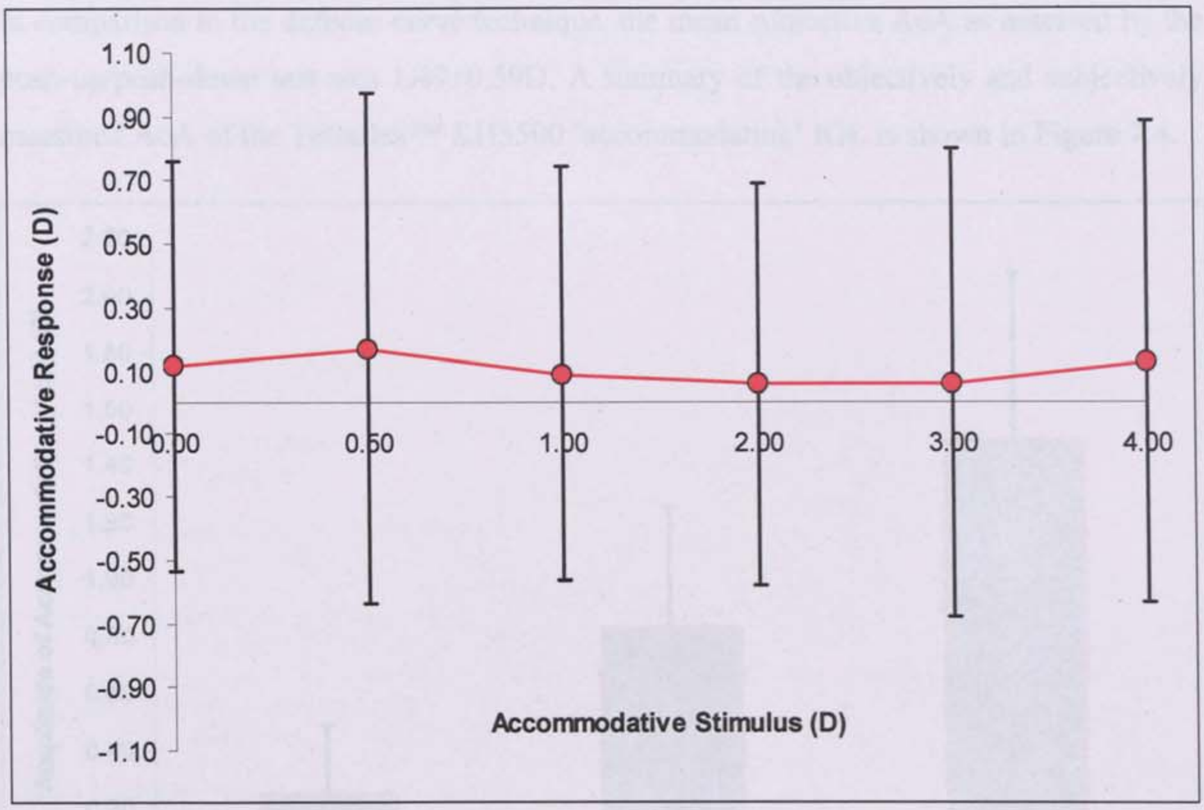

Figure 7.2 The mean stimulus-response curve of the Tetraflex™ KH3500 'accommodating' IOL, on average 2.6 years after implantation (n=48 eyes)

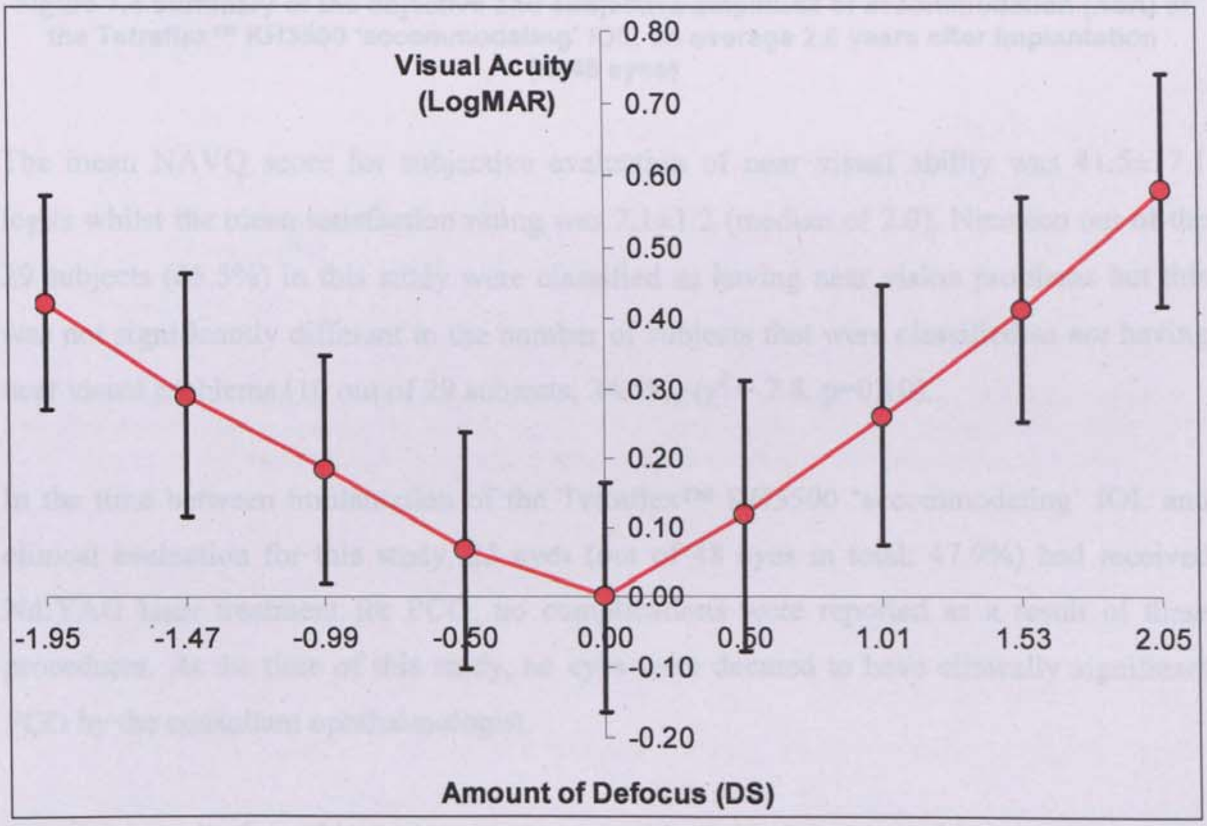

Figure 7.3 The mean defocus curve of the Tetraflex™ KH3500 'accommodating' IOL, on average 2.6 years after implantation (n=48 eyes)

In comparison to the defocus curve technique, the mean subjective AoA as assessed by the push-up/push-down test was 1.49±0.59D. A summary of the objectively and subjectively measured AoA of the Tetraflex™ KH3500 'accommodating' IOL is shown in Figure 7.4.

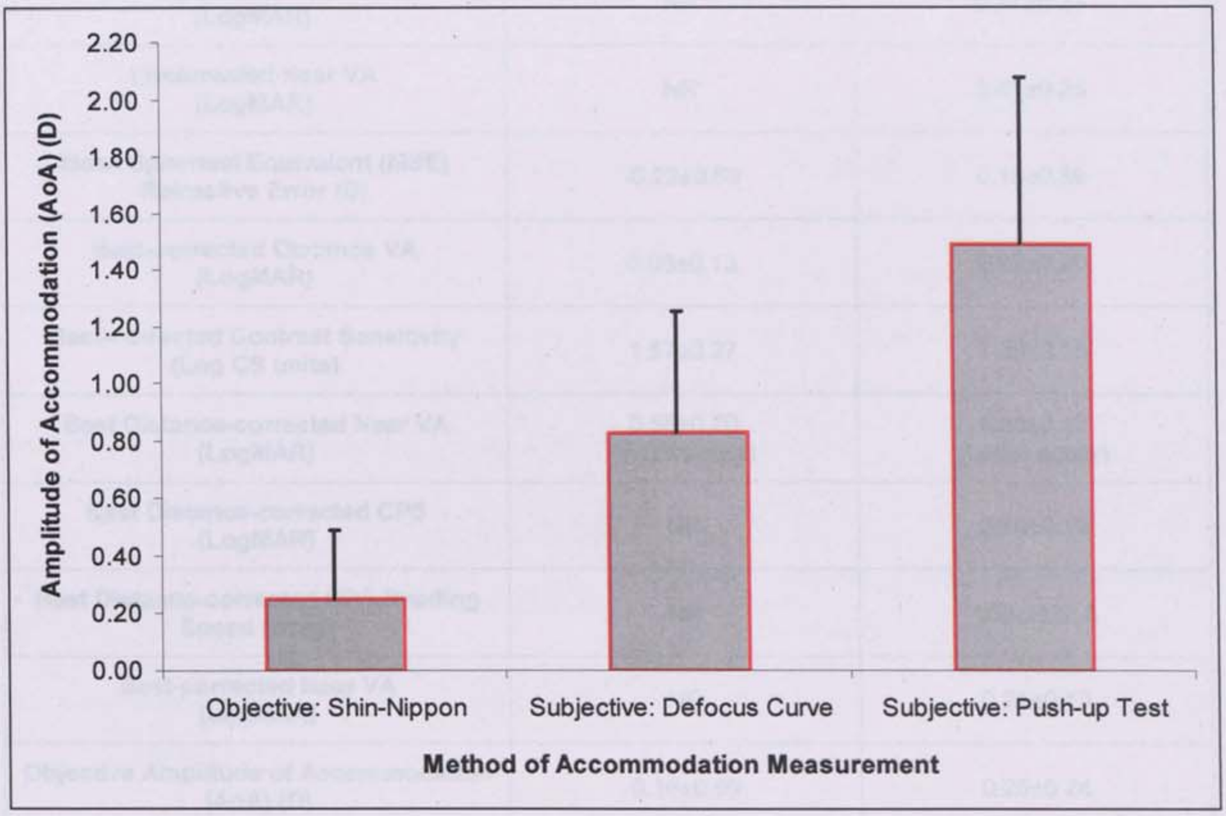

Figure 7.4 Summary of the objective and subjective amplitude of accommodation (AoA) of the Tetraflex™ KH3500 'accommodating' IOL, on average 2.6 years after implantation (n=48 eyes)

The mean NAVQ score for subjective evaluation of near visual ability was 41.5±17.1 logits whilst the mean satisfaction rating was 2.1±1.2 (median of 2.0). Nineteen out of the 29 subjects (65.5%) in this study were classified as having near vision problems but this was not significantly different to the number of subjects that were classified as *not* having near visual problems (10 out of 29 subjects; 34.5%) ($\chi^2 = 2.8$, p=0.10).

In the time between implantation of the Tetraflex™ KH3500 'accommodating' IOL and clinical evaluation for this study, 23 eyes (out of 48 eyes in total; 47.9%) had received Nd:YAG laser treatment for PCO; no complications were reported as a result of these procedures. At the time of this study, no eyes were deemed to have clinically significant PCO by the consultant ophthalmologist.

All of the results from this study are summarised in Table 7.1 along with a summary of the six-month data from the evaluation study of Wolffsohn et al. (2006b).

Clinical Measurement	Mean at 6 Months Post-operatively n=28 eyes (Wolffsohn *et al.* 2006b)	Mean at, on average, 31 Months Post-operatively n=48 eyes (Present study)
Uncorrected Distance VA (LogMAR)	NR	0.17±0.23
Uncorrected Near VA (LogMAR)	NR	0.61±0.25
Mean Spherical Equivalent (MSE) Refractive Error (D)	-0.23±0.69	0.15±0.89
Best-corrected Distance VA (LogMAR)	0.06±0.13	0.02±0.20
Best-corrected Contrast Sensitivity (Log CS units)	1.57±0.27	1.39±0.19
Best Distance-corrected Near VA (LogMAR)	0.58±0.20 (Word acuity)	0.58±0.17 (Letter acuity)
Best Distance-corrected CPS (LogMAR)	NR	0.80±0.16
Best Distance-corrected CPS Reading Speed (wpm)	NR	168.2±32.3
Best-corrected Near VA (LogMAR)	NR	0.21±0.19
Objective Amplitude of Accommodation (AoA) (D)	0.16±0.99	0.25±0.24
Subjective Amplitude of Accommodation (AoA) (D) (Defocus curve)	NR	0.83±0.42
Subjective Amplitude of Accommodation (AoA) (D) (Push-up/Push-down test)	1.70±2.20	1.49±0.59
Near Activity Visual Questionnaire (NAVQ) Score (logits) & Satisfaction rating (0 to 5)	NR NR	41.5±17.1 2.1±1.2

Table 7.1 Visual performance of the Tetraflex™ KH3500 'accommodating' IOL at 6 months after implantation, according to Wolffsohn et al. (2006b), and at, on average, 31 months (2.6 years) after implantation, according to the present study. 'NR' indicates that the measurement was not reported

7.5 Results: Binocular Comparison

The mean binocular best-corrected distance VA in the 19 bilaterally implanted subjects was -0.03±0.13 logMAR and whilst this was significantly better than the average measure of the monocular eyes (0.01±0.15 logMAR) ($t=-2.6$, $p<0.05$), this was not significantly better than the best monocular eye (-0.06±0.11 logMAR) ($t=1.6$, $p=0.13$).

The mean binocular best-corrected contrast sensitivity was 1.58±0.10 log CS units and this was significantly better than both the average measure of the monocular eyes (1.41±0.13 log CS units) ($t=8.8$, $p<0.001$) and the best monocular eye (1.46±0.14 log units) ($t=5.5$, $p<0.001$).

The mean binocular best distance-corrected near VA was 0.44±0.12 logMAR and this was significantly better than both the average measure of the monocular eyes (0.56±0.14 logMAR) ($t=-6.6$, $p<0.001$) and the best monocular eye (0.54±0.15 logMAR) ($t=-4.3$, $p<0.001$). The mean binocular subjective AoA as assessed by the push-up/push-down test was 1.88±0.90D and this was not significantly greater than the average measure of the monocular eyes (1.51±0.46D) ($t=1.9$, $p=0.08$) or the best monocular eye (1.47±0.46D) ($t=1.7$, $p=0.11$). All of these results are summarised in Table 7.2.

Clinical Measurement	Mean Binocular Measure	Average Monocular Measure & Significance (P-value)	Best Monocular Measure & Significance (P-value)
Best-corrected Distance VA (LogMAR)	-0.03±0.13	0.01±0.15 *p<0.05*	-0.06±0.11 p=0.13
Best-corrected Contrast Sensitivity (Log CS units)	1.58±0.10	1.41±0.13 *p<0.001*	1.46±0.14 *p<0.001*
Best Distance-corrected Near VA (LogMAR)	0.44±0.12	0.56±0.14 *p<0.001*	0.54±0.15 *p<0.001*
Subjective Amplitude of Accommodation (AoA) (Push-up/Push-down Test) (D)	1.88±0.90	1.51±0.46 p=0.08	1.47±0.46 p=0.11

Table 7.2 Comparison of visual performance between bilateral and unilateral implantation of the Tetraflex™ KH3500 'accommodating' IOL. Significant differences are highlighted in italic (n=19 subjects)

The potential benefit to visual function of bilateral implantation over unilateral (best eye) implantation of the Tetraflex™ KH3500 'accommodating' IOL could be statistically significantly predicted for the best-corrected contrast sensitivity (Figure 7.5; $r=-0.67$, $p<0.005$), best distance-corrected near VA (Figure 7.6; $r=-0.60$, $p<0.01$) and the subjective AoA, as assessed by the push-up/push-down test (Figure 7.7; $r=-0.53$, $p<0.05$). There was however no significant value of predicting any benefit from the best-corrected distance VA after second eye implantation of this 'accommodating' IOL (Figure 7.6; $r=0.01$, $p=0.96$). All of these results are summarised in Table 7.3.

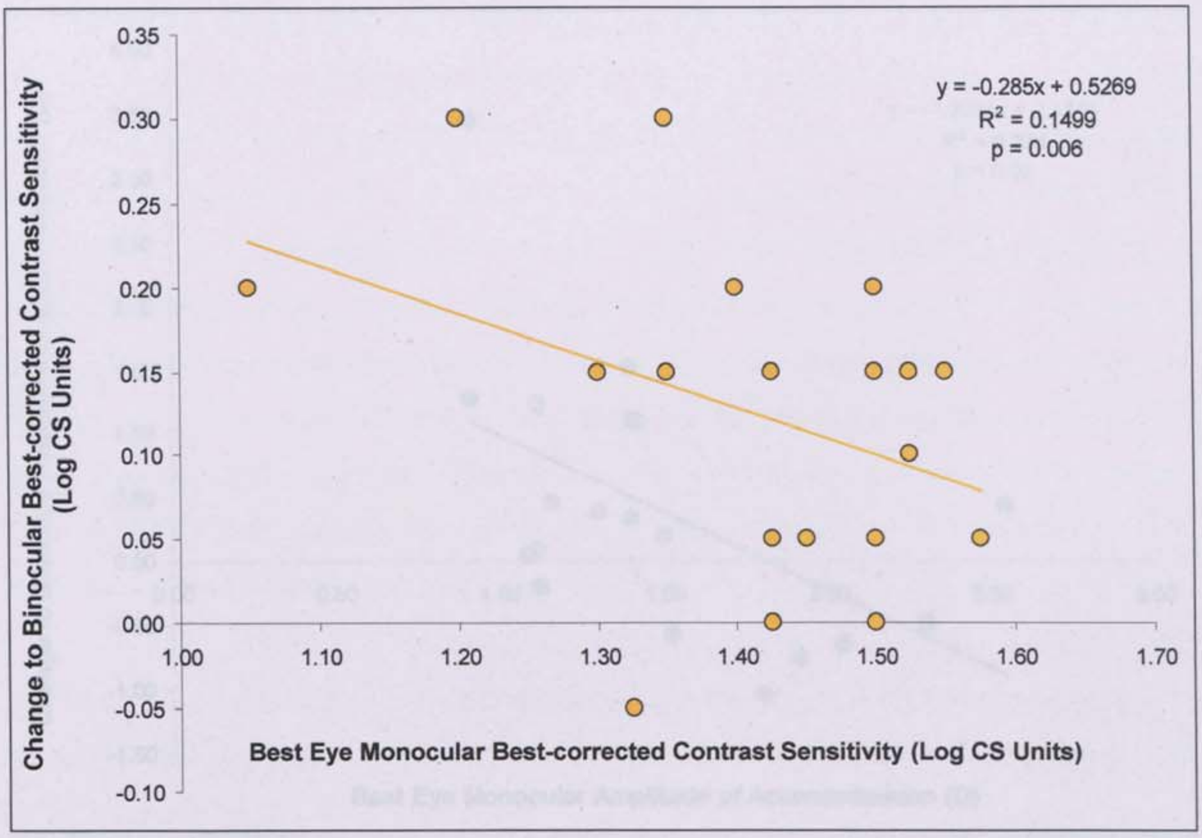

Figure 7.5 Predictive changes in best-corrected contrast sensitivity from unilateral (best eye) to bilateral implantation of the Tetraflex™ KH3500 'accommodating' IOL (n=19 subjects)

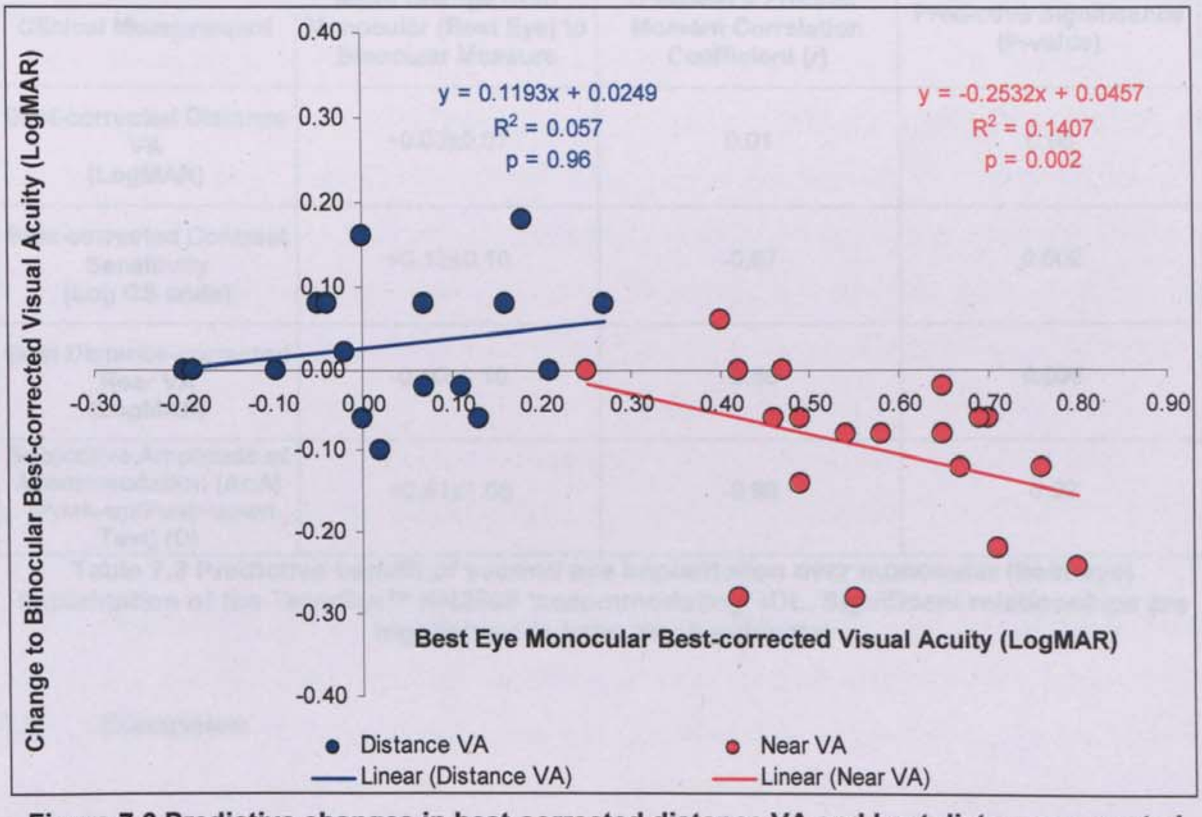

Figure 7.6 Predictive changes in best-corrected distance VA and best distance-corrected near VA from unilateral (best eye) to bilateral implantation of the Tetraflex™ KH3500 'accommodating' IOL (n=19 subjects)

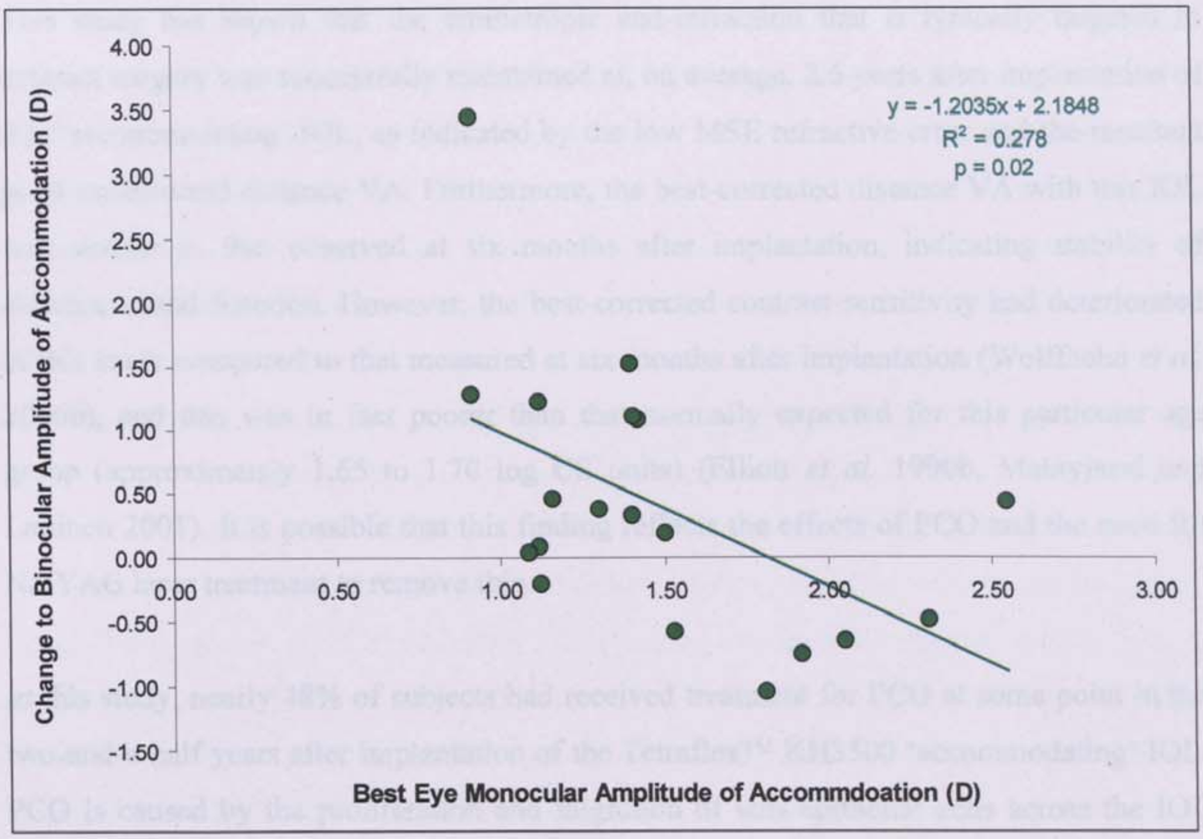

Figure 7.7 Predictive changes in the subjective amplitude of accommodation from unilateral (best eye) to bilateral implantation of the Tetraflex™ KH3500 'accommodating' IOL (n=19 subjects)

Clinical Measurement	Mean Change from Monocular (Best Eye) to Binocular Measure	Pearson's Product Moment Correlation Coefficient (r)	Predictive Significance (P-value)
Best-corrected Distance VA (LogMAR)	+0.03±0.07	0.01	0.96
Best-corrected Contrast Sensitivity (Log CS units)	+0.12±0.10	-0.67	*0.002*
Best Distance-corrected Near VA (LogMAR)	-0.10±0.10	-0.60	*0.006*
Subjective Amplitude of Accommodation (AoA) (Push-up/Push-down Test) (D)	+0.41±1.05	-0.53	*0.02*

Table 7.3 Predictive benefit of second eye implantation over monocular (best eye) implantation of the Tetraflex™ KH3500 'accommodating' IOL. Significant relationships are highlighted in italic (n=19 subjects)

7.6 Discussion

This study aimed to assess the long-term visual outcomes and potential benefit of bilateral implantation of the single piece single optic Tetraflex™ KH3500 'accommodating' IOL.

This study has shown that the emmetropic end-refraction that is typically targeted in cataract surgery was successfully maintained at, on average, 2.6 years after implantation of this 'accommodating' IOL, as indicated by the low MSE refractive error and the resultant good uncorrected distance VA. Furthermore, the best-corrected distance VA with this IOL was similar to that observed at six months after implantation, indicating stability of distance visual function. However, the best-corrected contrast sensitivity had deteriorated in this study compared to that measured at six months after implantation (Wolffsohn *et al.* 2006b), and this was in fact poorer than that normally expected for this particular age group (approximately 1.65 to 1.70 log CS units) (Elliott *et al.* 1990b, Mantyjarvi and Laitinen 2001). It is possible that this finding reflects the effects of PCO and the need for Nd:YAG laser treatment to remove this.

In this study, nearly 48% of subjects had received treatment for PCO at some point in the two-and-a-half years after implantation of the Tetraflex™ KH3500 'accommodating' IOL. PCO is caused by the proliferation and migration of lens epithelial cells across the IOL surface (see section 1.4.3, Chapter 1) and the rate of this in the present study was similar to that reported for the 1CU 'accommodating' IOL at a comparable time after implantation (Hancox *et al.* 2006, Wolffsohn *et al.* 2006a, Hancox *et al.* 2007). Of importance is the manner whereby PCO can cause a reduction in contrast sensitivity due to increased light scatter (Meacock *et al.* 2003) and it is possible that this occurred in the present study if a small amount was either re-developing in those eyes that had previously been treated, or was now developing in the 52% of subjects that had not yet required any treatment. Indeed, it has been reported that distance VA measures alone do not detect the effects of PCO, or significant improvements after Nd:YAG laser treatment, and therefore contrast sensitivity measurements with the Pelli Robson chart are strongly recommended (Tan *et al.* 1999).

PCO can also reportedly reduce the anterior optic movement of an 'accommodating' IOL, due to reduced capsular bag elasticity (see section 1.4.3.1, Chapter 1), and intuitively this will cause a reduction in the AoA (Hancox *et al.* 2006). A small increase in PCO appears to be an occurrence in this study since there was a deterioration in the subjective AoA, in addition to the changes in contrast sensitivity, compared to six months after implantation (Wolffsohn *et al.* 2006b). Although objective measurements suggested an improvement in the AoA, the accuracy of such methods has been questioned in pseudophakic eyes, primarily due to increased light scatter from the IOL surfaces (Langenbucher *et al.* 2003b, 2003c); in the presence of PCO, this is likely to be exacerbated.

The AoA of the Tetraflex™ KH3500 'accommodating' IOL approximately two-and-a-half years after implantation, as measured with the push-up/push-down test and the defocus curve method, does not appear to be as large as the 1CU 'accommodating IOL, which can purportedly provide between 1.09±0.58D (defocus curve) to 2.31±0.08D (push-up/push-down test) of 'accommodation' (Hancox *et al.* 2006, Wolffsohn *et al.* 2006a). It is therefore evident that this is the most likely reason for the large difference of nearly four lines of logMAR acuity between the best distance-corrected near VA and the best-corrected equivalent, observed in this study. However, the best distance-corrected near VA in this study was comparable to that reported at six months after implantation (Wolffsohn *et al.* 2006b), and to that reported for the 1CU 'accommodating' IOL at 18 months (Harman *et al.* 2008) to 24 months (Kriechbaum *et al.* 2005) after implantation, if not better (Wolffsohn *et al.* 2006a). It may be that pseudoaccommodative effects such as DoF (see section 1.4.4, Chapter 1) aided subjects to a greater extent in the present study. However, one must also consider that the word optotypes used by Wolffsohn et al. (2006b) to measure near VA tend to yield larger magnitudes compared to single letter near VA, despite high agreement (see Chapter 2), and therefore near VA may actually have deteriorated in the present study.

A reduced 'accommodative' ability of the Tetraflex™ KH3500 'accommodating' IOL also appears to impact upon the most comfortable (critical) readable print size achievable (CPS), since this was considerably larger than the near VA threshold. In addition, this was approximately three lines of logMAR acuity poorer than that reported for the 1CU 'accommodating' IOL at 18 months after implantation (0.50±0.12 logMAR) (Harman *et al.* 2008). It is not likely that the CPS reading speed was affected since that observed in this study was similar to that reported for the 1CU 'accommodating' IOL at 18 months after implantation (173.0±35.0 wpm) (Harman *et al.* 2008). However, in view of the findings of Chapter 6, where the CPS reading speed deteriorated significantly during the first six months after implantation of a prototype single piece single optic 'accommodating' IOL, most likely due to PCO, this possibility cannot be totally discounted. Unfortunately, no direct comparison of this function, with the IOL in this study, to that at six-months after implantation was possible since this metric was not reported (Wolffsohn 2008). Furthermore, the only other study that has assessed reading ability with the 1CU 'accommodating' IOL only reported the required CPS (0.46±0.14 logMAR) to achieve an arbitrarily set minimum reading speed of 80wpm. This in fact adds further support for the need to standardise measurements of near visual function with presbyopic corrections.

The individual stimulus-response curves in this study indicated that there was some active 'accommodative' function with the Tetraflex™ KH3500 'accommodating' IOL, since an increase in myopic refractive error, with increased stimulus demand, was observed in some subjects. It is evident however that this IOL does not produce enough anterior movement to confer adequate spectacle-free near vision for most subjects, as indicated by the NAVQ scores of perceived effects. Indeed, nearly half of the subjects were classified as having near visual difficulties by this questionnaire, although the high rating of overall satisfaction suggests that most were able to cope, or perhaps had lower demands and/or expectations.

The results of this study suggest that bilateral implantation of the Tetraflex™ KH3500 'accommodating' IOL can significantly improve visual outcomes compared to unilateral implantation, as assessed against the average measures of the monocular eyes, in terms of distance VA, contrast sensitivity and the best distance-corrected near VA. Even when assessed against the best monocular eye, bilateral implantation of this IOL produced significantly better contrast sensitivity and best distance-corrected near VA compared to unilateral implantation. This is in agreement with the findings of Sanders and Sanders (2007) and is most likely to be due to the effects of binocular summation (Campbell and Green 1965). There was however no significant improvement in the subjective AoA, suggesting that there is no substantial advantage to be gained for this particular function. Conversely, the subjective AoA was measured using the push-up/push-down test, which is known to be prone to variable DoF effects, due to pupil size and target size variation, which consequently may have resulted in inaccurate quantification of the true AoA (see section 3.1.7.3, Chapter 3). In view of this, use of the defocus curve technique would instead have been ideal, since these effects are minimal.

The finding in this study that NAVQ scores of unilaterally implanted subjects (mean of 31.4±22.9 logits) were not significantly different to those of bilaterally implanted subjects (mean of 46.9±10.4 logits) (independent samples Student's T-Test, $t=-2.0$, $p=0.07$) may suggest that there is no significant advantage to be gained from bilateral implantation of the Tetraflex™ KH3500 'accommodating' IOL. However, the mean score of the latter group was higher than the criterion score that is diagnostic of near visual problems (40.45 logits; see Chapter 4), whilst the mean score of the former group was lower. Consequently, it cannot be certain that NAVQ scores of unilaterally implanted subjects (all presbyopic) were not influenced by the visual function of the unoperated eye, particularly if this was much better, for example due to the presence of a relatively myopic refractive error.

Analysis of the NAVQ item that enquires about an individual's spectacle usage for near visual tasks revealed that only 30.0% (3 out of 10) of unilaterally implanted subjects relied on spectacles "most of the time or always", compared to 63.2% (12 out of 19) of bilaterally implanted subjects. This perhaps supports the likelihood that adequate near vision with the "unoperated" eye improves near visual function, and therefore reduces NAVQ scores.

It is at least evident from the results of this study that where visual performance with unilateral 'accommodating' IOL implantation is poor, in terms of the contrast sensitivity, best distance-corrected near VA and the subjective AoA, a greater and significant improvement in these functions can be predicted from bilateral implantation of this IOL. However, all of these findings are confounded by the possibility that the differences may be *purely* due to binocular summation, as opposed to the bilateral *implantation* and *function* of these IOLs, since the findings are based on a comparison of monocular to binocular subjects. Therefore, in order to fully appreciate the extent of any benefit of bilateral 'accommodating' IOL implantation, the comparison ought to have been made between binocular subjects in both groups i.e. those implanted bilaterally with two 'accommodating' IOLs compared to those implanted bilaterally with one 'accommodating' IOL and one single vision IOL, to remove the effects of binocular summation.

7.7 Conclusion

Distance visual performance with the single piece single optic Tetraflex™ KH3500 'accommodating' IOL remains stable for up to two-and-a-half years after implantation. Although considerable deterioration occurs in near visual ability, in terms of VA and the subjective AoA, subjects are generally reasonably satisfied with the overall near vision outcomes. The deterioration of visual function with this IOL can be attributed primarily to the effects of PCO, which appear to be no different to other 'accommodating' IOLs despite differences in functional design (single piece design vs. hinged-optic design).

Having investigated the standardisation of near visual metrics and subjective assessment of near visual function in presbyopia, and having applied these to the evaluation and comparison of presbyopic contact lenses and to the evaluation of short-term and long-term visual outcomes of single optic 'accommodating' IOL implantation, the next Chapter collectively discusses the outcomes of this thesis. Ideas for further research that may be necessary, in the area of evaluating visual performance in presbyopia, are also proposed.

CHAPTER 8

Discussion and Conclusions

8. Introduction

The rising life expectancy of humans means that there is an increasing need to tackle the many physiological disorders that are associated with the ageing process, not least those that affect the eyes. The condition of presbyopia is perhaps of great interest because the associated difficulties manifest approximately two-thirds of the way through the human lifespan, well before most other age-related physiological deficits occur. There are several techniques that can be used to correct presbyopia, including simple devices such as spectacles and contact lenses to more complex surgical methods, as described in Chapter 1. However, the development of such techniques continues since none can currently provide spectacle-free clear near vision as achieved by pre-presbyopes. Indeed, an incomplete understanding of the accommodative and presbyopic mechanisms considerably hinders this progress (see Chapter 1), which is likely to remain the case until these are resolved.

As modifications to existing techniques are developed, or as new presbyopic corrections are created, it becomes increasingly important that visual outcomes are evaluated and compared in a standardised and accurate manner, to obtain evidence of benefit. Whilst this may be more readily achievable with objective techniques, it is apparent from the reviews presented in this thesis that the same cannot be said of subjective alternatives. Indeed, subjective assessment of visual function is just as important as objective assessment since one can then determine if at least the individual's needs are met. In some cases, subjective tests are necessarily required if objective tests are not compatible with a type of correction (see section 8.2). The purpose of this thesis therefore was to develop standardisation for commonly conducted subjective assessments of near visual function in presbyopia.

8.1 Optimising Measurement of Near Visual Acuity and Reading

VA is perhaps the simplest measure that can be used to describe visual function and this allows fair inter-individual comparisons to be made when assessed using a chart that employs a geometric (e.g. logarithmic) progression for letter sizes and spacing.

Near VA can be assessed using a variety of different optotypes but word or letter optotypes are most commonly selected owing to their familiarity (face validity). There is however much debate as to which of these optotypes is the most appropriate to be used. On one hand, the use of single letter optotypes avoids any contextual advantages that may be gained from the use of words, which might then over-estimate the measure of visual resolution. In contrast, the use of word optotypes is considered to better reflect real world reading tasks that are commonly encountered in daily life, providing a more meaningful assessment for the individual. Indeed, for this reason charts such as the MNRead chart (Lighthouse Low Vision Products, Long Island City, NY., USA.) were created for the purpose of assessing low vision reading performance (see Chapter 2).

This thesis has shown that near VA measured with single letter (uppercase and lowercase) optotypes and word optotypes are highly correlated and in close agreement. This suggests redundancy in assessing near VA with all three optotypes for presbyopes corrected by a variety of techniques. Since uppercase letter optotypes are more commonly encountered on VA charts, these are suggested as the optotype of choice. Furthermore, since reading acuity as assessed with the MNRead chart was found to have a high ICC and close agreement with single letter acuity, there is redundancy in assessing this metric also. Instead, a more useful assessment of the ability to resolve word optotypes is achieved by evaluating the CPS, which denotes the smallest print size that can sustain the maximum reading speed, along with the associated reading speed itself. Neither metric was well matched to any of the other near vision metrics, primarily because the CPS represents an assessment of the 'comfortable' print size for reading, as opposed to the acuity threshold, whilst reading speed can be used to determine reading fluency. Both are therefore useful adjuncts to near VA measures, which ought to be assessed when evaluating and comparing different presbyopic corrections.

8.2 Optimising Measurement of Subjective Amplitude of Accommodation

The ability to see and read at near is dependent on the AoA and an assessment of this is of prime importance in presbyopia. Objective techniques are strongly preferred, due to their independence from the eye's DoF, but these cannot be used to assess the range of clear vision with corrections such as monovision and multifocal contact lenses, since these aim to enhance the natural DoF of the eye as opposed to creating a change in optical focus.

With these types of corrections, subjective techniques are therefore required. Whilst 'real-distance' tests such as the push-up/push-down test are the most ideal, and are perhaps the most common subjective tests of the AoA used, they unfortunately suffer from variable DoF due to pupil and target size variation during the measurement. For this reason, defocus curves are a better alternative technique since variable target size can be accounted for by correcting VA measures for lens magnification effects whilst also using only a single line of acuity in the criterion to define the AoA. Furthermore, pupil size variations are likely to be minor, in comparison to the push-up/push-down test, since all measurements are made with the subject viewing a consistently distant (far) target (see Chapter 3).

Defocus curve measurements can be implemented in several ways, with letter sequences and/or the order of lens presentation randomised, or not. It was found in this thesis that there were no significant differences between the different methods of measuring a defocus curve in both pre-presbyopic and presbyopic subjects. However, there may be individual variations based on different levels of honesty and memorisation. It was also evident that when defocus curves are measured without randomising the letter sequences, the measured VA at each level of defocus tends to be better compared to if both of these factors are randomised. In fact, even if the letter sequences were randomised, a lack of randomisation of the lens presentation order still resulted in similar better estimations of VA in presbyopic subjects. This is likely to represent the effects of subjects pre-empting the sequence of lenses and therefore responding accordingly. It is therefore recommended that both factors be randomised when measuring defocus curves.

Several studies have used defocus curves to quantify the AoA of presbyopic corrections but there is no consistent criterion that has been used to define this. As a consequence, comparisons between different studies, even of the same correction type, become difficult to make. This thesis has shown that the AoA from a defocus curve should be quantified as the full range of defocus for which the best level of VA can be maintained, with an allowance of 0.04 logMAR included to account for natural variations in repeated VA measures (a relative criterion); there is little need to alter this allowance for different age groups since this variability does not appear to change significantly with age (see section 3.6, Chapter 3). Indeed, this definition of the AoA is intuitive to the definition of *clear vision*, and includes minimal influence of artificial blur tolerance that can arise from variations in target size (for example through the use of absolute criteria for quantification) and pupil size, as associated with the push-up/push-down test.

8.3 Subjective Questionnaire Assessment of Perceived Effects

In addition to clinical evaluations of visual function such as VA, reading speeds and the AoA, it is also important to consider an individual's subjective perceptions of visual ability. Indeed, objective clinical observations may suggest, for example, that a presbyopic correction is under-performing compared to that which was hoped for. However, the advantage gained from the individual's own point of view, with respect to their needs and expectations, may still be sufficient. Several questionnaires have been created to assess various aspects of visual functioning and QoL but most tend to concentrate on visual function due to low vision or assess the direct effect of ocular disease. Few validated questionnaires are applicable to those with otherwise 'normal' vision or disease-free eyes, whilst those that are applicable tend to concentrate on issues of cosmetics, cost and social functioning only. Of primary importance, with respect to presbyopia, is the near visual ability that is conferred by various presbyopic correction techniques and following an extensive review of existing QoL questionnaires, it was ascertained that no current instrument addressed this particular area. This thesis therefore developed the NAVQ to meet this need.

The NAVQ was developed using the statistical concepts of Rasch Analysis owing to the sample independent inferences and greater objectivity that is conferred by this method compared to CTT. The NAVQ was found to be both a reliable and a valid questionnaire to measure near visual ability and satisfaction with a variety of presbyopic corrections. The items in the questionnaire were well targeted for the type of population intended whilst sufficient discrimination ability was displayed to differentiate at least two levels of subject difficulty. In addition, the weak magnitudes of the construct validity correlations that were made between NAVQ scores and clinical assessments of near vision (near VA, CPS, CPS reading speed and the subjective AoA) served to highlight the need for this questionnaire, since it was evident that these do not correspond strongly to subjective perceptions.

8.4 Standardised Evaluation of Current Presbyopic Corrections

The subjective near vision metrics standardised in this thesis were used to evaluate and compare the visual function conferred by best binocular spectacle correction, a centre-near aspheric simultaneous vision multifocal contact lens and monovision with contact lenses.

Whilst visual function was found to be optimal with best binocular spectacle-corrected vision, the standardised near vision metrics proved useful for detecting differences in near vision between monovision correction and the multifocal contact lens. Near VA was found to be better with the former whilst any compromise to binocularity was sufficient to cause a reduction in the CPS reading speed, since this was significantly and equally slower with both contact lens corrections compared to best binocular spectacle correction. The CPS itself however was not significantly different suggesting that the type of correction does not adversely affect the smallest achievable comfortable reading print size.

As expected, the range of clear vision when assessed with defocus curves was found to be significantly larger with monovision and the multifocal contact lens compared to best binocular spectacle correction. With monovision, alternate interocular blur suppression facilitates a change in perception from the 'distance eye' to the 'near eye', allowing the range of clear vision of the individual eyes to be summed, whilst the combination of aspheric surfaces and spherical regions of near refractive power with the multifocal contact lens act to create a 'varifocal' effect. In both cases, a greater range of 'clear' foci is produced, compared to the best binocular distance-corrected eyes. There was however no significant difference in subjective perceptions of near visual ability between the three types of correction, regardless of the magnitude of the near spectacle addition. This may be related to varying subject expectations and/or demands and warrants further investigation.

The standardised near vision metrics were also used to monitor the visual function of a prototype single piece single optic 'accommodating' IOL during a period of six months after implantation. It was found that early influences of PCO were likely to be the cause of a reduction in contrast sensitivity, whilst this in turn resulted in a significant deterioration in the CPS reading speed. There was no adverse effect on the best distance-corrected near VA and CPS itself, but due to the large difference in these measures compared to the best-corrected equivalents (with a near addition of +2.50DS), it was concluded that the near visual function, in terms of the AoA, was not as would have been expected of a truly 'accommodating' IOL. Indeed, the poor accommodative ability was confirmed using the defocus curve method, which revealed a decline in the AoA during the period of this study. Whilst a significant decline in overall satisfaction with near visual ability supported this, more specific subjective perceptions (questionnaire scores) were found to be no different. This may reflect subject adaptation to the correction or perhaps low subject demands and/or expectations.

Few studies have investigated whether the short-term visual outcomes of single optic 'accommodating' IOL implantation are maintained in the long-term, whilst only one previous study has investigated whether there is any significant benefit from bilateral IOL implantation compared to unilateral implantation. This thesis therefore sought to investigate these questions using a single-piece single optic 'accommodating' IOL and based on the standardised near vision metrics that had been developed. It was shown that visual function had deteriorated at, on average, two-and-a-half years after implantation compared to similar assessments on the same cohort at six months after implantation. This was primarily attributable to the effects of PCO, which can reduce IOL movement and subsequently the 'accommodative' effect. Consequently, near visual function was found to be poor, in terms of the best distance-corrected near VA and CPS, whilst contrast sensitivity also declined. This deterioration in near visual ability also resulted in a large proportion of the subjects being classified by the NAVQ as having near visual difficulties.

Of importance was the finding that visual function may be significantly enhanced by bilateral implantation of this 'accommodating' IOL, compared to unilateral implantation, whilst significant improvements from bilateral implantation may be predicted for contrast sensitivity, best distance-corrected near VA and the subjective AoA.

8.5 Further Research

The quest to develop new and improved methods of correcting presbyopia, to restore near visual ability, is ongoing and therefore use of the standardised near vision metrics described in this thesis will be of benefit during any investigations of visual function that these confer. Perhaps creation of a near vision chart that can measure near VA with single uppercase letter optotypes, CPS and CPS reading speed at once would be advantageous so that implementation time can be reduced. Of particular interest would be application of defocus curves and the NAVQ for the measurement of subjective AoA and subjective perceived effects, respectively, of theoretically promising techniques such as dual optic 'accommodating' IOLs and phaco-ersatz (see sections 1.4.3.2 and 1.4.6, Chapter 1). Certainly expansion of the validity of the NAVQ to include other corrections, both those that were not included in this thesis (e.g. multifocal IOLs) and those that will be developed in the future, would be of prime advantage, especially considering that the confidence in the statistical inferences made by Rasch Analysis will then be improved.

The correction of presbyopia by existing techniques, as evaluated in this thesis, has also raised questions regarding subject demands and expectations of such corrections. Indeed, where more objective assessments suggested that visual function was poorer than would have been desired, as corroborated by subjective assessment with the NAVQ, ratings of overall satisfaction with near visual ability with two types of presbyopic contact lens corrections, spectacle correction and single-piece single optic 'accommodating' IOLs (Chapters 5, 6 and 7 respectively) were consistently moderate to high, suggesting general contentment with the correction(s). Whilst this may indicate that the needs of the respective cohorts were met by the correction(s), it would be interesting to explore if there are any psychological aspects relating to expectations and/or demands that perhaps influences subject satisfaction. Furthermore, it would be interesting to investigate whether there are any differences in motivation that would lead subjects to select one type of correction over another.

Further research is also required to determine more definitively the effects of PCO on the performance of 'accommodating' IOLs, perhaps by comparing the visual function that is present before PCO occurs, to when PCO is present and then after treatment has been provided to remove PCO.

The standardisation of near vision metrics should also be expanded to include contrast sensitivity assessment and stereoacuity measurement so that a more comprehensive battery of tests can then be conducted, in addition to those described in this thesis, for the consistent and comparable evaluation of subjective near visual performance in presbyopia. This is of particular importance as current methodologies are modified and as new correction techniques are discovered.

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APPENDIX

A1. Statistical Test Selection

In this section, a detailed explanation is provided of how statistical analyses (tests) were selected (parametric versus non-parametric) for each of the thesis Chapters.

A1.1 Chapter 2

The one-sample Kolmogorov-Smirnov test was conducted to determine whether the observed data was significantly different to the normal distribution. The edited output from SPSS version 15.0 (SPSS Inc., Chicago, IL., USA.) is shown below.

	Uppercase Letters	Lowercase Letters	Words	Reading Acuity	Critical Print Size (CPS)	CPS Reading Speed
N	77	77	77	77	77	77
Mean	0.1976	.3023	.2675	.1535	.4714	170.4273
Std. Deviation	.2233	.2473	.2061	.2096	.2006	24.7565
Kolmogorov-Smirnov Z	1.418	1.565	1.673	1.283	1.497	0.573
Asymp. Sig. (2-tailed)	0.036	0.015	0.007	0.074	0.023	0.898

NB Test distribution is Normal.

All but reading acuity and CPS reading speed were significantly different to the normal distribution ($p<0.05$), suggesting that only non-parametric analyses ought to be used. However, the non-parametric Spearman's correlations are shown below (edited output from SPSS) and it can be seen that the correlations are similar to the Pearson's Product Moment Correlation Coefficients shown in Chapter 2, with statistical significance (indicated by asterisks) also the same. Since all of the parametric and non-parametric comparisons are in essence similar and since the variables are measured on an interval scale, this provides adequate support for use of the parametric Pearson's Product Moment Correlation Coefficient in Chapter 2.

** Correlation is significant at the 0.01 level (1-tailed).

		Uppercase Letters	Lowercase Letters	Words	Reading Acuity	Critical Print Size (CPS)	Reading Speed
Uppercase Letters	Correlation Coefficient	1.000	.945**	.866**	.907**	.761**	.095
	Sig. (1-tailed)	.	.000	.000	.000	.000	.207
Lowercase Letters	Correlation Coefficient	.945**	1.000	.902**	.926**	.729**	.095
	Sig. (1-tailed)	.000	.	.000	.000	.000	.206
Words	Correlation Coefficient	.866**	.902**	1.000	.916**	.689**	.174
	Sig. (1-tailed)	.000	.000	.	.000	.000	.065
Reading Acuity	Correlation Coefficient	.907**	.926**	.916**	1.000	.744**	.126
	Sig. (1-tailed)	.000	.000	.000	.	.000	.137
Critical Print Size (CPS)	Correlation Coefficient	.761**	.729**	.689**	.744**	1.000	.188
	Sig. (1-tailed)	.000	.000	.000	.000	.	.051
Reading Speed	Correlation Coefficient	.095	.095	.174	.126	.188	1.000
	Sig. (1-tailed)	.207	.206	.065	.137	.051	.

A1.2 Chapter 3

The one-sample Kolmogorov-Smirnov test was conducted on each of the defocus curve combinations in turn, for the pre-presbyopic subjects (n=18) and for the presbyopic subjects (n=20), to determine whether the observed data, for each level of defocus, was significantly different to the normal distribution. The edited outputs from SPSS are shown below. Since there was no significant difference between the data and the normal distribution for all of the defocus curve combinations and for both pre-presbyopic and presbyopic subjects, the data was confirmed as being amenable to parametric analyses.

A1.2.1 Pre-presbyopic Defocus Curves

Combination 1:

	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00
Mean	.6244	.4144	.1839	-.0278	-.1078	-.1011	-.1022	-.1022	-.0889
Std. Deviation	.1898	.1865	.1373	.0774	.0700	.0759	.0800	.0797	.0827
Kolmogorov-Smirnov Z	.551	.446	.670	.729	.659	.780	.535	.656	.525
Asymp. Sig. (2-tailed)	.922	.989	.761	.663	.778	.576	.937	.782	.945

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 2:

	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00
Mean	.5983	.4039	.1517	-.0356	-.1189	-.1250	-.1150	-.1056	-.1022
Std. Deviation	.2185	.1958	.1300	.0711	.0645	.0584	.0676	.0706	.0776
Kolmogorov-Smirnov Z	.660	.547	.655	.603	.774	.665	.612	.796	.682
Asymp. Sig. (2-tailed)	.776	.926	.784	.860	.587	.768	.848	.551	.741

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 3:

	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00
Mean	.6128	.4022	.1872	-.0278	-.1100	-.1133	-.1089	-.0989	-.0856
Std. Deviation	.1871	.1723	.1473	.1256	.0677	.0621	.0662	.0830	.0826
Kolmogorov-Smirnov Z	.499	.827	.432	.807	.540	.578	.578	.730	.663
Asymp. Sig. (2-tailed)	.965	.502	.992	.533	.932	.892	.892	.661	.772

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 4:

	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00
Mean	.6439	.4200	.1739	-.0133	-.0833	-.0989	-.0856	-.0856	-.0789
Std. Deviation	.1676	.1847	.1630	.0918	.0733	.0740	.0639	.0799	.0842
Kolmogorov-Smirnov Z	.433	.616	.572	.481	.545	1.018	.895	.598	.468
Asymp. Sig. (2-tailed)	.992	.843	.899	.975	.927	.251	.400	.867	.981

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 5:

	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00
Mean	.5767	.4094	.1639	-.0067	-.0822	-.1067	-.0856	-.0767	-.0878
Std. Deviation	.1961	.1924	.1255	.0854	.0791	.0636	.0709	.0871	.0730
Kolmogorov-Smirnov Z	.522	.652	.549	1.130	.781	.553	.604	.692	.731
Asymp. Sig. (2-tailed)	.948	.789	.924	.156	.575	.919	.859	.725	.660

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 6:

	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00
Mean	.6228	.4311	.1833	-.0122	-.1100	-.1089	-.0989	-.0900	-.0789
Std. Deviation	.1838	.1982	.1774	.0826	.0714	.0714	.0753	.0752	.0839
Kolmogorov-Smirnov Z	.630	.656	.485	.776	.485	.751	.817	.667	.494
Asymp. Sig. (2-tailed)	.823	.782	.973	.584	.972	.626	.516	.765	.968

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

A1.2.2 Presbyopic Defocus Curves

Combination 1:

	+3.00	+2.50	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00	-2.50	-3.00
Mean	.957	.804	.670	.509	.291	.069	-.074	-.059	.081	.263	.421	.532	.584
Std. Deviation	.155	.169	.171	.183	.168	.164	.092	.090	.156	.201	.224	.227	.222
Kolmogorov-Smirnov Z	.712	.531	.557	.601	.423	.760	.788	.646	.677	.611	.580	.790	.643
Asymp. Sig. (2-tailed)	.692	.941	.916	.863	.994	.610	.564	.798	.749	.850	.890	.561	.803

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 2:

	+ 3.00	+ 2.50	+ 2.00	+ 1.50	+ 1.00	+ 0.50	0.00	- 0.50	- 1.00	- 1.50	- 2.00	- 2.50	- 3.00
Mean	.864	.782	.634	.493	.272	.078	-.079	-.071	.083	.268	.401	.522	.615
Std. Deviation	.215	.180	.183	.141	.155	.147	.094	.079	.161	.201	.212	.224	.215
Kolmogorov-Smirnov Z	.613	.462	.588	.668	.580	.381	.690	.649	.483	.577	.578	.574	.543
Asymp. Sig. (2-tailed)	.847	.983	.880	.763	.890	.999	.728	.793	.974	.893	.892	.897	.930

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 3:

	+ 3.00	+ 2.50	+ 2.00	+ 1.50	+ 1.00	+ 0.50	0.00	- 0.50	- 1.00	- 1.50	- 2.00	- 2.50	- 3.00
Mean	.916	.814	.671	.488	.300	.094	-.072	-.029	.115	.282	.427	.554	.648
Std. Deviation	.147	.175	.160	.153	.188	.152	.086	.096	.122	.174	.194	.194	.190
Kolmogorov-Smirnov Z	.505	.713	.568	.438	.482	.614	.660	.682	.591	.816	.628	.686	.788
Asymp. Sig. (2-tailed)	.961	.690	.903	.991	.974	.845	.776	.741	.876	.519	.826	.734	.563

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 4:

	+ 3.00	+ 2.50	+ 2.00	+ 1.50	+ 1.00	+ 0.50	0.00	- 0.50	- 1.00	- 1.50	- 2.00	- 2.50	- 3.00
Mean	.932	.797	.647	.454	.263	.068	-.071	-.040	.128	.304	.436	.543	.617
Std. Deviation	.157	.160	.142	.183	.169	.131	.082	.095	.153	.178	.183	.180	.201
Kolmogorov-Smirnov Z	.670	.659	.656	.763	.446	.601	.503	.835	.370	.641	.812	.816	.888
Asymp. Sig. (2-tailed)	.761	.779	.783	.606	.989	.863	.962	.488	.999	.806	.524	.518	.409

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 5:

	+3.00	+2.50	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00	-2.50	-3.00
Mean	.902	.776	.654	.483	.295	.089	-.074	-.037	.105	.271	.400	.550	.615
Std. Deviation	.145	.144	.175	.150	.177	.159	.082	.086	.142	.179	.206	.204	.205
Kolmogorov-Smirnov Z	.714	.537	.717	.653	.570	.547	.740	.575	.577	.655	.658	.758	1.00
Asymp. Sig. (2-tailed)	.687	.935	.683	.787	.901	.926	.643	.895	.893	.784	.780	.613	.265

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

Combination 6:

	+3.00	+2.50	+2.00	+1.50	+1.00	+0.50	0.00	-0.50	-1.00	-1.50	-2.00	-2.50	-3.00
Mean	.940	.824	.671	.518	.262	.090	-.071	-.030	.116	.328	.458	.555	.642
Std. Deviation	.144	.154	.138	.152	.153	.136	.077	.101	.143	.182	.204	.217	.181
Kolmogorov-Smirnov Z	.949	.692	.529	.575	.477	.407	.769	.598	.488	.875	.693	.754	.971
Asymp. Sig. (2-tailed)	.329	.724	.943	.895	.977	.996	.595	.867	.971	.427	.723	.620	.302

NB Test distribution is Normal.

All p-values are greater than 0.05 therefore there is no significant difference to the normal distribution.

A1.3 Chapter 4

The one-sample Kolmogorov-Smirnov test was conducted on each of the measurements for validation of the Near Activity Visual Questionnaire (NAVQ) (n=87), including the questionnaire scores themselves, to determine whether the observed data was significantly different to the normal distribution. The edited output from SPSS is shown below.

	NAVQ	Best Distance-Corrected NVA	Best Distance-Corrected CPS	Best Distance-Corrected Reading Speed	Subjective AoA (Defocus Curves)
Mean	31.50	0.27	0.51	166.63	0.98
Std. Deviation	18.23	0.26	0.23	27.41	0.64
Kolmogorov-Smirnov Z	0.727	1.439	1.578	0.540	1.226
Asymp. Sig. (2-tailed)	0.667	0.032	0.014	0.932	0.099

a Test distribution is Normal.

Best distance-corrected NVA and Best distance-corrected CPS were significantly different to the normal distribution ($p<0.05$), suggesting that only non-parametric analyses ought to be used. However, the non-parametric Spearman's correlations are shown below (edited output from SPSS) and it can be seen that the correlations are similar to the Pearson's Product Moment Correlation Coefficients shown in Chapter 4, with similar significance. Since the variables are measured on interval scales, this provides adequate support for use of the parametric Pearson's Product Moment Correlation Coefficient in Chapter 4.

		Best Distance-Corrected NVA	Best Distance-Corrected CPS
NAVQ	Correlation Coefficient	.438**	.361**
	Sig. (1-tailed)	.000	.001

** Correlation is significant at the 0.01 level (1-tailed).

A1.4 Chapter 5

The one-sample Kolmogorov-Smirnov test was conducted on each of the clinical measurements made, for each of the three types of correction. The edited outputs from SPSS are shown in sections 1.4.1, 1.4.2 and 1.4.3 for best binocular spectacle correction, multifocal contact lens correction and monovision contact lens correction respectively.

It can be seen from the calculations that only the CSF, at distance and near, and stereoacuity had significantly different distributions to the normal distribution ($p<0.05$ on all occasions). With the CSF however, the measurements were converted into logarithmic units from whole numbers and are therefore measured on an interval scale to two decimal places. Furthermore, differences to the normal distribution only occurred at some of the spatial frequencies, not all, indicating that parametric analyses can be used. For stereoacuity, the TNO stereotest employs an arithmetical scale, and not an interval scale, whilst measurements are whole numbers to the nearest whole arc second. For this reason, stereoacuity ought to be analysed using non-parametric statistical tests.

A1.4.1 Best Binocular Spectacle Correction

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Distance VA	-0.10	0.07	0.759	0.612
Distance CSF 1.5 cpd	1.71	0.18	1.454	0.029
Distance CSF 3.0 cpd	2.04	0.17	1.461	0.028
Distance CSF 6.0 cpd	1.89	0.20	0.989	0.282
Distance CSF 12.0 cpd	1.55	0.27	1.167	0.131
Distance CSF 18.0 cpd	0.97	0.22	0.907	0.383
Intermediate VA	0.28	0.10	0.647	0.797
Near VA	0.03	0.12	0.643	0.803
CPS	0.32	0.15	1.333	0.057
CPS Reading Speed	173.43	24.12	0.831	0.495
Near CSF 1.5 cpd	1.60	0.15	2.247	0.0001
Near CSF 3.0 cpd	1.79	0.18	1.539	0.018
Near CSF 6.0 cpd	1.74	0.17	1.811	0.003
Near CSF 12.0 cpd	1.27	0.35	1.117	0.164
Near CSF 18.0 cpd	0.87	0.48	0.820	0.513
Stereoacuity	77.25	48.00	1.746	0.005
NAVQ	26.47	14.32	0.727	0.666
AoA (Defocus Curve)	0.46	0.23	0.435	0.992

NB Test distribution is Normal.

A1.4.2 Multifocal Contact Lens Correction

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Distance VA	0.05	0.08	0.965	0.310
Distance CSF 1.5 cpd	1.75	0.17	1.646	0.009
Distance CSF 3.0 cpd	1.93	0.21	1.139	0.149
Distance CSF 6.0 cpd	1.74	0.25	0.929	0.353
Distance CSF 12.0 cpd	1.12	0.47	1.110	0.170
Distance CSF 18.0 cpd	0.65	0.36	1.366	0.048
Intermediate VA	0.30	0.10	0.730	0.660
Near VA	0.21	0.13	0.424	0.994
CPS	0.37	0.11	1.458	0.029
CPS Reading Speed	154.90	17.91	0.717	0.682
Near CSF 1.5 cpd	1.58	0.20	1.682	0.007
Near CSF 3.0 cpd	1.73	0.14	1.960	0.001
Near CSF 6.0 cpd	1.53	0.18	1.572	0.014
Near CSF 12.0 cpd	1.09	0.32	1.246	0.090
Near CSF 18.0 cpd	0.58	0.44	0.984	0.287
Stereoacuity	174.00	95.17	1.184	0.121
NAVQ	34.1	17.41	0.763	0.605
Range of Clear Vision	1.59	0.70	0.484	0.973

NB Test distribution is Normal.

A1.4.3 Monovision Contact Lens Correction

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Distance VA	-0.01	0.07	0.841	0.479
Distance CSF 1.5 cpd	1.75	0.17	1.646	0.009
Distance CSF 3.0 cpd	1.89	0.20	1.271	0.079
Distance CSF 6.0 cpd	1.77	0.21	1.062	0.209
Distance CSF 12.0 cpd	1.33	0.29	1.128	0.157
Distance CSF 18.0 cpd	0.68	0.45	1.104	0.174
Intermediate VA	0.35	0.10	0.740	0.644
Near VA	0.11	0.11	0.490	0.970
CPS	0.37	0.11	1.140	0.149
CPS Reading Speed	157.97	19.45	0.644	0.801
Near CSF 1.5 cpd	1.62	0.14	2.071	0.0004
Near CSF 3.0 cpd	1.73	0.14	1.960	0.001
Near CSF 6.0 cpd	1.60	0.20	1.781	0.004
Near CSF 12.0 cpd	1.19	0.31	1.169	0.130
Near CSF 18.0 cpd	0.80	0.48	0.934	0.347
Stereoacuity	273.00	102.04	1.355	0.051
NAVQ	34.78	19.15	0.862	0.447
Range of Clear Vision	1.21	0.77	0.778	0.580

NB Test distribution is Normal.

A1.5 Chapter 6

The one-sample Kolmogorov-Smirnov test was conducted on each of the clinical measurements, for each of the three time points in the study. The edited outputs from SPSS are shown in sections 1.5.1, 1.5.2 and 1.5.3 for the 1-month post-operative visit, 3-month post-operative visit and 6-month post-operative visit, respectively.

It can be seen from the calculations that data for all of the clinical measurements did not have significantly different distributions to the normal distribution ($p>0.05$ on all occasions), apart from the "best-corrected CPS" measurement at the 3-month post-operative visit ($p=0.04$). However, this is not likely to substantially affect parametric statistical analyses of the study considering that all of the measurements were made on interval scales, and measured to an accuracy of 2 significant figures. Therefore, this confirmed that the data was amenable to parametric statistical analyses.

Since satisfaction with near visual ability was rated on arithmetical scale however, and not an interval scale, and considering that the measurements are whole numbers, this particular parameter ought to be assessed using non-parametric analyses, even though there is no significant difference in the distribution of this data compared to the normal distribution.

A1.5.1 One-month Post-operative Data

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Uncorrected Distance VA	0.35	0.23	0.46	0.99
Uncorrected Distance CSF	1.40	0.20	0.60	0.87
Uncorrected Near VA	0.65	0.23	0.48	0.97
Mean Spherical Equivalent	0.94	1.05	0.66	0.78
Best-corrected Distance VA	0.09	0.18	0.81	0.53
Best-corrected Distance CSF	1.45	0.16	0.94	0.34
Best dist.-corr. Near VA	0.48	0.19	0.60	0.86
Best dist.-corr. CPS	0.75	0.18	0.95	0.33
Best dist.-corr. Reading Speed	213.95	40.49	0.74	0.64
Best-corrected Near VA	0.22	0.20	1.29	0.07
Best-corrected CPS	0.51	0.22	0.99	0.28
Best-corrected Reading Speed	216.97	41.93	0.66	0.77
Best dist.-corr. Intermediate VA	0.54	0.19	0.52	0.95
Subjective AoA (Push-up test)	2.25	1.14	0.65	0.80
Subjective AoA (Defocus Curve)	0.89	0.42	0.50	0.96
NAVQ	41.91	24.24	1.00	0.27
Satisfaction	2.32	1.73	0.87	0.43
Objective AoA	0.39	0.25	0.63	0.83

NB Test distribution is Normal.

A1.5.2 Three-month Post-operative Data

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Uncorrected Distance VA	0.37	0.24	0.61	0.85
Uncorrected Distance CSF	1.38	0.20	0.83	0.50
Uncorrected Near VA	0.71	0.23	0.56	0.92
Mean Spherical Equivalent	0.91	1.25	0.94	0.34
Best-corrected Distance VA	0.04	0.14	0.89	0.41
Best-corrected Distance CSF	1.42	0.18	0.84	0.48
Best dist.-corr. Near VA	0.53	0.23	0.58	0.89
Best dist.-corr. CPS	0.76	0.20	1.02	0.25
Best dist.-corr. Reading Speed	200.82	46.28	0.69	0.73
Best-corrected Near VA	0.21	0.22	0.82	0.51
Best-corrected CPS	0.52	0.24	1.42	0.04
Best-corrected Reading Speed	210.82	39.63	0.65	0.79
Best dist.-corr. Intermediate VA	0.67	0.56	1.32	0.06
Subjective AoA (Push-up test)	2.36	1.50	0.97	0.30
Subjective AoA (Defocus Curve)	0.87	0.48	0.92	0.37
NAVQ	40.09	17.26	0.73	0.66
Satisfaction	3.18	1.37	1.03	0.24
Objective AoA	0.35	0.27	1.09	0.19

NB Test distribution is Normal.

A1.5.3 Six-month Post-operative Data

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Uncorrected Distance VA	0.34	0.25	0.63	0.82
Uncorrected Distance CSF	1.32	0.21	0.84	0.49
Uncorrected Near VA	0.68	0.25	0.70	0.71
Mean Spherical Equivalent	0.29	1.63	0.83	0.50
Best-corrected Distance VA	0.06	0.19	0.89	0.41
Best-corrected Distance CSF	1.35	0.19	0.98	0.29
Best dist.-corr. Near VA	0.53	0.22	0.60	0.86
Best dist.-corr. CPS	0.77	0.23	1.28	0.07
Best dist.-corr. Reading Speed	195.67	33.25	0.85	0.46
Best-corrected Near VA	0.23	0.25	1.08	0.19
Best-corrected CPS	0.54	0.28	1.05	0.22
Best-corrected Reading Speed	203.85	26.48	0.98	0.30
Best dist.-corr. Intermediate VA	0.57	0.23	1.08	0.19
Subjective AoA (Push-up test)	2.06	0.90	0.42	0.99
Subjective AoA (Defocus Curve)	0.57	0.45	0.53	0.94
NAVQ	35.91	20.30	0.82	0.52
Satisfaction	3.41	1.33	0.80	0.54
Objective AoA	0.49	0.42	0.89	0.40

NB Test distribution is Normal.

A1.6 Chapter 7

The one-sample Kolmogorov-Smirnov test was conducted on each of the clinical measurements made binocularly (see section 1.6.1), whilst this was also conducted for the corresponding data of the average eyes (see section 1.6.2), the best monocular eye (see section 1.6.3), the right eye (see section 1.6.4), and the left eye (see section 1.6.5). The edited outputs from SPSS are shown in the respective sections and it can be seen that all of the clinical measurements did not have significantly different distributions to the normal distribution ($p>0.05$ on all occasions). Also, since all of the measurements were made on interval scales, and measured to an accuracy of 2 significant figures, the data was confirmed as being amenable to parametric statistical analyses.

A1.6.1 Binocular Data

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Distance VA	-0.03	0.13	0.58	0.86
Distance CS	1.58	0.10	1.18	0.13
Near VA	0.44	0.12	0.50	0.96
Amplitude of Accommodation	1.88	0.90	0.70	0.71

NB Test distribution is Normal.

A1.6.2 Average Eyes Data

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Distance VA	0.01	0.15	0.56	0.92
Distance CS	1.41	0.13	0.75	0.62
Near VA	0.56	0.14	0.64	0.80
Amplitude of Accommodation	1.51	0.46	0.61	0.85

NB Test distribution is Normal.

A1.6.3 Best Monocular Eye Data

Clinical Measurement	Mean	Std. Deviation	Kolmogorov-Smirnov Z	Asymp. Sig. (2-tailed)
Distance VA	-0.06	0.11	0.79	0.56
Distance CS	1.46	0.14	1.16	0.13
Near VA	0.54	0.15	0.59	0.88
Amplitude of Accommodation	1.47	0.46	0.82	0.51

NB Test distribution is Normal.

A2. Calculation of the Intraclass Correlation Coefficient (ICC)

The Intraclass Correlation Coefficient (ICC) assesses the concordance between two measurements made under the same conditions. Generally, there are three experimental research designs that are likely to be encountered:

(a) Each measure is carried out on a different group of people, with each group originating from a larger population, or
(b) Each measure is carried out on each person and each person is representative of a larger group, or
(c) Each measure is carried out on each person and only these people are of interest.

The experimental design described in option (b) is typically applicable for assessments of concordance in the context of testing questionnaire test-retest reliability or repeatability of VA measures. In this situation, the ICC is referred to as a *two-way random effects model* (R_2) since the coefficient accounts for variation due to subjects as well as due to the measures themselves and an unknown residual error; a random effects model is selected since the subjects are to be representative of the larger population.

First, the measurements of interest are tabulated and used to derive a table of expected measures (Tables below) (Streiner and Norman 1995).

Subject	**Attempt 1**	**Attempt 2**	**Attempt 3**	*Mean of Attempts*
1				
2				
3				
Etc.				
Mean				

Table of observed measures

Subject	**Attempt 1**	**Attempt 2**	**Attempt 3**
1			
2			
3			
Etc.			

Table of calculated expected measurements

From these, the 'Sum of Squares' for subjects (SSs) (Equation A1), number of measures (SSm) (Equation A2), and measurement error (SSe) (Equation A3) can be calculated.

SSs = $n \sum (\text{Subject 'x' Mean Score} - \text{Overall Mean})^2$ **Equation A1**

where n = the number of measurements made
'x' = a particular subject 'x' mean score for the measurements made

SSm = $n \sum (\text{Measure 'x' Mean} - \text{Overall Mean})^2$ **Equation A2**

where n = the number of subjects
'x' = the mean measure of all subjects for a particular measure 'x'

SSe = $\sum$ (actual measure – expected measure)^2 **Equation A3**

where 'actual measure' is that obtained by a subject on a particular test
'expected measure' is that expected, as calculated in Table 2.9

Next, the number of Degrees of Freedom (Df) is calculated for subjects (Equation A4), measures (Equation A5) and measurement error (Equation A6).

Df Subjects (Dfs) = number of subjects -1 **Equation A5**

Df Measures (Dfm) = number of measures -1 **Equation A6**

Df Error (Dfe) = Total Df – (Dfs + Dfm) **Equation A7**

where *Total Df = (Total number of Patients x Total number of Measures) - 1*

The Mean Square is then calculated for subjects (Equation A8), measures (Equation A9) and measurement error (Equation A10), before deriving the ANOVA table.

MS Subjects (MSs) = SSs / Dfs **Equation A8**

MS Measures (MSm) = SSm / Dfm **Equation A9**

MS Error (MSe) = SSe / Dfe **Equation A10**

Source of Variation	*SS*	*df*	*MS*
Attempts	SSa	Dfa	MSa
Subjects	SSs	Dfs	MSs
Error	SSe	Dfe	MSe
Total	SSa + SSs + SSe	Total Df	

The ANOVA Table

The two-way random effects model ICC (R_2) can be calculated from Equation A11 and as is evident, if variance due to error and the measures is low, the ICC will be high displaying greater concordance between the measures (Kramer and Feinstein 1981).

$$R_2 = \frac{\sigma^2 \text{ subjects}}{\sigma^2 \text{ subjects} + \sigma^2 \text{ measures} + \sigma^2 \text{ error}}$$ **Equation A11**

where σ^2 subjects = (MSs – MSe) / no. of measures
σ^2 attempts = (MSm – MSe) / no. of patients
σ^2 error = MSe

A3. Statistical Power Analysis Calculations

In this section, the statistical power analysis calculations that were conducted *a priori* and retrospectively (*post hoc*) are explained. In all cases, it is the lowest possible power that could be present in the study that was calculated

A3.1 Chapter 3

Based on the two-Factor repeated measures ANOVA test (from Cohen (1988)):

I is Factor 1 (the defocus curve combination type) and 'i' is the number of levels of I (=6 combinations)
J is Factor 2 (the number of levels of defocus) and 'j' is the number of levels of J (=9 for pre-presbyopes and 13 for presbyopes)
The power tables are based on a single source of error (single factor ANOVA) but for a two-factor design there is a need to account for the fact that there is more than one source of error variance. This is done by altering the number of subjects to n' using Equation A12.

$$n' = [N - (i \times j)/(\text{df of factor we are interested in} + 1)] + 1 \qquad \textbf{Equation A12}$$

where i x j is the total number of inputs (number of cells)
N is the total number of subjects in the whole table (=n_c x i x j)
n_c is the number of subjects

For ANOVA 'f' describes the spread of the data of the F statistic, according to the F-distribution, and this is calculated from Equation A13.

$$f = \sigma_m / \sigma \qquad \textbf{Equation A13}$$

where σ is the standard deviation of the population measurement
σ_m is calculated from Equation A14

$$\sigma_m = \sqrt{\left[\frac{\sum_{i=1}^{k} (m_i - m)^2}{k}\right]} \qquad \textbf{Equation A14}$$

where m_i is the mean of each population for the factor of interest
m is the mean of the means of each population
k is the number of levels of the factor of interest

This is done for all factors present. However, it is known in this study that VA will vary considerably for different levels of defocus and since the only factor of interest is defocus curve combination, the calculation was done for this factor only.

For the **pre-presbyopic** population in this study, (n=18) n'=154 and:

$\sigma_m = \sqrt{(0.0004/6)} = 0.008212$
$f = 0.008212 / 0.08 = 0.10$

From Cohen (1988), at p=0.05, u=5, and f = 0.10, power = **0.64** (64%)

For the **presbyopic** population in this study (n=20) n' = 248 and:

$\sigma_m =$ $\sqrt{(0.0007/6)}$ $= 0.0108$
$f =$ $0.0108 / 0.09$ $= 0.12$

From Cohen (1988), at p=0.05, u=5, n'= 248 and f = 0.12 power = **0.70** (70%)

For a power of 80% (0.8), n' would need to be 215 (from Cohen (1988)) and therefore n = 1350/54 = 25. Therefore **25** subjects were needed.

A3.2 Chapter 5

(a) Paired-samples Student's T-Tests (two-tailed) for pair-wise comparisons

The calculations were carried out *a priori* based on the requirement to detect a significant difference in pair-wise comparisons between the multifocal contact lens and monovision, which would be conducted by SPSS (using the two-tailed paired samples Student's T-test) if an overall significant difference between the three types of correction were found. This comparison was selected as this was expected to display the smallest effect size. The calculations were conducted for distance and near VA, based on clinical expectations and the observations from the Richdale et al. (2006) study who used the *SofLens® Multi-focal* which is similar in design to the *PureVision® Multi-focal*. Standard deviations (SD) (0.10 for DVA and NVA) were derived from clinical expectation and from observations in the Richdale et al. (2006) study. These calculations are shown below, along with the post hoc calculations based on the actual sample size and observations, and are based on determination of the effect size 'd' from the mean and standard deviation of each population (Equation A15) (Russo 2003).

$$d = (M_1 - M_2) / SD_D$$ **Equation A15**

SD however is assumed to be the same for each population and SD_D is taken as the standard deviation of the differences.

(i) DVA

$d = 0.06 / 0.1 = 0.6$
For power = 0.8, (at $\alpha = 0.01$) $\delta = 3.4$
$n = \delta^2 / d^2 \quad = 3.4^2 / 0.6^2 \quad = 32.11$
Therefore **32** subjects are needed

Post-hoc:

Based on actual sample of 20 subjects, at $\alpha = 0.01$
$d = 0.05 / 0.08 = 0.63$
$\delta = d \times \sqrt{n} = 0.63 \times \sqrt{20} = 2.8$
Therefore power = **0.59**

(ii) NVA

$d = 0.06 / 0.1 = 0.6$
For power = 0.8, (at $\alpha = 0.01$) $\delta = 3.4$
$n = \delta^2 / d^2 \quad = 3.4^2 / 0.6^2 \quad = 32.11$
Therefore **32** subjects are needed

Post-hoc: Based on actual sample of 20 subjects, at $\alpha = 0.01$
$d = 0.10 / 0.14 = 0.66$
$\delta = d \times \sqrt{n} = 0.66 \sqrt{20} = 2.95$
Therefore power = **0.65**

(b) Two-factor repeated measures ANOVA for distance and near CSF

Based on Equations A12, A13 and A14 (from Cohen (1988)), and calculating for the factor 'type of correction' only (since each SF is known to be considerably different)

n=20 and therefore n' was calculated to be 72.25.

For the distance CSF:

$\sigma_m =$ $\sqrt{(0.0065/3)}$ $= 0.0804$
$f =$ $0.00804 / 0.17$ $= 0.46$

From Cohen (1988), at p=0.05, u=2, and f = 0.46, power >**0.99** (>99%)

For the near CSF:

$\sigma_m =$ $\sqrt{(0.004/3)}$ $= 0.0620$
$f =$ $0.00620 / 0.18$ $= 0.35$

From Cohen (1988), at p=0.05, u=2, and f = 0.35, power = **0.99** (99%)

(c) Independent-samples Student's T-Test (two-tailed) – 'low add' vs. 'high add'

Calculations were conducted *post hoc* based on the comparison between the 'low addition' multifocal lens and the 'high addition' multifocal lens, for distance VA and near VA. According to Russo (2003), the SD of the samples is assumed to be the same, whilst the value for "n" is calculated from Equation A16 as the harmonic mean if sample sizes are different in each group.

$$n = (2 n_1 n_2) / (n_1 + n_2)$$ **Equation A16**

The effect size is then calculated from Equation A15, with delta (δ) then calculated from Equation A17.

$$\delta = d \times \sqrt{(n / 2)}$$ **Equation A17**

(i) DVA $n_1 = 11$ and $M_1 = 0.08$, $n_2 = 9$ and $M_2 = 0.02$ and SD = 0.09
Therefore n = 9.9 and d = 0.58
Finally, δ = 1.3 and power = **0.26** (from (Russo 2003))

(ii) NVA $n_1 = 11$ and $M_1 = 0.27$, $n_2 = 9$ and $M_2 = 0.13$ and SD = 0.09
Therefore n = 9.9 and d = 1.60
Finally, δ = 3.5 and power = **0.94** (from (Russo 2003))

(d) Two-Factor ANOVA for distance and near CSF

Based on Equations A12 and A13, power was calculated to be 0.99 and this was confirmed from the SPSS version 15.0 (SPSS Inc., Chicago IL., USA.) outputs, although power for the distance CSF was indicated to be 0.79 by SPSS.

A3.3 Chapter 6

(a) Paired-samples Student's T-Tests (two-tailed) for pair-wise comparisons

The calculations were carried out *a priori* based on the requirement to detect a significant difference in pair-wise comparisons between the 1-month and 3-month data, which would be conducted by SPSS (using the two-tailed paired samples Student's T-test) if an overall significant difference between the three time points was found. This comparison was selected as this was expected to display the smallest effect size. The calculations were conducted for distance VA, near VA an the amplitude of accommodation (AoA), based on clinical expectations and the observations of Langenbucher et al. (2003a, 2003b), Mastropasqua et al. (2003), and Hancox et al. (2007) using the 1CU 'accommodating' IOL. Standard deviations (SD) (0.12 for DVA, 0.10 for NVA and 0.50 for AoA) were derived from clinical expectation and from observations in the Langenbucher et al. studies (2003a, 2003b). These calculations are shown below, along with the post hoc calculations based on the actual sample size and observations, and are based on determination of the effect size from Equation A15 (Russo 2003).

(i) DVA

$d = 0.06 / 0.12 = 0.5$
For power = 0.8, (at $\alpha = 0.01$) $\delta = 3.4$
$n = \delta^2 / d^2 \quad = 3.4^2 / 0.5^2 \quad = 46.24$
Therefore **46** subjects are needed

Post-hoc:

Based on actual sample of 22 subjects, at $\alpha = 0.01$
$d = 0.03 / 0.07 = 0.40$
$\delta = d \times \sqrt{n} = 0.40 \times \sqrt{22} = 1.90$
Therefore power = **0.25**

(ii) NVA

$d = 0.06 / 0.10 = 0.6$
For power = 0.8, (at $\alpha = 0.01$) $\delta = 3.4$
$n = \delta^2 / d^2 \quad = 3.4^2 / 0.6^2 \quad = 32.11$
Therefore **32** subjects are needed

Post-hoc:

Based on actual sample of 22 subjects, at $\alpha = 0.01$
$d = 0.05 / 0.13 = 0.38$
$\delta = d \times \sqrt{n} = 0.38 \times \sqrt{22} = 1.80$
Therefore power = **0.22**

(iii) AoA

$d = 0.30 / 0.50 = 0.6$
For power = 0.8, (at $\alpha = 0.01$) $\delta = 3.4$
$n = \delta^2 / d^2 \quad = 3.4^2 / 0.6^2 \quad = 32.11$
Therefore **32** subjects needed

Post-hoc: Based on actual sample of 22 subjects, at $\alpha = 0.01$
$d = 0.05 / 0.26 = 0.19$
$\delta = d \times \sqrt{n} = 0.19 \times \sqrt{22} = 0.90$
Therefore power = **0.05**

(b) Single factor ANOVA – for detection of overall significant differences

Calculations were conducted *post hoc* based on Equations A13 and A14

(i) DVA

$\sigma_m =$	$\sqrt{(0.0012/3)}$	$= 0.0202$
$f =$	$0.0202 / 0.17$	$= 0.12$

From Cohen (1988), at p=0.05, u=2 (k = u + 1 therefore u degrees of freedom = k - 1), and n=22, f = 0.12 and power = **0.15**. For power = 0.8, **n = 170**.

(ii) NVA

$\sigma_m =$	$\sqrt{(0.0016/3)}$	$= 0.023$
$f =$	$0.023 / 0.21$	$= 0.11$

From Cohen (1988), at p=0.05, u=2, and n=22, f = 0.11 and power = **0.11**. For power = 0.8, **n = 250**.

(iii) AoA

$\sigma_m =$	$\sqrt{(0.0105/3)}$	$= 0.059$
$f =$	$0.059 / 0.31$	$= 0.19$

From Cohen (1988), at p=0.05, u=2, and n=22, f = 0.19 and power = **0.34**. For power = 0.8, **n = 60**.

Large 'n' indicated for DVA and NVA because actual differences were small, indicating no significant changes over the 6-month period.

A3.4 Chapter 7

Based on the paired-samples Student's T-Tests (two-tailed):

The calculations were carried out *a priori* based on the requirement to detect a significant difference in two of the four comparisons between binocular and monocular visual outcomes, using the two-tailed paired-samples Student's T-Test. The calculations were based on Equation A15. The expected differences (effect sizes) were derived from clinically expected differences (binocular VA known to be √2 times better than monocular (Campbell and Green 1965)) and those observed in the Wolffsohn et al. (2006) and Sanders & Sanders (2007) studies. Standard deviations were estimated from clinical expectation and from those observed in the Wolffsohn et al. (2006) study (0.10 for NVA and 0.70 for AoA). These calculations are shown below along with the post hoc calculations based on the actual sample size and observations.

(i) NVA	$d = 0.14\text{-}0.10 / 0.10 = 0.4$ For power = 0.8, (at $\alpha = 0.05$) $\delta = 2.8$ $n = \delta^2 / d^2 \quad = 2.8^2 / 0.4^2 \quad = 49$ Therefore **49** subjects are needed
Post-hoc:	Based on actual sample of 19 subjects, at $\alpha = 0.05$ $d = (0.56\text{-}0.44) / 0.13 = 0.92$ $\delta = d \times \sqrt{n} = 0.92 \times \sqrt{19} = 4.02$ Therefore power = **0.98**
(ii) AoA	$d = 3.17 - 2.77 / 0.70 = 0.57$ For power = 0.8, (at $\alpha = 0.05$) $\delta = 2.8$ $n = \delta^2 / d^2 \quad = 2.8^2 / 0.57^2 \quad =$ Therefore **24** subjects needed
Post-hoc:	Based on actual sample of 19 subjects, at $\alpha = 0.05$ $d = (1.88 - 1.51) / 0.70 = 0.53$ $\delta = d \times \sqrt{n} = 0.53 \times \sqrt{19} = 2.3$ Therefore power = **0.63**

A4. Curve-Fitting Analysis for Determination of Defocus Curve AoA

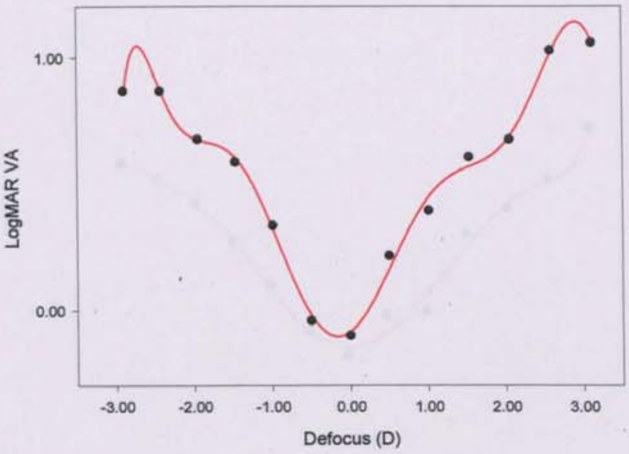
All of the defocus curves measured in Chapter 3 for determination of the most appropriate criterion to quantify the AoA were analysed to determine the best-fit polynomial regression curve (shown on the next few pages). From these an equation was determined and the output provided by SigmaPlot indicated various 'y-values' for various 'x-values'. These were used as starting points for trial and error determination of the AoA using with the equations for different criteria; the difference in the two x-values giving a particular criterion was defined as the AoA. The criteria tested were:

Absolute (0.3 LogMAR)
Absolute (0.4 LogMAR)
Best VA*
Best VA + 0.1 LogMAR
Best VA + 0.2 LogMAR
Best VA + 0.3 LogMAR
Best VA + 0.4 LogMAR

*This criterion was taken as the defocus range that gives 'Best VA + 0.04 logMAR' to allow for the natural expected variation in repeated VA measures

For the 'negative defocus only' criteria, the AoA was calculated from the above as the difference between zero defocus and the maximum negative defocus that corresponded to the criterion definition. For all defocus curves measured in this, the method described here was used to quantify the AoA, but only for the criterion of 'Best VA + 0.04 logMAR'.

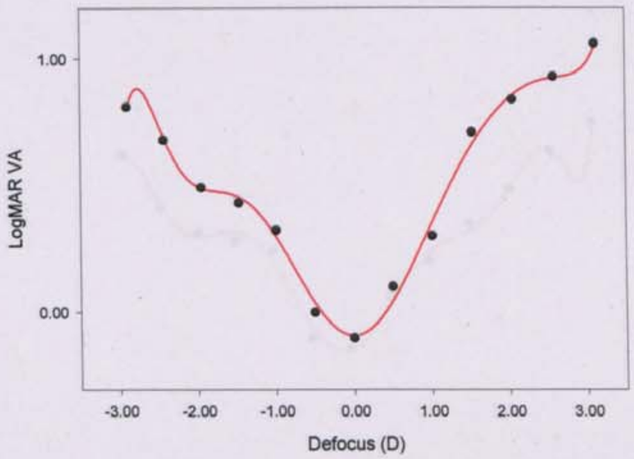
Person 1: SA



$R^2 = 0.995$

$Y = 0.0007x^9 - 0.003x^8 - 0.01x^7 + 0.04x^6 + 0.1x^5 - 0.3x^4 - 0.3x^3 + 0.7x^2 + 0.3x - 0.08$

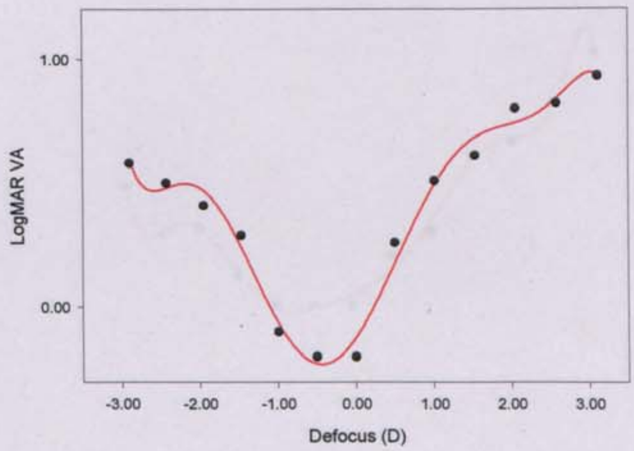
Person 2: TA



$R^2 = 0.993$

$Y = 0.0004x^9 - 0.001x^8 - 0.006x^7 + 0.03x^6 + 0.02x^5 - 0.2x^4 - 0.007x^3 + 0.6x^2 + 0.02x - 0.09$

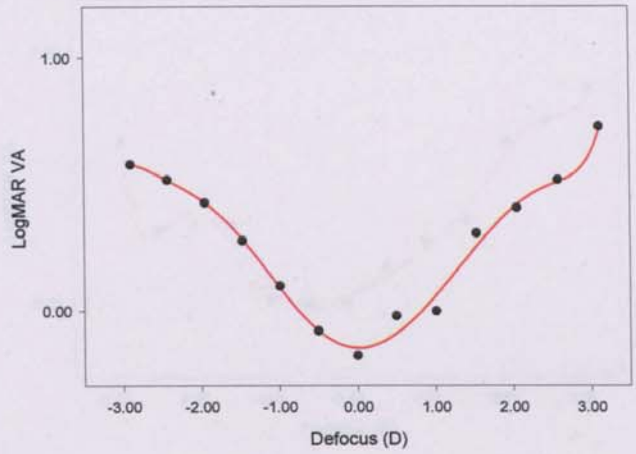
Person 3: DA



$R^2 = 0.982$

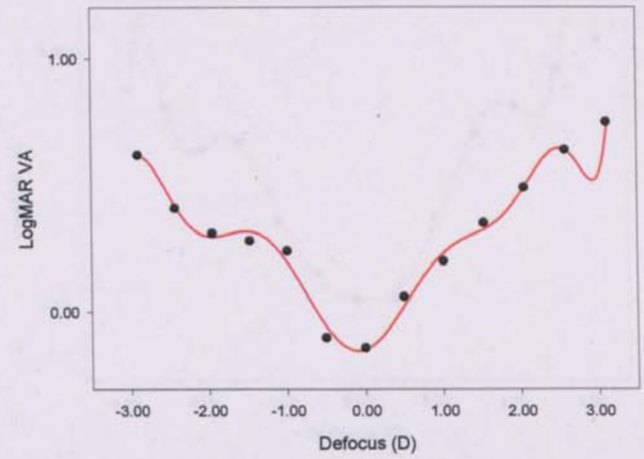
$Y = -0.00008x^8 - 0.002x^7 + 0.006x^6 + 0.04x^5 - 0.08x^4 - 0.2x^3 + 0.4x^2 + 0.5x - 0.1$

Person 4: JB



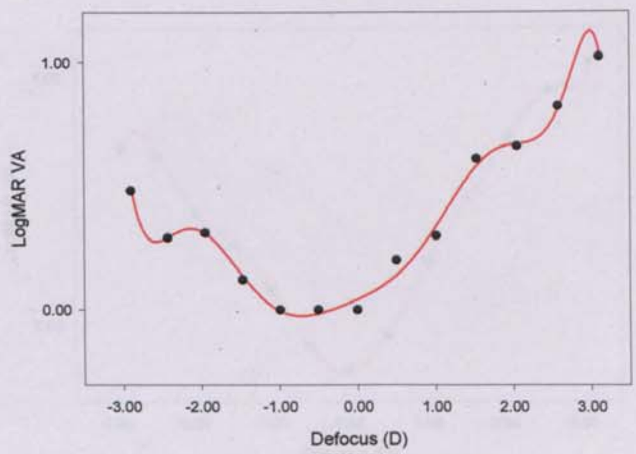
$R^2 = 0.987$
$Y = 0.00009x^9 - 0.00006x^8 - 0.002x^7 + 0.003x^6 + 0.01x^5 - 0.04x^4 - 0.02x^3 + 0.3x^2 - 0.001x - 0.1$

Person 5: CB



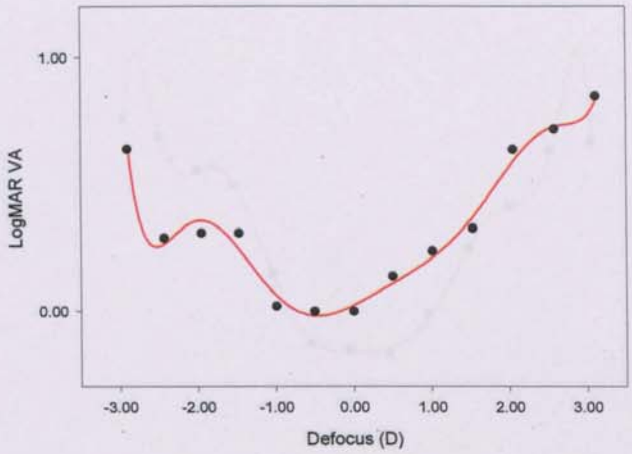
$R^2 = 0.990$
$Y = 0.0003x^{10} + 0.0005x^9 - 0.007x^8 - 0.01x^7 + 0.07x^6 + 0.07x^5 - 0.3x^4 - 0.2x^3 + 0.6x^2 + 0.1x - 0.1$

Person 6: CB



$R^2 = 0.994$
$Y = -0.0002x^{10} - 0.0005x^9 + 0.004x^8 + 0.009x^7 - 0.03x^6 - 0.05x^5 + 0.09x^4 + 0.07x^3 + 0.06x^2 + 0.1x + 0.04$

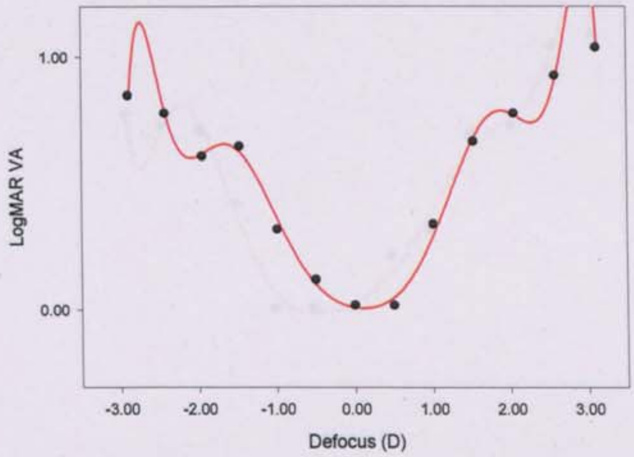
Person 7: MB



$R^2 = 0.984$

$Y = 0.001x^8 - 0.002x^7 - 0.01x^6 + 0.03x^5 + 0.05x^4 - 0.1x^3 + 0.08x^2 + 0.2x + 0.03$

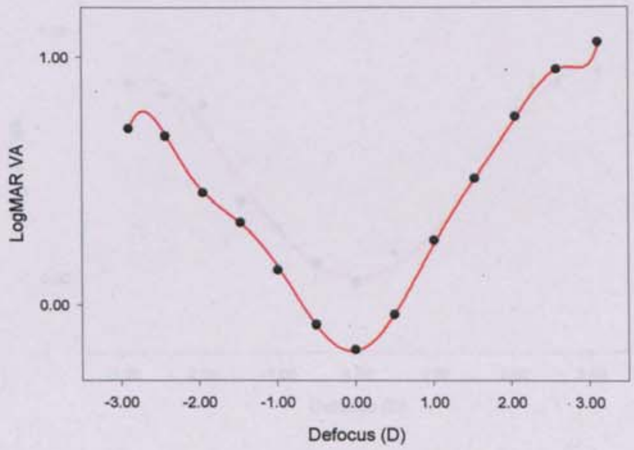
Person 8: AB



$R^2 = 0.996$

$Y = -0.0008x^{10} + 0.0006x^9 + 0.02x^8 - 0.009x^7 - 0.1x^6 + 0.04x^5 + 0.2x^4 - 0.02x^3 + 0.2x^2 - 0.04x + 0.01$

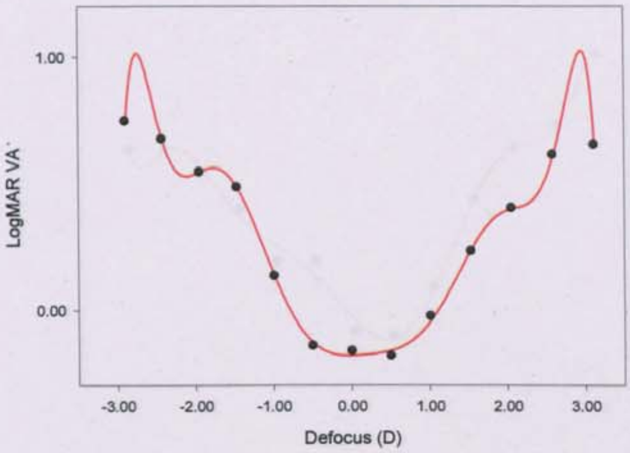
Person 9: JD



$R^2 = 1.000$

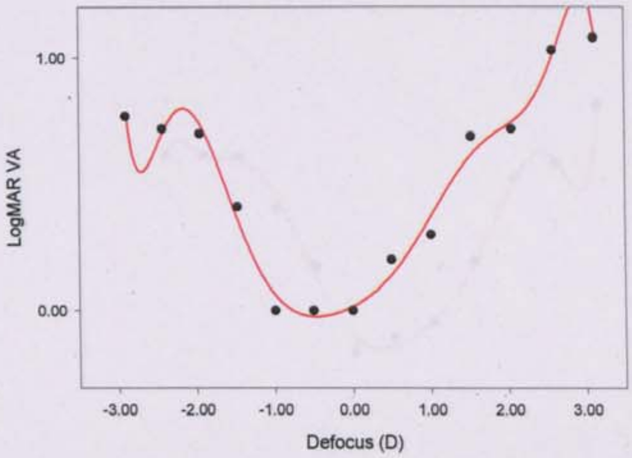
$Y = 0.0001x^{10} + 0.0002x^9 - 0.004x^8 - 0.004x^7 + 0.04x^6 + 0.02x^5 - 0.2x^4 - 0.02x^3 + 0.5x^2 + 0.06x - 0.2$

Person 10: SG



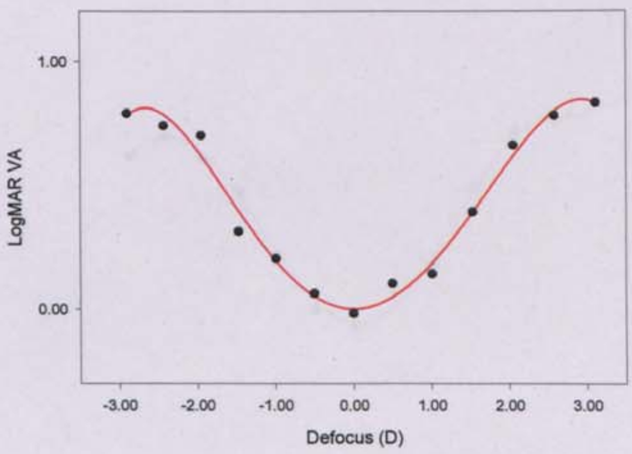
$R^2 = 0.999$
$Y = -0.0008x^{10} + 0.0009x^9 + 0.02x^8 - 0.02x^7 - 0.1x^6 + 0.09x^5 + 0.2x^4 - 0.2x^3 + 0.09x^2 + 0.01x - 0.2$

Person 11: GM



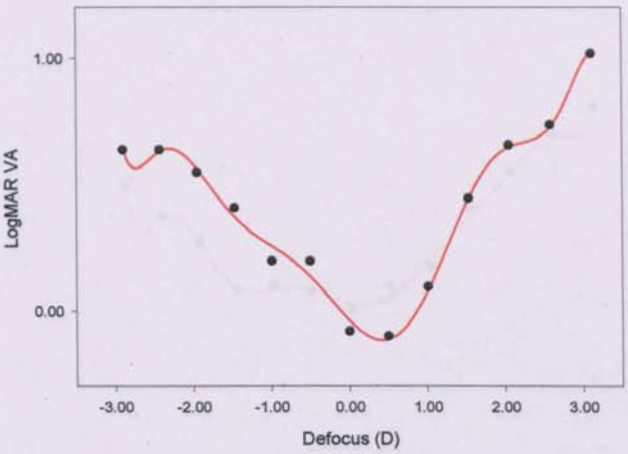
$R^2 = 0.986$
$Y = -0.0009x^9 + 0.001x^8 + 0.01x^7 - 0.02x^6 - 0.07x^5 + 0.05x^4 + 0.05x^3 + 0.2x^2 + 0.2x + 0.02$

Person 12: JP



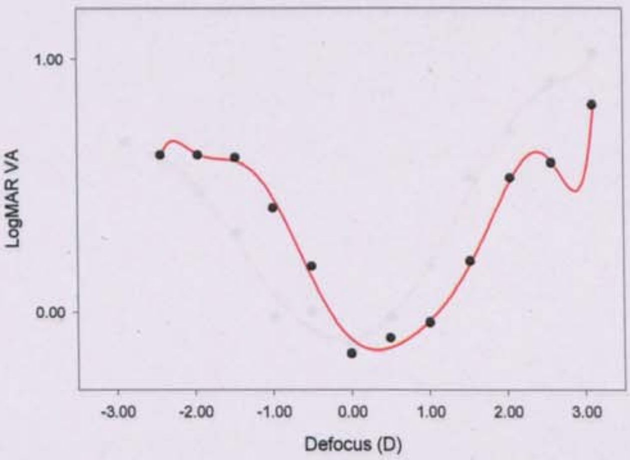
$R^2 = 0.981$
$Y = -0.0003x^6 + 0.0009x^5 - 0.01x^4 - 0.007x^3 + 0.2x^2 + 0.004x - 0.0009$

Person 13: AR



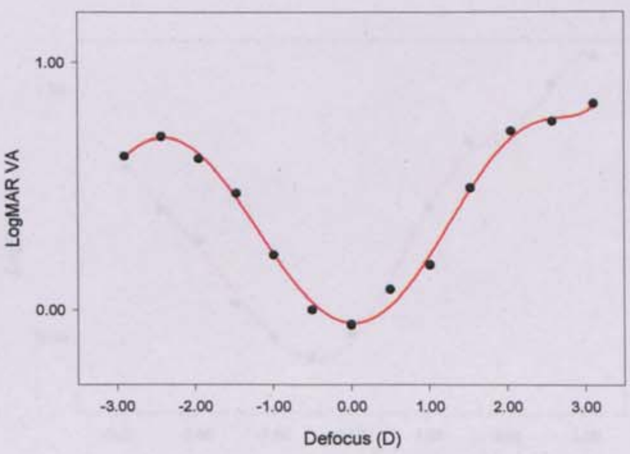
$R^2 = 0.992$
$Y = -0.0007x^9 + 0.0006x^8 + 0.01x^7 - 0.008x^6 - 0.1x^5 + 0.01x^4 + 0.3x^3 + 0.2x^2 - 0.3x - 0.04$

Person 14: VS



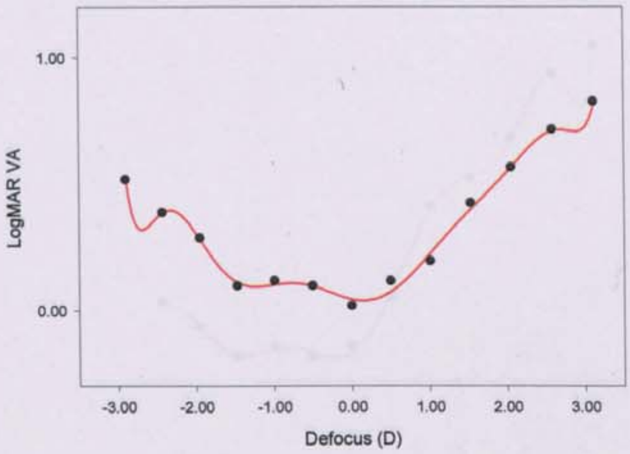
R^2 0.993
$Y = 0.001x^9 - 0.003x^8 - 0.02x^7 + 0.04x^6 + 0.08x^5 - 0.2x^4 - 0.04x^3 + 0.5x^2 - 0.3x - 0.1$

Person 15: JS



$R^2 = 0.993$
$Y = 0.0002x^7 + 0.002x^6 - 0.002x^5 - 0.04x^4 + 0.01x^3 + 0.3x^2 - 0.008x - 0.05$

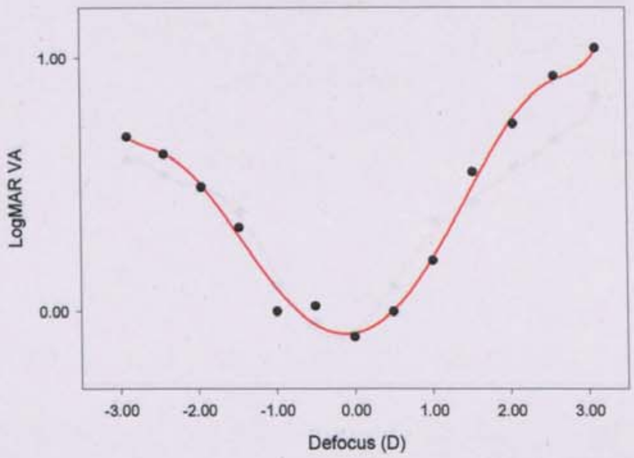
Person 16: BS



R^2 0.995

$Y = 0.0003x^{10} - 0.0007x^9 - 0.006x^8 + 0.01x^7 + 0.04x^6 - 0.08x^5 - 0.1x^4 + 0.2x^3 + 0.2x^2 - 0.06x + 0.05$

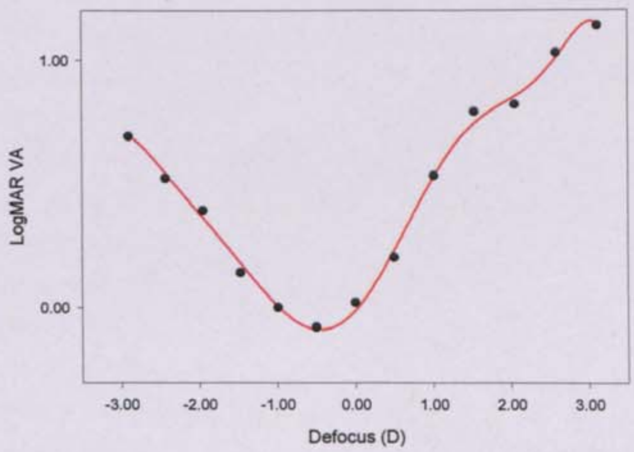
Person 17: KS



$R^2 = 0.990$

$Y = 0.0002x^8 - 0.000003x^7 - 0.002x^6 - 0.0002x^5 - 0.01x^4 - 0.0005x^3 + 0.2x^2 + 0.06x - 0.08$

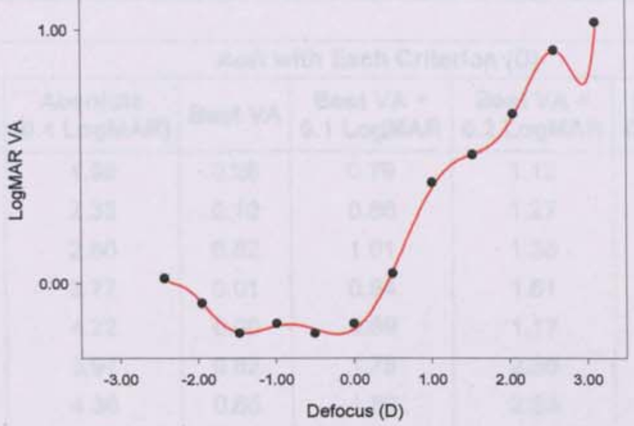
Person 18: KT



$R^2 = 0.996$

$Y = -0.0005x^8 - 0.0005x^7 + 0.01x^6 + 0.01x^5 - 0.08x^4 - 0.1x^3 + 0.3x^2 + 0.4x - 0.007$

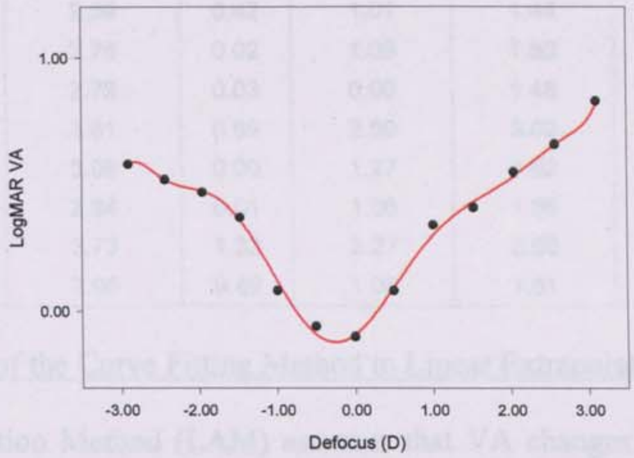
Person 19: RW



$R^2 = 0.999$

$Y = 0.0008x^{10} - 0.001x^9 - 0.02x^8 + 0.02x^7 + 0.1x^6 - 0.09x^5 - 0.4x^4 + 0.1x^3 + 0.6x^2 + 0.2x - 0.2$

Person 20: MW



R^2 0.995

$Y = 0.0003x^9 - 0.0006x^8 - 0.007x^7 + 0.01x^6 + 0.06x^5 - 0.1x^4 - 0.2x^3 + 0.4x^2 + 0.2x - 0.09$

A4.1 Summary of Quantified Defocus Curve AoA with Each Criterion

Subject	AoA with Each Criterion (D)						
	Absolute (0.3 LogMAR)	Absolute (0.4 LogMAR)	Best VA	Best VA + 0.1 LogMAR	Best VA + 0.2 LogMAR	Best VA + 0.3 logMAR	Best VA + 0.4 logMAR
SA	1.67	1.99	0.28	0.79	1.12	1.41	1.70
TA	1.94	2.33	0.10	0.86	1.27	1.61	1.96
DA	2.25	2.60	0.52	1.01	1.36	1.67	1.97
JB	3.14	3.77	0.01	0.94	1.61	2.14	2.65
CB1	3.41	4.22	0.00	0.69	1.17	1.58	2.06
CB2	2.84	3.97	0.82	1.78	2.36	2.90	3.98
MB	2.92	4.36	0.65	1.59	2.35	2.98	4.39
AB	1.91	2.20	0.16	1.20	1.61	1.93	2.21
JD	2.48	3.06	0.49	1.04	1.43	1.82	2.23
SG	2.82	3.30	0.59	1.58	2.00	2.30	2.61
GM	2.26	2.57	0.78	1.50	1.93	2.29	2.60
JP	2.58	3.04	0.04	1.51	2.01	2.52	2.98
AR	2.49	2.99	0.42	1.01	1.44	1.93	2.54
VS	2.46	2.76	0.02	1.09	1.59	1.97	2.29
JS	2.31	2.72	0.03	0.90	1.48	1.94	2.35
BS	3.18	3.81	0.69	2.50	3.02	3.55	4.59
KS	2.65	3.06	0.00	1.27	1.82	2.28	2.69
KT	2.40	2.84	0.01	1.06	1.56	2.01	2.44
RW	3.51	3.73	1.33	2.27	2.90	3.17	3.37
MW	2.34	2.95	0.49	1.08	1.51	1.92	2.38

A4.2 Comparison of the Curve Fitting Method to Linear Extrapolation

The Linear Assumption Method (LAM) assumes that VA changes linearly between two defocus points. As such the proportion of VA change that is still within the criterion of 'Best VA + 0.04 logMAR' can be apportioned to a similar change in defocus. The following table compares this approach to the curve fitting method used in Chapter 3:

	Push-up test	Curve-fitting	LAM
Mean AoA ± SD (D)	1.35±0.47	0.82±0.40	0.73±0.42
Pearson's Correlation:			
To push-up test	-	0.84	0.82
Curve-fitting v LAM		0.95	
Significance (Regression):			
To push-up test	-	p=0.000004	p=0.00001
Curve-fitting v LAM		p<0.000001	
Concordance			
To push-up test	-	0.47	0.38
Curve-fitting v LAM		0.78	
Bland-Altman Limits of Agreement (D):			
To push-up test	-	0.50	0.53
Curve-fitting v LAM		0.25	
Curve-Fitting: range of r values		0.9905 to 0.9999	

A5. Review of Vision Related-Quality of Life (VR-QoL) Questionnaires

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
VFI (Bernth-Petersen 1981)	Assess the effect of cataract on daily visual tasks	Interview	11	'Yes / No' & 3-point Likert scales	N/A	Construct Validity by inter-item correlations & correlation of total questionnaire score to VA	None
PERK Study Psychometric Questionnaire *(Has pre- and post-operative elements)* (Waring *et al.* 1983, Bourque *et al.* 1984, Bourque *et al.* 1986)	Evaluate demographic and psychological characteristics of myopic subjects having radial keratotomy, and their perceptions of visual ability before and after surgery	Self-administration	140 in pre-op. version 16 (112) in post-op. version	2 to 5-point Likert scales in pre-op. version 7-point Likert scale in post-op. version	N/A	Comparison of pre-op. data to that obtained in the Rand Health Insurance Experiment, which was a large-scale health assessment study conducted in the USA from 1974 to 1982	Factor Analysis used to reduce the post-op. version into three subscales (Satisfaction Index, Fluctuating Vision Index and Glare Index)
ALB (Becker *et al.* 1985)	To aid rehabilitation of the blind by assessing the difficulties experienced with various activities	Telephone	74 (124)	3 to 9-point Likert scales depending on the type of question	Conformance to Rasch Model	Inter-correlations of scores for rehabilitated & non-rehabilitated blind persons, & rehabilitation workers	Rasch Analysis
VSI (Coren and Hakstian 1987)	Indicate visual health status without using technology	Self-administered & Post	52 (357)	5-point Likert scale - no values	Cronbach's α for each domain (0.86-0.94)	Construct Validity by correlation of domain scores with VA, colour vision & binocularity	Factor Analysis
PVD (Elliott *et al.* 1990)	Assess visual disability in cataract patients	Self-administered	20 plus 3 qualitative	• 10cm visual analogue scales • Max. Score = 200	N/A	Correlation of individual items to VA, CS & glare disability	None
NAS (Dodds *et al.* 1991, Dodds *et al.* 1993)	Identify the variables involved with acquired vision loss	Interview	47 (55)	7 domains	N/A	Comparison of scores pre to post rehabilitation	Factor Analysis
VAQ (Sloane *et al.* 1992)	Asses the effect of vision loss on daily life activities in the elderly	Self-administered	33 (100)	5-point Likert scale	Cronbach's α for each domain (all >0.80)	• Content Validity by item-domain correlation • Criterion Validity by correlation of each domain score with appropriate clinical tests	Factor Analysis

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
ADVS (Mangione *et al.* 1992)	Assess visual function loss cataract patients	Telephone Interview	22	• 5-point Likert scale plus 'N/A' • 0-100 rating of satisfaction with overall vision	• Correlations for inter-rater & Test-retest • Cronbach's α (0.94)	Criterion Validity by correlation of total scores to binocular vision loss & overall satisfaction	• Correlation with SF-36 score • Factor Analysis • Rasch Analysis (Pesudovs *et al.* 2003)
VFQOL (Brenner *et al.* 1993)	Determine whether quality of life & visual function change in the same direction	Interview	19	3, 4 or 5-point Likert scales	Cronbach's α for visual (0.85) & social (0.89) domains	None	None
VF-14 (Steinberg *et al.* 1994)	Assess & measure functional impairment in cataract patients	Interview (person & telephone) & Self-administered	18	• 'Yes / No / N/A' then rating on a 5-point Likert scale • Total score = mean x 25	Cronbach's α (0.85)	Criterion Validity by Spearman's correlations with VA, overall satisfaction & trouble ratings	• Factor Analysis • Multiple Linear Regression to identify best predictor of VF-14 score
Catquest (Lundstrom *et al.* 1994, Lundstrom *et al.* 1997)	Assess daily living & visual activities, & independence pre & post cataract extraction	Telephone & Self-administered	7 activities 24 overall (37)	4-point Likert scale plus 'cannot say' option	• Spearman's item-total correlations • Test-retest – ANOVA ($p>0.05$)	Spearman's correlation with global ratings of general vision & problems, satisfaction, best DVA, and to non-cataract patients	None
ABS (Massof 1995, 1998)	Aid rehabilitation by classifying activities as a hierarchy of goals, tasks & objectives	Telephone	24	6-point Likert scale	N/A	N/A	Rasch Analysis
SOCA (Wu *et al.* 1996, Martin *et al.* 2001)	Assess perceived visual function in cytomegalovirus retinitis patients	Self-administered	18 (21)	• 5-point Likert scale • Total score = mean x a linear factor	Cronbach's α (0.68-0.87)	Construct Validity by inter-item & item-scale correlations, & correlations with VA, visual fields, retinitis area, & correlation of global vision with VA & visual fields	• Frequency of endorsement • Correlations of general health scales to clinical measures e.g. CD4+ & haemoglobin
Cataract TyPE Spec (Javitt *et al.* 1997, Javitt *et al.* 2003)	Assess functional & quality of life outcomes of cataract surgery	Interview, Self-administered & Post	13	• 5-point Likert scale • 0-10 satisfaction & global vision rating • Total = sum of domain totals	Cronbach's α (0.94)	Criterion Validity by correlation with VA in better eye & change in overall satisfaction	None

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
NEI-VFQ (Mangione *et al.* 1998a, 1998b, 2001)	Assess visual function & influence of various eye conditions on HR-QoL	Interview & Self-administered	25 or 51 (2623)	• 5 or 6-point Likert scale • Max. Score = 100	• Cronbach's α (0.66-0.91) • Test-retest –ICC (0.68-0.91)	Construct Validity by correlation with SF-36, VF-14, ADVS, VAQ, best & worst eye VA & visual fields	• Comparison of low VA patient scores to high VA • Linear regression to identify variance
VQOL & VCMI (Frost *et al.* 1998, Frost *et al.* 2001)	Define vision-related quality of life & devise a fast means of assessing it	Telephone Interview & Self-administered	10 (107)	6-point Likert scale	• Cronbach's α (0.93) • Test-retest –ICC (0.89)	Construct Validity by Spearman's correlation of VCMI with SF-36, EuroQol, VF-14, TyPE, & NAS	Factor Analysis
VDA (Pesudovs and Coster 1998)	Assess visual disability & outcomes of cataract surgery	Interview	18 (37)	• 4-point Likert scale • Final score = mean of answered items	• Cronbach's α (0.92) • Test-retest – ICC (0.98)	Criterion validity by Spearman's correlation with ADVS score	Factor Analysis
GO-QOL (Terwee *et al.* 1998, Terwee *et al.* 1999)	Assess perceived quality of life in patients with Graves' Ophthalmopathy	Self-administered	16	• 3-point Likert scale • Total score = sum x a linear factor for 0-100 range	• Cronbach's α (0.86-0.89) • Test-retest – ICC (0.83)	Construct Validity by Spearman's correlation with MOS-24, 3 scales of SIP & 'NO SPECS' classification	Factor Analysis
AVL (Horowitz and Reinhardt 1998)	Assess older people's adaptations to late-life vision loss	Interview	24 (33)	4-point Likert scale reduced to 'Agree / disagree'	Cronbach's α (0.84-0.86)	Correlation to global self well-being ratings & life satisfaction ratings	• Skew • Item-total correlations • Factor Analysis
IMQ (Turano *et al.* 1999)	Determine perceived ability for independent mobility in patients with retinitis pigmentosa, to aid rehabilitation	Self-administered	35	5-point Likert scale plus 'N/A' & 'don't do due to non-visual reasons'	Rasch Reliability Coefficients for person (0.96) & item (0.98) parameters	• Content Validity from the separation index • Construct Validity from the Rasch fit statistics • Criterion Validity by ROC Curve Analysis	• Rasch Analysis • Comparisons with VA, contrast sensitivity & visual fields for covariance
VDQ (Nelson *et al.* 1999)	Assess visual disability in glaucoma patients	Self-administered	62	5-point Likert scale plus 'don't do for non-visual reasons'	Cronbach's α (0.96) for glaucoma scale	Spearman's correlation with loss in visual field	Factor Analysis
TyPE (Lawrence *et al.* 1999)	Measure outcomes of cataract surgery	Self-administered	13	5-point Likert scale	Kappa Coefficient (0.84) & Spearman's correlations (0.93)	Construct Validity by correlation of change in total score with change in perceived visual function	None
MIOLS Instruments (Ellwein *et al.* 1994, Fletcher *et al.* 1997, Fletcher *et al.* 1998)	Measure outcomes of cataract surgery in a developing country	Interview	12	4-point Likert scale	Cronbach's α >0.90	Correlation to VA (0.40)	Comparison of repeated scores

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
VF-7 (Uusitalo *et al.* 1999)	Shorten the VF-14 for measuring functional impairment in cataract	Interview	7 (14)	5-point Likert scale	N/A	Correlations with VA, cataract symptom score & overall trouble rating	Spearman's rank correlations with patient satisfaction
CSS (Crabtree *et al.* 1999)	Measure functional disability & visual symptoms due to cataract in older UK residents	Interview	15	• 6 & 5-point Likert scales • Total = percentage score of answered items only	• Cronbach's α (0.88) • Test-retest – Spearman's correlation (0.91)	Spearman's correlations with VA in better, worst, & operated eyes, VF-14, ADL, GHQ, HAD & global rating of visual symptoms	Factor Analysis
DLTV (Hart *et al.* 1999, Denny *et al.* 2007)	Evaluate visual function in AMD	Interview	17 (22 plus 2 overall ability ratings)	4-point Likert scale	Rasch Separation Indices for Person (0.86 and 0.77) and Item (0.99 and 0.98) measures	• Spearman's correlation with DVA in better, worse & both eyes for each item • Pearson's correlations of global ability ratings	• Stepwise regression analysis to identify best predictors of variance • Factor Analysis • Rasch Analysis (2007)
LVQOL (Wolffsohn and Cochrane 2000)	Evaluate vision-specific low-vision rehabilitation strategy & management	Interview (in person & telephone) & Self-administered (post)	25 (74)	• 6-point Likert scale plus N/A option • Missed items given an average score	• Cronbach's α (0.88) • Test-retest - 0.72)	Correlations with DV, DVA, NV, NVA, & CS	• Frequency of endorsement • Item-total correlations • Factor Analysis
MOOD (Foss *et al.* 2000)	Assess visual function & the impact of eye treatment in ocular melanoma	Self-administered	21	5-point Likert scale plus a global question rated on a 0-100 visual analogue scale	• Cronbach's α (0.92) • Test-retest – Spearman's correlation (0.88)	Construct Validity by inter-item correlations within own scale & with other scales, & correlations to VA & SF-36	• Frequency of endorsement • Item-total correlations
RSVP (Vitale *et al.* 2000)	Assess self-reported functioning, symptoms, health perceptions & expectations in individuals with refractive error	Self-administered	42 (64)	• 5-point Likert scale plus a 'N/A' option • Total scores re-scaled to 0-100	• Cronbach's α (0.92; 0.70-0.93) • Test-retest – ICC (0.61; 0.68-0.84)	• Criterion Validity by correlation with clinical measures, ratings of satisfaction, overall vision, & general health • Construct Validity by item-total correlations & various hypotheses	• Factor Analysis • Multitrait analysis
HVAT (Prager *et al.* 2000)	Aid the clinical decision to proceed with cataract extraction	Self-administered	10 (30)	• 6-point Likert scale • Total score = sum of part (a) score x part (b) score • Part (b) acts as a weighting factor	Cronbach's α (0.96 pre-surgery, 0.94 post-surgery)	Correlation with VA at varying contrasts	• Item-total correlations • Stepwise regression analysis to identify the best predictors of outcomes

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
IVI (Hassell *et al.* 2000, Weih *et al.* 2002, Lamoureux *et al.* 2007)	Assess how vision impairment impacts on a person's ability to participate in society, to do what they want & need to do	Interview & Self-administered	32 (76)	6-point Likert scale	• Cronbach's α (0.80-0.96) • Test-retest – Guttman Split Half reliability (0.73-0.94)	Construct Validity by Spearman's correlations with DVA, NVA & SF-12, & by correlating with global rating of restriction in participation	• Inter-tem Spearman's correlations • Frequency of endorsement • Factor Analysis • Rasch Analysis (2007 paper)
CRSRGQ (Brunette *et al.* 2000)	Assess patient satisfaction & perceived outcome after bilateral PRK	Self-administered	39 (41)	• 5-point Likert scales for 29 items • Yes/No responses for 10 items	• Cronbach's α (0.83-0.96) • Test-retest – ICC (0.85-0.92)	Construct validity by item-total & item-scale correlations & by correlating scales to corrected & uncorrected VA, & global satisfaction	None
MLVAI (Haymes *et al.* 2001)	Assess activities of daily living in the low-vision population	Interview / practitioner	25 (27)	5-point Likert scale	• Cronbach's α (0.96) • Test-retest – ICC (0.95) & Spearman's correlation (0.94) • Inter-rater – Spearman's correlation (0.90)	• Content Validity from the separation index • Construct Validity by conforming to the Rasch fit statistics & by correlation with VA overall, & central vs. peripheral impairment, & by Principal Components Analysis / Factor Analysis	• Skew for each item • Item-total correlations • Rasch Analysis
NEI-RQL (Berry *et al.* 2003, Hays *et al.* 2003)	Assess the impact of refractive correction in subjects with normal vision (6/9 or better) on vision-related function & well-being	Self-administered	42 (94)	4, 5 or 6-point Likert scales	• Cronbach's α (0.64-0.90) • Test-retest – ICC (0.55-0.83)	Construct Validity by testing hypothesized scores for myopes, hyperopes & emmetropes on NEIVFQ-25 & SF-36, & by correlating scores with MSE	Item discrimination by item-scale correlations
QoLQ (Chan *et al.* 2003)	Evaluate of quality of life before & after cataract surgery with a more culturally relevant questionnaire	Self-administered	20	5-point Likert scale plus 'N/A' option if unable to read due to illiteracy & unable to drive	• Cronbach's α (0.92) • Test-retest – weighted Kappa (0.93)	Construct Validity by correlations of pre & post-op. scores with VA in operated, better & worst eyes & by correlating change in QoL score with visual improvement & overall satisfaction ratings	None

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
LVP-FVQ (Gothwal *et al.* 2003)	Assess self-reported visual function problems in visually impaired school children	Interview	19 (26) plus overall ability	'Yes/No' followed by a rating of difficulty if 'Yes' on a 5-point Likert scale	Rasch Reliability Coefficients for person (0.65) & item (0.93) parameters	• Content Validity from the separation index & by comparing to DVA • Construct Validity from the Rasch fit statistics • Criterion Validity by ROC Curve Analysis	Rasch Analysis
VA LV-VFQ-48 (Stelmack *et al.* 2004, Szlyk *et al.* 2004)	Assess difficulty in performing daily living tasks by the visually impaired & evaluate low-vision outcomes	Telephone	48	6-point Likert Scale reduced to a 4-point Likert scale	• Separation index (0.98) • Test-retest – Item ICC (0.98) & person ICC (0.84)	Conformance to Rasch Model	• Rasch Analysis • Factor Analysis
QIRC (Pesudovs *et al.* 2004)	Quantify quality of life of people with different types of refractive correction	Self-administered	20 (115)	5-point Likert scale	• Cronbach's α (0.78) • Test-retest – ICC (0.88) • Coefficient of Repeatability	• Content Validity from focus groups • Conformance to Rasch Model	• Factor Analysis • Rasch Analysis
PVQQ (Aslam *et al.* 2004)	Quality of vision after cataract surgery with intraocular lens implantation	Self-administered	17	4-point Likert scale for Question 1 5-point Likert Scale for the remaining questions	• Cronbach's α (0.93) • BSI repeatability coefficient (mean –0.20, ± 6.66)	• Comparison of questionnaire scores between subjects with no PCO and no difficulty to those with difficulty and a need for PCO treatment	None
APEDS-VFQ (Nutheti et al. 2004)	Perceived visual ability in adults with low vision in India	Self-administered	16	5-point Likert Scale reduced to a 4-point Likert Scale	• Rasch Cronbach's α (0.97) • Separation Index (5.44)	• Conformance to Rasch Model • Criterion Validity by ROC Curve Analysis	• Rasch Analysis
VisQoL (Misajon *et al.* 2005)	Economically evaluate eye care & rehabilitation	Self-administered	6 (33)	5, 6 & 7-point Likert scales	Cronbach's α (0.88)	Conformance to Rasch Model	• Frequency of Endorsement (>80%) • Item Mean Score (<20%) • Item Discrimination • Factor Analysis • Rasch Analysis

Questionnaire	Aim of Instrument	Administration Method(s)	No. of Items (original no.)	Response Scale Format & Scoring	Reliability	Validity	Other Analyses
Focus-QOL (Fylan *et al.* 2005)	Assess social & psychological well-being & ability to use residual vision, in low vision patients	Self-administered	25	• 5-point Likert scale • Max score =100	• Cronbach's α (0.96) • Test-retest	N/A	Factor Analysis
AI (Massof *et al.* 2005, Massof *et al.* 2007)	Evaluate the relation between visual ability measured at the task level to the goal level	Telephone	459 (50 goals, 3 objectives)	5 and 6-point Likert scales	Rasch Separation reliabilities (0.86 goal rating, 0.96 task rating)	Conformance to Rasch Model	• Rasch Analysis • Factor Analysis
IND-VFQ *(Gupta et al. 2005, Murthy et al. 2005)*	Develop a patient-defined vision function questionnaire for visually impaired and blind people living in a low income country	Interview	33 (103 plus an open-ended item)	4 and 5-point Likert Scales	• Cronbach's α (0.88 to 0.97) • Item-total correlations (0.51 to 0.66) • Test-retest by correlation (0.90-096)	• Focus groups for Content Validity • Construct Validity by comparison of scores to normal subjects, VA, and change over time	• Frequency of Endorsement • Item-total correlations for item reduction
SLQ (Subramanian and Dickinson 2006)	Assess self-reported difficulty with spatial localisation tasks in the visually impaired & determine if such tests are better predictors than VA & CS	Self-administered	28 (39)	5-point Likert scale plus N/A	Rasch subject reliability (0.95) & item reliability (0.94)	• Correlation with VA, CS, reading speed, stereoacuity, vernier acuity, bisection acuity & visual direction • Conformance to Rasch Model provides validity	• Rasch Analysis • Stepwise regression analysis to identify best predictors of ability
AFREV (Altangerel *et al.* 2006)	Evaluate vision-related function in a spectrum of aetiologies & types of impairment	Interview	5 (9)	0-10 rating of ability to carry out the task	Internal consistency from Rasch fit statistics	Correlation with NEI-VFQ subscale & total scores, CS, binocular VA, better & worse eye VA, & visual fields	• Rasch Analysis • Factor Analysis • Stepwise regression analysis to identify best predictors of ability
CLIQ (Pesudovs *et al.* 2006)	Measure the impact of contact lenses on quality of life	Self-administered	28 (115)	5-point Likert scale	• Rasch real reliability (0.80) • Test-retest – ICC (0.86) • Coefficient of Repeatability	Conformance to Rasch Model	Rasch Analysis

A6. Differential Item Functioning of the NAVQ

The tables below are the outputs obtained from the Winsteps® Rasch Measurement Program giving evidence of Differential Item Functioning (DIF). DIF describes whether there are any significant differences in the relative difficulty of the various items between constituent groups i.e. between those corrected with 'accommodating' IOLs, multifocal or monovision contact lenses, or varifocal spectacles. The probability values in the tables indicate the likelihood of observing DIF due to chance for that particular item, for that particular comparison of presbyopic correction - if "p" is less than 0.05 ($p<0.05$) then there is a definite contrast in the items between constituent groups i.e. significant DIF exists.

Before item reduction (see section A6.1) there were 10 pair-wise comparisons where $p<0.05$, whilst after item reduction (see section A6.2) there were 8 pair-wise comparisons where $p<0.05$. This suggested that DIF was present in the NAVQ and therefore separate Rasch Analysis procedures were needed for each type of presbyopic correction.

A6.1 DIF Prior to Overall Group NAVQ Item Reduction

Person CLASS	DIF MEASURE	DIF S.E.	Person CLASS	DIF MEASURE	DIF S.E.	DIF CONTRAST	JOINT S.E.	t	d.f.	Prob.	MantelHanzl Prob.	Size	Item Number	Name
C	35.00	2.55	I	31.59	1.92	3.41	3.19	1.07	47	.2902			1	Q1 Small Print
C	35.00	2.55	V	37.30	2.06	-2.30	3.27	-.70	56	.4846	.3701	-.	1	Q1 Small Print
I	31.59	1.92	C	35.00	2.55	-3.41	3.19	-1.07	47	.2902			1	Q1 Small Print
I	31.59	1.92	V	37.30	2.06	-5.71	2.81	-2.03	65	.0465	.5637	+.	1	Q1 Small Print
V	37.30	2.06	C	35.00	2.55	2.30	3.27	.70	56	.4846	.3701	+.	1	Q1 Small Print
V	37.30	2.06	I	31.59	1.92	5.71	2.81	2.03	65	.0465	.5637	-.	1	Q1 Small Print
C	33.05	2.50	I	31.02	1.92	2.03	3.16	.64	47	.5239			2	Q2 Labels
C	33.05	2.50	V	33.76	1.88	-.71	3.13	-.23	56	.8216	.7009	-.	2	Q2 Labels
I	31.02	1.92	C	33.05	2.50	-2.03	3.16	-.64	47	.5239			2	Q2 Labels
I	31.02	1.92	V	33.76	1.88	-2.74	2.69	-1.02	65	.3130	.3173	+.	2	Q2 Labels
V	33.76	1.88	C	33.05	2.50	.71	3.13	.23	56	.8216	.7009	+.	2	Q2 Labels
V	33.76	1.88	I	31.02	1.92	2.74	2.69	1.02	65	.3130	.3173	-.	2	Q2 Labels
C	45.19	2.97	I	41.87	2.01	3.32	3.59	.93	47	.3587	.3173	+.	3	Q3 Mail
C	45.19	2.97	V	50.70	3.64	-5.50	4.70	-1.17	55	.2469	.2207	-.	3	Q3 Mail
I	41.87	2.01	C	45.19	2.97	-3.32	3.59	-.93	47	.3587	.3173	-.	3	Q3 Mail
I	41.87	2.01	V	50.70	3.64	-8.83	4.16	-2.12	64	.0376	.3173	+.	3	Q3 Mail
V	50.70	3.64	C	45.19	2.97	5.50	4.70	1.17	55	.2469	.2207	+.	3	Q3 Mail
V	50.70	3.64	I	41.87	2.01	8.83	4.16	2.12	64	.0376	.3173	-.	3	Q3 Mail
C	61.50	5.12	I	58.07	3.15	3.42	6.01	.57	46	.5715			4	Q4 Large Print
C	61.50	5.12	V	70.06	<11.95	-8.56	13.00	-.66	56	.5129			4	Q4 Large Print
I	58.07	3.15	C	61.50	5.12	-3.42	6.01	-.57	46	.5715			4	Q4 Large Print
I	58.07	3.15	V	70.06	<11.95	-11.99	12.36	-.97	64	.3359			4	Q4 Large Print
V	70.06	<11.95	C	61.50	5.12	8.56	13.00	.66	56	.5129			4	Q4 Large Print
V	70.06	<11.95	I	58.07	3.15	11.99	12.36	.97	64	.3359			4	Q4 Large Print
C	48.06	3.16	I	48.74	2.28	-.68	3.90	-.17	47	.8629			5	Q5 Own Writing
C	48.06	3.16	V	57.03	4.90	-8.97	5.84	-1.54	56	.1299			5	Q5 Own Writing
I	48.74	2.28	C	48.06	3.16	.68	3.90	.17	47	.8629			5	Q5 Own Writing
I	48.74	2.28	V	57.03	4.90	-8.29	5.41	-1.53	65	.1299			5	Q5 Own Writing
V	57.03	4.90	C	48.06	3.16	8.97	5.84	1.54	56	.1299			5	Q5 Own Writing
V	57.03	4.90	I	48.74	2.28	8.29	5.41	1.53	65	.1299			5	Q5 Own Writing
C	39.69	2.80	I	43.18	2.58	-3.49	3.81	-.92	33	.3665			6	Q6 Computer
C	39.69	2.80	V	50.63	4.26	-10.94	5.10	-2.15	36	.0386	.5637	+.	6	Q6 Computer
I	43.18	2.58	C	39.69	2.80	3.49	3.81	.92	33	.3665			6	Q6 Computer
I	43.18	2.58	V	50.63	4.26	-7.46	4.98	-1.50	35	.1434	.7055	-.	6	Q6 Computer
V	50.63	4.26	C	39.69	2.80	10.94	5.10	2.15	36	.0386	.5637	-.	6	Q6 Computer
V	50.63	4.26	I	43.18	2.58	7.46	4.98	1.50	35	.1434	.7055	+.	6	Q6 Computer
C	41.42	2.78	I	41.26	1.99	.16	3.41	.05	47	.9624			7	Q7 Telephone
C	41.42	2.78	V	45.72	2.76	-4.30	3.91	-1.10	56	.2770	.2207	-.	7	Q7 Telephone
I	41.26	1.99	C	41.42	2.78	-.16	3.41	-.05	47	.9624			7	Q7 Telephone
I	41.26	1.99	V	45.72	2.76	-4.46	3.40	-1.31	65	.1947			7	Q7 Telephone
V	45.72	2.76	C	41.42	2.78	4.30	3.91	1.10	56	.2770	.2207	+.	7	Q7 Telephone
V	45.72	2.76	I	41.26	1.99	4.46	3.40	1.31	65	.1947			7	Q7 Telephone
C	48.06	3.16	I	51.57	2.57	-3.51	4.08	-.86	45	.3942	.3173	-.	8	Q8 Watch
C	48.06	3.16	V	51.71	3.64	-3.65	4.82	-.76	56	.4525			8	Q8 Watch
I	51.57	2.57	C	48.06	3.16	3.51	4.08	.86	45	.3942	.3173	+.	8	Q8 Watch
I	51.57	2.57	V	51.71	3.64	-.14	4.45	-.03	63	.9753	.3173	-.	8	Q8 Watch
V	51.71	3.64	C	48.06	3.16	3.65	4.82	.76	56	.4525			8	Q8 Watch
V	51.71	3.64	I	51.57	2.57	.14	4.45	.03	63	.9753	.3173	+.	8	Q8 Watch
C	66.76	6.89	I	64.61	3.87	2.15	7.90	.27	46	.7870			9	Q9 Money
C	66.76	6.89	V	61.98	6.75	4.78	9.65	.50	56	.6220			9	Q9 Money
I	64.61	3.87	C	66.76	6.89	-2.15	7.90	-.27	46	.7870			9	Q9 Money
I	64.61	3.87	V	61.98	6.75	2.63	7.78	.34	64	.7360			9	Q9 Money
V	61.98	6.75	C	66.76	6.89	-4.78	9.65	-.50	56	.6220			9	Q9 Money
V	61.98	6.75	I	64.61	3.87	-2.63	7.78	-.34	64	.7360			9	Q9 Money
C	40.27	2.72	I	47.27	2.30	-7.00	3.57	-1.96	45	.0558			10	Q10 Hobbies
C	40.27	2.72	V	46.94	2.90	-6.68	3.98	-1.68	56	.0993	.4855	-.	10	Q10 Hobbies
I	47.27	2.30	C	40.27	2.72	7.00	3.57	1.96	45	.0558			10	Q10 Hobbies
I	47.27	2.30	V	46.94	2.90	.33	3.71	.09	63	.9295			10	Q10 Hobbies
V	46.94	2.90	C	40.27	2.72	6.68	3.98	1.68	56	.0993	.4855	+.	10	Q10 Hobbies

Person CLASS	DIF MEASURE	DIF S.E.	Person CLASS	DIF MEASURE	DIF S.E.	DIF CONTRAST	JOINT S.E.	t	d.f.	Prob.	MantelHanzl Prob.	Size	Item Number	Name
V	46.94	2.90	I	47.27	2.30	-.33	3.71	-.09	63	.9295			10	Q10 Hobbies
C	25.64	2.54	I	27.61	2.14	-1.97	3.32	-.59	42	.5571	.3173	-.	11	Q11 Handwork
C	25.64	2.54	V	28.61	1.85	-2.97	3.14	-.95	50	.3488	.4609	+.	11	Q11 Handwork
I	27.61	2.14	C	25.64	2.54	1.97	3.32	.59	42	.5571	.3173	+.	11	Q11 Handwork
I	27.61	2.14	V	28.61	1.85	-1.00	2.83	-.36	56	.7237	.5637	+.	11	Q11 Handwork
V	28.61	1.85	C	25.64	2.54	2.97	3.14	.95	50	.3488	.4609	-.	11	Q11 Handwork
V	28.61	1.85	I	27.61	2.14	1.00	2.83	.36	56	.7237	.5637	-.	11	Q11 Handwork
C	46.09	3.13	I	53.46	3.43	-7.37	4.64	-1.59	33	.1219	.3173	-.	12	Q12 Tools
C	46.09	3.13	V	49.37	3.69	-3.28	4.84	-.68	45	.5021	.1824	+.	12	Q12 Tools
I	53.46	3.43	C	46.09	3.13	7.37	4.64	1.59	33	.1219	.3173	+.	12	Q12 Tools
I	53.46	3.43	V	49.37	3.69	4.09	5.04	.81	44	.4207	.3173	-.	12	Q12 Tools
V	49.37	3.69	C	46.09	3.13	3.28	4.84	.68	45	.5021	.1824	-.	12	Q12 Tools
V	49.37	3.69	I	53.46	3.43	-4.09	5.04	-.81	44	.4207	.3173	+.	12	Q12 Tools
C	53.31	3.65	I	52.93	2.59	.38	4.48	.08	45	.9331	.3173	+.	13	Q13 Meals
C	53.31	3.65	V	51.71	3.64	1.60	5.15	.31	56	.7580			13	Q13 Meals
I	52.93	2.59	C	53.31	3.65	-.38	4.48	-.08	45	.9331	.3173	-.	13	Q13 Meals
I	52.93	2.59	V	51.71	3.64	1.22	4.46	.27	63	.7859			13	Q13 Meals
V	51.71	3.64	C	53.31	3.65	-1.60	5.15	-.31	56	.7580			13	Q13 Meals
V	51.71	3.64	I	52.93	2.59	-1.22	4.46	-.27	63	.7859			13	Q13 Meals
C	66.76	6.89	I	67.11	4.30	-.35	8.12	-.04	45	.9657			14	Q14 Utensils
C	66.76	6.89	V	70.10	<12.01	-3.35	13.85	-.24	56	.8099			14	Q14 Utensils
I	67.11	4.30	C	66.76	6.89	.35	8.12	.04	45	.9657			14	Q14 Utensils
I	67.11	4.30	V	70.10	<12.01	-3.00	12.76	-.23	63	.8151			14	Q14 Utensils
V	70.10	<12.01	C	66.76	6.89	3.35	13.85	.24	56	.8099			14	Q14 Utensils
V	70.10	<12.01	I	67.11	4.30	3.00	12.76	.23	63	.8151			14	Q14 Utensils
C	61.50	5.12	I	55.18	2.75	6.31	5.81	1.09	46	.2829	.3173	+.	15	Q15 Appliances
C	61.50	5.12	V	57.03	4.90	4.46	7.09	.63	56	.5313			15	Q15 Appliances
I	55.18	2.75	C	61.50	5.12	-6.31	5.81	-1.09	46	.2829	.3173	-.	15	Q15 Appliances
I	55.18	2.75	V	57.03	4.90	-1.85	5.62	-.33	64	.7435			15	Q15 Appliances
V	57.03	4.90	C	61.50	5.12	-4.46	7.09	-.63	56	.5313			15	Q15 Appliances
V	57.03	4.90	I	55.18	2.75	1.85	5.62	.33	64	.7435			15	Q15 Appliances
C	51.38	3.45	I	53.17	2.56	-1.78	4.30	-.42	47	.6800	.3173	+.	16	Q16 Grooming
C	51.38	3.45	V	53.98	4.10	-2.60	5.36	-.48	56	.6300	.1573	-.	16	Q16 Grooming
I	53.17	2.56	C	51.38	3.45	1.78	4.30	.42	47	.6800	.3173	-.	16	Q16 Grooming
I	53.17	2.56	V	53.98	4.10	-.81	4.84	-.17	65	.8670			16	Q16 Grooming
V	53.98	4.10	C	51.38	3.45	2.60	5.36	.48	56	.6300	.1573	+.	16	Q16 Grooming
V	53.98	4.10	I	53.17	2.56	.81	4.84	.17	65	.8670			16	Q16 Grooming
C	66.76	6.89	I	74.86	5.94	-8.10	9.10	-.89	47	.3780			17	Q17 Dressing
C	66.76	6.89	V	72.89	<14.78	-6.13	16.31	-.38	56	.7083			17	Q17 Dressing
I	74.86	5.94	C	66.76	6.89	8.10	9.10	.89	47	.3780			17	Q17 Dressing
I	74.86	5.94	V	72.89	<14.78	1.97	15.93	.12	65	.9020			17	Q17 Dressing
V	72.89	<14.78	C	66.76	6.89	6.13	16.31	.38	56	.7083			17	Q17 Dressing
V	72.89	<14.78	I	74.86	5.94	-1.97	15.93	-.12	65	.9020			17	Q17 Dressing
C	61.50	5.12	I	58.07	3.15	3.42	6.01	.57	46	.5715			18	Q18 Shelf
C	61.50	5.12	V	53.64	4.12	7.86	6.57	1.20	55	.2371			18	Q18 Shelf
I	58.07	3.15	C	61.50	5.12	-3.42	6.01	-.57	46	.5715			18	Q18 Shelf
I	58.07	3.15	V	53.64	4.12	4.43	5.19	.85	63	.3967			18	Q18 Shelf
V	53.64	4.12	C	61.50	5.12	-7.86	6.57	-1.20	55	.2371			18	Q18 Shelf
V	53.64	4.12	I	58.07	3.15	-4.43	5.19	-.85	63	.3967			18	Q18 Shelf
C	75.02	<12.00	I	62.58	3.55	12.44	12.51	.99	47	.3252			19	Q19 Colours
C	75.02	<12.00	V	51.71	3.64	23.31	12.53	1.86	56	.0682			19	Q19 Colours
I	62.58	3.55	C	75.02	<12.00	-12.44	12.51	-.99	47	.3252			19	Q19 Colours
I	62.58	3.55	V	51.71	3.64	10.87	5.08	2.14	65	.0361			19	Q19 Colours
V	51.71	3.64	C	75.02	<12.00	-23.31	12.53	-1.86	56	.0682			19	Q19 Colours
V	51.71	3.64	I	62.58	3.55	-10.87	5.08	-2.14	65	.0361			19	Q19 Colours
C	66.76	6.89	I	70.41	4.92	-3.65	8.47	-.43	47	.6685			20	Q20 Faces
C	66.76	6.89	V	61.98	6.75	4.78	9.65	.50	56	.6220			20	Q20 Faces
I	70.41	4.92	C	66.76	6.89	3.65	8.47	.43	47	.6685			20	Q20 Faces
I	70.41	4.92	V	61.98	6.75	8.43	8.35	1.01	65	.3164			20	Q20 Faces
V	61.98	6.75	C	66.76	6.89	-4.78	9.65	-.50	56	.6220			20	Q20 Faces
V	61.98	6.75	I	70.41	4.92	-8.43	8.35	-1.01	65	.3164			20	Q20 Faces
C	40.27	2.72	I	45.09	2.11	-4.82	3.44	-1.40	47	.1680	.3173	-.	21	Q21 Poor Light
C	40.27	2.72	V	36.05	1.99	4.22	3.37	1.25	56	.2166	.7009	+.	21	Q21 Poor Light
I	45.09	2.11	C	40.27	2.72	4.82	3.44	1.40	47	.1680	.3173	+.	21	Q21 Poor Light
I	45.09	2.11	V	36.05	1.99	9.04	2.90	3.12	65	.0027	1.000	.000	21	Q21 Poor Light
V	36.05	1.99	C	40.27	2.72	-4.22	3.37	-1.25	56	.2166	.7009	-.	21	Q21 Poor Light
V	36.05	1.99	I	45.09	2.11	-9.04	2.90	-3.12	65	.0027	1.000	.000	21	Q21 Poor Light
C	40.27	2.72	I	41.26	1.99	-.99	3.37	-.29	47	.7698	.3173	-.	22	Q22 Haloes
C	40.27	2.72	V	33.76	1.88	6.50	3.31	1.96	56	.0545	.4855	+.	22	Q22 Haloes
I	41.26	1.99	C	40.27	2.72	.99	3.37	.29	47	.7698	.3173	+.	22	Q22 Haloes
I	41.26	1.99	V	33.76	1.88	7.50	2.74	2.74	65	.0080	.5637	+.	22	Q22 Haloes
V	33.76	1.88	C	40.27	2.72	-6.50	3.31	-1.96	56	.0545	.4855	-.	22	Q22 Haloes
V	33.76	1.88	I	41.26	1.99	-7.50	2.74	-2.74	65	.0080	.5637	-.	22	Q22 Haloes
C	39.15	2.68	I	38.32	1.94	.83	3.31	.25	47	.8031	.3173	-.	23	Q23 Focus
C	39.15	2.68	V	32.19	1.82	6.96	3.24	2.15	56	.0360	.5637	+.	23	Q23 Focus
I	38.32	1.94	C	39.15	2.68	-.83	3.31	-.25	47	.8031	.3173	+.	23	Q23 Focus
I	38.32	1.94	V	32.19	1.82	6.13	2.66	2.31	65	.0243	.1444	+.	23	Q23 Focus
V	32.19	1.82	C	39.15	2.68	-6.96	3.24	-2.15	56	.0360	.5637	-.	23	Q23 Focus
V	32.19	1.82	I	38.32	1.94	-6.13	2.66	-2.31	65	.0243	.1444	-.	23	Q23 Focus
C	32.62	2.99	I	35.77	2.15	-3.15	3.68	-.85	47	.3970			24	Q24 Change
C	32.62	2.99	V	33.98	2.31	-1.36	3.78	-.36	56	.7206	.8638	-.	24	Q24 Change
I	35.77	2.15	C	32.62	2.99	3.15	3.68	.85	47	.3970			24	Q24 Change
I	35.77	2.15	V	33.98	2.31	1.79	3.16	.57	65	.5727	.5637	-.	24	Q24 Change
V	33.98	2.31	C	32.62	2.99	1.36	3.78	.36	56	.7206	.8638	+.	24	Q24 Change
V	33.98	2.31	I	35.77	2.15	-1.79	3.16	-.57	65	.5727	.5637	+.	24	Q24 Change
C	42.87	3.29	I	27.31	2.22	15.56	3.97	3.92	47	.0003	.1797	+.	25	Q25 Use Aids
C	42.87	3.29	V	33.18	2.26	9.69	3.99	2.43	56	.0184	.1985	+.	25	Q25 Use Aids
I	27.31	2.22	C	42.87	3.29	-15.56	3.97	-3.92	47	.0003	.1797	-.	25	Q25 Use Aids
I	27.31	2.22	V	33.18	2.26	-5.87	3.17	-1.86	65	.0680	.0201	-.	25	Q25 Use Aids
V	33.18	2.26	C	42.87	3.29	-9.69	3.99	-2.43	56	.0184	.1985	-.	25	Q25 Use Aids
V	33.18	2.26	I	27.31	2.22	5.87	3.17	1.86	65	.0680	.0201	+.	25	Q25 Use Aids

A6.2 DIF After Overall Group NAVQ Item Reduction

Person CLASS	DIF MEASURE	DIF S.E.	Person CLASS	DIF MEASURE	DIF S.E.	DIF CONTRAST	JOINT S.E.	t	d.f.	Prob.	MantelHanzl Prob.	Size	Item Number	Name
C	45.81	3.46	I	41.82	2.62	3.99	4.34	.92	47	.3628	.5485	+.	1	Q1 Small Print
C	45.81	3.46	V	50.17	2.88	-4.36	4.51	-.97	56	.3378	.7027	-.	1	Q1 Small Print
I	41.82	2.62	C	45.81	3.46	-3.99	4.34	-.92	47	.3628	.5485	-.	1	Q1 Small Print
I	**41.82**	**2.62**	**V**	**50.17**	**2.88**	**-8.35**	**3.89**	**-2.14**	**65**	**.0358**	**.4609**	**-.**	**1**	**Q1 Small Print**
V	50.17	2.88	C	45.81	3.46	4.36	4.51	.97	56	.3378	.7027	+.	1	Q1 Small Print
V	50.17	2.88	I	41.82	2.62	8.35	3.89	2.14	65	.0358	.4609	+.	1	Q1 Small Print
C	59.60	4.11	I	55.79	2.74	3.81	4.94	.77	47	.4438	1.000	-.	2	Q3 Mail
C	59.60	4.11	V	69.24	5.08	-9.64	6.53	-1.48	55	.1457	.7276	-.	2	Q3 Mail
I	55.79	2.74	C	59.60	4.11	-3.81	4.94	-.77	47	.4438	1.000	+.	2	Q3 Mail
I	**55.79**	**2.74**	**V**	**69.24**	**5.08**	**-13.45**	**5.78**	**-2.33**	**64**	**.0230**	**.2743**	**-.**	**2**	**Q3 Mail**
V	69.24	5.08	C	59.60	4.11	9.64	6.53	1.48	55	.1457	.7276	+.	2	Q3 Mail
V	69.24	5.08	I	55.79	2.74	13.45	5.78	2.33	64	.0230	.2743	+.	2	Q3 Mail
C	52.21	3.81	I	58.69	3.57	-6.48	5.22	-1.24	33	.2234	.6682	-.	3	Q6 Computer
C	**52.21**	**3.81**	**V**	**69.28**	**5.99**	**-17.08**	**7.10**	**-2.41**	**36**	**.0214**	**.6880**	**-.**	**3**	**Q6 Computer**
I	58.69	3.57	C	52.21	3.81	6.48	5.22	1.24	33	.2234	.6682	+.	3	Q6 Computer
I	58.69	3.57	V	69.28	5.99	-10.60	6.97	-1.52	35	.1375	.9324	+.	3	Q6 Computer
V	69.28	5.99	C	52.21	3.81	17.08	7.10	2.41	36	.0214	.6880	+.	3	Q6 Computer
V	69.28	5.99	I	58.69	3.57	10.60	6.97	1.52	35	.1375	.9324	-.	3	Q6 Computer
C	54.44	3.80	I	54.96	2.73	-.52	4.68	-.11	47	.9125	.6015	+.	4	Q7 Telephone
C	54.44	3.80	V	62.05	3.85	-7.60	5.41	-1.40	56	.1658	.2482	-.	4	Q7 Telephone
I	54.96	2.73	C	54.44	3.80	.52	4.68	.11	47	.9125	.6015	-.	4	Q7 Telephone
I	54.96	2.73	V	62.05	3.85	-7.08	4.72	-1.50	65	.1382	.2743	-.	4	Q7 Telephone
V	62.05	3.85	C	54.44	3.80	7.60	5.41	1.40	56	.1658	.2482	+.	4	Q7 Telephone
V	62.05	3.85	I	54.96	2.73	7.08	4.72	1.50	65	.1382	.2743	+.	4	Q7 Telephone
C	33.31	3.46	I	36.91	2.91	-3.60	4.52	-.80	42	.4300	.8084	+.	5	Q11 Handwork
C	33.31	3.46	V	38.02	2.59	-4.71	4.32	-1.09	50	.2805	.2952	-3.67	5	Q11 Handwork
I	36.91	2.91	C	33.31	3.46	3.60	4.52	.80	42	.4300	.8084	-.	5	Q11 Handwork
I	36.91	2.91	V	38.02	2.59	-1.11	3.89	-.29	56	.7766	.2324	-.	5	Q11 Handwork
V	38.02	2.59	C	33.31	3.46	4.71	4.32	1.09	50	.2805	.2952	3.67	5	Q11 Handwork
V	38.02	2.59	I	36.91	2.91	1.11	3.89	.29	56	.7766	.2324	+.	5	Q11 Handwork
C	52.88	3.72	I	60.11	2.86	-7.23	4.70	-1.54	47	.1306	.1573	-.	6	Q21 Poor Light
C	52.88	3.72	V	48.40	2.79	4.48	4.65	.96	56	.3390	.6398	6.28	6	Q21 Poor Light
I	60.11	2.86	C	52.88	3.72	7.23	4.70	1.54	47	.1306	.1573	+.	6	Q21 Poor Light
I	**60.11**	**2.86**	**V**	**48.40**	**2.79**	**11.71**	**3.99**	**2.93**	**65**	**.0046**	**.2511**	**+.**	**6**	**Q21 Poor Light**
V	48.40	2.79	C	52.88	3.72	-4.48	4.65	-.96	56	.3390	.6398	-6.28	6	Q21 Poor Light
V	48.40	2.79	I	60.11	2.86	-11.71	3.99	-2.93	65	.0046	.2511	-.	6	Q21 Poor Light
C	52.88	3.72	I	54.96	2.73	-2.08	4.61	-.45	47	.6544	1.000	.000	7	Q22 Haloes Glare
C	52.88	3.72	V	45.16	2.64	7.72	4.56	1.69	56	.0961	.8640	+.	7	Q22 Haloes Glare
I	54.96	2.73	C	52.88	3.72	2.08	4.61	.45	47	.6544	1.000	.000	7	Q22 Haloes Glare
I	**54.96**	**2.73**	**V**	**45.16**	**2.64**	**9.80**	**3.79**	**2.58**	**65**	**.0120**	**.1610**	**+.**	**7**	**Q22 Haloes Glare**
V	45.16	2.64	C	52.88	3.72	-7.72	4.56	-1.69	56	.0961	.8640	-.	7	Q22 Haloes Glare
V	45.16	2.64	I	54.96	2.73	-9.80	3.79	-2.58	65	.0120	.1610	-.	7	Q22 Haloes Glare
C	51.38	3.66	I	50.97	2.66	.41	4.52	.09	47	.9278	.1336	-.	8	Q23 Focus
C	51.38	3.66	V	42.93	2.55	8.45	4.46	1.89	56	.0633	.8340	+.	8	Q23 Focus
I	50.97	2.66	C	51.38	3.66	-.41	4.52	-.09	47	.9278	.1336	+.	8	Q23 Focus
I	**50.97**	**2.66**	**V**	**42.93**	**2.55**	**8.04**	**3.69**	**2.18**	**65**	**.0329**	**.0172**	**+.**	**8**	**Q23 Focus**
V	42.93	2.55	C	51.38	3.66	-8.45	4.46	-1.89	56	.0633	.8340	-.	8	Q23 Focus
V	42.93	2.55	I	50.97	2.66	-8.04	3.69	-2.18	65	.0329	.0172	-.	8	Q23 Focus
C	42.64	4.09	I	47.75	2.88	-5.11	5.00	-1.02	47	.3124	.1573	-.	9	Q24 Change
C	42.64	4.09	V	45.34	3.19	-2.70	5.18	-.52	56	.6048	.7837	-.	9	Q24 Change
I	47.75	2.88	C	42.64	4.09	5.11	5.00	1.02	47	.3124	.1573	+.	9	Q24 Change
I	47.75	2.88	V	45.34	3.19	2.41	4.30	.56	65	.5771	.8282	+.	9	Q24 Change
V	45.34	3.19	C	42.64	4.09	2.70	5.18	.52	56	.6048	.7837	+.	9	Q24 Change
V	45.34	3.19	I	47.75	2.88	-2.41	4.30	-.56	65	.5771	.8282	-.	9	Q24 Change
C	**56.25**	**4.43**	**I**	**36.59**	**3.02**	**19.66**	**5.37**	**3.66**	**47**	**.0006**	**.0477**	**+.**	**10**	**Q25 Use Aids**
C	**56.25**	**4.43**	**V**	**44.24**	**3.12**	**12.01**	**5.42**	**2.22**	**56**	**.0308**	**.0409**	**+.**	**10**	**Q25 Use Aids**
I	36.59	3.02	C	56.25	4.43	-19.66	5.37	-3.66	47	.0006	.0477	-.	10	Q25 Use Aids
I	36.59	3.02	V	44.24	3.12	-7.65	4.34	-1.76	65	.0827	.0453	-.	10	Q25 Use Aids
V	44.24	3.12	C	56.25	4.43	-12.01	5.42	-2.22	56	.0308	.0409	-.	10	Q25 Use Aids
V	44.24	3.12	I	36.59	3.02	7.65	4.34	1.76	65	.0827	.0453	+.	10	Q25 Use Aids

A7. Final Near Activity Visual Questionnaire (NAVQ)

How much difficulty do you have:	Not Applicable *Or* Stopped for Non-visual Reasons	No Difficulty	A Little Difficulty	Moderate Difficulty	Extreme Difficulty *Or* Stopped for Visual Reasons
1. Reading small print, e.g. newspaper articles, books, magazine articles, menu at a restaurant, telephone directories, etc.?	X	0	1	2	3
2. Reading your post / mail, e.g. electric bills, greetings cards, bank statements, letters, etc.?	X	0	1	2	3
3. Seeing the screen & keyboard when using a computer?	X	0	1	2	3
4. Seeing the display & keypad on a mobile or fixed telephone, or calculator?	X	0	1	2	3
5. Doing fine handwork, e.g. threading a needle, sewing, knitting, crochet, etc.?	X	0	1	2	3
6. Seeing objects near to you in poor or dim light?	X	0	1	2	3
7. Seeing objects near to you if there is glare or haloes from lights and shiny surfaces?	X	0	1	2	3
8. Maintaining focus for prolonged near work?	X	0	1	2	3
9. How quickly does your focus change from distance vision to near vision?	Instantly *Or* Very Quickly (0)		Moderately (1)	Very Slowly *Or* Never Changes (2)	
10. How often do you have to rely on reading or magnifying aids to do near tasks?	Never *or* Rarely (0)		Occasionally (1)	Most of the Time *or* Always (2)	

FINALLY	Completely Satisfied	Very Satisfied	Very to Moderately Satisfied	Moderately to A Little Satisfied	A Little Satisfied	Completely Unsatisfied
Overall how satisfied are you with the near visual ability that you have?	0	1	2	3	4	5

A8. List of Publications

Is randomisation necessary for measuring defocus curves in pre-presbyopes?
Contact Lens and Anterior Eye 30;2:119-124 (May 2007)
Navneet Gupta, Shehzad A. Naroo & James S. Wolffsohn.

Development of a near activity visual questionnaire to assess accommodating intraocular lenses
Contact Lens and Anterior Eye 30;2:134-143 (May 2007)
Navneet Gupta, James S. Wolffsohn, Shehzad A. Naroo, Leon N. Davies, George A. Gibson & Sunil Shah.

Optimising measurement of subjective amplitude of accommodation using defocus curves
Journal of Cataract and Refractive Surgery 34;8:1329-1338 (August 2008)
Navneet Gupta, James S. Wolffsohn & Shehzad A. Naroo

Comparison of Visual Function with a Multifocal Contact Lens to Monovision with Contact Lenses
Optometry & Vision Science (in press), due to be published in 2009
Navneet Gupta, James S. Wolffsohn & Shehzad A. Naroo

Comparison of Near Visual Acuity and Reading Metrics in Presbyopia Correction
Journal of Cataract and Refractive Surgery (in press), due to be published in 2009
Navneet Gupta, James S. Wolffsohn & Shehzad A. Naroo

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