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OPTICAL, NEURAL AND PERCEPTUAL BASIS OF BLUR SENSITIVITY AND THE EFFECT OF TEXT DETAIL IN MYOPES AND EMMETROPES

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A thesis in partial fulfilment of the requirements of Anglia Ruskin University for the degree of Doctor of Philosophy

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ABSTRACT

FACULTY OF SCIENCE AND TECHNOLOGY

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Optical, neural and perceptual basis of blur sensitivity and the effect of text detail in myopes and emmetropes

By Heather Shorrock

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Retinal blur experienced by myopes during near work has been linked to myopia development and progression. Whether poor responses to blur signals are due to poor perceptual blur sensitivity (subjective depth of focus), poor neural accommodation responses (objective depth of focus) to blur or optical differences such as higher order aberrations making blur detection difficult is yet unclear. This study investigates whether myopes respond to blur differently compared to emmetropes and whether filtering spatial frequencies in reading text influence accommodation responses.

Accommodative functions were investigated using spatial frequency filtered text targets of two different sizes (N10 and N20). Monocular objective depth of focus (DOF), accommodative microfluctuations, and dynamic accommodation were measured. Subjective DOF after cycloplegia was also recorded with the same targets. Higher order aberration measurements explored optical contributions to blur. Peripheral refraction and accommodative lag were also measured to consider how in combination they might increase peripheral retinal blur for near tasks.

Results showed that myopes demonstrated larger subjective DOF. Subjective DOF was larger when viewing the peak text spatial frequency in both refractive error groups. The optimum focus was more myopic for text peak spatial frequencies. Levels of spherical aberration were correlated with the point of optimum focus. Objective DOF and accommodative microfluctuations were larger in myopes when viewing the peak text spatial frequencies. Dynamic accommodation showed that while myopes were not poorer at initiating accommodation responses they had longer positive response times. Accommodative lag, although not different in myopes, increases the peripheral hyperopic blur experienced for near tasks.

Conclusion: Myopes were poorer at using retinal blur cues to refine accommodation responses especially when viewing peak text spatial frequencies. Larger positive response times, DOF and accommodative microfluctuations in myopes resulted in accommodative error and hyperopic blur for near tasks. Spherical aberration, previously thought to provide a myopigenic stimulus, was not different between refractive groups and is unlikely to be large enough to enhance DOF during naturalistic viewing.

Blur adaptation studies might consider using peak text spatial frequencies as adaptation targets to reduce accommodation differences in myopes and emmetropes.

Optical treatment strategies aimed at correcting peripheral refraction to control myopia should consider the combined effect of accommodative lag which increases levels of hyperopic peripheral blur experienced by myopes.

Keywords: Myopia, blur sensitivity, spatial frequency, accommodation

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accommodative sensory gain (ASG). The threshold for oculomotor control is represented by deadspace (DSP) or the DOF. The resulting signal goes into the accommodative controller, a linear operator with gain, the accommodative controller gain (ACG). Output from here is summed with vergence accommodation (CA) (not applicable in the current study) and tonic accommodation (ABIAS) to drive the accommodative plant which results in the accommodation response

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Notations

ACD Anterior chamber depth

AL Axial length

ANS Autonomic nervous system

BVD Back vertex distance

CLEERE Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study

COMET Correction of Myopia Evaluation Trial

CSF Contrast sensitivity function

DOF Depth of focus

D Dioptres

DPI Dots per inch

HFC High frequency component

IOL Intraocular lens

LFC Low frequency component

LORIC Longitudinal Orthokeratology research in Children study

MFC Medium frequency component

PAL Progressive addition lens

RMS Root mean squared

RT Response time

Chapter 1: Introduction

1.1 Background to myopia

Myopia affects around 1.6 billion people worldwide (Holden, 2004) and its prevalence is increasing (Morgan and Rose, 2005; Bloom, Friedman and Chuck, 2010; Pan, Ramamurthy and Saw, 2012). A literature review by Parssinen (2011) suggested an increase in myopia prevalence in Finland, from <10% to 21-30% from the beginning to the end of the 20th century. Vitale, Sperduto and Ferris (2009) reported increasing myopia prevalence in the USA in 12-54 year olds from 25% (1971-1972) to 42% (1999-2004). Lin *et al.* (2001) using nationwide surveys showed that between 1983 and 2000 myopia increased from 5.8% to 21% in 7 year olds, from 36.7% to 61% in 12 year olds, from 64.2% to 81% in 15-year-olds, and from 74% to 84% in 16 to 18 year olds. Similar findings have been made in Hong Kong where Wu and Edwards (1999) found the odds of having myopia in three generations increased for the younger generations (grandparents', parents', and children's generation odds were 0.06, 0.26, and 0.35, respectively) suggesting an increasing prevalence. Matsumura and Hirai (1999) found an increase from 50 to 66% myopia in 17 year olds over a 13 year period in Japan.

The increasing myopia prevalence has cost implications in terms of spectacles and also health implications, increasing the risk for certain pathological conditions, such as myopic degeneration, retinal detachment and glaucoma. In some rural communities of developing countries such as China, Nepal, India and South Africa, access to eye care is limited (Naidoo *et al.*, 2010; He *et al.*, 2012; Naidoo and Jaggernath, 2012). In addition certain occupations require good unaided visual acuity including the military, aviation industry, fire officers and LGV drivers (Royal College of Ophthalmologists, Ophthalmic service guidelines) which restricts myopes in their chosen profession. Pathological myopia has also been shown to reduce quality of life due to disability in Japan caused by ocular disease (Takashima *et al.*, 2001).

1.2 Myopia development and progression

1.2.1 Links to near work

Myopia has a genetic predisposition (Ashton, 1985; Goss, Hampton and Wickham, 1988; Mutti and Zadnik, 1995; Pacella *et al.*, 1999; Wu and Edwards, 1999; Guggenheim, Kirov and Hodson, 2000; Saw *et al.*, 2001; Mutti *et al.*, 2002; Czepita *et al.*, 2011). It has been shown that even where a genetic predisposition to myopia exists that environmental triggers may also contribute to myopia development and progression (Saw *et al.*, 2000; Gwiazda *et al.*, 2004). Lower prevalence of myopia have been found in communities who live outdoor (such as Canadian Arctic Inuit populations) and who have not had access to formal education (Johnson, 1988). Outdoor activity may provide a protective effect against myopia development (Rose *et al.*, 2008; Dirani *et al.*, 2009; Jones-Jordan *et al.*, 2011; Yi and Li, 2011). Studies have shown strong correlations between myopia prevalence and higher education levels (Goldschmidt, 1968; Wong *et al.*, 1993) and also higher levels of IQ (Grosvenor, 1970; Young *et al.*, 1970; Ashton, 1985; Mutti *et al.*, 2002). Increased levels of near work and accommodative lag have been linked with myopia development (Gwiazda *et al.*, 2004). Angle and Wissmann (1980) considered data from the US National Health Examination Survey of 12-17 year olds and found a link between near work and myopia. They suggested that a portion of myopia may be preventable by avoiding near work. Kinge *et al.* (2000) explored myopia progression in 200 engineering students from Norway and reported a significant relationship with time spent on near work. Although little can be done to affect the genetic component the increasing requirement to limit myopia progression needs to concentrate on the environmental component. Therefore environmental causes of myopia need to be identified in order that treatment strategies can be designed to control it.

1.2.2 Form deprivation myopia

It is well recognised that myopia is due to axial elongation which can be seen in MRI studies (Atchison *et al.*, 2004). Form deprivation has been shown to cause ocular elongation (and hence myopia) in animal studies. Wallman *et al.* (1987) demonstrated visually guided ocular growth in chicks, where myopia developed in the area of retina affected by hemiretinal translucent occluders. Smith *et al.* (1999) showed that in all four adolescent monkeys, where form deprivation, induced by fusing the eyelids of one eye, myopia resulted. Troilo, Nickla and Wildsoet (2000) demonstrated a similar effect in adult marmosets suggesting that as ocular elongation occurred after the early developmental emmetropisation, it might support the theory that visual factors may influence myopia development in adult humans as evidenced in late onset myopia.

1.2.3 Lens induced ocular growth

Animal studies have shown ocular growth to be guided by visual feedback (in chicks, Schaeffel, Glasser and Howland, 1988; Irving, Callender and Sivak, 1991; Irving, Sivak and Callender, 1992; Zhu *et al.*, 2005; in rhesus monkeys, Hung, Crawford and Smith, 1995; Smith and Hung, 1999; in marmosets, Whatham and Judge, 2001; Troilo, Totonelly and Harb, 2009; and guinea pigs, McFadden, Howlett and Mertz, 2004; see Wallman and Winawer, 2004 for review). These studies have shown that minus lenses which induce hyperopic retinal defocus, where the image is formed behind the retina, provide a stimulus to ocular elongation and myopia. Plus lenses which induce myopic retinal defocus, where the image is formed in front of the retina, may provide a 'stop' signal and prevent further ocular elongation. Schaeffel, Glasser and Howland (1988) showed evidence of this when they looked at the development of chickens' eyes following treatment with lens induced defocus. They examined the eyes using infrared retinoscopy which consistently showed altered refractions in a direction to compensate for the treatment lens. Smith and Hung (1999) examined infant rhesus monkeys and found that lens induced defocus resulted in compensatory refractive change similar to the change found in chickens. This shows evidence of an adaptive visually guided feedback process responding to defocus, allowing the eye to elongate to eliminate hyperopic defocus.

The manipulation of ocular development in humans is limited ethically. However the findings from animal studies support many theories that human myopia is partly influenced by environmental factors (Goldschmidt, 1968; Gwiazda *et al.*, 2004; Morgan and Rose, 2005) and supports the theory that human emmetropisation is also driven by visually guided feedback (Wallman and Winawer, 2004).

1.2.4 Sources of defocus in humans

The animal studies reviewed in section 1.2.3 have led to theories that hyperopic defocus may provide a stimulus to axial elongation and myopic defocus may provide a ‘stop signal’ and slow down myopia progression. Inaccurate accommodation, resulting in hyperopic retinal defocus, has been suggested as a stimulus for myopia development in humans (Gwiazda *et al.*, 1993; Gwiazda *et al.*, 1995; Jiang, 1997; Abbott, Schmid and Strang, 1998; Gwiazda *et al.*, 2004; Allen and O'Leary, 2006; Langaas *et al.*, 2008; Strang *et al.*, 2011). The cause of inaccurate accommodation may be due to a poor neural response to blur stimuli (Gwiazda *et al.*, 1993) or a structural deficiency (Mutti, 2010). It has been found that myopes have a thickened ciliary body (Bailey, Sinnott and Mutti, 2008). Mutti (2010) hypothesised that this may be linked with poor accommodation and myopia development.

1.3 Accommodation

1.3.1 The accommodation process

The accommodation response is controlled by the autonomic nervous system (ANS) where the sympathetic nervous system is responsible for near to far (negative) accommodation and parasympathetic responsible for far to near (positive) accommodation (McBrien and Millodot, 1986). The sympathetic signal is carried by the nasociliary nerve (a branch of the ophthalmic nerve) and passes through the ciliary ganglion, causing an increase in ciliary body size. This, in turn, tightens the zonule fibres and results in a decrease in lens power. In positive accommodation a blur signal is transmitted through the magnocellular layer of the Lateral Geniculate Nucleus (LGN) to the visual cortex. The cortical cells pass the blur signal on to the midbrain, oculomotor nucleus and Edinger Westphal nucleus where the motor command is initiated. Parasympathetic signals are carried by the ciliary muscle via the oculomotor nerve, ciliary ganglion and short ciliary nerves and produces the appropriate change in contraction. This causes a passive biomechanical relaxation of the anterior zonules and increases the lens power, increasing accommodation and reducing retinal defocus.

1.3.2 Accommodation components

A model of static accommodation by Hung and Semmlow (1980) later modified by Jiang (1997) described the initiation of the accommodation response (Figure 8.2). Defocus blur is regarded as the primary stimulus for accommodation (Fincham, 1951; Campbell and Westheimer, 1960; Phillips and Stark, 1977; Tucker and Charman, 1979; Kruger and Pola, 1986; Morgan, 1986; Kruger and Pola, 1987; Ciuffreda, 1991) and serves to maintain a clear retinal image. The second major influence on accommodation is retinal disparity where vergence accommodation is initiated (Fincham and Walton, 1957). Proximal accommodation is initiated by perceptual cues relating to the proximity of the object of regard (Rosenfield and Ciuffreda, 1991). In the absence of directional information (perception of nearness of the target), when only information from the blur pattern is available, the accommodation system responds, but may not respond in the correct direction (Troelstra *et al.*, 1964). It is an ‘even – error control system’ which can detect the magnitude of the blur signal but not the direction. Tonic accommodation reflects the baseline neural innervations and is always found even in the absence of blur, disparity and proximal cues.

The accommodation response system is dependent on the detection of retinal blur. Myopes may respond less well to blur either due to poorer blur perception or poorer neural accommodation responses to retinal blur. These can be investigated separately by considering blur perception without accommodation (using cycloplegia) and investigating the neural accommodation responses in order that accommodation can take place before blur is perceived.

Neural response to blur

Studies have suggested that an inability to accommodate correctly may be linked with myopia development (section 1.2.4). Other studies maintain that poor accommodation is not responsible for myopia development (Mutti *et al.*, 2006; Berntsen *et al.*, 2011a) and hypothesise instead that it may be due to structural deficiency. Gwiazda *et al.* (1993) reported that the accommodative responses in myopic children were reduced when viewing through negative lenses compared with emmetropes when presented with static blur stimuli. Later Gwiazda *et al.* (1995) found a positive correlation between the change in accommodative response and in refractive error over a 6-12 month period in myopes but not emmetropes suggesting a link between poor accommodation and myopia development.

Perception of blur

Inaccurate accommodation may be due to an inability to detect blur and studies have investigated the possibility that myopes are poorer at detecting and discriminating blur. Rosenfield and Abraham-Cohen (1999) found myopes had poorer blur sensitivity compared with emmetropes. However, Schmid *et al.* (2002) found no correlation between blur detection or discrimination and refractive error although there was greater individual variation in myopic children.

It may be that accommodative responses are less accurate in myopes due to an inability to detect retinal blur. The nature of the target may also affect the way in which the accommodation response system detects blur. Text detail, size and spatial frequency information may influence the detection systems of myopes and emmetropes differently.

1.3.3 Accommodative lag

If the accommodation response (measured using an autorefractor) is less than that required by the accommodative stimulus (dependent on target vergence), retinal hyperopic defocus results. This is known as accommodative lag (Figure 1.1). This may occur if the target image lies within the subjects' depth of focus (DOF). No further accommodative response would occur until the target moves outside the DOF. The effect of induced hyperopic defocus on eye elongation has been shown in animal models (section 1.2.3).

Figure 1.1

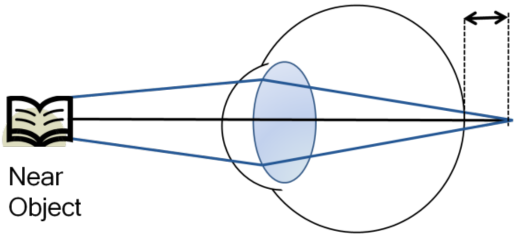

Figure 1.1 Black arrow shows accommodative lag where a subject's eye accommodates less than required by the accommodative stimulus and the target image is formed behind the retina (hyperopic defocus)

Various studies have investigated accommodative lag and its potential to provide a stimulus for ocular growth in humans but competing theories are still disputed (Goss, 1991; Gwiazda *et al.*, 1993; Gwiazda *et al.*, 1995; Drobe and de Saint-Andre, 1995; Abbott, Schmid and Strang, 1998; Schor, 1999; Vera-Diaz, Strang and Winn, 2002; Nakatsuka *et al.*, 2005; Allen and O'Leary, 2006; Langaas *et al.*, 2008; Weizhong *et al.*, 2008). Abbott, Schmid and Strang (1998) found progressing myopes had poorer accommodation responses to negative lens induced defocus compared to stable myopes. A large study conducted by Mutti *et al.* (2006) suggested that accommodative lag was a consequence rather than cause of myopia development.

Although evidence of accommodative lag differences in myopes and emmetropes has been equivocal, more consistent findings of larger levels of accommodative variability in myopes have been reported (Seidel, Gray and Heron, 2005; Day *et al.*, 2006; Radhakrishnan, Allen and Charman, 2007; Langaas *et al.*, 2008). Seidel, Gray and Heron

(2003) and Seidel, Gray and Heron (2005) found no difference in accommodative lag between myopes and emmetropes but suggested that larger accommodative microfluctuations in myopes might suggest larger accommodative variability. Radhakrishnan, Allen and Charman (2007) also found no difference in accommodative lag in refractive error groups but found myopes to have a slower velocity of accommodation. Langaas *et al.* (2008) conducted a study on children (under the age of 15 years) and found no difference in accommodative lag between refractive error groups and also suggested that myopes had more variable accommodation. If accommodative lag is not the source of hyperopic blur it may be accommodative variability that provides a contributing factor towards the development of myopia. This shows that it is not only accommodative lag which needs to be considered but other sources of inaccuracies, such as variability in the accommodative response.

1.3.4 Dynamic accommodation

Other sources of accommodative variability, besides static measurements, need to be considered between myopes and emmetropes to discover the causes of hyperopic defocus. Dynamic accommodation measurements are related to the time taken to initiate accommodation (accommodative latency) and to complete the response (response time). If a large change in target vergence occurs (step change), it follows that there is a delay, a period of reaction time or accommodative latency, before an accommodative response is initiated. Further time will elapse before the accommodation reaches a stable level and the accommodative response is complete.

Campbell and Westheimer (1960) investigated the monocular dynamic accommodation components and found accommodation latency was an average of 0.37s±0.08. They found maximum velocities were about $10Ds^{-1}$ and that when tracking the focus of a target the accommodation system managed this in a serious of step changes rather than a smooth gradual change. They also reported that the time taken to reach a steady accommodation level, following a change in stimulus, was about 1s. Heron and Winn

(1989) found similar latencies to Campbell and Westheimer (1960) and reported the monocular negative response times (1.03s±0.22) to be significantly longer than positive response times (0.82s±0.12). However, Kasthurirangan, Vilupuru and Glasser (2003) found that negative accommodation occurs progressively faster than positive accommodation and this difference is greater with increasing accommodative amplitude. These differences highlight the importance of experimental design.

Dynamic aspects of accommodation in this study are measured by recording the refraction dynamically (using the PRII Power Refractor) whilst altering a subjects' attention between a far and near target. Positive and negative accommodative latencies and response times (RT) were calculated using the start and end of the accommodation response as determined by a predetermined protocol (section 2.6.4). In a study by Seidel, Gray and Heron (2003) blur cues only, resulted in longer accommodative latencies in myopes compared to emmetropes. Studies allowing retinal blur and proximal cues have found significantly longer RTs but no difference in accommodative latencies in myopes compared to emmetropes (Culhane and Winn, 1999; Seidel, Gray and Heron, 2005). This showed that in natural open view conditions where proximal cues were available, myopes were not slower to initiate an accommodative response but were poorer at responding to small errors in retinal blur which may be a consequence of a larger DOF and poorer blur sensitivity.

Dynamic accommodation methods used in the current study provided large proximal cues as the subject altered their attention between a far and near target and the change in target vergence was large. The objective DOF methods provided more subtle proximal cues as only a gradual movement of the target forwards or backwards occurred. This allowed comparisons between refractive error groups in their use of proximal and retinal blur cues to stimulate accommodation.

1.3.5 Accommodative microfluctuations

Accommodative microfluctuations have been reported as another source of accommodative inaccuracy. Microfluctuations have been found to be larger in myopes compared with emmetropes (Seidel, Gray and Heron, 2003; Day *et al.*, 2006; Harb, Thorn and Troilo, 2006; Langaas *et al.*, 2008) supporting evidence from Vasudevan, Ciuffreda and Wang (2006a) that myopes have larger objective DOF. This supports the theory that myopes may be poorer at correcting small errors in hyperopic retinal blur when compared to emmetropes.

Accommodation fluctuations are known to occur when observing stationary stimuli and increase as target vergence increases (Strang *et al.*, 2004). The current understanding is that accommodative microfluctuations provide feedback to ensure that accommodation response is sufficient for the accommodative stimulus (Kotulak and Schor, 1986b; Winn *et al.*, 1990a; Gray, Winn and Gilmartin, 1993b) and also to provide directional cues for dynamic accommodation responses to changes in target vergence (Campbell, Robson and Westheimer, 1959; Kotulak and Schor, 1986b; Charman and Heron, 1988; Gray, Winn and Gilmartin, 1993b). Many factors influence the magnitude of microfluctuations including size (Campbell, Robson and Westheimer, 1959; Campbell and Westheimer, 1960; Gray, Winn and Gilmartin, 1993a; Stark and Atchison, 1997; Charman and Radhakrishnan, 2009), target luminance (Alpern, 1958a; Schor, Johnson and Post, 1984; Gray, Winn and Gilmartin, 1993b), spatial frequency content of the stimulus (Bour, 1981; Niwa and Tokoro, 1998; Day *et al.*, 2009a), and also the stimulus vergence demand (Krueger, 1978; Usui and Stark, 1978; Denieul, 1982; Kotulak and Schor, 1986b; Heron and Schor, 1995; Stark and Atchison, 1997; Day *et al.*, 2006). Day *et al.* (2009b) found that the root mean square (RMS) of microfluctuations was constant as target luminance was decreased with neutral density filters but significantly reduced with a low target luminance of 0.002cd/m^2 and when artificial pupil size was less than 2mm.

Studies conducting power spectrum analysis of accommodative microfluctuation waveforms agree on two frequency bands, a low frequency component <0.6Hz and a high frequency component 1-2.1Hz (Denieul, 1982; Kotulak and Schor, 1986a;b; Charman and Heron, 1988; Winn *et al.*, 1990a; Gray, Winn and Gilmartin, 1993a; b; Heron and Schor, 1995; Gray, Gilmartin and Winn, 2000). The low frequency component is thought to be responsible for guiding the accommodation response (Hung and Semmlow, 1982; Charman and Heron, 1988; Winn *et al.*, 1989; Winn and Gilmartin, 1992; Gray, Winn and Gilmartin, 1993a; b). It has been reported that the high frequency components are due to the structural properties of the lens, zonules and ciliary body (Charman and Heron, 1988).

Day *et al.* (2009a) found that microfluctuations were smallest for mid-spatial frequency sine-wave targets (2 and 4 $cdeg^{-1}$) and increase for low (0.5 $cdeg^{-1}$) and high (16 $cdeg^{-1}$) spatial frequencies. They also found myopes to have larger microfluctuations for all spatial frequency sine waves especially the high spatial frequency target. However, to date no study had investigated the effect of the spatial frequencies contained within text on microfluctuations in refractive error groups.

1.3.6 Accommodation in myopes and emmetropes

Hyperopic blur is thought to drive myopia progression. If the source of hyperopic blur is increased accommodative variability, rather than accommodative lag, then treatment strategies need to concentrate on improving and stabilising accommodative responses particularly to near targets. Poor accommodation responses may be due to mechanical restriction in myopes which would be difficult to remedy. However, if the poor accommodation responses are due to poor blur perception or neural accommodation responses to blur stimuli then potential improvements could be achieved. As there is known link between myopia development and near work (Zadnik, 1997 for review; Angle and Wissmann, 1980; Kinge *et al.*, 2000) particularly for reading (Saw *et al.*, 2002; Ip *et al.*, 2008), then it may be a feature of text detail which accounts for poor blur perception and inaccurate neural accommodation responses in myopes. This study aimed to investigate what features of text contribute to poorer blur sensitivity and accommodation responses so that treatment strategies such as blur training and accommodative facility training might be designed using appropriate targets.

1.4 Peripheral refraction and ocular shape

Animal studies have long suggested that hyperopic retinal blur stimulates ocular growth and myopia development (Wallman and Winawer, 2004 for review). Many studies on myopia have concentrated on the effects of lens induced defocus at the central retina, however peripheral hyperopic retinal defocus has also recently been shown to have the potential to influence ocular growth (Smith *et al.*, 2010). Photoreceptor density is far higher in the central retina decreasing out towards the periphery and it has therefore been the assumption that the central retina would provide the majority of the influence in refractive development. However, the area of the central retina is relatively small and therefore cumulatively the peripheral retina may contribute more towards refractive development (Wallman and Winawer, 2004).

An early study by Hoogerheide, Rempt and Hoogenboom (1971) investigated peripheral refraction in pilots and suggested that emmetropes with relative hyperopic peripheral refractions were more likely to develop myopia during their training. As accommodative lag has not been found conclusively as a precursor to myopia development, recently more emphasis has been put on considering the influence of peripheral retina when investigating hyperopic retinal blur as an influence to myopia development (Mutti *et al.*, 2000; Logan *et al.*, 2004; Stone and Flitcroft, 2004; Atchison, Pritchard and Schmid, 2006; Lundstrom, Mira-Agudelo and Artal, 2009; Charman and Radhakrishnan, 2010; Kang *et al.*, 2010; Lin *et al.*, 2010; Chan, 2011; Ehsaei *et al.*, 2011; Mutti *et al.*, 2011; Sankaridurg *et al.*, 2011; Schmid, 2011; Smith, 2011; Sng *et al.*, 2011b; Backhouse *et al.*, 2012).

1.4.1 Animal models of peripheral refraction

Miles and Wallman (1990) demonstrated locally driven ocular growth and considered the peripheral influence in chicks reared in a low ceiling environment. The chicks developed greater superior visual field myopia than chicks raised in a high ceiling environment. Gottlieb, Fugate-Wentzek and Wallman (1987) and Wallman *et al.* (1987) demonstrated locally driven ocular growth in chicks by inducing hemiretinal form deprivation which resulted in asymmetric retinal profiles and myopia evident only in the deprived area of retina. Smith *et al.* (2005), investigated peripheral retinal form deprivation in infant monkeys and showed that the peripheral retina was influential in emmetropisation. Diffusing filters obstructed the peripheral vision whilst allowing unobstructed central vision. The monkey's recoveries were studied following filter removal. Treated monkeys showed more myopia/ less hyperopia compared with untreated monkeys, and even after monocular foveal ablation these monkeys still underwent recovery towards emmetropisation. Restricted central vision did not prevent emmetropisation in infant monkeys, indicating the peripheral retina also played a part in emmetropisation. Smith *et al.* (2009) also showed that ocular growth could be locally controlled. They induced hemiretinal form deprivation on monkeys and found that myopic changes were limited to the treated retina. Smith *et al.* (2010) conducted a similar experiment with full field and hemiretinal lens induced defocus and found monkeys which underwent full field hyperopic defocus developed myopia. Those which had hemiretinal hyperopic lens induced defocus had their myopic shift mainly limited to the treated retina. Based on their earlier findings suggesting that peripheral retinal blur can influence emmetropisation, Smith (2011) also made a case for considering the peripheral retina in future myopia treatment strategies in humans.

1.4.2 Peripheral ocular shape

Studies measuring human ocular shapes have found myopes to have a more prolate shape (Figure 1.2) and have achieved this measuring eye length (Schmid, 2003), using A-scan ultrasonography (Logan *et al.*, 2004) and MRI techniques (Chen, 1992; Cheng *et al.*, 1992; Atchison *et al.*, 2004; Atchison *et al.*, 2005). Correspondingly, hyperopes have a more oblate shape and a relatively myopic periphery.

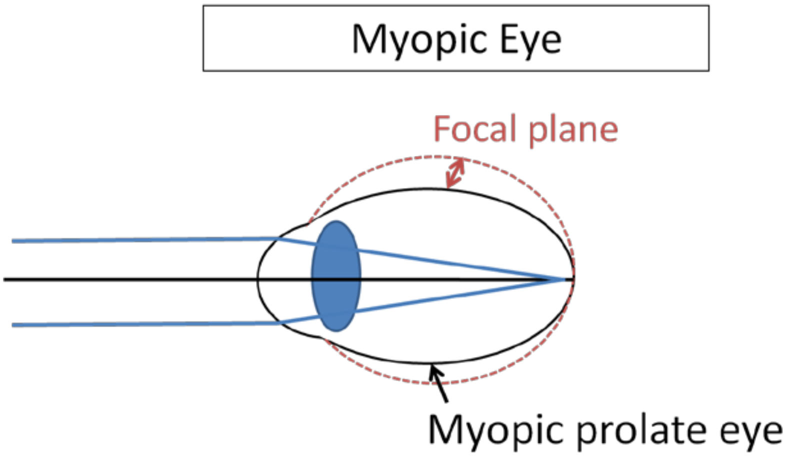

Figure 1.2 The profile of a typical oblate myopic eye. The peripheral refraction is shown to be hyperopic and the focal plane lies behind the retina hypothesised to provide a stimulus to ocular growth and myopia development

1.4.3 Peripheral refraction

The ocular shape has been inferred from many peripheral refraction studies although measurements of peripheral refraction also include the influence of anterior optics (Mutti *et al.*, 2000; Kang *et al.*, 2010; Ehsaei *et al.*, 2011). Myopic eyes show less myopic or more hyperopic peripheries whilst emmetropes show a more myopic periphery (Mutti *et al.*, 2000; Seidemann *et al.*, 2002; Atchison, Pritchard and Schmid, 2006; Charman *et al.*, 2006; Calver *et al.*, 2007; Mutti *et al.*, 2007; Davies and Mallen, 2009; Lundstrom, Mira-Agudelo and Artal, 2009; Kang *et al.*, 2010; Lin *et al.*, 2010; Ehsaei *et al.*, 2011; Mutti *et al.*, 2011; Sng *et al.*, 2011a; Faria-Ribeiro *et al.,* 2013). Mutti *et al.* (2000) showed this in a large study of 822 children. This was supported by Atchison, Pritchard and Schmid (2006) who also considered the vertical peripheral refraction, finding refractive error to have less of an influence on vertical compared to horizontal peripheral refraction. The degree of astigmatism is known to increase in the periphery in myopes and emmetropes and peripheral astigmatism is shown to be higher in the temporal compared with nasal retina beyond 30 degrees (Millodot, 1981). The asymmetry in the temporal and nasal fields was considered in early studies although the peripheral refractions and application to potential myopia development was not yet realised (Ferree, 1932).

1.4.4 Peripheral refraction, acuity and blur thresholds

The fovea forms a small part of the overall visual field. Although visual acuity decreases with retinal eccentricity (Jennings and Charman, 1981), the consideration that the peripheral retina also influences ocular growth has become increasingly more popular. Animal studies have shown that the peripheral retina has the potential to influence ocular growth (section 1.4.1). However, as peripheral defocus is not noticed clinically, it is questionable how much influence this can have on central ocular growth. Studies have suggested that levels of defocus in the periphery have little impact on the peripheral resolution (Millodot *et al.*, 1975; Anderson, 1996; Wang, Thibos and Bradley, 1997; Lundstrom, Gustafsson and Unsbo, 2007; Lundstrom *et al.*, 2007) suggesting that the peripheral retina would not be able to offer a contribution to eye growth and emmetropisation. However, Rosen, Lundstrom and Unsbo (2011) investigated spatial frequency thresholds for detection and resolution tasks with high and low contrast grating targets with up to +/-4D of optical defocus at 20° in the nasal visual field. They reported that optical defocus as small as 1D had a large impact on most peripheral visual tasks especially with low contrast resolution. As real life viewing does not consist of high contrast peripheral stimuli only, then it is possible that low contrast peripheral tasks can be affected by small errors in defocus. However, what contribution low contrast tasks make to myopisation when most of the near vision tasks, such as reading, with which it has been attributed to, are not known.

Few studies have investigated the DOF in the periphery in humans. Ronchi and Molesini (1975) found that DOF increased by several dioptres with retinal eccentricity out to 60° although experimentally examined blur detection rather than perception. Wang and Ciuffreda (2004) reported that DOF in the near retinal periphery increased from around 0.9D centrally to 3.5D at 8 degrees eccentrically. Blur discrimination and blur detection decrease in the periphery although blur discrimination remains more sensitive than blur detection (Wang and Kenneth, 2006). It has been shown that centrally blur discrimination is poorer in myopes (Rosenfield and Abraham-Cohen, 1999) so it is possible that blur discrimination peripherally as well as centrally contributes towards myopia development. On the other hand, other studies have reported that peripheral detection of movement, direction and flicker can be sensitive to defocus of as little as 0.50D, at eccentricities of 20-30° (Ronchi, 1971; Artal, Derrington and Colombo, 1995; Wang, Thibos and Bradley, 1997; Anderson, McDowell and Ennis, 2001). Gu and Legge (1987) also suggested that accommodation could be induced by stimuli lying several degrees outside the fovea (up to 30°). These studies suggest that in naturalistic viewing conditions peripheral focus information may be drawn from a variety of sources. The possibility that the peripheral retina can influence eye growth is dependent on peripheral defocus being detectable, even if not perceptually. Although peripheral defocus is rarely noticed clinically, it can still influence peripheral visual tasks especially at low contrast and affect movement, direction and flicker detection. The importance of peripheral vision is also supported by studies finding that patients with central vision loss can still notice benefits of peripheral refractive correction (Lundstrom, Gustafsson and Unsbo, 2007). This combined with the small but significant treatment effects of reducing peripheral hyperopic defocus (section 1.8.5) to slow myopia progression suggest that for future myopia treatments the influence of peripheral retinal blur cannot be ignored.

1.4.5 Peripheral refraction as a stimulus to myopia development

Whether the peripheral refraction is a precursor to the development of myopia or is a consequence of myopia development was investigated by Mutti *et al.* (2007). This study was part of the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study (CLEERE) and examined children aged 6-14 participating between 1995 and 2003. Of these children 605 became myopic and 374 emmetropic. They measured axial length (AL) using A-scan ultrasonography and relative peripheral refractive error (at 30 degrees in the temporal retina compared to primary gaze) using an autorefractor. Children were examined 5 years prior to and 5 years post myopia onset. They found children who became myopic had a more hyperopic peripheral refractive error but only from 2 years prior to onset. It was also shown that these children started with lower hyperopia and longer AL for their age. They suggested that these variables may provide useful predictors for the onset of myopia but only for 2-4 years prior to onset. However, a follow up of their study (Mutti *et al.*, 2011) found that although relative peripheral hyperopia was related to myopia progression the amounts were small and they concluded that peripheral refraction may not provide the influence on axial elongation previously thought. Sng *et al.* (2011b) measured relative peripheral refraction in 187 Chinese children (mean age 7.2 +/- 3.0 years) at two appointments (average of 1.26 years apart) and found that initial relative peripheral refraction could not be used to predict myopia development.

1.4.6 The effect of near viewing on peripheral refraction

It has been well documented that prolonged near work is linked with the development of myopia and that hyperopic retinal blur can lead to axial elongation. As animal studies have shown that blur experienced at the peripheral retina can affect ocular elongation (Smith *et al.*, 2005; Smith *et al.*, 2009) the effect of near viewing on peripheral refraction is important. Calver *et al.* (2007) measured peripheral astigmatic and mean spherical equivalent errors in emmetropic and myopic participants for distance and near viewing. They concluded that viewing distance had little effect on peripheral refraction, or any change in nasal-temporal asymmetry. Davies and Mallen (2009) found little change in peripheral refraction whilst viewing targets requiring different accommodative demands, and suggested changes due to accommodation were not different in refractive error groups. These studies consider how near viewing affects the relative peripheral refraction but not how accommodative lag might affect the blur experienced in the peripheral retina at different viewing distances.

1.4.7 Peripheral refraction in myopes and emmetropes

The hypothesis that accommodative lag and peripheral hyperopic blur act as stimuli to myopia development is still up for debate. However, it is certain that peripheral and central retinal blur need to be considered together when considering hyperopic retinal blur as a stimulus for myopia development. Studies investigating peripheral refraction have concentrated on the mean spherical equivalent data. Charman and Radhakrishnan (2010) suggested that as well as considering the mean spherical equivalent peripheral refractions it may be important to evaluate both the sagittal and tangential astigmatic image planes. It might be that one of these provides more of a stimulus for ocular growth. To date it is not known whether viewing distance affects the blur experienced in the peripheral retina with respect to the two astigmatic image planes.

Although levels of accommodative lag in myopes and emmetropes may not differ, it may still affect the peripheral blur experienced for near viewing tasks. Manipulation of peripheral refraction as a treatment strategy for myopia will be discussed fully in section 1.8.5. However, treatment strategies aimed at reducing levels of peripheral hyperopic defocus may need to consider peripheral refraction in conjunction with accommodative lag and levels of near work in order to fully address the peripheral blur experienced by the individual and improve treatment effects.

1.5 Depth of focus

1.5.1 Definition

Depth of focus (DOF) is the variation in target vergence which can be tolerated without the perception of blur or the need for a corrective accommodative response. As retinal defocus is thought to drive the accommodation system, the DOF provides stability to the accommodative feedback, closed loop system. Subjective DOF is the distance over which a target can be moved before blur is perceived. If there is a large subjective DOF and therefore poor blur sensitivity then blur could be tolerated in everyday visual tasks.

Objective DOF assesses the dioptric change in target vergence occurring before a corrective accommodative response is required although methodologies determining the accommodation response endpoint differ.

Factors that can increase the DOF include aberrations such as chromatic aberration, myopia and increasing age; factors that decrease the DOF include increasing target contrast and target luminance (Ciuffreda, Wang and Wong, 2005).

Table1.1 Values of subjective and objective DOF found in previous studies

Study	Measurement	Values
Kotulak and Schor (1986a)	Objective DOF	0.24-0.28D
Mordi and Ciuffreda (1998)	Objective DOF Subjective DOF	1.28D 0.76D
Rosenfield and Abraham-Cohen (1999)	Subjective DOF	Emmetropes 0.22D Myopes 0.38D
Wang and Ciuffreda (2004)	Subjective DOF	0.89D
Vasudevan, Ciuffreda and Wang (2006b)	Objective DOF	0.61D
Vasudevan, Ciuffreda and Bin (2007)	Objective DOF Subjective DOF	1.18D 1.26D
Yao *et al.* (2010)	Objective DOF Subjective DOF	0.18D 1.04D

Table 1.1 shows values of total DOF (sum of distal and proximal halves of the DOF). Rosenfield and Abraham-Cohen (1999), Wang and Ciuffreda (2004) and Vasudevan, Ciuffreda and Bin (2007) measured subjective DOF using cycloplegia and although Rosenfield and Abraham-Cohen (1999) found smaller levels using a 2mm artificial pupil than Wang and Ciuffreda (2004) who used a 5mm artificial pupil, the instruction for detecting blur was different. Rosenfield and Abraham-Cohen (1999) used a bipartite target and one side remained stationary whilst the other side was moved toward or away from the subject. This constitutes a blur discrimination task. Wang and Ciuffreda (2004) asked subjects to report first detectable blur. It has been reported that blur discrimination is easier to detect over blur detection (Jacobs, Smith and Chan, 1989).

Objective DOF levels are usually found to be smaller than those measured subjectively. Kotulak and Schor (1986a) dilated their three subjects using 2.5% phenylephrine so pupil margins did not interfere with refraction measurements from the optometer. Vasudevan, Ciuffreda and Wang (2006b) used an open view naturalistic experimental set up allowing proximal cues and measured 20 subjects' refractions whilst they observed a moving target with start position at 25cm (4D). The experimental set up, subject instruction and target type will affect the dioptric value of objective and subjective DOF and Ciuffreda (1998) offers a review.

The DOF is an important consideration in the accurate retinal focus and has been reported to be larger in myopes compared with emmetropes (Vasudevan, Ciuffreda and Wang, 2006a). Reduced blur sensitivity could contribute to inaccurate accommodation during prolonged near-work resulting in retinal hyperopic defocus. Whether the poor response to blur signals is due to poor perceptual blur sensitivity (subjective DOF), an inefficient neural accommodation response (objective DOF) to blur or optical differences such as higher order aberrations making blur detection difficult is as yet unclear.

1.5.2 Subjective DOF

Subjective measures of DOF rely on the use of a Badal optometer which ensures a constant image size regardless of target vergence which in turn helps to rule out proximal cues. Atchison, Charman and Woods (1997) investigated subjective DOF as a function of pupil size and target size. They found DOF values of 0.86, 0.59, and 0.55 D for 2-, 4-, and 6-mm pupils respectively and showed that DOF increase with target size.

Wang, Ciuffreda and Irish (2006) assessed blur discrimination and blur detection in five subjects using cycloplegia and a Badal optical system. They found that less retinal defocus was required to discriminate blur than to first detect its presence. Watson and Ahumada (2011) reviewed many studies investigating blur thresholds, concluding that the level of blur required for detection and discrimination increases towards a threshold, and that as blur increases further this threshold decreases. They reported the threshold for blur discrimination is lower than blur detection.

Studies in humans have shown that myopes have poorer blur sensitivity than emmetropes (Gwiazda *et al.*, 1993; Jiang, 1997; Abbott, Schmid and Strang, 1998; Rosenfield and Abraham-Cohen, 1999) but results depend on the criteria for determining the edge of the subjective DOF (blur detection or discrimination criteria).

1.5.3 Objective DOF

Objective DOF measures accommodative responses to changes in target vergence and rely on the closed accommodation feedback loop and the subject's ability to make neural responses to the retinal defocus. The point at which the accommodation makes a significant change as a target moves towards or away from a subject defines the distal and proximal edge of the DOF.

Vasudevan, Ciuffreda and Wang (2006a) measured the objective DOF in 16 myopes, 13 emmetropes and 6 hyperopes. They measured the accommodation responses to a moving target dynamically using a Power Refractor (PRII) and found the objective DOF to be significantly larger in myopes (0.61D±0.07) than emmetropes (0.53D±0.09) supporting the theory that myopes may tolerate more retinal blur for near viewing.

Accommodative lag (accommodative stimulus minus accommodative response) must exceed the DOF for further accommodative response to be initiated. Accommodative lag may not be different in myopes and emmetropes but if DOF is larger in myopes, then the accommodative error may lie within the DOF and no corrective accommodative response would be initiated. This may result in hyperopic retinal defocus which is a potential myopigenic stimulus.

Objective DOF values (Table 1.1) have been found to be smaller than those measured subjectively (Yao *et al.*, 2010). Marcos, Moreno and Navarro (1999) found subjective to be smaller than objective DOF, although they also commented that their absolute values could not be directly compared. They had also used different criteria to other studies. They measured the retinal image quality and defined the objective DOF as the dioptric range over which retinal image quality did not fall below 80%. They based subjective DOF measurements on the accuracy of their subjects being able to focus a point source of light. Other studies measured subjective DOF by recording the dioptric range over which a target could be described as clear and found subjective to be larger than objective DOF (Mordi and Ciuffreda, 1998; Yao *et al.*, 2010) supporting the theory that the accommodation system responds before blur can be perceived. Vasudevan, Ciuffreda and Bin (2007) found no significant difference between the subjective and the objective DOF (±0.63 and ±0.59D respectively) although they found more variability in subjective measurements. The differences in these studies may be due to the criteria used to determine the edges of the DOF as well as the targets used and refractive errors of the subjects. Vasudevan, Ciuffreda and Bin (2007) measured 10 subjects with refractive errors ranging from +1D to -3D whilst viewing a Maltese cross target. Yao *et al.* (2010) investigated 10 emmetropic subjects whilst viewing a square wave grating. Mordi and Ciuffreda (1998) investigated 30 subjects (ages 21-50 years) whilst viewing a Maltese cross target. None of these studies investigated the differences between refractive error groups or the effect of target spatial frequency on both subjective and objective DOF.

1.5.4 Depth of focus, accommodation and microfluctuations

Larger DOF in myopes are thought to be responsible for larger accommodative microfluctuations (Day *et al.*, 2009b). Winn *et al.* (1989) considered the perceptual detectability of the level of accommodative microfluctuations. They recorded microfluctuations during steady state viewing of targets using an IR optometer. They paralysed accommodation and placed a target at the far point of accommodation such that the target was at optimal focus. The target was oscillated so the vergence changed sinusoidally with time at the same dioptric level as the previously measured microfluctuations. They showed that the RMS values of the fluctuations were the same as the threshold for the detection of blur under cycloplegia suggesting that at least an amount of the microfluctuations span the DOF and concluded that microfluctuations are capable of providing information to aid the feedback loop of the accommodation system. Larger microfluctuations resulting from larger DOF may increase accommodative inaccuracies and would increase levels of retinal defocus.

1.5.5 External factors affecting depth of focus

Various factors affect DOF and include those outside the optical system which affect the visual target or test environment. Factors affecting DOF have been discussed by Wang and Ciuffreda (2006) and include spatial frequency, target size, luminance and contrast.

Spatial frequency

DOF has been shown to decrease as the target spatial frequency increases (Tucker and Charman, 1986; Legge *et al.*, 1987a; Marcos, Moreno and Navarro, 1999). Marcos, Moreno and Navarro (1999) used psychophysical methods to investigate objective and subjective DOF and the effect of target characteristics. They concluded that DOF decreased with increasing spatial frequency but over 3cdeg^{-1} the decrease would be less than expected in an aberration free system. This supported previous studies by Legge *et al.* (1987b) and Tucker and Charman (1986) concluding that DOF decreased with increasing spatial frequencies. Other studies suggest that mid-range spatial frequencies best drive accommodation (Owens, 1980; Bour, 1981; Ward, 1987). This might lead to theories that mid-range spatial frequencies would elicit the smallest DOF.

Taylor *et al.* (2009) found no significant difference in the accommodative response between myopes and emmetropes regardless of target spatial frequency, although only one measurement of static accommodation for each grating target was taken. Strang *et al.* (2011) conducted a study which compared accommodative step responses in myopes and emmetropes who viewed different spatial frequency grating targets. They showed that myopes had a poorer percentage of correct responses (calculated as the percentage of all responses made in the correct direction) for small step changes when compared with emmetropes for low and high spatial frequency targets only (0.5 and 16cdeg^{-1}). To date, studies investigating the effects of spatial frequency on accommodation responses have used gratings. As it has been suggested that there is a link between myopia and prolonged near-work (Angle and Wissmann, 1980; Kinge *et al.*, 2000) particularly reading, it may be the spatial frequencies and detail contained within text which are responsible for the accommodation response differences in myopes and emmetropes. Myopes may have a different peak spatial frequency when compared to emmetropes. Few studies have investigated accommodative differences in refractive error groups to different spatial frequencies and to date no studies have investigated the effect of text target spatial frequency content on the DOF to consider any features of the text which may contribute to poorer accommodation responses seen in myopes.

Target size

Proximal cues are known to be involved in accommodative control (Kruger and Pola, 1986). McLin Jr, Schor and Kruger (1988) suggested that increasing stimulus size stimulated accommodation directly. Kruger and Pola (1987) also found that changes in target size that alter the perception of apparent distance can drive the accommodative system. Alpern (1958b) investigated the effect of target size on vergence and accommodation and found that increasing the size of a playing card on a screen at a fixed distance elicited an increase in vergence and accommodation. The present study was conducted monocularly, limiting the influence of disparity cues but the objective DOF experiment was conducted in an open view system, allowing blur and proximity cues. Examining different text sizes filtered for the same spatial frequency bands helped consider whether differences between myopes and emmetropes seen with spatial frequency targets are due to specific spatial frequency bands or the target detail (as the same spatial frequency filter had a different effect on the two target sizes). Atchison, Charman and Woods (1997) found that subjective DOF increased with increasing target size but the current study will investigate whether the neural accommodation response and objective DOF are also altered by changing target size.

Target luminance

DOF increases as luminance decreases due to the loss of high spatial frequency information as light levels decrease to scotopic levels (Tucker and Charman, 1986). For luminance levels of <0.02cd/m^2, DOF and microfluctuations have been shown to increase (Day *et al.*, 2009b). A reduction in target luminance causes high spatial frequency information to become undetectable (VanNes, 1967).

Kotulak and Schor (1987) reported that the accommodative accuracy improves with increasing spatial frequency with mean luminance of 10cd/m^2, but as luminance decreased below this level, there is a corresponding fall off of accommodative response accuracy especially at high spatial frequencies. Various studies investigating DOF have used different target luminance although most in the photopic range from 3.7cd/m^2 in Vasudevan, Ciuffreda and Wang (2006b), 25cd/m^2 in Mordi and Ciuffreda (1998) and 180cd/m^2 in Yao *et al.* (2010). Experimentally there is a requirement to maintain photopic light levels for the target of at least 10cd/m^2.

Target contrast

Contrast of the target and the effect on DOF has also been considered and results, although variable, have shown slight increases in DOF with low contrast levels (Atchison, Charman and Woods, 1997). Contrast has been shown to affect accommodation responses only when an accommodation response threshold is reached (Ward, 1987). Ward (1987) used sinusoidal gratings (1.67, 5.0 and 15 cdeg^{-1}) and found that accommodation changed very little as contrast was reduced when the accommodation response was sub-threshold. Higher contrast was required for the high spatial frequency targets to maintain a good accommodative response.

1.5.6 Internal factors influencing depth of focus

Internal factors include the subject's pupil size, visual acuity and retinal eccentricity (Wang and Ciuffreda, 2006).

Pupil size

Many studies have found that larger DOF are found with smaller pupils (Campbell, 1957; Ogle and Schwartz, 1959; Tucker and Charman, 1975; Charman and Whitefoot, 1977; Tucker and Charman, 1986; Legge *et al.*, 1987b; Walsh and Charman, 1988; Atchison, Charman and Woods, 1997; Marcos, Moreno and Navarro, 1999), although the DOF is not significantly affected until the pupil size is less than 3mm (Campbell, 1957; Charman and Whitefoot, 1977). This is thought to be due to the reduced blur circle on the retina and reduced spherical aberrations seen with smaller pupils. Pupil sizes have not been found to differ in myopes and emmetropes (Jones, 1990)

Visual acuity

The higher the visual acuity, the smaller the DOF (Wang and Ciuffreda, 2006). This is thought to be due to a smaller detectable blur circle on the retina with improved visual acuity. If retinal blur is thought to be a primary stimulus to accommodation then detection of smaller changes in retinal blur would lead to smaller DOF. This was suggested in mathematical models produced by Green, Powers and Banks (1980). Reduced visual acuity in myopes compared to emmetropes has been previously suggested (Strang, Winn and Bradley, 1998).

Retinal eccentricity

Ciuffreda, Wang and Wong (2005) investigated the DOF psychophysically under monocular Badal viewing conditions with accommodation paralysed and a 5mm artificial pupil. The target was moved until the subject reported 'just noticeable blur' and repeated for 'just noticeable clarity'. They reported DOF increased at a rate of 0.11±0.01Ddegree^{-1}

of increased target size from 1.46D±0.42 for a 0.5degree radius target to 2.30D±1.12 for an 8 degree target radius. It has been shown that the larger the extent across the near retinal periphery covered by the target image, the larger the DOF, thought to be due to reduced cone density and increased aberrations (Wang, Thibos and Bradley, 1997; Wang and Ciuffreda, 2004; Ciuffreda, Wang and Wong, 2005).

Age

Subjective DOF has been shown to increase with age (Mordi and Ciuffreda, 1998) as a result of gradual presbyopia onset allowing a gradual tolerance to blur. Mordi and Ciuffreda (1998) also reported no change in objective DOF with age.

1.5.7 Depth of focus in myopes and emmetropes

Accommodative lag may be the same in myopes and emmetropes but if the DOF is larger in myopes then accommodative inaccuracies will need to be larger to extend beyond the DOF and initiate a corrective accommodative response. This would result in extended periods of hyperopic defocus.

Gwiazda *et al.* (1993), Abbott, Schmid and Strang (1998) and Jiang (1997) concluded that myopes were poorer at using blur signals to make correct accommodation responses. As near work, particularly reading has been linked with myopia development it is of interest what features of text influence the subjective DOF seen in different refractive error groups, which to date, has not been investigated.

This study investigated the influence of text detail on the subjective and objective DOF. Any differences found between myopes and emmetropes for both subjective and objective DOF, especially if the differences are seen with the same targets, would prove important for future studies considering blur training to improve accommodation responses and reduce the DOF.

1.6 Higher order aberrations

1.6.1 Definition

The eye is not a perfect optical system, and the deviation from the perfect point source formed at the retina is called an aberrated wavefront. Low order aberrations include the spherical and cylindrical components of the refractive error. Higher order aberrations include the third order coma, trefoil and fourth order spherical aberrations, secondary astigmatism and quadrafoil. The wave aberration can be modelled using mathematical equations (Campbell, 2003) and described using Zernike polynomial equations (Table 1.2). Each aberration has either a positive or negative form and although there is no limit to the number of terms in optics, the first six orders are most commonly used. The root mean square (RMS) is limited in its use to consider and compare higher order aberrations as it does not describe how the aberrations affect the retinal image.

Table 1.2 Zernike descriptions of the second, third and fourth orders (Z_n^m, where *n* is the radial order and *m* is the angular frequency)

Zernike order	Zernike mode	Description
2	Z_2^{-2}	Oblique astigmatism
2	Z_2^{0}	Spherical defocus
2	Z_2^{2}	Against/with the rule astigmatism
3	Z_3^{-3}	Oblique trefoil
3	Z_3^{-1}	Vertical coma
3	Z_3^{1}	Horizontal coma
3	Z_3^{3}	Horizontal trefoil
4	Z_4^{-4}	Oblique quadrafoil
4	Z_4^{-2}	Oblique second order astigmatism
4	Z_4^{0}	Spherical aberration
4	Z_4^{2}	With/against the rule astigmatism
4	Z_4^{4}	Quadrafoil

1.6.2 Effects on retinal image

Results of investigations into the relationship between higher order aberrations in different refractive error groups have been equivocal. Charman (2005) suggested that if myopes had higher levels of higher order aberrations and therefore a diminished foveal image quality then this might encourage ocular elongation and myopia development although stated that the 'evidence for higher levels of axial aberration in myopes in comparison with other refractive error groups is weak'. Cheng *et al.* (2004) also reported that RMS values of third and fourth order higher order aberrations were not correlated with refractive error. Hartwig and Atchison (2012) found that although most higher order aberration terms were correlated with spherical equivalent refraction, the proportion of the higher order aberrations which could be explained by refraction was less than 2% except for horizontal coma (9%) and spherical aberration (12%).

1.6.3 Effects on accommodation and depth of focus

Many studies have investigated the effects of accommodation on aberrations (Koomen, Tousey and Scolnik, 1949; Ivanoff, 1956; Jenkins, 1963; Millodot and Thibault, 1985; Howland and Buettner, 1989; Atchison *et al.*, 1995b; He *et al.*, 1998; He, Burns and Marcos, 2000; Ninomiya *et al.*, 2002; Vilupuru, Roorda and Glasser, 2004). There is general agreement that accommodation causes a negative change of spherical aberration although there appears to be large variability amongst subjects and studies (Koomen, Tousey and Scolnik, 1949; Ivanoff, 1956; Jenkins, 1963; He, Burns and Marcos, 2000; Ninomiya *et al.*, 2002; Hazel, Cox and Strang, 2003; Cheng *et al.*, 2004; Buehren, Collins and Carney, 2005; Chen *et al.*, 2006). There is even less agreement regarding the effect of accommodation on coma (Howland and Buettner, 1989; He, Burns and Marcos, 2000).

Fewer studies have investigated how higher order aberrations affect the accommodation response. Wilson, Decker and Roorda (2002) reported that monochromatic aberrations are used to identify the direction of retinal defocus. Based on this finding Fernandez and Artal (2005) considered the effect of correcting these aberrations on accommodation responses. They corrected higher order aberrations using adaptive optics, and found no effect on the accommodation response level or latency time but a significant increase in accommodation RT.

Studies investigating effects of higher order aberrations on accommodation and DOF have often done so to investigate how aberrations affect the range of clear near viewing in presbyopes. Rocha *et al.* (2009) measured DOF subjectively (the distance over which a letter could be correctly identified) and used an adaptive optics simulator to introduce spherical aberration, coma and trefoil. They found that only spherical aberration had the effect of increasing the DOF (by up to 2D with 0.6 micron of spherical aberration). Benard, Lopez-Gil and Legras (2011) found that with large (6mm) pupils inducing 0.3 and 0.6 microns of spherical aberration, using adaptive optics, increased the subjective DOF by 45 % and 64% respectively. Gambra *et al.* (2009) found inducing positive spherical aberration and coma increased accommodative lag. They also found that inducing higher order aberrations, particularly negative spherical aberration increased accommodative microfluctuations. Marcos, Moreno and Navarro (1999) highlighted the importance of considering the higher order aberrations in conjunction with DOF measurements. Measuring higher order aberrations alongside DOF measurements may help to explain DOF differences between subjects.

1.7 Spatial frequency channels

1.7.1 Background

Various studies have shown links between myopia development and near work particularly reading (Angle and Wissmann, 1980; Kinge *et al.*, 2000). The presence of spatial frequency specific channels in visual processing is known (Blakemore and Campbell, 1969; Boden and Giaschi, 2009). Reading text contains a range of spatial frequencies although studies investigating effects of spatial frequency content on accommodation have primarily used gratings which are simple targets that do not contain the same spatial frequency distribution as text. Differences in results may be seen when comparing sine and square wave gratings as low spatial frequency square wave gratings still contain high spatial frequency information in the sharp edges. The targets designed in this study filtered particular spatial frequencies contained within text.

It is known that cortical neurons have a spatial frequency bandwidth of around 1-1.5 octaves and an orientation bandwidth of 25-35 degrees (Bass, 2009). Spatial frequency information is usually considered in octaves and the measurements are nonlinear. Spatial frequency measurements are discussed in detail in section 2.4 for the purposes of target production.

1.7.2 Spatial frequency versus object frequency

The human contrast sensitivity function (CSF) shows a peak spatial frequency in photopic conditions around 4-6cdeg^{-1} when viewing sine wave gratings (Figure 5.1). However, studies considering the influence of spatial frequency on letter identification have shown that the peak spatial frequency depends on letter detail. Peak frequency recorded as retinal frequency (cycles per degree) has been shown to scale with letter size (Parish and Sperling, 1991; Solomon and Pelli, 1994).

Previous studies have investigated the influence of spatial frequencies on letter recognition (Braje, Tjan and Legge, 1995; Chung, Legge and Tjan, 2002; Majaj *et al.*, 2002). Majaj *et al.* (2002) investigated the stroke frequency (average number of lines crossed by a slice through the letter divided by letter width) of a variety of targets including Roman numerals and Chinese letters. They suggested that the stroke frequency determined the cortical spatial frequency selective channel employed regardless of target font and size. They suggested that large letters are identified by the finer detail and smaller letters by their gross strokes. Braje, Tjan and Legge (1995) investigated the efficiency for detecting and recognizing low pass filtered objects. They tested the hypothesis that humans are inefficient at using high spatial frequency information but did not find this to be the case. Chung, Legge and Tjan (2002) used filtered spatial frequency letter targets, one octave in width, to compare the peak spatial frequency of letter identification of their subjects to that expected from an ideal CSF. They reported the peak sensitivity occurs at a frequency 0.34 octaves (27%) higher in humans than the ideal CSF would predict. They suggested this may be due to the visual system requiring broadband spatial frequency channels for pattern perception. Studies investigating spatial frequency effects on accommodation have largely used grating targets which consider only narrow band spatial frequency information and does not consider object detail.

1.7.3 Spatial frequency and accommodation

Owens (1980) investigated the accuracy of steady state accommodation for high contrast sinusoidal gratings and found the best performance for accommodation and contrast sensitivity was for spatial frequencies 3-5cdeg^{-1}. Ward (1987) also found that using sinusoidal gratings of 5cdeg^{-1} elicited the best accommodative responses compared to gratings of 1.67 and 15cdeg^{-1}, taking static measurements whilst subjects' maintained fixation on a -5D target vergence. Strang *et al.* (2011) showed an improved percentage of correct large accommodative step responses with the 4cdeg^{-1} sine wave gratings compared to 16cdeg^{-1}.

Bour (1981) measured the magnitude of microfluctuations while subjects viewed sine waves of low (1cdeg^{-1}), medium (4cdeg^{-1}) and high (16cdeg^{-1}) spatial frequencies. They found that microfluctuations were smallest when viewing the medium (4cdeg^{-1}) spatial frequency gratings suggesting that dynamic accommodation is optimal for these spatial frequencies. However, Bour (1981) examined only two subjects. Niwa and Tokoro (1998) also measured accommodative microfluctuations when the observers viewed square wave gratings and found an increase in magnitude of microfluctuations for low spatial frequency square wave gratings.

Day *et al.* (2009b) compared microfluctuations between myopic and emmetropic observers viewing different spatial frequency targets. When viewing sine wave targets the microfluctuations were found to be significantly larger when viewing 0.5 and 16cdeg-1 targets when compared with 4cdeg-1, and the microfluctuations were larger in myopes. Taylor *et al.* (2009) also investigated the effect of target spatial frequency on accommodative response in different refractive groups. Although they did not investigate accommodation dynamically, and could not consider microfluctuations, they found emmetropes and myopes showed similar accommodative behaviour regardless of the spatial frequency of sinusoidal gratings. Strang *et al.* (2011) suggested that myopes had poorer small step accommodative responses compared to emmetropes when viewing low (0.5cdeg^{-1}) and high (16cdeg^{-1}) spatial frequency gratings. These studies are not conclusive about which spatial frequency targets elicit the smallest DOF but those investigating differences between refractive error groups do highlight the importance of considering many aspects of accommodation response in order to draw conclusions about refractive error group differences. These previous studies have used grating targets which do not adequately represent text. If it is a feature of reading that influences the poor accommodation in myopes compared to emmetropes then the effects of spatial frequency and detail of text on accommodation needs to be considered.

1.7.4 The influence of defocus and pupil size on contrast

The human contrast sensitivity function has a drop in sensitivity at high spatial frequencies attributed to blurring from two main factors: optical limitations of the eye and spatial summation of the nervous system (Campbell and Green, 1965). The drop in sensitivity at low spatial frequencies has been attributed to lateral inhibition (Georgeson and Sullivan, 1975).

When attempting to accommodate accurately to an initially out of focus image, Charman and Heron (1979) commented that this must be based on low spatial frequency information and as the image comes more into focus higher spatial frequency information will be available for accommodation refinement.

Radhakrishnan *et al.* (2004) found that in non myopes increasing levels of defocus blur (positive and negative) resulted in reduced contrast sensitivity. They reported more contrast sensitivity loss in non myopes compared with myopes for low-medium spatial frequency gratings (1-8cdeg^{-1}) with negative defocus. This might suggest that in the current study when investigating DOF, the impact of defocus (by moving the targets towards or away from subjects) may result in reduced CSF functions more so in emmetropes than myopes when viewing low-medium spatial frequency filtered text targets. The findings the Radhakrishnan *et al.* (2004) study may suggest the current study would find emmetropes to have smaller DOF compared to myopes when viewing these spatial frequency filtered text targets.

The reduction in contrast sensitivity with decreasing pupil size has been investigated by Campbell and Green (1965). However, the effect of pupil size on the human contrast sensitivity function is not straight forward as Sloane, Owsley and Alvarez (1988) reported that the decreasing pupil size in the aging eye also decreases spherical aberration and that in some subjects offsets the negative effect of reduced luminance limiting the effects on the contrast sensitivity.

Defocus blur has the effect of reducing the CSF resulting in oscillations (“notches”) between the peak spatial frequency and the cut off spatial frequency. This has been well predicted by Atchison, Woods and Bradley (1998) in aberration free models with small pupils. With larger pupils with larger aberrations, it might be expected that the impact of defocus blur on the CSF would be larger but this is not always the case (Strang, Atchison and Woods, 1999). Strang, Atchison and Woods (1999) reported that for certain subjects, at some spatial frequencies, contrast sensitivity with larger pupils was better than with smaller pupils. They found for one subject with induced hyperopic defocus the contrast sensitivity around 8cdeg^{-1} was better with 4mm compared to 2mm pupils. Although the aim of the current study was not to investigate the influence of pupil size on DOF, the study by Strang, Atchison and Woods (1999) showed that it would not always be the case that those subjects with larger pupils would have reduced CSF functions and perhaps smaller DOF.

1.7.5 Spatial frequency adaptation

It has been shown that after extended periods of blur adaptation (positive defocus), uncorrected acuity is improved in myopes. Vera Diaz *et al.* (2004) showed that after a period of only 3 minutes of blur adaptation using diffusing filters in myopes resulted in an increase in the near accommodative response although the same did not occur in emmetropes. Adaptation to particular spatial frequencies been shown to result in a loss in sensitivity centred around the adaptation frequency (De Valois, 1977) whilst enhancing sensitivity to spatial frequencies further removed than one octave higher than the adaptation frequency (De Valois, 1977; Wilson and Regan, 1984). These findings require consideration when designing experiments requiring extended periods of observing spatial frequency specific targets. Subjects viewing spatial frequency specific targets should be limited to less than 3 minutes of constant viewing and targets presented in a randomised order to limit adaptation effects.

1.8 Attempts at prevention of myopia and myopia progression

The increasing prevalence of myopia with associated risk factors means that potential myopia prevention is becoming important. Many lines of investigation have examined the possibility of limiting myopic progression.

1.8.1 Overcorrection and under-correction of myopia

As hyperopic defocus is thought to provide a stimulus to ocular growth, studies have considered the possibility that under-correction of myopia would lead to improved retinal focus. However, Adler and Millodot (2006) found that over an 18 month period, under-correction of 0.50D resulted in a significant but clinically small difference in myopia progression of 0.17D. Chung, Mohidin and O'Leary (2002) found that under-correction of myopia led to larger levels of myopia progression and suggested that under-correction enhances rather than inhibits myopia progression. Goss (1984) considered overcorrection and found that the rates of myopia progression were not different in the treatment and control group.

1.8.2 Progressive addition lenses and bifocals

Reducing accommodative effort at near, thereby reducing accommodative lag and hyperopic blur for near tasks using progressive addition lenses (PALs), has been a popular idea (COMET study: Leung and Brown, 1999; Edwards *et al.*, 2002; Gwiazda *et al.*, 2002; Gwiazda *et al.*, 2003; Gwiazda *et al.*, 2004; Hyman and Gwiazda, 2004; Kurtz *et al.*, 2007; Hasebe *et al.*, 2008; Berntsen *et al.*, 2011b; COMET2, 2011). General consensus is PALs show a significant (but clinically small) treatment effect on slowing myopia progression. The Correction of Myopia Evaluation Trial (COMET) was a multicentre randomised clinical trial evaluating the effects of PALs on slowing myopia progression. PALs were found to slow progression by 0.20D over 3 years with most of the treatment effect occurring in the first year. Fulk, Cyert and Parker (2000) found similar results using bifocal lenses compared to single vision lenses in children (0.25D treatment effect over 30 months) although made no reference to sustainability. The COMET2 study investigated the effect of PALs in children with high levels of accommodative lag and similarly found a small (0.28D) but significant treatment effect over 3 years. Berntsen *et al.* (2011b) reported that in the year after PALs treatment, treated subjects showed no significant difference in myopia progression to untreated subjects.

1.8.3 Contact lenses

The Contact Lens and Myopia Progression study (CLAMP) is based on anecdotal evidence that reshaping of the cornea slows myopia progression. Walline *et al.* (2004) found a small but significant effect (0.63D treatment effect in 3 years) of rigid gas permeable lenses (RGPs) compared with soft lenses in slowing myopia progression. However, they suggested that this effect was likely to reverse if lens wear was stopped.

Attempts to correct and control myopia progression using orthokeratology have also been attempted by Cho, Cheung and Edwards (2005) in the Longitudinal Orthokeratology research in Children study (LORIC). Although they did find a positive effect on myopia progression, data were varied among subjects. They reported a significant reduction in axial length growth in children wearing treatment contact lenses (0.25mm treatment effect over 2 years).

Contact lenses specially designed to provide a clear retinal image whilst simultaneously presenting 2D of myopic defocus were used in a study by Anstice and Phillips (2011). Over a 10 month period myopia progression was significantly less in subjects assigned to the treatment lens group. The possibility that multifocal soft contact lenses which alter the peripheral refraction could be used to slow myopia progression has been considered with small but significant results (section 1.8.5). Studies are now considering the effects of multifocal contact lenses on the peripheral refraction in order to improve future treatment results (Rosén *et al.*, 2012; Kollbaum *et al.*, 2013; Ticak and Walline, 2013). Further studies over longer periods using these lenses are needed to assess further sustainability of the treatment effects.

1.8.4 Pharmacological intervention

Pharmacological attempts using atropine to control myopia progression have shown promise, although the mechanism of action is not entirely clear (Shih *et al.*, 2001; Chua *et al.*, 2006; Lee *et al.*, 2006; Chia *et al.*, 2011; Walline *et al.*, 2011). However, these studies do not comment on sustainability. Pirenzepine, another muscarinic antagonist, has also been shown to reduce myopia progression (Tan *et al.*, 2005; Siatkowski *et al.*, 2008). Side effects of near blurring and light sensitivity limit their use beyond that of a study.

1.8.5 Peripheral refraction correction

Smith (2011) stated the case for considering peripheral retinal blur in future optical treatment strategies for myopia. It is known that standard single vision lens myopia correction increases the effect of hyperopic defocus in the peripheral retina (Lin *et al.*, 2010; Backhouse *et al.*, 2012). Research groups have considered the possibility that manipulating the peripheral blur experienced by myopes may slow progression (Holden *et al.*, 2010; Sankaridurg *et al.*, 2011; Smith, 2011). Holden *et al.* (2010) found that if the relative peripheral hyperopia was reduced with specially designed contact lenses, myopia progression was 54% reduced over a sixth month period compared to standard single vision lens correction, although the differences in progression were small (-0.34D). Sankaridurg *et al.* (2011) used contact lenses to control relative peripheral refraction in myopic children aged 7-14, and found that over 1 year myopia progression was 34% less than those treated with standard single vision lenses although this only equated to 0.31D. However, the contact lenses were not individually designed so the exact levels of hyperopic blur corrected were difficult to ascertain and the levels of hyperopic blur may be different depending on the distance of near tasks undertaken. Also they did not comment on accommodative lag of individual subjects or levels of near work carried out by subjects. Although practically difficult to achieve individually designed lenses to correct the peripheral refraction may have improved effects.

1.8.6 Treatment strategies

The use of near adds to reduce hyperopic blur experienced for near tasks rely on the theory that accommodative lag has a causative effect on myopia. Berntsen *et al.* (2012) suggested that the lack of a rebound of the treatment effect following PALs cessation ruled out the possibility that the treatment effect was due to reduction of mechanical tension. Instead they suggested that the treatment effect was due to reduction of retinal blur at near. However, they also stated that lack of association between accommodative lag and myopia progression might be the reason for clinically small treatment effects. Refractive error group differences in accommodative lag are inconclusive. Weizhong *et al.* (2008) conducted one of the only longitudinal studies investigating accommodative lag and myopia progression and found no statistically significant relationship between the two. If accommodative lag is not a causative factor for myopia development then treatment strategies aimed at manipulating lag are unlikely to prove successful. If accommodative variability (see section 1.3.3) is the source of hyperopic blur in myopes rather than just levels of accommodative lag then treatment strategies aimed at improving the stability of accommodation responses may be more successful in slowing myopia progression.

Newer treatment strategies aimed at reducing peripheral hyperopic blur have proved promising although treatment effects have been small. Further studies considering the levels of near work in conjunction with peripheral refraction correction for individual requirements need to be conducted.

1.9 Study aims

1.9.1 Objective 1: Peripheral refraction

This study examined the effects of accommodative inaccuracy on peripheral retinal blur experienced in myopes and emmetropes at different viewing distances and with reference to the two astigmatic image planes. One image plane may provide more of a stimulus for ocular growth particularly for near tasks. Astigmatic image planes, accommodative inaccuracy and viewing distance may prove to be important considerations in future studies attempting peripheral refraction correction as a treatment strategy for myopia.

1.9.2 Objective 2: Subjective DOF

No study to date has investigated the effect of spatial frequencies contained in text on the subjective DOF in myopes and emmetropes. The current study investigated blur sensitivity differences in myopes and emmetropes using spatial frequency filtered text targets. If blur perception is linked with the accommodation response system, myopes may have been found to perceive blur and accommodate differently with particular text spatial frequencies. Future studies attempting blur adaptation training might use the aspects of text where myopes showed poorer blur sensitivity, in order to improve their blur sensitivity and accommodation responses and reduce hyperopic retinal blur.

1.9.3 Objective 3: Dynamic accommodation

Bour (1981) suggested that dynamic accommodation was optimal for mid-range spatial frequency sine wave gratings. Grating stimuli do not adequately represent text, which contains a range of spatial frequencies. No studies have considered the effect of spatial frequencies and detail contained in text on dynamic accommodation responses in myopes and emmetropes. This study investigated dynamic accommodation responses in refractive error groups with spatial frequency filtered text targets, alongside DOF measurements.

1.9.4 Objective 4: Objective DOF

To date no study had investigated the effect of text target spatial frequency content on objective DOF in different refractive error groups. No study to date had investigated objective and subjective DOF in myopes and emmetropes. Considering both the subjective and objective DOF results helped clarify whether accommodative inaccuracies in myopes were due to a poorer neural response to retinal blur stimuli (objective DOF) or poorer perceptual blur sensitivity (subjective DOF). Investigating DOF using spatial frequency filtered text targets highlighted what text detail would result in the smallest objective DOF and best drive accommodation and what is most critical for blur perception. If spatial frequency filtered text targets affected the DOF in myopes and emmetropes differently and myopes showed larger DOF with particular spatial frequency filtered targets, it would be these text spatial frequencies eliciting the largest DOF which would be best targeted in future blur adaptation and training programmes, in order to improve myopes blur sensitivity and reduce levels of hyperopic defocus experienced for near tasks.

1.9.5 Objective 5: Accommodative microfluctuations

Accommodative microfluctuations are thought to provide a feedback loop to detect change in target vergence and initiate accommodative responses. Larger microfluctuations resulting from larger DOF may increase accommodative inaccuracies. Larger microfluctuations have been found with very high (16cdeg^{-1}) or very low (0.5cdeg^{-1}) spatial frequency sine wave targets (Day *et al.*, 2009b). The effects of text target spatial frequency content on microfluctuations in refractive error groups had not been previously investigated. If objective DOF and accommodative microfluctuations are similarly affected by text target spatial frequencies this would support the theory that microfluctuations are involved in the accommodative response system. We hypothesised that myopes would show a larger DOF and larger microfluctuations which would support the theory that myopes are poorer at responding to retinal blur signals. If myopes showed larger microfluctuations for very high and very low spatial frequency filtered targets, it would suggest that although mid-spatial frequencies are meant to best drive accommodation, low and high spatial frequencies also play a part in accommodation response feedback.

1.9.6 Objective 6: Higher order aberrations

Studies have induced high order aberrations using adaptive optics and found that spherical aberration (both positive and negative) had the effect of increasing DOF (Rocha *et al.*, 2009; Benard, Lopez-Gil and Legras, 2011). To date, no study has considered the influence of individuals' higher order aberrations on objective and subjective DOF, microfluctuations and dynamic accommodation. Positive and negative spherical aberrations cause image degradation which is likely to have a more detrimental effect on high spatial frequency filtered text targets. We therefore hypothesised that subjects with larger levels of spherical aberration would have larger DOF, accommodative microfluctuations and poorer dynamic accommodation, particularly when viewing higher spatial frequency filtered text targets. The current study aimed to measure higher order aberrations, not primarily to compare myopes and emmetropes, but to investigate any relationship between higher order aberration terms and the DOF measured both objectively and subjectively.

Chapter 2: Methodology

2.1 Participants

Subjects were recruited according to the inclusion criteria below:

- Aged 18-35
- Emmetropic (refractive error +1.00 to -0.50D) or myopic (refractive error >-0.50D)
- Cylinder values of <1.25DC
- Corrected visual acuity at least 0.00 logMAR in each eye
- No history of or current ocular pathology
- No family history of or risk factors for closed angle glaucoma

Sample size

Previous studies on peripheral refraction showed a difference between the relative peripheral refraction in myopes and emmetropes at 30 degrees temporally of 1.30D±0.95 (Calver *et al.*, 2007), 0.85D±0.41 (Lundstrom, Mira-Agudelo and Artal, 2009) and 1.20D±1.06 (Mutti *et al.*, 2000). These results, showed that a minimum of 16 subjects in each refractive group were required to allow a type 1 error α=0.05 and type 2 error ß=0.20.

A previous study on objective DOF differences in myopes and emmetropes (Vasudevan, Ciuffreda and Wang, 2006a) found an effect size difference of 0.08DS±0.08. A sample size calculation showed 16 participants were required for each refractive group to allow for a type 1 error α=0.05 and type 2 error ß=0.20.

Table 2.1 describes recruited subject numbers for each part of the study. The 4 subjects found not to comply with inclusion criteria comprised of 1 anisometrope, 1 high astigmat, 1 amblyope and 1 subject with mild keratoconus. Due to the difficulty measuring accommodation dynamically with the Power Refractor some subjects were found to have incomplete accommodation recordings which could not be analysed.

Table 2.1 Subject numbers for each part of the study and those subjects which failed to complete the study

Experiment	Recruited	Failed to complete	Poor accommodation recordings	Outside inclusion criteria	Completed
1. Peripheral refraction	87	0	N/A	3	84
2.Subjective DOF	58	5	2*	4	47
3. Dynamic accommodation	58	6	5	4	43
4. Objective DOF	58	5	3	4	46

***2 subjects who had pupils too small to record with the Power Refractor were excluded from all parts of the study including the subjective DOF experiments**

Ethics

Participants meeting the inclusion criteria were recruited from the student and staff population at Anglia Ruskin University, their friends and family via emails sent to university email addresses. Recruits were fully informed in writing and verbally of the processes and procedures involved in the study via a participant information leaflet (Appendix A). Written consent was obtained (Appendix B) following a verbal and written explanation of the procedures. They were advised of their right to withdraw from the study at any time without consequence. This study was granted ethical approval from Anglia Ruskin University Ethics Committee and adhered to the tenets of the Declaration of Helsinki.

2.2 Subjective refraction and biometric measurements

2.2.1 Classification

Myopia can be classified by degree of refractive error or by age of onset (Grosvenor, 1987). Subjective refraction of subjects in this study allowed them to be classified by degree of refractive error. Biometric measurements of the subjects helped to identify the type of myopia and also compare the influence of biometric parameters on peripheral refraction.

2.2.2 Instrumentation

The IOL Master (Zeiss, UK) was used to take biometric measurements including axial length (AL), anterior chamber depth (ACD), keratometry readings and horizontal visible iris diameter (corneal diameter). The IOL Master is a non contact device and uses partial coherence interferometry to take AL measurements. It is unaffected by high ametropia, pupil size or accommodative state. It uses lateral slit lamp illumination to determine the ACD (the distance between posterior cornea and anterior crystalline lens). Repeatability of the IOL Master has been verified by Sheng, Bottjer and Bullimore (2004) who found the IOL master to be more repeatable than ultrasound and measurements were not affected by observer experience. They found the mean difference between first and second readings of AL with the IOL master were -0.015mm for non cycloplegic measurements and 0.00mm for cycloplegic measurements. They also found the mean difference between first and second readings of ACD were 0.01mm for non cycloplegic measurements and -0.01mm for cycloplegic measurements. Hussin *et al.* (2006) investigated the reliability and validity of the IOL master compared to ultrasound techniques in children and found the IOL master to be more accurate and reproducible.

2.2.3 Methods

Subjective refraction was conducted in a standard 3m testing room with a 6m Snellen chart. The refraction was tested using the best sphere technique with the aid of retinoscopy, finding the maximum amount of positive power or the minimum amount of negative power that could be tolerated by the eye, without causing blurring of the image. Astigmatism was measured using the cross cylinder technique. Refraction was measured to 0.25DS.

Biometric measurements were taken using the Zeiss IOL Master according to manufacturer’s instructions with undilated pupils. Three measurements of AL were taken and accepted if within 0.01mm of each other. Three keratometry readings were taken and the median value taken, as slight differences in astigmatic axis would mean calculation of mean values was not straight forward. The mean of five ACD measurements was taken.

2.3 Peripheral refraction

Studies investigating the impact of blur experienced at the retina can no longer be limited to considering only the effects at the fovea (section 1.4). This study investigated the peripheral refractions in order to consider the retinal blur experienced by different refractive error groups at different viewing distances. Studies investigating peripheral refraction have drawn more attention in recent years as consideration has been given to correcting peripheral blur either via spectacles or contact lenses in order to slow myopia progression (section 1.8.5: Holden *et al.*, 2010; Sankaridurg *et al.*, 2010).

2.3.1 Previous work

Earlier studies on human eyes have also found discrepancies in relative peripheral refraction between refractive groups (Hoogerheide, Rempt and Hoogenboom, 1971; Rempt, Hoogerheide and Hoogenboom, 1971; Millodot, 1981). The prolate shape in myopic eyes and the oblate shape found in emmetropes have been confirmed using A scan ultrasonography (Logan *et al.*, 2004), MRI scans (Atchison *et al.*, 2005) and peripheral refraction techniques (Millodot, 1981; Seidemann *et al.*, 2002; Atchison, Pritchard and Schmid, 2006; Lundstrom, Mira-Agudelo and Artal, 2009). Whether relatively hyperopic peripheral refractive profiles in myopes are a precursor to myopia development or the result of eye elongation is still up for debate. Prolate retinal profiles found in myopes would mean that conventional myopia correcting spectacle lenses would increase the relative hyperopia in the periphery (Tabernero and Schaeffel, 2009; Lin *et al.*, 2010). Animal models (section 1.4.1) have suggested that peripheral retinal defocus can influence eye growth (Smith *et al.*, 2005; Smith *et al.*, 2010). Mutti *et al.* (2011) concluded that relative peripheral hyperopia in humans does not provide a consistent influence on myopia development (section 1.4.4).

It is known that astigmatism increases in the peripheral retina and is approximated to oblique astigmatism with two focal lines approximately radial or tangential to the axis (Charman and Radhakrishnan, 2010). It is also necessary to consider the peripheral astigmatism and the two image shells across the retina as it is possible that one astigmatic image shell might favour myopia development.

Fedtke, Ehrmann and Holden (2009) reviewed peripheral refraction techniques and compared the variety of ways peripheral refraction can be measured. These included subjective refraction, double pass technique (custom made for experimental set up), manual optometers, retinoscopy, photorefraction using the PlusOptix Power Refractor, and perhaps more commonly using autorefractors or wavefront sensors. They found the best instruments for eccentric refraction to be Hartmann Shack wavefront sensor technique and the open-field autorefractors. Lundstrom *et al.* (2005) compared different methods of assessing the peripheral refraction: subjective refraction, photorefraction with a PowerRefractor, wavefront measurements with a Hartmann Shack sensor and retinoscopy. They found the Power Refractor was unable to measure 15 of 50 subjects and underestimated high myopia but that subjective refraction methods had a larger spread of refractive results. They suggested that the Hartmann Shack wavefront technique was the most useful. The advantage of the Shin Nippon open view autorefractor is it allows an unobstructed view of real distance targets and for this reason the current study used the Shin Nippon SRW-5000. As well as being one of the better instruments for eccentric refraction it also allows viewing of peripheral targets out to 30 degrees temporally and nasally and central targets placed at different distances.

There are then three ways to take this peripheral refraction measurement:

1. Turn the head and eye whilst the instrument remains stationary
2. Keep the head and instrument stationary and turn the eye
3. Move the instrument around a stationary head and eye.

Previous studies have investigated these methods and both Radhakrishnan (2008) and Mathur *et al.* (2009) found that it was not critical whether the eye was rotated with respect to the head during axial or peripheral refraction measurements.

2.3.2 Instrumentation

Peripheral refraction and accommodation measurements were taken using the Shin Nippon SRW-5000 autorefractor. This is an infra-red open view autorefractor, allowing static refractive error measurements, with a range of ±22D sphere and ±10D cylinders in 0.125D steps and measures cylinder axis to 1°. Vertex distance can be altered and measurements can be taken to a minimum pupil size of 2.9mm (Mallen *et al.*, 2001). A ring image of an infrared source of wavelength 850nm is reflected from the retina and analysed over a pupil diameter of 3mm. Mallen *et al.* (2001) verified the Shin Nippon SRW-5000 autorefractor validity and repeatability compared to subjective refraction of 200 eyes of 100 adult subjects and found that the autorefractor read slightly more positive prescriptions (0.16D±0.44). Chat and Edwards (2001) found the SRW-5000 autorefractor to be both reliable and repeatable for children, aged 4-8 years, (44 for cycloplegic measures and 53 for non-cycloplegic) when compared with its predecessor, the Canon R-1.

2.3.3 Procedure

Large ‘X’ shaped targets were placed at 0, 5, 10, 15, 20, 25, 30 degrees right and left of centre 3m away from the subject’s right eye. A minimum of three readings were taken from the subject’s uncorrected right eye, whilst the left eye was occluded, with the subject fixating each target in turn. Targets had a central fixation point and a laser pointer was projected at the centre of each cross to aid fixation especially for those subjects with poor unaided acuities. Back vertex distance (BVD) was set to 0mm to give the refraction in the corneal plane, the step size was set to 0.12D and the cylinder set to record in minus form. The first reading was taken with the subject viewing the central target. The measurement was taken with the central dots aligned with the visual axis and then with the centre of the pupil. The instrument calculated the average refraction for each measurement.

Monocular accommodative responses in free space were measured. The refraction was placed in a trial frame in front of the left eye which fixated the targets. The participants were instructed to keep the target clear. Readings were taken from the right eye occluded using a Wratten 88A infrared filter (Eastman Kodak, Rochester, NY). The targets consisted of a 6/6 letter of a Snellen chart at 6m and then a near text target (Times Roman N10 paragraph of text) at 1m, 0.5m, 0.40m, 0.33m and 0.25m presented in sequence. The targets were aligned so that the measurement was taken along the visual axis of the measured eye. Three readings were taken for each target and the mean refraction calculated by the autorefractor.

2.3.4 Data analysis

The mean spherical equivalent refraction (the full sphere plus half the cylinder value) was calculated and then normalised for each peripheral retinal location by subtracting the spherical equivalent of the subjective refraction at zero back vertex distance. Normalising the data meant that the relative rather than absolute peripheral refraction could be considered allowing comparison of refractive error groups. The distance lead of individual subjects taken along the visual axis was calculated using Equation 2.1. This was then added to the individual subjects' normalised peripheral refraction values and the average of the refractive error groups plotted.

The accommodative lag at 33cm viewing distance was calculated for each individual subject (Equations 2.2-2.4). Near accommodative lag requires the calculation of accommodative demand dependent on the subject's refractive error. The lag value for each individual subject was added to the same subjects' relative peripheral refraction values and the average of each refractive group plotted. These plots allow relative peripheral defocus to be considered for different viewing distances. Asymmetry in the nasal and temporal retina was also considered. In order to make comparisons, asymmetry values were calculated by subtracting the mean spherical equivalent value at 30 degrees nasally from the same value at 30 degree temporally.

Equation 2.1 Distance lead is calculated as follows:

$$DLA = AS - (MSE - DR)$$

Where DLA is the distance lead of accommodation, AS is the accommodative stimulus (0.17D at 6m), MSE is the mean spherical equivalent of the subjective refraction at 0mm BVD and DR is the mean spherical equivalent refraction taken at 6m viewing distance.

Equation 2.2 (from Tunnacliffe, 1993)

$$AD = \frac{-Ls}{(1-dFs)(1-d(Ls+Fs))}$$

Where AD is the accommodative demand, Ls is accommodative stimulus (D) measured in the correcting lens plane, Fs is the dioptric power of the correcting lens (D) and d is the vertex distance (m).

Equation 2.3

$$AR = NR – MSE$$

Accommodative response (AR) can be calculated by subtracting the spherical equivalent subjective refraction (MSE, 0mm BVD) from the measured accommodative response at the desired working distance (NR).

Equation 2.4

$$NLA = AD – AR$$

Accommodative lag can be calculated. Where NLA is near lag of accommodation (at 33cm), AD is accommodative demand as previously calculated and AR is accommodative response (at 33cm).

Sagittal and tangential powers were then calculated from the sphero-cylindrical refractions at each retinal location (equations 2.5-6) and plotted against the peripheral location in degrees.

Equation 2.5
The power (F_θ) along the horizontal (sagittal) meridian is:

$$F_\theta = F_s+F_c\sin^2(180-\alpha)$$

Equation 2.6
The power (F_θ) along the vertical (tangential) meridian is:

$$F_\theta = F_s + F_c \cos^2(180-\alpha)$$

where F_s is the power of the sphere, F_c is the cylinder power and α is the cylinder axis.

2.4 Target design

The experiments on subjective and objective DOF, dynamic accommodation and accommodative microfluctuations used the same spatial frequency filtered targets. For this reason the target design is discussed in the following section.

2.4.1 Target spatial frequency

Studies have suggested mid-range spatial frequencies best drive accommodation (Owens, 1980; Bour, 1981; Ward, 1987). These studies have been summarised in section 1.7.3, and used grating targets that do not adequately represent text. Reading has been shown to be supported by a broad range of spatial frequencies (reviewed section 1.7.2; Braje, Tjan and Legge, 1995; Chung, Legge and Tjan, 2002; Majaj *et al.*, 2002). As spatial frequencies present in text have been shown to influence reading and letter recognition it may be that this detail also influences accommodation responses. The effect of spatial frequency filtered text on accommodation in myopes and emmetropes should, therefore, be considered.

The text in this experiment was filtered for different spatial frequencies using a MATLAB program. Low-pass and high-pass filters for different spatial frequency cut offs were applied to text, but this allowed too much low or high spatial frequency information through the filter, so the letters were not obviously different. Also, this would have meant bandwidths were hard to quantify. In the current study the letters were band-pass filtered.

Spatial frequency information is usually described in octaves (Figure 2.1).

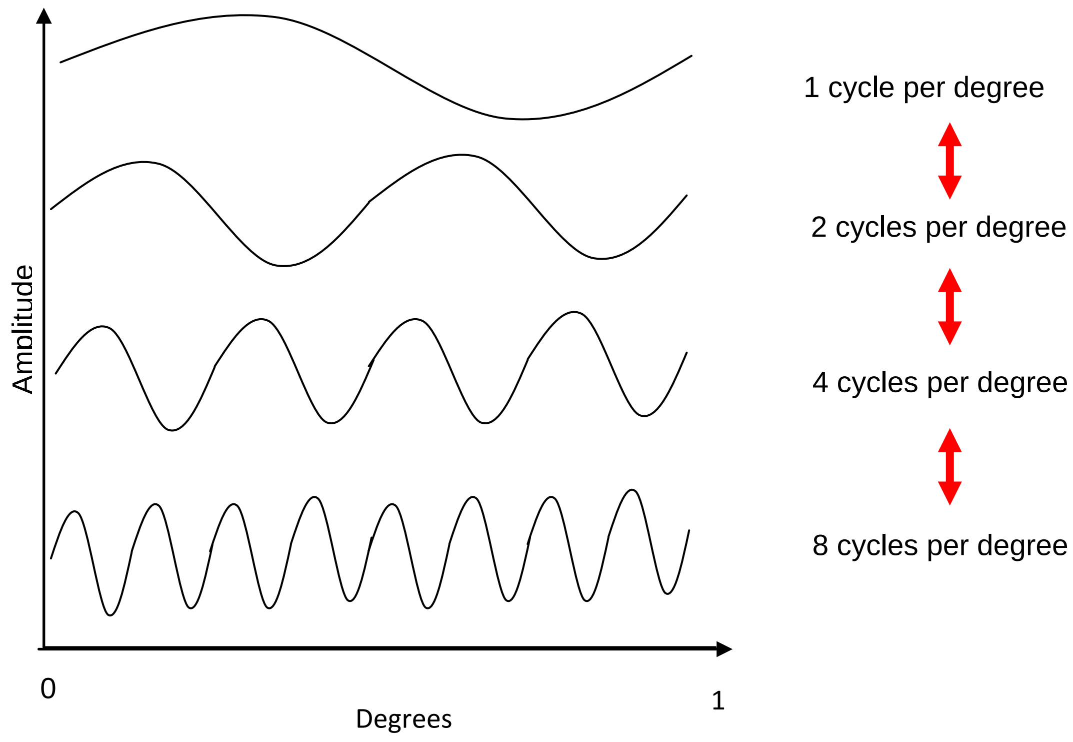

Figure 2.1 Spatial frequency is measured in cycles per degree but can be described in octaves. Red arrows denote 1 octave

If a band-pass filter was designed with a peak spatial frequency of 4cdeg^{-1} and a bandwidth of 2 octaves, the bandwidth boundaries would be between 2 and 8cdeg^{-1}. If the peak spatial frequency was 4cdeg^{-1} and 1 octave in width (0.5 octaves either side) the bandwidth boundaries would be between 2.82 and 5.66cdeg^{-1}. This was calculated using equation 2.7. As N20 text is double the size of N10 text, if we wanted the two text sizes to appear the same after band-pass filtering we would have to double the bandwidths (1-4cdeg^{-1} for the N20 and 2-8cdeg^{-1} for N10).

Equation 2.7

Lower bandwidth boundary = $SFP / 2^{b}$
Upper bandwidth boundary = $SFP \times 2^{b}$

The boundaries of band-pass filters can be calculated in octaves using the equations where *SFP* is the peak spatial frequency and *b* is half the bandwidth required in octaves.

If the main limb width of a letter is considered to provide the text peak spatial frequency then the spatial frequency for text at different viewing distances can be calculated. The N10 Times Roman text has an ‘x’ height of 1.875mm. The limb width is 1/5th of the text height (0.375mm). One cycle (1 dark bar and 1 light bar) would be 0.75mm. One cycle placed at 40cm equates to 9.31cdeg^{-1}. For an N20 letter at 40cm the spatial frequency would be half of this at 4.65cdeg^{-1}.

2.4.2 Target size

Two text sizes; N10 a standard book print and a larger N20 size were examined. The same band-pass filter would cause the two text sizes to appear differently (Figure 2.4).

If we consider a large DOF extending 1D either side of the start point the N10 text target will subtend 4.3° vertically at the eye and ranging from 2.1° to 4.9° from the distal to proximal edge. The N20 text target will start at 40cm subtending 7.0° vertically at the eye ranging from 4.2° to 9.7° from the distal to the proximal edge.

2.4.3 Target luminance

Refraction measurements taken with the PlusOptix PRII relied on a minimum pupil diameter of 4mm. Therefore, ambient illumination was reduced to maximise pupil size, and kept constant between trials and observers. Target illumination was maintained with a direct additional light source fitted to the motorised track which moved with the target. Target illumination was maintained at between 70 and 110 lux for all subjects and monitored using a Professional digital light metre (CEM).

2.4.4 Target contrast

Few studies using spatially band-pass filtered targets comment on contrast correction. The targets in the current study were filtered for spatial frequencies using a MATLAB program and as they were filtered contrast was affected. Boden and Giaschi (2009) also used a MATLAB program to produce spatial frequency filtered text targets to investigate the effects on letter recognition. This was one of the few studies which commented on contrast control of the targets and stated that they had adjusted the grey-scale of their filtered targets to the same Michelson contrast. Contrast correction (Michelson contrast) using MATLAB was applied to ensure all filtered targets had the same Michelson contrast. Michelson contrast can be calculated from equation 2.8.

Equation 2.8

$$(L_{max} - L_{min}) / (L_{max} + L_{min})$$

where Lmax is the maximum luminance and Lmin in the minimum luminance

The contrast correction ensured the difference between the lightest and darkest pixels were the same for all band-pass filters applied, so that the Michelson contrast remained unchanged. This did result in certain targets appearing to have a grey background (Figure 2.4).

2.4.5 Target production

Text targets were designed with words taken from standard MNREAD near acuity charts (Figure 2.2). The targets were created using a standard image manipulation application (GIMP 2.6). The N10 and N20 Times Roman text in this experiment were band-pass filtered for different spatial frequencies and contrast corrected using MATLAB. The working distance for the experimental set up was 40cm, a realistic working distance.

nowhere pain kept advance
enjoyed pond mess occurrence
candles productive lost tonight
leading poor distribute chickens
bolt copy resistance crystal
characters filling sold evening
wire accordance mood

Figure 2.2 Representation of the final target before band-pass filters applied

The spatial frequency filtering program for MATLAB was used (written by Paul van Diepen, University of Leuven, Belgium) and relied on knowledge of the pixels per degree of the image to be filtered. This was therefore set up for a 300DPI (dots per inch) image for the N20 targets and 600DPI image for the N10 targets in order that the text contained the same number of pixels per letter (Table 2.2). This value was chosen due to printer capabilities and because for the Badal lens set up target sizes would need to be halved and therefore DPI of the resultant images doubled.

Table 2.2 Parameters of each target size

Target Parameters	N10	N20
Letter height (mm)	1.875	3.750
Limb width (mm)	0.375	0.750
Angle subtended at the eye when at 40cm(degrees)	0.269	0.537
Height of letter in pixels	44.5	44.5
A4 page size (mm)	297 x 210	297 x 210
Dot per inch (DPI)	600	300
A4 page dots size	7020 x 4980	3510 x 2490
Dots per mm	23.64 x 23.71	11.82 x 11.86
Pixels per degree	191.84 x 179.79	95.92 x 89.90
Potential highest spatial frequency ($cdeg^{-1}$)	92.91	46.46
Letter main spatial frequency ($cdeg^{-1}$)	9.31	4.65

Initial bandwidths were based around the peak spatial frequencies of the human CSF (4-6$cdeg^{-1}$). Targets were designed with the first bandwidth set at 3-8$cdeg^{-1}$ to encompass spatial frequencies thought to elicit the most accurate accommodation responses. The low-pass spatial frequency band was set at 0.01-3$cdeg^{-1}$ and the higher spatial frequency content information at 8-12$cdeg^{-1}$ and 12-16$cdeg^{-1}$. Although the band-pass filters for even higher spatial frequency information were created, they were unreadable and therefore thought to offer little benefit to this study. These targets were used in a pilot experiment (section 6.2) but later refined.

A filter order applied to the band-pass filter made a significant difference to the appearance of the target. The order is a reference of the ‘sharpness’ of the edges of the band-pass filter. An order of zero would allow no overlap of the band-pass filters but would mean the resulting targets were illegible. Although an arbitrary figure, the order of 30 was applied, and did not alter the peak spatial frequency of the band-pass filter.

It was then decided that the limb width of the N10 and N20 text would be used to calculate the peak text spatial frequency. This spatial frequency formed the peak of the first bandwidth filter. The edges of this band-pass filter could then be calculated depending on the desired width (in octaves) using equation 2.7. A one octave bandwidth was designed (half an octave either side of the peak text spatial frequency). A narrow bandwidth was preferable when considering the previously reported 1 to 1.5 bandwidth of cortical neurons. For the peak spatial frequency of an N10 letter of 9.31cdeg^{-1} a 1 octave width band-pass filter was between 6.58-13.15cdeg^{-1} (Table 2.3). For a peak spatial frequency of N20 letters of 4.65cdeg^{-1} a 1 octave width band-pass filter was between 3.29-6.58cdeg^{-1}. Lower and higher band-pass filters were then calculated with the same one octave bandwidths at 1.65-3.29cdeg^{-1}, 13.15-26.33cdeg^{-1}, 26.33-52.66cdeg^{-1} and 52.66-105cdeg^{-1}. The band-pass filters applied to the text are shown in Table 2.3 and represented in Figure 2.3.

Table 2.3 Target codes and the bandwidths included. ()*denotes targets designed but excluded from the study. The labels were given to each spatial frequency band in order to aid randomised target selection

Target	N10 – spatial frequency bands (cdeg^{-1})	Peak spatial frequency of band (cdeg^{-1})	Target	N20 – spatial frequency bands (cdeg^{-1})	Peak spatial frequency of band (cdeg^{-1})
A	Unfiltered	**9.31**	**G**	Unfiltered	**4.65**
B	3.29-6.58	**4.65**	**H**	1.65-3.29	**2.33**
C	6.58-13.15	**9.31**	**I**	3.29-6.58	**4.65**
D	13.15-26.33	**18.62**	**J**	6.58-13.15	**9.31**
E	26.33-52.66	**37.23**	**K**	13.15-26.33	**18.62**
(F)*	*52.66-105.00*		**(L)***	26.33-52.66	

For the N20 300DPI image at 40cm, the highest spatial frequency content available can be grossly calculated to be 41cdeg^{-1}, and for the N10 600DPI image at 40cm; 82cdeg^{-1}. This was based on the definition that one dark spot and one white spot would produce 1 cycle. This meant it was impossible to create the N20 text target filtered with the highest two band-pass filters and the N10 target with the highest band-pass filter as the limits of resolution of the image did not extend to the upper boundary of the band-pass filter.

The lowest 2.33 cdeg^{-1} filter for the N10 text target appeared no different to the band adjacent to it. This was due to the slight overlap in the bands and the small number of cycles and therefore was excluded from the N10 range. Final targets are shown in Figure 2.4.

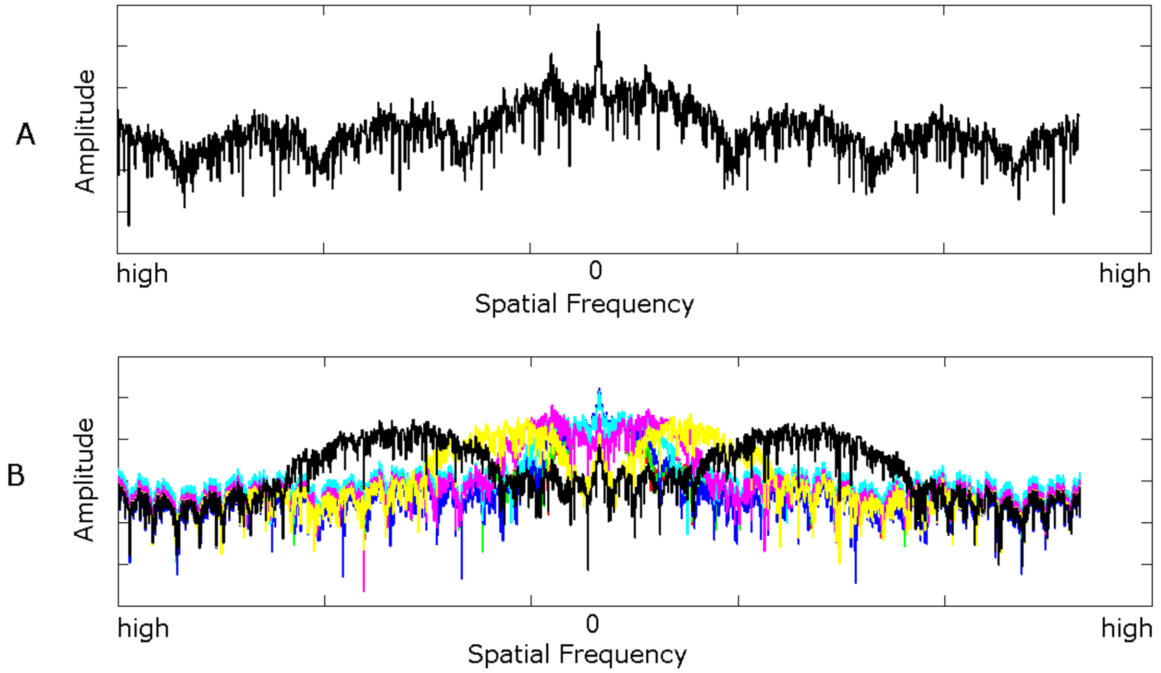

Figure 2.3 The Fourier Amplitude Spectra

A: Unfiltered text B: Band-pass filters

This represents the band-pass filters applied to the N10 targets. The colours denoted different band pass filters applied; turquoise 4.65cdeg^{-1}, pink 9.31cdeg^{-1}, yellow 18.62cdeg^{-1} and black filter 37.23cdeg^{-1}

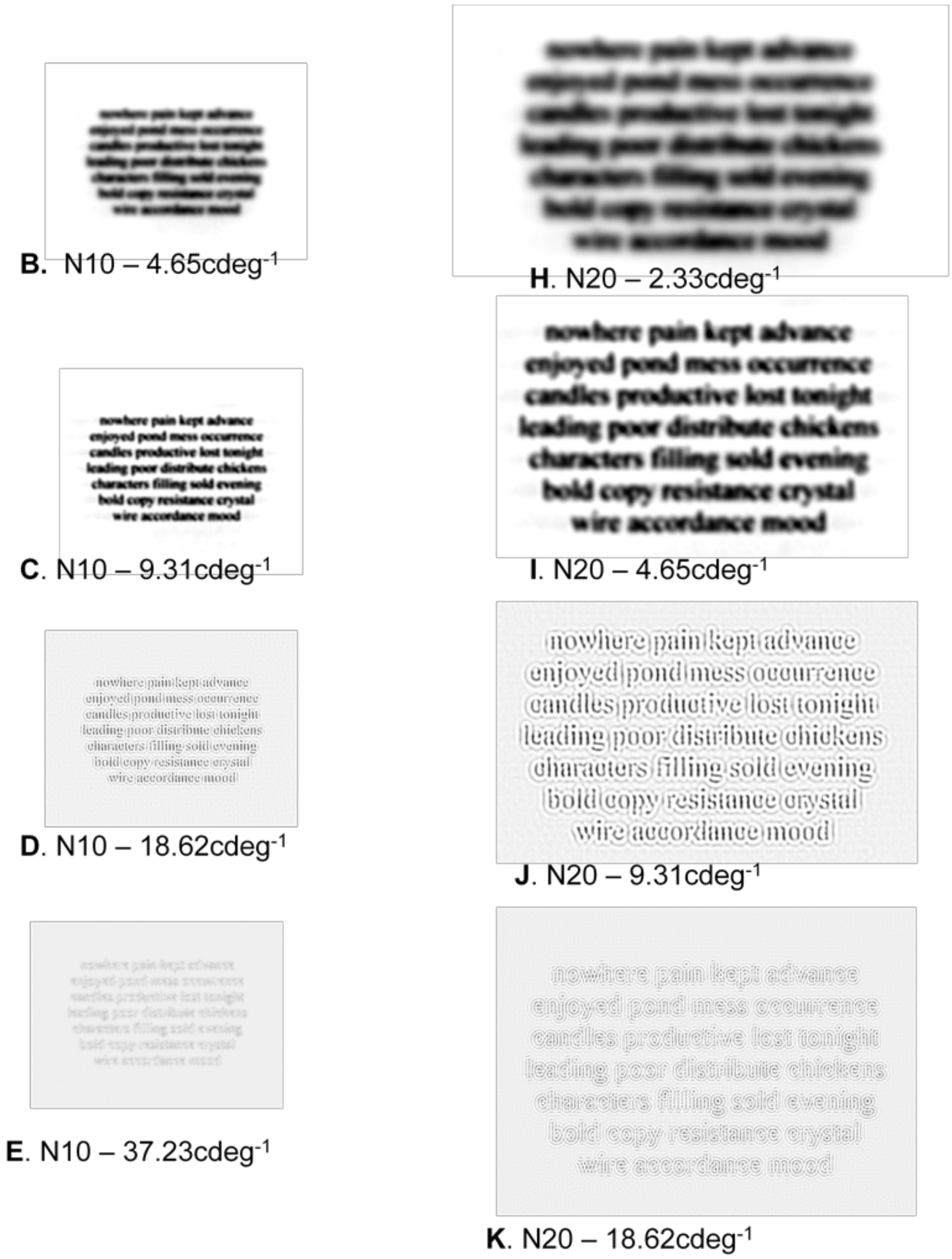

Figure 2.4 Final targets used in the study

The targets were printed on high quality paper using a printer which met the DPI requirements.

2.5 – Subjective depth of focus

Subjective DOF can be defined as the range in target vergence which can be tolerated without incurring blur. The current study aimed to consider the subjective DOF with different spatial frequency filtered text targets in different refractive groups to establish which spatial frequencies influence perceptual judgements on blur.

2.5.1 Instrumentation

A 5D Badal optometer was placed at its focal distance of 20cm from the right eye of the subject. The target was positioned 20cm beyond this and the centre of the target was aligned with the centre of the lens. Cycloplegia eliminated accommodation and a 6mm artificial pupil was placed in a trial frame in front of the right eye whilst the left eye was occluded. A motorised track moving at 2.1cms^{-1} maintained the speed of target movement between subjects (Figure 2.5). With this Badal lens system displacement of the target by 1mm corresponded to 0.025D change in target vergence.

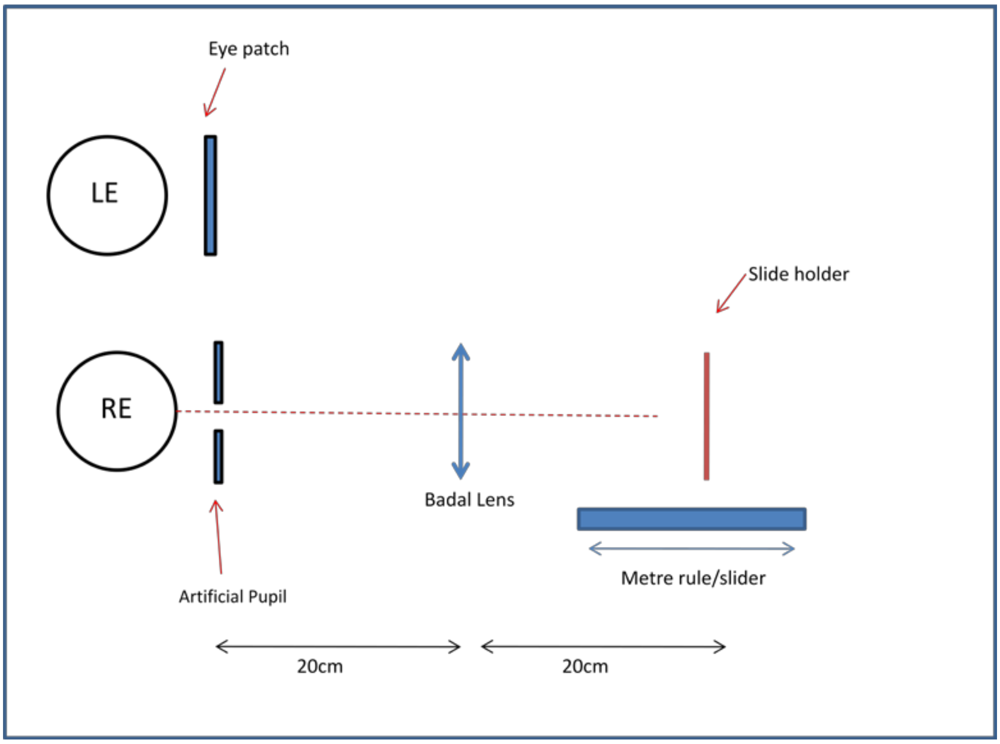

Figure 2.5 Diagram of the apparatus used to measure the subjective DOF. RE and LE denote the right and left eyes

The ‘x’ height of an N10 Times Roman lower case letter is known to be 1.875mm. The image subtended an angle of 0.269° at the eye in the open view system (Figure 2.6). The Badal system magnification was then considered. For target size to be maintained using the Badal system, the text needed to have an ‘x’ height of 0.9375mm (Figure 2.7). This is half the size of the ‘x’ height used in the open view system and equates to the Badal system providing 2X magnification.

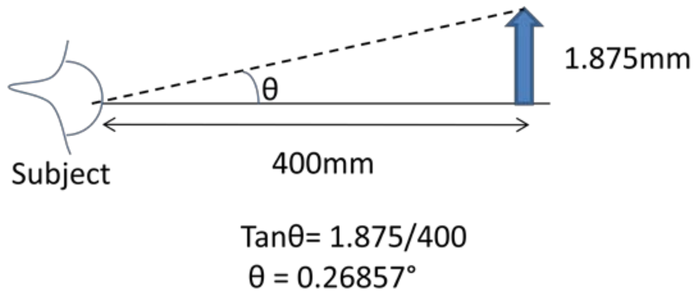

Figure 2.6 The angle of an image subtended at the eye

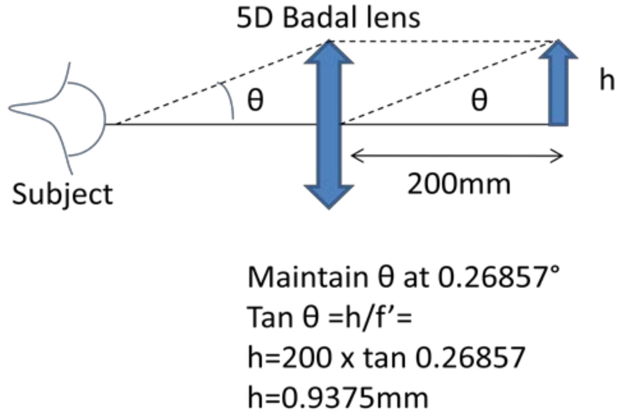

Figure 2.7 Badal magnification in this experimental set up

2.5.2 Methods

Subjective DOF measurements required the use of cyclopentolate 1%, instilled two times at five minute intervals and cycloplegic refraction checked 30 minutes after drop instillation. Cycloplegia was also verified using the dynamic mode on the PRII and getting subjects to alter their attention between near and distance targets, ensuring no change in refraction.

The target was positioned in line with the subject's right eye and Badal lens and moved proximally on the motorised track which moved at 2.1cms^{-1}. The subjects were given a handheld button which controlled the movement of the motorised track and were instructed to depress the button when they first noticed blur of the target. The distance at which the target stopped was recorded. This proximal movement was repeated so that the subject could also report the 'first point at which the target became unreadable'. This was repeated three times each for the proximal and distal measurements. The targets were presented in a random order using a random number table.

2.5.3 Data analysis

The average dioptric value of three proximal and distal readings for each target were calculated and added to give the total DOF. Data analysis for all experiments was conducted using SPSS. Normality of the data was investigated using Kolmogorov-Smirnov test.

The effects of refractive group, target size and spatial frequency content of the target on objective and subjective DOF, accommodative microfluctuations and dynamic accommodation was assessed using one-way ANOVA and repeated measures ANOVA. Z-scores calculated using SPSS (equation 2.10) were used to identify outliers in the data. Z-scores express scores in terms of a distribution with a mean of 0 and a standard deviation of 1. In a normal distribution it might be expected that 5% of the data had z-scores greater than 1.96, 1% to be greater than 2.58 and none to be greater than 3.29. Where z-scores are greater than 3.29 this identifies outliers in the data and one way of dealing with these outliers is to replace the outlier with the mean plus 3 times the standard deviation.

Equation 2.10

$$z = \frac{X - \bar{X}}{sd}$$

where z is the z-score, X is the value in the data set, $\bar{X}$ is the mean and sd is the standard deviation

Repeatability

Subjective DOF measurements from ten subjects were repeated for an unfiltered N10 text target. Paired sample t-tests revealed no significant difference between the first and second recordings of subjective DOF, either just noticeable [$t(9)=1.06$, $p=0.32$] or non resolvable DOF [$t(9)=1.22$, $p=0.26$].

2.6 Dynamic accommodation

2.6.1 Instrumentation

Accommodation dynamics were measured in free space by monitoring accommodation continuously using the Plusoptix Power Refractor PRII (Plusoptix, Germany). The PRII uses infra-red eccentric photorefraction. It allows dynamic measurements of refraction, monocularly or binocularly, whilst simultaneously measuring pupil diameter, and gaze direction, with a refractive test range of +5D to -7D. Its validity compared with subjective refraction has been previously confirmed by Jainta, Jaschinski and Hoormann (2004). The PRII is pre-calibrated at the factory. Although calibration of the PRII for individual subjects is not possible, no significant difference was found between the PRII measurement of refraction and subjective refraction [paired sample t-test: $t(26)=-0.98$ $p=0.34$] and an average difference of -0.04D±0.87 was found between the two measurements. Dynamic measurements were taken every 40ms (12.5Hz) and it has a dioptric resolution of 0.12D. The PRII used in this study also included licence R (PlusOptix, Germany) which allowed the export of dynamic measurements to an excel file.

2.6.2 Methods

Dynamic accommodation measurements were taken by placing the near target at 40cm and a far target at 2m. Refractive error was corrected in the trial frame for the right eye. The near target was aligned slightly nasal to the right eye and the left eye was fully occluded. The PRII was positioned at 1m from the subject's right eye. A stop watch and the PRII recording were started simultaneously, whilst the subject viewed the distance target. At 10s intervals the subject was instructed to look to the near target when requested and then to look at the far target when requested. The recording was stopped after 70s to allow three far to near (positive) accommodation changes and three near to far (negative) recordings.

2.6.3 Data cleaning

A designed MATLAB program (Mathworks, Inc., Nantick, MA) analysed the columns for Time (ms), Pupil size (mm) and Refraction (D). The PRII inserted a value of '-100' into the refraction column where no valid data was captured, which could result from a loss of recording due to blink or a reflection caught from the light source or from the trial frame. These readings needed to be removed. If a blink is assumed to be 250ms (Doane, 1980), then in the PRII recording this would account for approximately 6-7 consecutive readings. Therefore a program was written which identified gaps of three or more consecutive readings and eliminated one reading before and two readings after the gap. Solitary gaps in the data where '-100' had been inserted were deleted but left as gaps.

Time [ms]	Pupil(mm)	Refraction(D)
13920	5.163002	-0.995095
13960	5.38748	-1.094898
14000	5.163002	-0.9334
14040	5.163002	-1.011649
14080	5.498574	-1.026499
14120	5.382802	-1.083029
14160	0	-100
14200	0	-100
14240	0	-100
14280	0	-100
14320	0	-100
14360	5.274047	-1.206483
14400	5.274047	-1.249591
14440	5.274047	-1.398212
14480	5.38748	-1.32276
14520	5.498574	-1.344344
14560	5.498574	-1.363847
14600	5.498574	-1.487422
14640	5.274047	-1.14185
14680	5.274047	-1.078983

Figure 2.8 Part of excel file showing a possible blink where numerical values of '-100' have been applied to missing data (circled in red)

Measurements of the velocity of accommodation vary from 3.7Ds^{-1} to 10Ds^{-1} (Campbell and Westheimer, 1960; Schor, 1999; Heron, Charman and Schor, 2001). Assuming a maximum velocity change of 10Ds^{-1} then the maximum possible change in 40ms (each consecutive PRII reading) would be 0.40D. Therefore differences between two consecutive readings more than 0.40D were removed. Cufflin and Mallen (2008) recorded accommodation dynamically using the Shin Nippon SRW 5000 autorefractor. As microfluctuations are believed to be present up to 5Hz, they applied a smoothing function to their data to remove frequencies of more than 6Hz. The current study applied a smoothing function within the MATLAB program with a sliding window of five data points to remove sampling errors.

Summary of steps in the MATLAB cleaning program (Figure 2.9):

1. Data sorted into columns and those of interest identified (time, refraction, pupil size and gaze deviation)
2. Removed all '-100' values from the refraction columns
3. Where more than 3 consecutive '-100' values, considered a blink and removed 1 reading preceding the gap and 2 readings after
4. Removed any outliers from refraction column where the pupil size was beyond the normal recording (>8mm or <4mm)
5. Where there was a difference between 2 consecutive points of more than 0.40D these were removed and a line drawn on the graph to fill the gaps
6. Sliding window (5 data points) applied to the refraction data to minimise sampling errors
7. Cleaned reading plotted with time along the x-axis and refraction along the y-axis

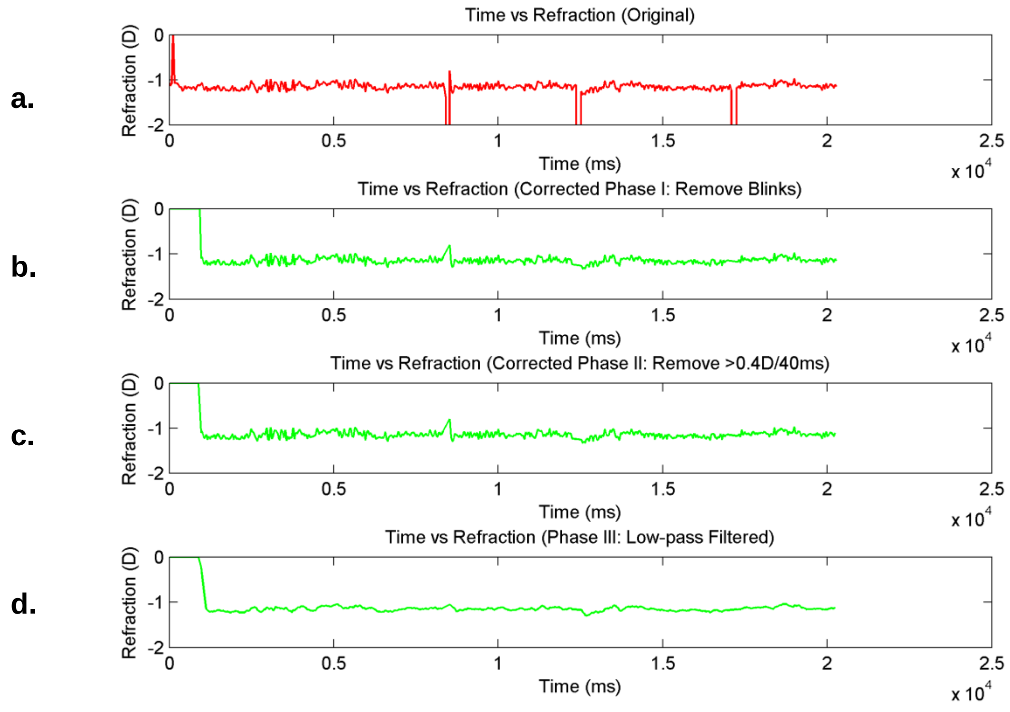

Figure 2.9 A MATLAB representation of the steps taken in the data cleaning program.
a. shows a plot of original data where straight lines show where missing data occurs (assigned values of '-100')
b. shows the data following the removal of missing data
c. shows the data following removal of erroneous data
d. shows the data following the application of a smoothing function

2.6.4 Data analysis

The data file was a 70 second recording consisting of three positive (far to near) changes and three negative (near to far) changes in accommodation. The MATLAB program initially indentified the six 10s segments of interest. Analysis was then conducted on each segment individually.

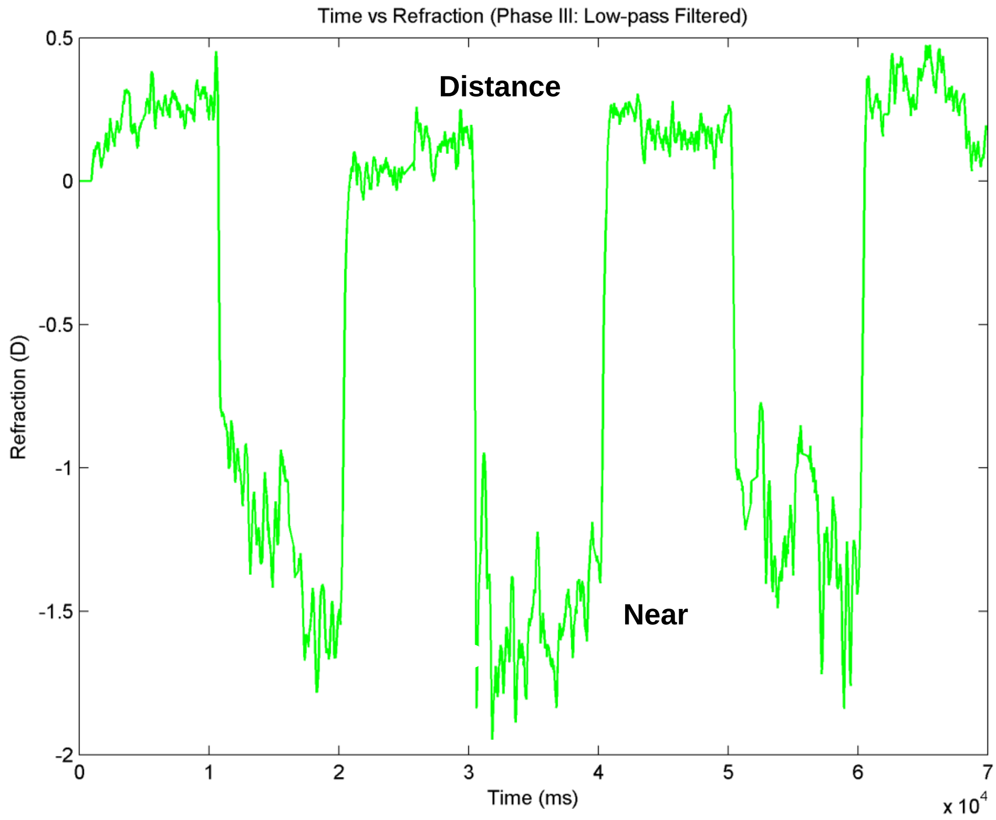

Figure 2.10 MATLAB plot of a dynamic recording with three positive and three negative accommodation changes

Previous studies have highlighted the difficulties in determining the start of an accommodative response (Tucker and Charman, 1979; Heron and Winn, 1989). Cufflin and Mallen (2008) used a modified version of an algorithm used by Kasthurirangan, Vilupuru and Glasser (2003) to identify the start and end points of accommodation response changes. They defined the start of an accommodative response as the point where three preceding samples showed no systematic accommodation increase followed by five data samples all exhibiting consecutive increases. This method was initially used for our data analysis, however as much of the plot seemed to consist of a ‘dog tooth’ appearance this algorithm did not pick the most accurate sample for the start of the accommodation change.

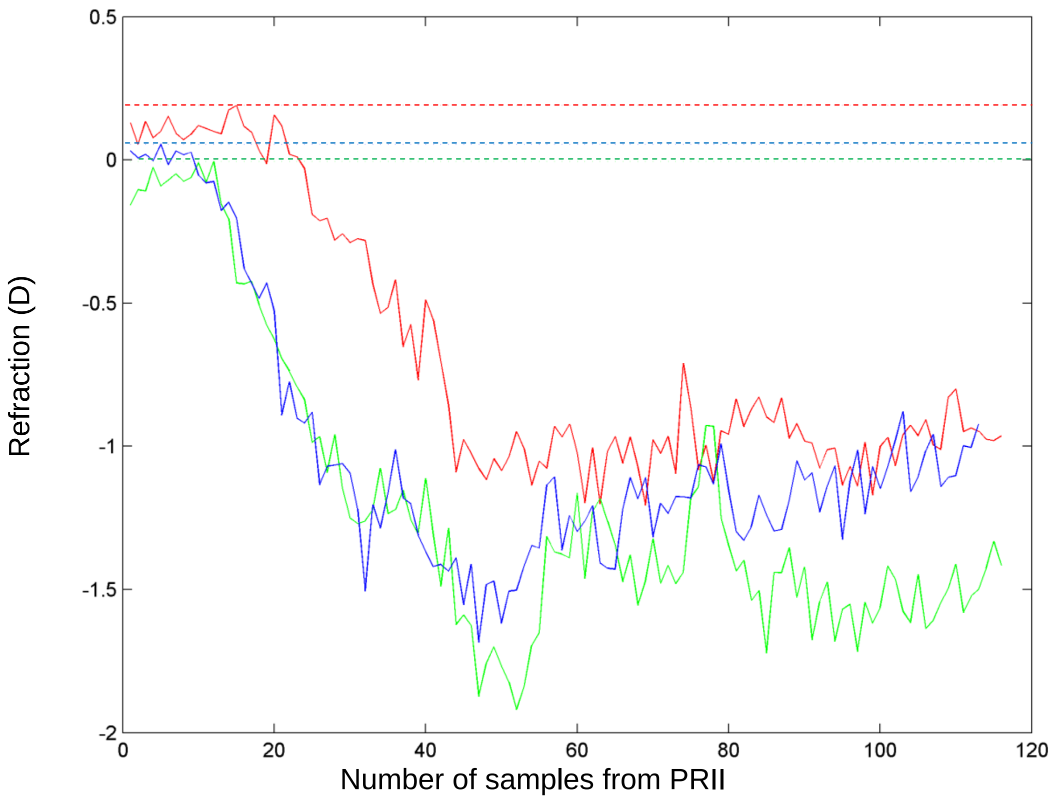

Figure 2.11 An example of three positive dynamic accommodation plots of one subject showing a 'dogtooth' appearance of accommodation change. This would make a protocol requiring 5 consecutive increases in accommodation to define the point of accommodation change difficult. Dotted lines show the point of accommodation change from the protocol used in the current study. '0' on the x-axis denotes the point at which the target vergence changed

For this reason an algorithm identifying the initial point of accommodative change and end of accommodation change was defined (Figure 2.12). The time lapse between the beginning of the 10s segment (change in target vergence) and the point of accommodation change was taken as the accommodative latency. The time between the beginning and end of the defined accommodation change was taken as the accommodation response time (RT).

Figure 2.13 shows the application of the algorithm to a response from one subject. An average of the three positive and three negative accommodative latencies and RTs were calculated along with the standard deviation of the three values.

Data analysis was conducted as before (section 2.5.3).

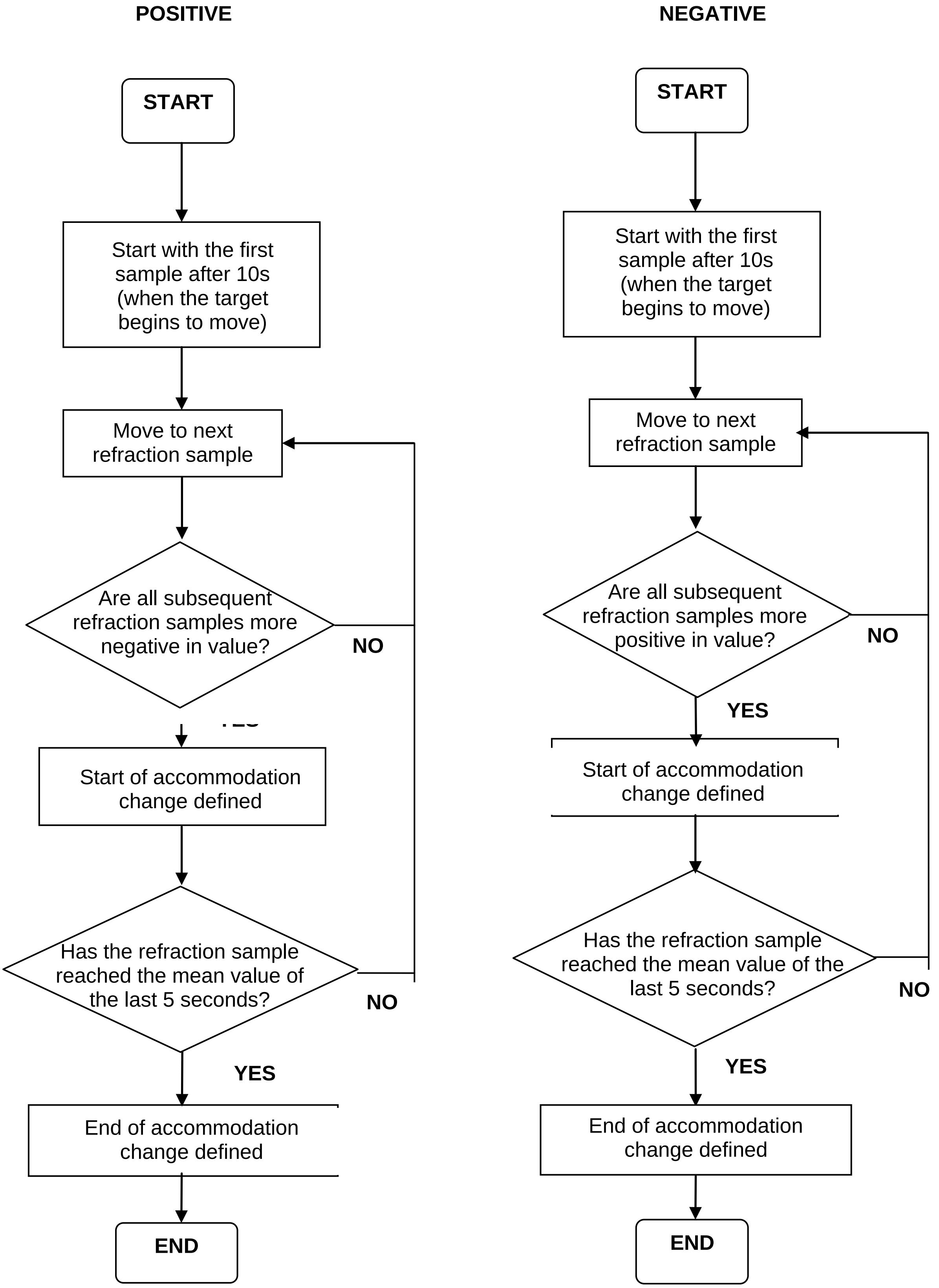

Figure 2.12 Algorithm used to identify the start and end of accommodation response in order to calculate latency and RT

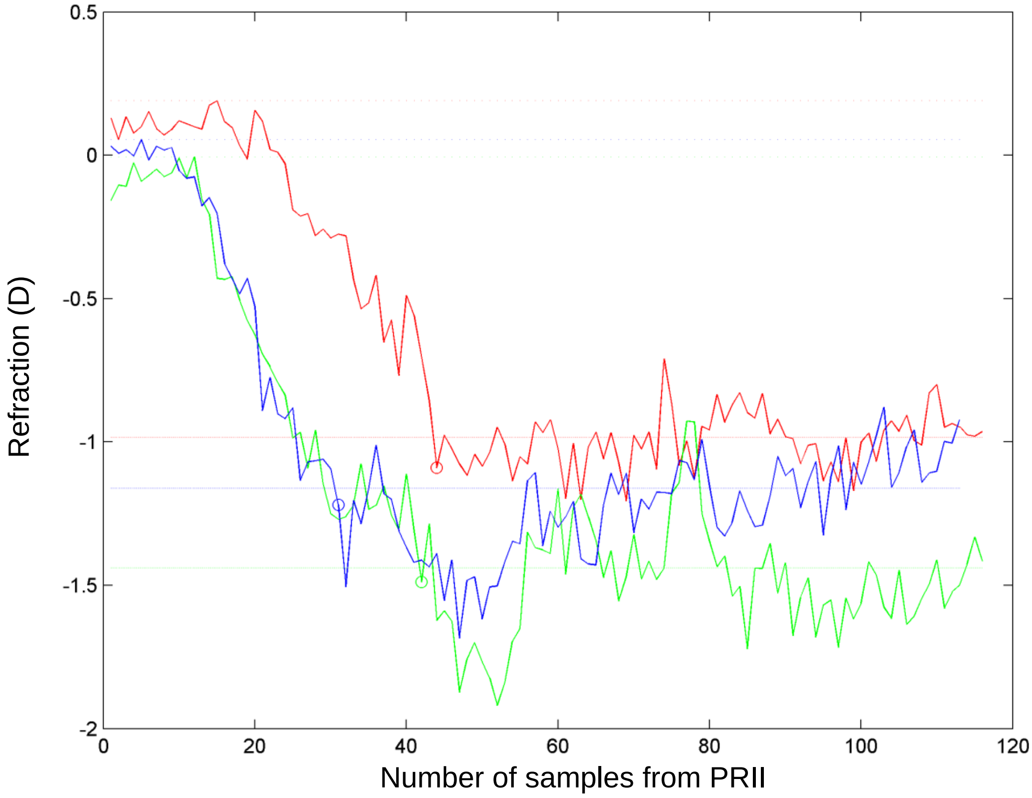

Figure 2.13 Positive accommodation plots for one subject with the end point of accommodation (circled) defined from the protocol used in the current study. Solid lines show the average accommodation level for the last 5s of the 10s segment

2.7 Objective depth of focus and accommodative microfluctuations

2.7.1 Instrumentation

The current study aimed to investigate objective DOF with different spatial frequency filtered targets using an open view, free space system for more naturalistic viewing conditions allowing proximal and blur cues.

Objective DOF was measured by sampling accommodation continuously using the PRII as described above (section 2.6.1). The edge of the objective DOF was defined as the point at which a significant stable accommodation change was made in response to changing target vergence.

The targets, described in section 2.4, were displaced on a motorised track at a constant speed of 2.1cms^{-1}.

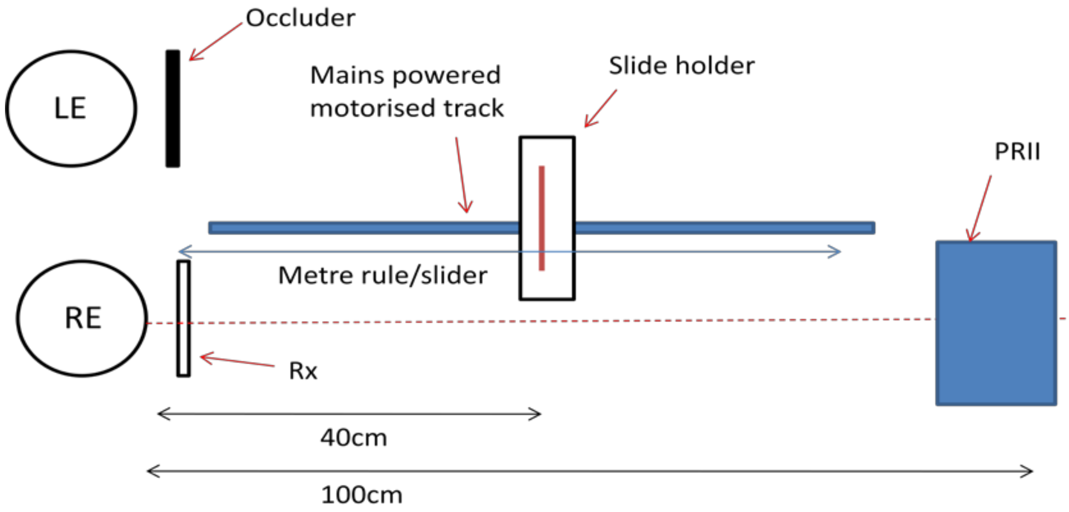

Figure 2.14 Diagram of the apparatus used to measure the objective DOF

2.7.2 Methods

A trial of the objective DOF set up took measurements from the right eye of subjects through an infrared filter whilst the left eye fixated the target to allow the right eye to be recorded in the absence of trial lenses. However the filter made measurements difficult and the PRII limits on the maximum refraction (+5 to -7DS) meant that with accommodative effort, it was necessary to leave the trial lenses in place.

The new experimental set up recorded the right eye directly using the PRII, with the left eye occluded. The ten targets were presented in a randomised order (using a random number table). A stop watch and the PRII recording were started together and a measurement of accommodation whilst the subject viewed the static target at 40cm was taken for a period of 10 seconds. After 10s the motorised track was started and as the motor displaced the target at 2.1cms^{-1}, the linear and dioptric DOF could be calculated. The subject was asked to maintain target clarity. Four proximal recordings were taken before four distal recordings. Multiple readings were taken due to the difficulty in obtaining complete recordings without blink so that as many complete readings could be analysed and averaged.

Assessment of microfluctuations used a 60s continuous recording, taken whilst the subject viewed the ten static targets at 40cm. The subject was asked to direct their attention to the near target only and maintain target clarity.

2.7.3 Data Analysis

The objective DOF data was cleaned using the MATLAB program as described in section 2.6.3.

Previous assessments of DOF have simplified the identification of accommodative change which denotes the edge of the DOF. Vasudevan, Ciuffreda and Wang (2006b) applied the rule that the accommodative response change needed to be in the correct direction and a change of at least 0.25D for at least 2s. Their protocol was used to analyse data from the current study but it was found to simplify the accommodative response. Accommodative microfluctuations can affect the start point of accommodation change as this can occur at any point along the sinusoidal wave of a microfluctuation. The accommodation level may take much longer to reach the protocol criteria of a stable 0.25DS change if it begins at a microfluctuation trough. The accommodation change was identified using a MATLAB program designed to apply the following algorithm:

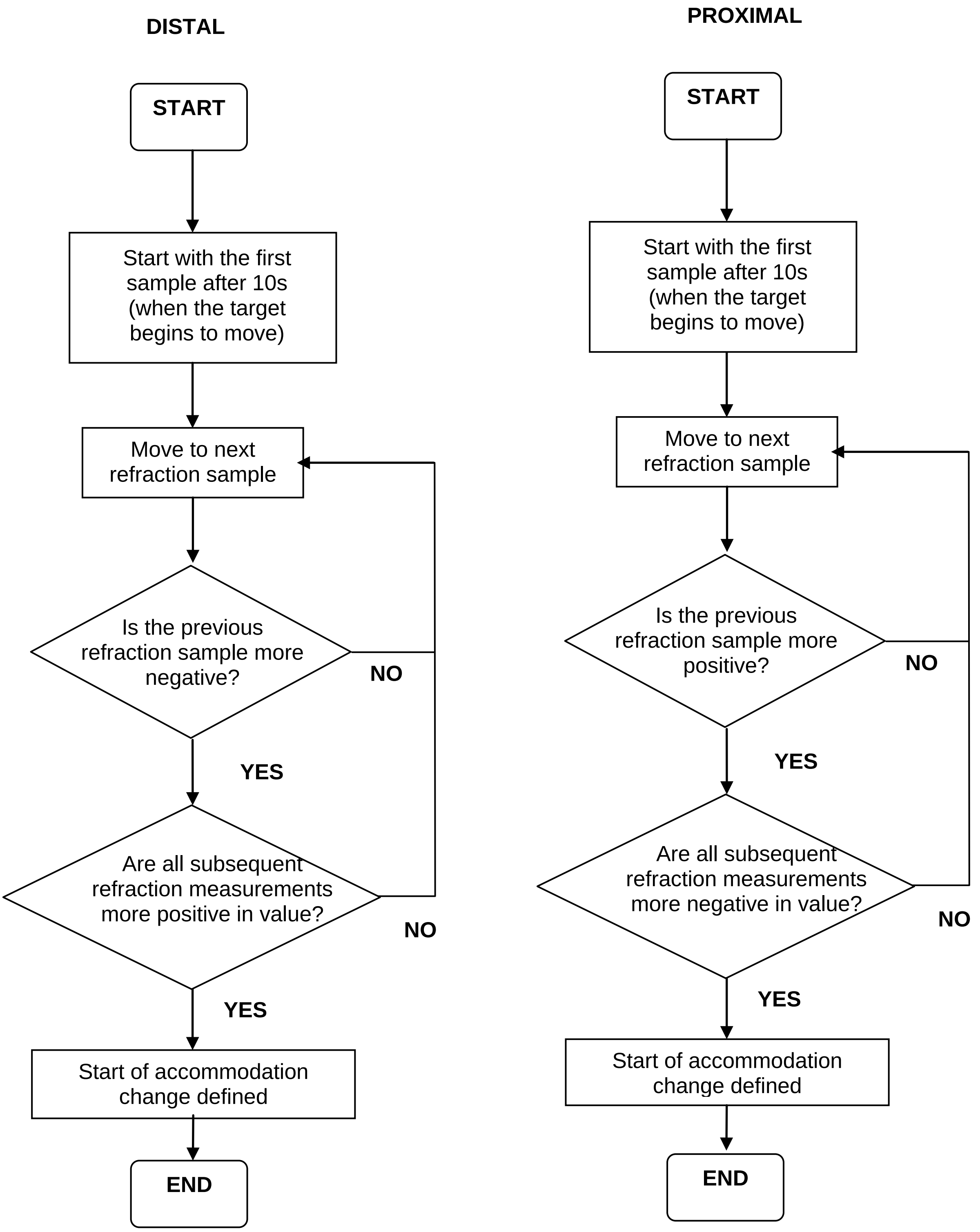

Figure 2.15 Algorithm demonstrating the method used to determine the point of accommodation change

Once the points of accommodation change were defined for each plot, the three proximal and three distal recordings were averaged. This was then converted to the dioptric point of change. The proximal and distal DOF values were calculated and the sum of these gave the total DOF. An example of a distal plot is shown in Figure 2.16.

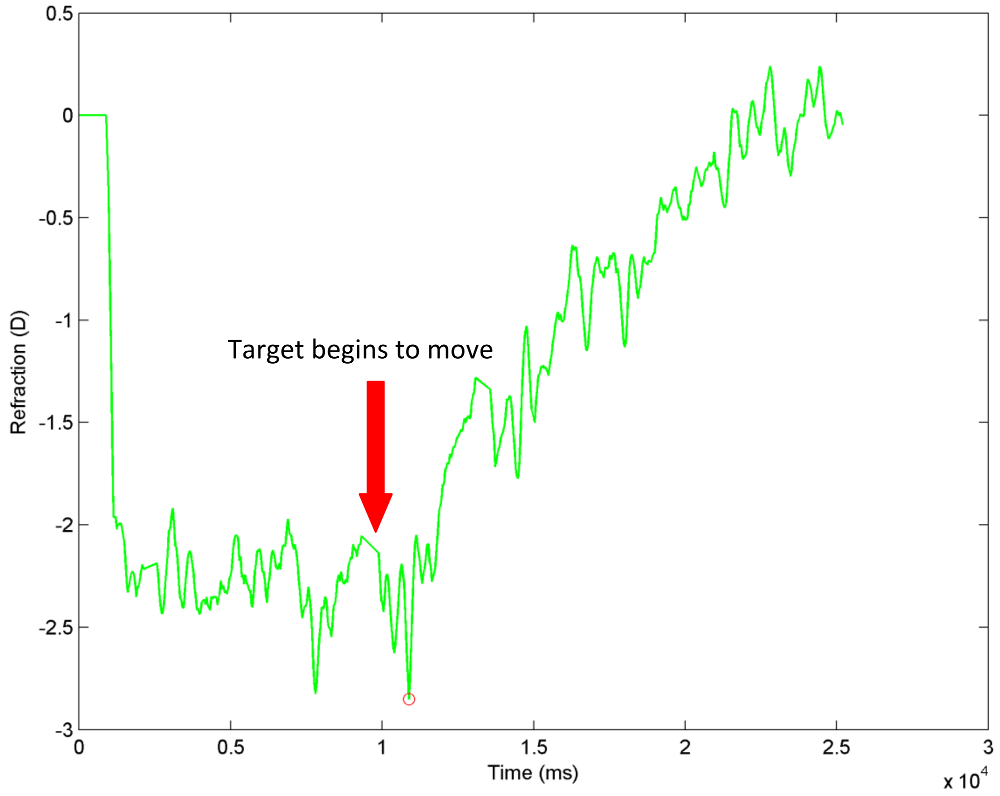

Figure 2.16 A MATLAB distal accommodation plot (target moved from 40cm distally) after data cleaning has taken place. The PRII recording was started at 0ms. The target began to move at 10s and the point of accommodation change is circled in red

Accommodative microfluctuations were analysed using a MATLAB program written for this purpose. Data cleaning was applied similarly to other PRII recorded data (section 2.6.3) with a few modifications:

1. Data after 60s was removed
2. The first 1s of data was removed
3. Removed bad pupil sizes and blinks as previously
4. Bad samples were replaced with a random sample (taken from acceptable samples)
5. Adjacent samples with a change of >0.4D/s were removed as previously

6. A second correction was made where bad samples were replaced by random samples

7. No smoothing function was applied to microfluctuation data

Day *et al.* (2006) interpolated areas of missing data which adds low spatial frequencies to the recording and removes high spatial frequencies. The current study added random samples taken from acceptable samples within the recording which avoids the limitations of altering spatial frequency content as occurs in the protocol applied by Day *et al.* (2006).

The MATLAB program then plotted the power spectrum analysis (fast Fourier transform) and calculated the RMS of the whole data sample. The power in each low (0-0.6Hz), medium (0.6-0.9Hz) and high frequency (1.0-2.0Hz) segment were calculated as done by other studies (Kotulak and Schor, 1986b; Charman and Heron, 1988; Winn *et al.*, 1990b; Day *et al.*, 2006)

Data analysis was conducted as before (section 2.5.3).

2.7.4 Repeatability

Objective DOF measurements were repeated for ten subjects whilst viewing the unfiltered N10 text target. Paired sample t-tests revealed no significant differences between the results for proximal [$t(9)=0.03$, $p=0.98$], distal [$t(9)=1.04$, $p=0.34$] or total objective DOF [$t(9)=1.61$, $p=0.15$].

2.8 Higher order aberrations

2.8.1 Instrumentation

The COAS-HD (Complete Ophthalmic Analysis System; Wavefront Sciences) is based on Shack-Hartmann wavefront sensing technology and provides data to 10th order aberrations. The COAS uses a number of lenslets that sample the wavefront in the pupil at 210μm intervals allowing 600 sample points within a 6mm pupil. Refractive error can be measured between -15D and +7D with a resolution of 0.01D and pupil size to 0.1mm. Salmon *et al.* (2003) found the accuracy and repeatability of this instrument to be similar to the Nidek ARK-2000 autorefractor with and without the use of cycloplegia. Baskaran *et al.* (2010) found the COAS aberrometer to be repeatable in young emmetropes.

2.8.2 Methods

Three aberrometry measurements were taken undilated from each subject's right eye with the left eye observing a near target placed at 40cm, to assess aberrations whilst accommodating. The subject's full subjective refractive correction and appropriate base out prism were placed in front of the left eye to align the visual axis of the right eye with the internal target. The target was a paragraph of N10 Times Roman text mounted within the illumination plane of a torch placed as close to the head of the COAS aberrometer as possible and placed at left eye height.

Three aberrometry measurements were also taken with dilated pupils for comparison with the subjective DOF data. A 6mm analysis diameter was applied before aberration values were exported.

2.8.3 Data analysis

Zernike coefficients were used to describe the wavefront errors (Table 1.2). Data up to the fourth order terms were exported to Excel for analysis. Average values for each higher order term as well as the RMS value of the third and fourth order terms were calculated. SPSS was used to investigate correlations between DOF and higher order aberrations.

Chapter 3: Experiment 1 Peripheral Refraction in different refractive groups

3.1 Introduction

Hyperopic retinal blur is thought to stimulate ocular elongation and myopia progression. Animal studies have found that hyperopic blur in the peripheral retina can also stimulate myopia (section 1.4.1: Wallman *et al.*, 1987; Schmid and Wildsoet, 1997; Smith *et al.*, 2010). Early studies suggested a link between peripheral refraction and myopia development in humans (Hoogerheide, Rempt and Hoogenboom, 1971; Rempt, Hoogerheide and Hoogenboom, 1971). Mutti *et al.* (2011) modified conclusions from their previous studies (section 1.4.4) reporting that peripheral refractive error was not a significant risk factor for myopia development. However, a limitation of this study was that only one peripheral retinal location was measured (30 degrees in the nasal visual field) and also that myopia onset was defined at -0.75D and a lower value may have given a more accurate picture.

Charman and Radhakrishnan (2010) demonstrated the importance of considering the different components of peripheral astigmatism. Astigmatism increases in the peripheral retina resulting in an increasing distance between the two focal lines (the sagittal and tangential image shells). One hypothesis based on findings from a study on monkeys (Kee *et al.*, 2004) is that one of these astigmatic image shells may play a more significant role in myopia development. Rempt, Hoogerheide and Hoogenboom (1971) developed skiagrams to illustrate refractive change across the horizontal peripheral retina (Figure 3.1). Hoogerheide, Rempt and Hoogenboom (1971) later used these skiagrams to investigate myopia development in a longitudinal study of pilots in training. They suggested that subjects in which both sagittal and tangential image shells were relatively hyperopic had about a 40% chance of myopia development, whereas if either one or both image shells showed relative myopia or emmetropia the chance of developing myopia was far less (4%). Time intervals for refractive changes were not specified which did not allow an estimation of myopia development over time and as the subjects were pilots and all over the age of 18 they could only make conclusions regarding late onset myopia.

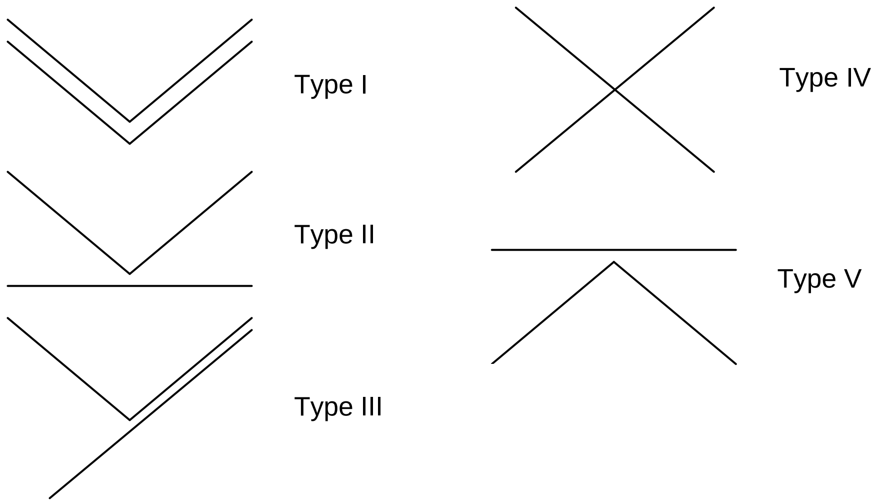

Figure 3.1 Skiagrams as designed by Rempt, Hoogerheide and Hoogenboom (1971), showing the sagittal and tangential image shells across the horizontal meridian. Lines in an upward direction denote hyperopic shift whilst downward sloping lines denote myopic shift with respect to the axial refraction

Studies have considered the effect of accommodation on peripheral refraction (Walker and Mutti, 2002; Calver *et al.*, 2007; Davies and Mallen, 2009; Lundstrom, Mira-Agudelo and Artal, 2009; Tabernero and Schaeffel, 2009) but to date no study has investigated the effect of accommodative lag on peripheral retinal blur. The current study investigated the effect of accommodative inaccuracy on the peripheral retinal blur.

3.2 Methods

Subjects

82 subjects were recruited from the staff and students of Anglia Ruskin University. Refractive groups were divided into emmetropes, low myopes and moderate to high myopes with relatively equal group sizes (Table 3.1). However, further analysis showed the high myopes to have very different peripheral refractions to moderate myopes and have therefore been considered separately.

The classification of low, moderate and high myopes is generally accepted to be in the following categories (Cline, 1997):

Low myopes: 0 to -3D

Moderate myopes: -3 to -6D

High myopes: above -6D

Table 3.1 Refractive error range of each group

<table>
<tr><th>Refractive Error Group</th><th>n</th><th colspan="4">Refractive error (mean ± SD; range)</th></tr>
<tr><td>Emmetropes</td><td>26</td><td colspan="4">0.12DS ± 0.25; +0.50 to -0.37</td></tr>
<tr><td>Low myopes</td><td>27</td><td colspan="4">-1.85DS ± 0.77; -0.50 to -3.01</td></tr>
<tr><td rowspan="2">Moderate/High myopes</td><td rowspan="2">29</td><td rowspan="2">-5.64 ± 2.31;
-3.16 to -12.44</td><td>Moderate myopes</td><td>n=19</td><td>-4.30 ± 0.70;
-3.16 to -5.87</td></tr>
<tr><td>High myopes</td><td>n=10</td><td>-8.17DS ± 2.18;
-6.31 to -12.44</td></tr>
</table>

Procedure

Full methodology has been described in the methodology section 2.3 but a summary follows here.

- Non-cycloplegic subjective refractive error was obtained for 82 subjects (see Table 3.1)
- Peripheral refractive error of the right eye was measured using the Shin Nippon SRW5000 auto-refractor with the left eye occluded
- Peripheral refractive error was measured referenced to the pupillary axis at 5° intervals out to 30° in the horizontal nasal and temporal retina
- Accommodative responses at 6.0m and 0.33m along the visual axis, for each individual subject were assessed and lead or lag (making allowances for accommodative demand depending on refractive error) calculated for each viewing distance

- The spherical equivalent refraction for each peripheral location was normalised by subtracting the spherical equivalent of the subjective refraction resulting in relative peripheral refraction
- The accommodative lag and lead for each individual was calculated and applied to their relative peripheral refraction values
- Refractive error group averages of relative peripheral refraction for each retinal location were plotted for distance and near viewing and the standard deviations of each group presented as error bars
- Biometric data was taken using the IOL Master (Zeiss, UK) including AL, ACD, keratometry readings and corneal diameter

3.3 Results

Preliminary examination of individual peripheral refractions revealed two clear outliers. One emmetropic subject showed significant peripheral astigmatism which contributed to larger myopic relative peripheral refraction. Another moderately myopic subject showed a large amount of asymmetry with a large amount of peripheral myopia in the nasal retina. These two subjects were removed from statistical analysis leaving 82 subjects. Normality of the remaining cohort was investigated using Kolmogorov-Smirnov test of normality for all peripheral points and all were found to follow a normal distribution (p>0.05).

No significant difference in accommodative lag was found between refractive groups (emmetropes 0.85D±0.45, low myopes 0.91D±0.66, moderate myopes 0.88D±0.66, high myopes 0.85D±0.58; one-way ANOVA: p=0.69) or accommodative lead (emmetropes 0.14D±0.31, low myopes 0.14D±0.29, moderate myopes 0.17D±0.25, high myopes -0.13D±0.30; one-way ANOVA: p=0.37).

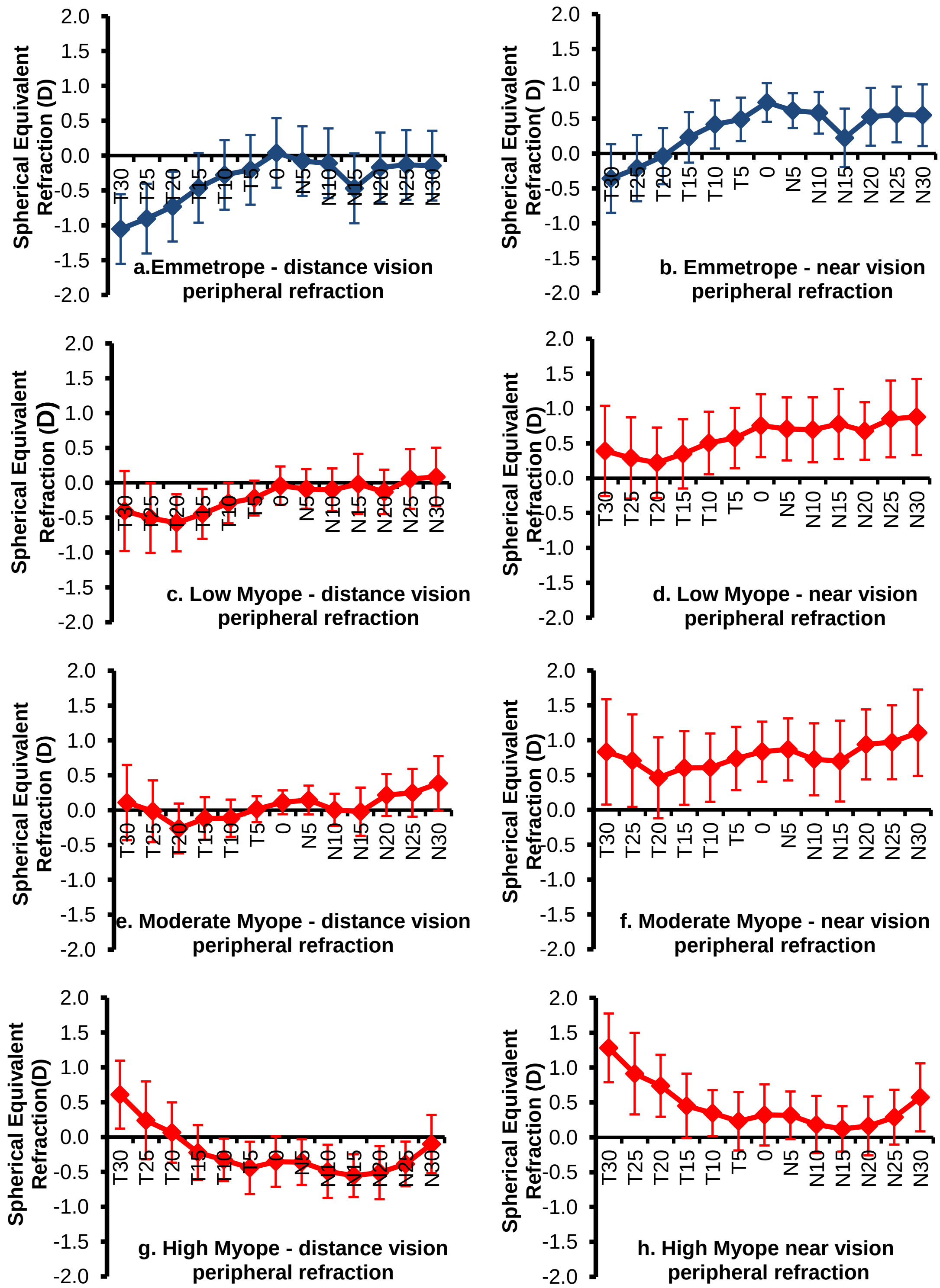

Figure 3.2a-h Relative peripheral refraction of emmetropes (shown in blue), low, moderate and high myopes (shown in red) for distance (left) and near viewing (right). N= nasal retina, T= temporal retina. Error bars demonstrate standards deviations of the refractive error groups at each peripheral location. Note that due to different accommodative demands of the individual subjects this results in different standard deviations of distance and near relative peripheral refraction plots.

Figure 3.2 shows the relative peripheral refractions incorporating the distance accommodative lead (at 6m) and near accommodative lag (at 33cm) of the individual subjects. The average relative peripheral refractions were plotted for distance and near viewing although individual data can be found in Appendix C.

The distance and near plots allow an assessment of the blur experienced at the peripheral retina for different task distances. Emmetropes showed a relative myopic peripheral retina with some nasal-temporal asymmetry (Figure 3.2a). With the addition of accommodative lag for near viewing tasks, the relative peripheral refraction of emmetropes lay closer to plano. Emmetropes therefore experience less peripheral blur for near viewing tasks. Although distance plots showed low and moderate myopes to have quite even peripheral refractions with little peripheral blur (Figure 3.2c+e), accounting for the accommodative lag at near, showed hyperopic blur would be experienced in the peripheral as well as central retina (Figures 3.2d+f). High myopes showed significant relative peripheral hyperopia more so in the temporal retina for distance viewing tasks (Figure 3.2g). This peripheral hyperopia was exaggerated at near with values over 1.0D at the 30 degree temporal retinal location (Figure 3.2h).

Peripheral refraction differed significantly between refractive error groups at temporal locations; 30 degrees ($p<0.001$), 25 degrees ($p=0.003$) and 20 degrees ($p=0.03$). Post hoc tests, with Bonferroni correction, showed that high myopes had significantly more hyperopic relative peripheral refractions when compared with emmetropes at 30 degrees ($p<0.001$), 25 degrees ($p=0.01$) and 20 degrees ($p=0.04$). Post hoc tests also revealed that moderate myopes had significantly more hyperopic relative peripheral refractions when compared with emmetropes at 30 degrees ($p=0.002$) and 25 degrees ($p=0.01$). Comparisons made between only two groups (myopes and emmetropes) in the current cohort still showed significant differences at the temporal retinal locations of 30 degrees ($p<0.001$), 25 degrees ($p=0.004$) and 20 degrees ($p=0.05$).

Peripheral asymmetry (temporal - nasal 30 degree) was found to be significantly different between refractive error groups (emmetropes -0.91D±0.70, low myopes -0.49D±1.00, moderate myopes -0.22D±1.03, high myopes +0.71D±0.76; one-way ANOVA: $p<0.001$).

Negative values of asymmetry denote a more myopic temporal compared to nasal relative peripheral refraction. Positive values of asymmetry denote a more hyperopic temporal compared to nasal relative peripheral refraction. Post hoc analysis, with Bonferroni correction, showed high myopes to have significantly more positive values of asymmetry compared to emmetropes (p<0.001) and low myopes (p=0.003).

Table 3.2 shows the correlation between axial length (AL) and anterior chamber depth (ACD) and relative peripheral refraction at each location. Temporal refractive error correlated with AL at 30 degrees (Pearson's correlation: r=0.352, p<0.001), at 25 degrees (r=0.275, p=0.01) and 5 degrees (r=-0.250, p=0.03). Temporal refractive error correlated with ACD at 30 degrees (Pearson's correlation: r=0.413, p<0.001), at 25 degrees (r=0.362, p=0.001) and 20 degrees (r=0.321, p=0.003). Nasal refractive error is correlated with ACD at 30 degrees (Pearson's correlation: r=0.225, p=0.04). The horizontal iris diameter measurement did not correlate with any peripheral points so is not an influential factor in the peripheral refraction. This showed that the longer the AL and the larger the ACD, the more hyperopic the relative refraction in the temporal peripheral retina. The nasal retina did not show similar results as the correlations between the AL and the nasal relative peripheral refraction are negative correlations. Also differences between refractive groups were not significant in the nasal retina [one-way ANOVA; 30 degrees (p=0.19), 25 degrees (p= 0.16), 20 degrees (p=0.11), 15 degrees (p=0.09), 10 degrees (p=0.22) and 5 degrees (p=0.17)].

Table 3.2 Pearson's correlation between spherical equivalent refraction (SERx), anterior chamber depth (ACD) and axial length (AL). T=temporal, N=nasal retina. Numbers in the peripheral refraction column denote horizontal peripheral retinal location

Peripheral Refraction		SERx	AL	ACD
T30	Pearson Correlation	-.478**	.352**	.413**
	Sig. (2-tailed)	.000	.001	.000
T25	Pearson Correlation	-.339**	.275*	.362**
	Sig. (2-tailed)	.002	.013	.001
T20	Pearson Correlation	-.282*	.191	.321**
	Sig. (2-tailed)	.010	.087	.003
T15	Pearson Correlation	-.094	.069	.216
	Sig. (2-tailed)	.402	.538	.053
T10	Pearson Correlation	.061	-.040	.213
	Sig. (2-tailed)	.585	.720	.056
T5	Pearson Correlation	.188	-.248*	.086
	Sig. (2-tailed)	.090	.025	.446
O	Pearson Correlation	.295**	-.319**	.000
	Sig. (2-tailed)	.007	.004	.997
N5	Pearson Correlation	.196	-.295**	.021
	Sig. (2-tailed)	.078	.007	.849
N10	Pearson Correlation	.247*	-.360**	-.074
	Sig. (2-tailed)	.026	.001	.514
N15	Pearson Correlation	.080	-.277*	-.012
	Sig. (2-tailed)	.477	.012	.912
N20	Pearson Correlation	.133	-.103	.114
	Sig. (2-tailed)	.237	.364	.315
N25	Pearson Correlation	.085	-.097	.129
	Sig. (2-tailed)	.449	.387	.252
N30	Pearson Correlation	-.051	.009	.225*
	Sig. (2-tailed)	.649	.938	.043

**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed).

The tangential and sagittal image planes were also considered in each refractive group. The image shells are calculated using the equations 2.5 and 2.6 (section 2.3.4) and have average values shown in Figure 3.3. Individual data for the tangential and sagittal image shells can be found in Appendix C.

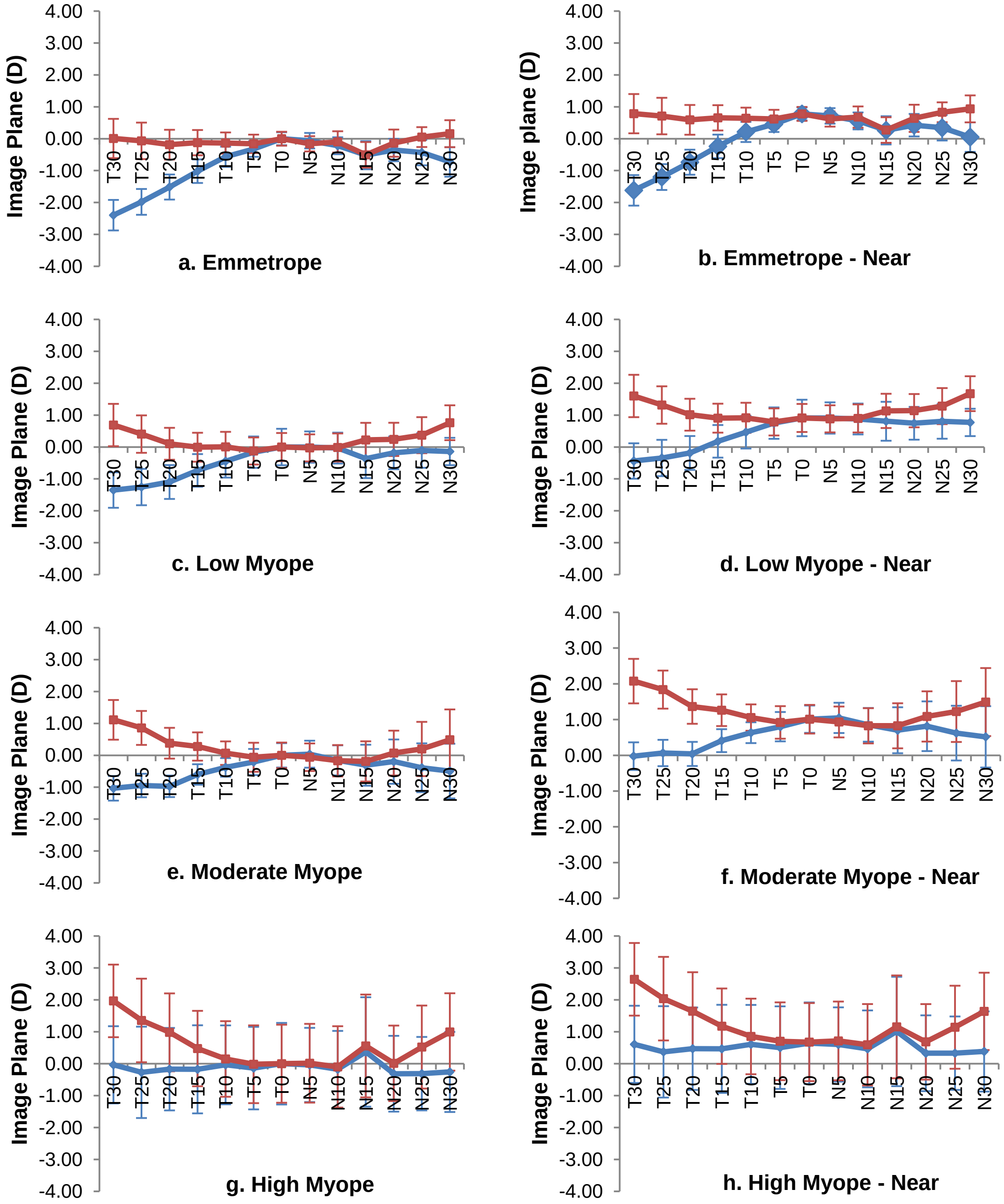

Figure 3.3a-h. Tangential (blue) and sagittal (red) image planes normalized for the different refractive groups showing relative peripheral refractions. The x-axis shows the peripheral location from 30 degrees temporally (T30) to 30 degrees nasally (N30). Plots on the left show tangential and sagittal image shells for normal distance viewing and plots on the right show the tangential and sagittal image shells with the addition of accommodative lag. Error bars denote the standard deviations at each peripheral location

The emmetropes sagittal peripheral image plane lay near to the retina and the tangential image plane lay further in front of the retina (Figure 3.3a). For near viewing the tangential image shell lay closer to emmetropia and the sagittal image shell provides hyperopic defocus across the retina (Figure 3.3b). Low and moderate myopes (Figures 3.3c-f) showed a similar pattern with the relative tangential image shell providing myopic defocus for distance viewing whilst the sagittal image plane showed relative hyperopic defocus. With the addition of accommodative lag for near viewing these image shells both provided hyperopic defocus, although less for the tangential image shell in the temporal retina. High myopes (Figures 3.3g-h) showed an even further shift of the relative sagittal image plane behind the retina and for near viewing both image shells provided relative hyperopic defocus across the retina.

3.4 Discussion

This study found increasingly hyperopic relative peripheral refraction in the temporal retina with larger levels of myopia similar to other studies (Ferree, 1932; Rempt, Hoogerheide and Hoogenboom, 1971; Millodot, 1981; Charman and Jennings, 1982; Mutti *et al.*, 2000; Seidemann *et al.*, 2002; Logan *et al.*, 2004; Atchison *et al.*, 2005; Atchison, Pritchard and Schmid, 2006; Calver *et al.*, 2007; Bakaraju, 2009; Lundstrom, Mira-Agudelo and Artal, 2009; Lin *et al.*, 2010; Mutti *et al.*, 2011).

Emmetropes showed a relatively myopic periphery in the temporal more than nasal retina. Low and moderate myopes showed some hyperopic shift of 0.12D and 0.28D respectively at 30 degrees nasally and little change temporally. High myopes showed a relative hyperopic shift of 0.26D nasally and 1D temporally. Atchison, Pritchard and Schmid (2006) measured refraction horizontally out to 35 degrees nasally and temporally and found a larger hyperopic shift of 1D at 30 degrees eccentricity for a group of -4D myopes and 0.5D hyperopic shift for their group of -3D myopes. In the current study myopes with this level of refractive error demonstrated less hyperopic shift but higher myopes showed larger levels of hyperopic shift. Seidemann *et al.* (2002) used an infrared Power Refractor to measure peripheral refraction out to 25 degrees. A double pass technique provided further peripheral refraction data out to 45 degrees in the temporal horizontal meridian. They reported a relatively myopic peripheral refraction of about 1D at 30 degrees temporally in 9 myopes and a larger myopic shift in the horizontal periphery of about 2D in 11 emmetropic subjects. This finding differs to other studies but may be due to their chosen recording technique. Millodot (1981) measured refraction in the horizontal retina out to 60 degrees temporally and nasally and found about 1D hyperopic shift at 30 degrees nasally and temporally in myopes (30 subjects between -1.00 and -7.87D). A significant difference in the relative peripheral refraction was found between their three refractive groups (hyperopes, myopes and emmetropes) temporally at 30 degrees ($p<0.01$) and from 20 degrees nasally ($p<0.01$). These are similar findings to our study although differences in relative peripheral refraction were only found temporally from 20 to 30 degrees.

There is a known link between longer AL and myopia (Mutti *et al.*, 2000). The current study also found that AL was correlated with relative temporal refractive error (25 and 30 degree locations) and ACD was correlated with relative refractive error (temporal 20, 25 and 30 degrees and nasal 30 degrees). Whether the peripheral refraction is a cause or consequence of myopia development needs further longitudinal investigation but this study suggested that peripheral refraction alongside AL and ACD measurements could be considered together as a predictor of myopia development.

Peripheral asymmetry has been found previously in studies on peripheral refraction (Ferree, 1932; Rempt, Hoogerheide and Hoogenboom, 1971; Millodot, 1981; Logan *et al.*, 2004; Atchison, Pritchard and Schmid, 2006; Calver *et al.*, 2007; Lundstrom, Mira-Agudelo and Artal, 2009). In this study peripheral asymmetry was found to differ in refractive error groups. Peripheral asymmetry in animals has been induced with experimental manipulation of the visual environment (Hodos and Kuenzel, 1984; Gottlieb, Fugate-Wentzek and Wallman, 1987; Wallman *et al.*, 1987; Miles and Wallman, 1990) and suggested locally driven feedback mechanisms based on visual experience. Near-work for typical reading tasks may cause images to be formed at different positions at different peripheral retinal locations and locally driven ocular growth mechanisms might respond accordingly. Mutti *et al.* (2000) suggested that the distorted ocular shape and peripheral asymmetry might be due to mechanical restrictions of equatorial expansion.

The current study found the relative peripheral refraction in the temporal retina was more myopic in emmetropes shifting towards hyperopia in myopes. It might be hypothesized that the temporal retina provides a protective effect against ocular growth in emmetropes and a stimulus in myopes. Whether the nasal or temporal retina is more influential in myopia development and whether the asymmetry interacts with the position of targets within the visual field during near-work requires further investigation.

Schmid and Wildsoet (1997) investigated the effect of inducing astigmatic defocus in the eyes of chicks whilst Kee *et al.* (2004) conducted a similar experiment in monkeys and both studies suggested that the refractive development was most influenced by the more myopic or least hyperopic (tangential) focal plane. However, whether the same effect would be seen in human eyes is unknown. In the current study the tangential image shell in emmetropes was the one providing the relative peripheral myopic defocus and it is possible that this image shell provides a 'stop' signal to prevent eye elongation.

Hoogerheide, Rempt and Hoogenboom (1971) commented that of the skiagrams designed by Rempt, Hoogerheide and Hoogenboom (1971) (Figure 3.1), type I-III applied to myopes and types IV and V applied to hyperopes. Hoogerheide, Rempt and Hoogenboom (1971) reported that initially emmetropic pilots in a longitudinal study who became myopic largely belonged to types I and III. These are the types in which at least a portion of both tangential and sagittal image shells provided hyperopic defocus. The emmetropes from the current study belonged to type V. The low and moderate myopes from the current study belong to type IV which would suggest less risk of further myopia development. The high myopes belong to group II. According to Hoogerheide, Rempt and Hoogenboom (1971) those subjects with skiagrams type II, IV and V were at much lower risk of developing myopia. However, they had not specified the time over which these changes occurred and also only considered late onset myopia. Rosen *et al.* (2012) also questioned the interpretations of Hoogerheide, Rempt and Hoogenboom (1971) arguing that data for the skiagrams was not taken at initial examination, limiting conclusions that peripheral refraction is a causative factor for myopia development.

Whether the peripheral refraction has the potential to influence ocular growth has been discussed in section 1.4.4, especially as peripheral defocus is not noticed clinically. Animal studies (section 1.4.1) as well as the studies by Hoogerheide, Rempt and Hoogenboom (1971) and Rempt, Hoogerheide and Hoogenboom (1971) and the small but significant results of studies reducing peripheral hyperopic defocus to slow myopia progression (Holden *et al.*, 2010; Sankaridurg *et al.*, 2011) have suggested a possible influence of peripheral refraction on myopia progression. However there is the opposing view that the peripheral refraction is a consequence of myopia development (Charman and Jennings, 1982; Mutti *et al.*, 2011; Sng *et al.*, 2011). The current study might suggest that accommodative inaccuracy increases the peripheral hyperopic blur experienced in myopes for near viewing distances. Accommodative lag and peripheral refraction may have a combined influence. It might be noted that in combination with accommodative lag for near tasks the position of sagittal and tangential image shells of low and moderate myopes were shifted towards hyperopic blur (more like skiagram type III) previously reported to increase the risk of myopia development. Accommodative lag in emmetropes moved the tangential image shell towards plano and the sagittal image shell towards hyperopic defocus. This would suggest that at least for near viewing the tangential image shell provides less hyperopic defocus in emmetropes. For distance viewing low and moderate myopes showed myopic tangential and hyperopic sagittal image shells. If peripheral refraction is a causative factor for myopia development then it may be the sagittal image plane is more influential in myopia development whilst the tangential image shell provides a protective effect against myopia development.

High myopes showed that, in conjunction with accommodative lag both tangential and sagittal peripheral image planes were shifted towards hyperopic defocus. When both image planes provide peripheral hyperopic defocus, they may have a cumulative myopigenic effect. Although Schmid and Wildsoet (1997) and Kee *et al.* (2004) reported the tangential image plane was the most influential factor in myopia development, it may be a combination of the two image shells with the tangential image shell providing more of a protective effect in emmetropes and the sagittal image shell providing increasing hyperopic peripheral defocus with near viewing distances. Where accommodative lag shifts both astigmatic image shells into hyperopia, the risk of myopia may be greater.

3.5 Conclusion

Accommodative lag decreased the peripheral myopic defocus experienced by emmetropes and increased the peripheral hyperopic defocus experienced by myopes at near. It is not universally agreed whether peripheral refraction is a precursor to or consequence of myopia development, but it could be hypothesised that the myopic periphery seen in emmetropes has a protective effect against hyperopic blur resulting from accommodative lag during near viewing.

The possibility that accommodative lag provides a stimulus for ocular growth has been widely investigated and is still unclear (section 1.3.3). Our study found no difference between the accommodative lag in myopes and emmetropes (section 3.3) but the peripheral hyperopic defocus experienced was still different. Accommodative lag and peripheral refraction need to be considered together to examine blur experienced at different viewing distances. This would be especially important when investigating the effects of blur as a stimulus to ocular growth and manipulation of peripheral refraction in myopia control programmes.

This study gives more evidence towards considering peripheral astigmatism as a stimulus for myopia development. Although future longitudinal studies are required to determine whether the differences in peripheral astigmatism are a cause or consequence of myopia development, it is possible that the sagittal image plane is more influential in driving ocular elongation and myopia development. The peripheral tangential image shell in emmetropes, may provide a protective effect and a ‘stop’ signal to ocular elongation. Accommodative lag considered in conjunction with the peripheral astigmatic image shells may negate any protective effect of the relatively myopic tangential image shell. It may be the conjunction of the two image shells providing hyperopic defocus across the retina at near which acts as the largest stimulus to ocular elongation and myopia progression. This serves to show the importance of considering not only the mean spherical equivalent peripheral refractions but the astigmatic components in conjunction with accommodative lag in future studies of peripheral refraction.

Chapter 4: Experiment 2 Subjective depth of focus in myopes and emmetropes

4.1 Introduction

Subjective DOF, defined as the dioptric range of retinal defocus which can be tolerated without blur perception, has been widely investigated (Campbell, 1957; Ogle and Schwartz, 1959; Atchison, Charman and Woods, 1997; Marcos, Moreno and Navarro, 1999; Wang, Ciuffreda and Vasudevan, 2006; Yao *et al.*, 2010). Few studies have investigated refractive error group differences but Rosenfield and Abraham-Cohen (1999) showed myopes have poorer blur sensitivity than emmetropes using a blur discrimination task. Schmid *et al.* (2002) found no correlation between refractive error and blur thresholds (blur discrimination or detection) using stationary targets with increasing levels of blur. The current study compared just noticeable and non resolvable blur of text targets in myopes and emmetropes.

Studies investigating the effects of spatial frequency on DOF have suggested that higher spatial frequencies elicit smaller DOF (Tucker and Charman, 1986; Legge *et al.*, 1987b; Marcos, Moreno and Navarro, 1999). No study to date has considered the effect of spatial frequency filtered text targets on the subjective DOF in myopes and emmetropes. If the accommodation response system relies on blur sensitivity then poorer blur sensitivity to spatial frequencies contained within text may contribute to poorer accommodation responses. The current study aimed to investigate whether myopes had poorer blur sensitivities to spatial frequency filtered text targets when compared to emmetropes.

4.2 Methods

Subjects

47 subjects were recruited from the staff and students of Anglia Ruskin University.

Table 4.1 Subject numbers and subjective refractions of the two refractive groups

Group	n	Refractive error (mean ± SD; range)
Emmetropes	**18**	**0.15DS ± 0.30; +0.50 to -0.63**
Myopes	**29**	**-4.12DS ± 2.24; -1.11 to -12.44**

Procedure

Full methodology has been described in the methodology section 2.5 but a summary follows here:

- Subjective DOF is the change in target distance without the perception of blur. Corrections in accommodation usually prevent the perception of blur. Therefore cyclopentolate 1% was used to paralyse accommodation and 6mm artificial pupil were used to obtain measurements of subjective blur perception
- Times roman text targets were band-pass filtered for different spatial frequencies. The band-pass filters were one octave in width and based around the peak spatial frequency of the limb width of the text; N10 calculated to be $9.31cdeg^{-1}$ and N20 $4.65cdeg^{-1}$. Other band-pass filters applied were one octave away from the peak text spatial frequencies; $2.33cdeg^{-1}$, $18.62cdeg^{-1}$ and $37.23cdeg^{-1}$ (section 2.4.5)
- The same targets were used in the subjective as the objective DOF experiments, except half the size to allow for Badal system magnification (section 2.5). The targets were produced so that the text had the same number of pixels per letter to maintain spatial frequencies and bandwidths
- Two text sizes; N10 and N20; allowed consideration as to whether it was the specific spatial frequency band or a feature of text detail which affected blur sensitivity
- The target was positioned in line with the subject's right eye and 20cm from the 5D Badal lens. A Badal optometer maintains target size as it moves (Atchison *et al.*, 1995a)

- The target was moved proximally and then distally on the motorised track at a speed of 2.1cms^{-1}
- The subjects' had a handheld button when depressed halted the movement of the target. It was assumed the reaction times of emmetropes and myopes were the same
- They were first instructed to depress the button when they first noticed that the target became blurred. They were then asked to depress the button at the first point at which the target became unreadable
- Three just noticeable and three non resolvable recordings for each spatial frequency filtered text targets were recorded proximally and distally
- Although adaptation to spatial frequencies has been reported (section 1.7.4), the targets were presented in a randomised order for each individual to limits the effects of adaptation on the results
- Dioptric proximal and distal measurements were added to give total DOF values

Pilot study to investigate subject numbers and refractive groups

The first 37 subjects were divided into emmetropes, low myopes and moderate to high myopes. Similar group sizes were used; 12 emmetropes (0.22D±0.27), 11 low myopes (-2.44D±1.04) and 14 moderate to high myopes (-5.73D±2.16). One-way ANOVA was used to investigate the differences in just noticeable and non resolvable DOF whilst viewing an N10 text target. No significant difference was found between refractive groups for just noticeable (p=0.24) or non resolvable DOF (p=0.17). DOF values shown by low myopes and moderate to high myopes were not different for just noticeable (0.24D±0.04 and 0.24D±0.05 respectively) or non resolvable DOF (0.37D±0.05 and 0.38D±0.08). Power calculations of this data suggested that to achieve significant differences between low myopes and moderate to high myopes, an infinitely large number of subjects would be required. For this reason the remaining experiments combined the low and moderate to high myopes in one group.

4.3 Results

Normality of the complete cohort for total DOF were found to follow a normal distribution (K-S test; $p>0.05$). Levene's test revealed that variances between refractive error groups were homogenous for all repeated measure variables. Calculation of z-scores revealed no outliers and therefore all data was included in the analysis.

A mixed design repeated measures ANOVA was conducted, with refractive error group as an independent variable and target size and spatial frequency filter as within subject variables. Target size had two levels (N10 and N20) and spatial frequency filter had six levels (unfiltered, 2.33cdeg^{-1}, 4.65cdeg^{-1}, 9.31cdeg^{-1}, 18.62cdeg^{-1} and 37.25cdeg^{-1}). The N10 2.33cdeg^{-1} and the N20 37.25cdeg^{-1} text targets had been excluded from the study (explained in section 2.4.5). For this reason initial analysis considered the results for the two target sizes separately. Dependent variables measured in this experiment were subjective just noticeable and non resolvable total DOF (measured in dioptres) and the proximal and distal standard deviations of subject responses.

4.3.1 Just noticeable and non resolvable DOF differences

Just noticeable total DOF for N10 targets

Repeated measures ANOVA showed no significant effect of refractive group on just noticeable total DOF [$F(1,45)=0.24$, $p=0.63$] but a significant main effect of spatial frequency filtered text [Figure 4.1; corrected using Greenhouse-Geisser; $F(2.66, 119.71)=10.53$, $p<0.001$, $\eta^2=0.19$]. Contrasts revealed that all filtered targets elicited a significantly smaller just noticeable DOF when compared to the unfiltered target (0.23D±0.04), for 4.65cdeg^{-1} [0.20D±0.06; $F(1,45)=8.34$, $p=0.01$ $\eta^2=0.16$] for 9.31cdeg^{-1} [0.21D±0.05; $F(1,45)=16.79$, $p<0.001$, $\eta^2=0.27$] for 18.62cdeg^{-1} [0.20D±0.04; $F(1,45)=82.08$, $p<0.001$, $\eta^2=0.65$] and for 37.25cdeg^{-1} [0.18D±0.06; $F(1,45)=35.74$, $p<0.001$, $\eta^2=0.44$]. When repeated measures ANOVA were conducted on the emmetropes and myopes separately it was revealed that the significant main effect was only found in the myopes [F(4,112)=14.19, p<0.001] and not the emmetropes [F(4,68)=2.47, p=0.053, η^2=0.34]. This would suggest that the myopes are responsible for the main effect of spatial frequency filtered text observed.

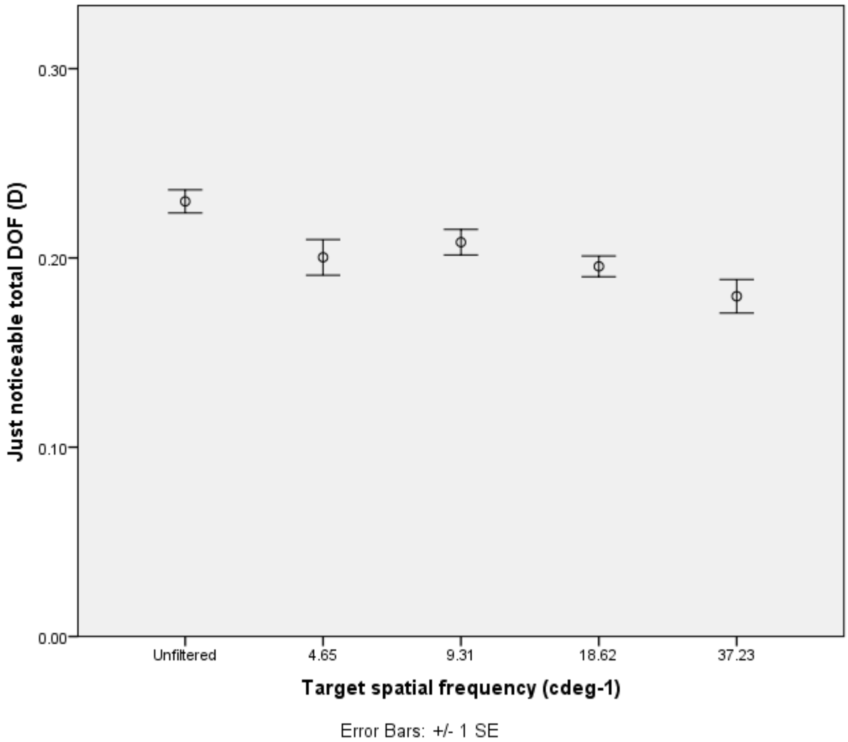

Figure 4.1 Just noticeable DOF for all the N10. There was a significant main effect of spatial frequency filtered text [corrected using Greenhouse-Geisser; F(2.66, 119.71)=10.53, p<0.001, η^2=0.19]

There was no significant interaction effect between refractive group and spatial frequency filtered text for just noticeable total DOF [corrected using Greenhouse-Geisser; F(2.66, 119.71)=2.01, p=0.12].

There was no significant difference between standard deviations of refractive groups for proximal [F(1,45)=0.38, p=0.54] or distal recordings [F(1,45)= 2.55, p=0.12]. This suggested that myopes did not have more variable responses when compared to emmetropes.

Just noticeable total DOF for N20 targets

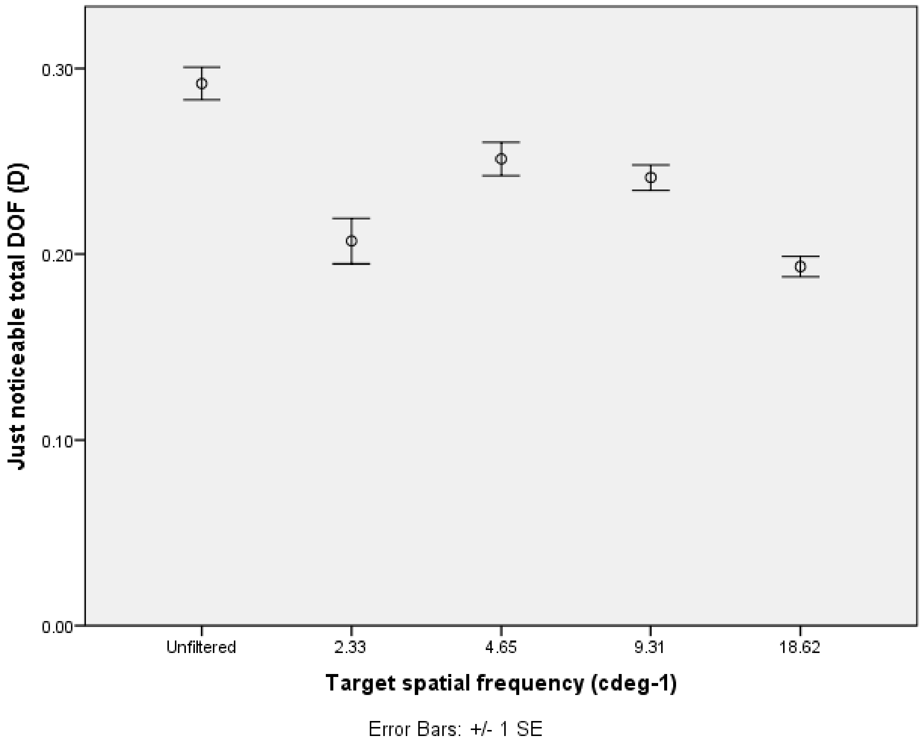

Figure 4.2 Just noticeable total DOF for all N20 targets. There was a significant main effect of the spatial frequency filtered text on the just noticeable DOF [corrected using Greenhouse-Geisser; $F(2.39, 107.47)=34.33$, $p<0.001$, $\eta^2=0.43$]

There was no significant effect of refractive group on just noticeable DOF for N20 targets [$F(1,45)=0.20$, $p=0.66$]. There was a significant main effect of the spatial frequency filtered text on the just noticeable DOF [Figure4.2*;* corrected using Greenhouse-Geisser; $F(2.39, 107.47)=34.33$, $p<0.001$, $\eta^2=0.43$]. Contrasts revealed the just noticeable DOF was significantly larger with the unfiltered target (0.29D±0.06) when compared to all the filtered targets; 2.33cdeg^{-1} [0.21D±0.08; $F(1,45)= 43.02$, $p<0.001$ $\eta^2=0.49$], 4.65cdeg^{-1} [0.25D±0.06; $F(1,45)=24.40$, $p<0.001$ $\eta^2=0.35$], 9.31cdeg^{-1} [0.24D±0.05; $F(1,45)=51.14$, $p<0.001$, $\eta^2=0.53$] and 18.62cdeg^{-1} [0.19D±0.04; $F(1,45)=226.98$, $p<0.001$, $\eta^2=0.84$]. When repeated measures ANOVA were conducted on the emmetropes and myopes separately it was revealed that the significant main effect was found in myopes [$F(4,112)=29.89$, $p<0.001$, $\eta^2=0.52$] and emmetropes [$F(4,68)=10.77$, $p<0.001$, $\eta^2=0.39$]. This would suggest both refractive groups are responsible for the main effect of spatial frequency filtered text observed.

There was no significant interaction effect between refractive group and spatial frequency filtered text for just noticeable DOF [F(2.39, 107.47)=1.72, p=0.18].

Standard deviations of the subjective DOF measurements were not significantly different for the refractive error groups for either proximal [F(1,45)=0.32, p=0.56] or distal recordings [F(1,45)= 1.81, p=0.19] showing limited difference in variability in the responses of myopes and emmetropes.

Non resolvable total DOF for N10 targets

A mixed design repeated measures ANOVA was conducted as before. The repeated measures variable, spatial frequency filter of N10 text had three levels; unfiltered, 9.31cdeg^{-1} and 18.62cdeg^{-1}. The other filtered N10 targets could not be resolved and therefore data could not be obtained.

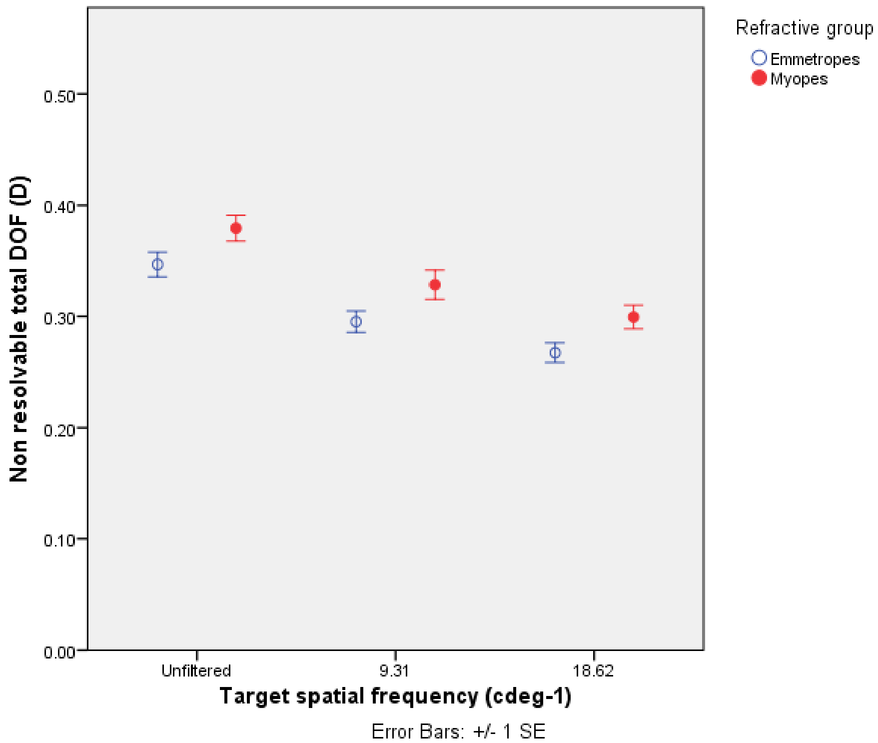

Figure 4.3 Non resolvable total DOF for all N10 targets for both myopes and emmetropes. There was a significant effect of refractive group on non resolvable total DOF [F(1,45)=4.36, p=0.04]

There was a significant effect of refractive group on non resolvable total DOF [Figure 4.3; F(1,45)=4.36, p=0.04, η^2=0.09]. Total non resolvable DOF individual data for the unfiltered N10 target can be found in Appendix D. Myopes showed significantly larger non resolvable DOF when compared with emmetropes for the unfiltered targets (0.379D and 0.347D respectively) and for filtered targets; 9.31cdeg^{-1} (0.329D and 0.295D respectively) and 18.62cdeg^{-1} (0.299D and 0.267D respectively). There was a significant main effect of the spatial frequency filtered text on the non resolvable DOF [$F(2,90)=91.89$, $p<0.001$, $\eta^2=0.67$]. Contrasts revealed that all filtered targets elicited a significantly smaller non resolvable DOF when compared to the unfiltered target (0.37D±0.06), for 9.31cdeg^{-1} [0.32D±0.06; $F(1,45)=67.45$, $p<0.001$, $\eta^2=0.60$] and for 18.62cdeg^{-1} [0.29D±0.05; $F(1,45)=254.63$, $p<0.001$, $\eta^2=0.85$].

There was no significant interaction effect between refractive group and spatial frequency filtered text for non resolvable DOF [$F(2, 90)=0.01$, $p=0.99$].

There was no significant difference of standard deviations of subjective DOF recordings between refractive groups for proximal [$F(1,45)=0.28$, $p=0.60$] or distal recordings [$F(1,45)= 0.08$, $p=0.78$].

Non resolvable total DOF for N20 targets

A mixed design repeated measures ANOVA was conducted as before. The repeated measures variable, spatial frequency filter of N20 text had four levels, as the 2.33cdeg^{-1} target could not be resolved and therefore data could not be obtained.

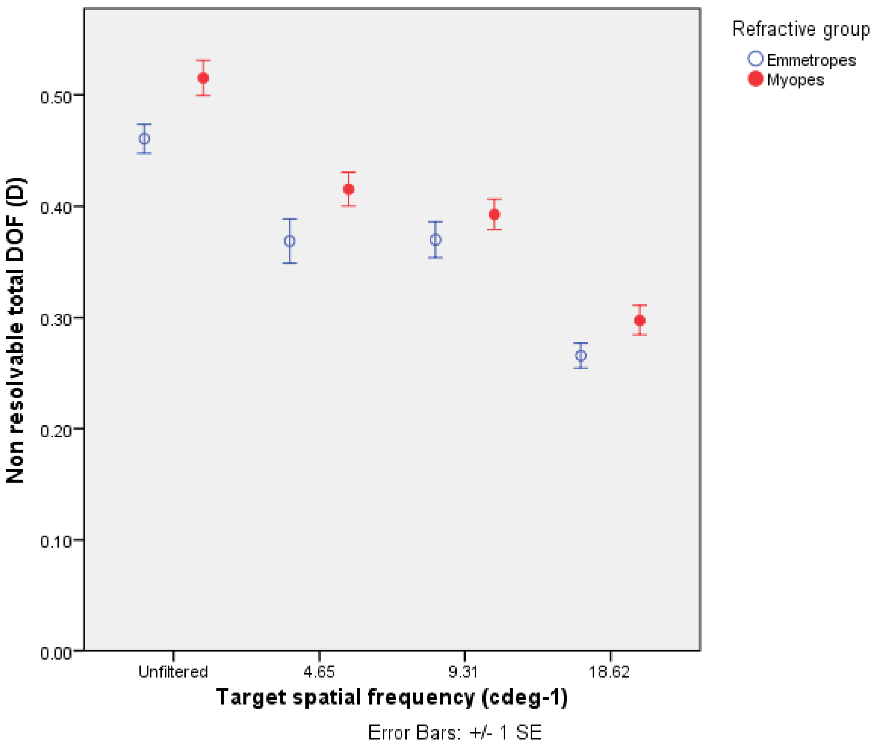

Figure 4.4 Non resolvable total DOF for all the N20 targets. There was a significant effect of refractive group on non resolvable total DOF [$F(1,45)=4.71$, $p=0.05$, $\eta^2=0.10$]

There was a significant effect of refractive group on non resolvable total DOF [Figure 4.4; $F(1,45)=4.71$, $p=0.05$, $\eta^2=0.10$]. Total non resolvable DOF individual data for the unfiltered N20 target can be found in Appendix D. Myopes demonstrated significantly larger non resolvable DOF when compared to emmetropes for the unfiltered target (0.515D and 0.461D respectively) and for filtered targets; 4.65cdeg^{-1} (0.415D and 0.369D respectively), 9.31cdeg^{-1} (0.393D and 0.370D respectively) and 18.62cdeg^{-1} (0.297D and 0.266D respectively). There was a significant main effect of the spatial frequency filtered text on the non resolvable DOF [$F(3,135)=126.69$, $p<0.001$, $\eta^2=0.74$]. Contrasts revealed that all filtered targets elicited a significantly small non resolvable DOF when compared to the unfiltered target (0.49D±0.08), for 4.65cdeg^{-1} [0.40D±0.08; $F(1,45)=94.97$, $p<0.001$ $\eta^2=0.68$] for 9.31cdeg^{-1} [0.38D±0.07; $F(1,45)=101.70$, $p<0.001$, $\eta^2=0.69$] and for 18.62cdeg^{-1} [0.29D±0.06; $F(1,45)=386.55$, $p<0.001$, $\eta^2=0.90$].

There was no significant interaction effect between refractive group and spatial frequency filtered text for non resolvable total DOF [$F(1,45)=0.16$, $p=0.69$, $\eta^2<0.01$].

No significant difference in the standard deviations of subjective DOF measurements between refractive error groups was found for proximal [$F(1,45)=0.64$, $p=0.43$] or distal recordings [$F(1,45)= 0.25$, $p=0.62$] showing little difference in the variability of the responses of myopes and emmetropes.

Target size comparisons

A repeated measures ANOVA compared the effect of target size on just noticeable DOF. This mixed design included one independent variable with two levels (myopes and emmetropes) and two within subjects' variables: target size with two levels (N10 and N20) and spatial frequency filter with four levels (unfiltered, 4.65cdeg^{-1}, 9.31cdeg^{-1} and 18.62cdeg^{-1}). The N10 2.33cdeg^{-1} and the N20 37.28cdeg^{-1} targets could not be created and therefore are not included.

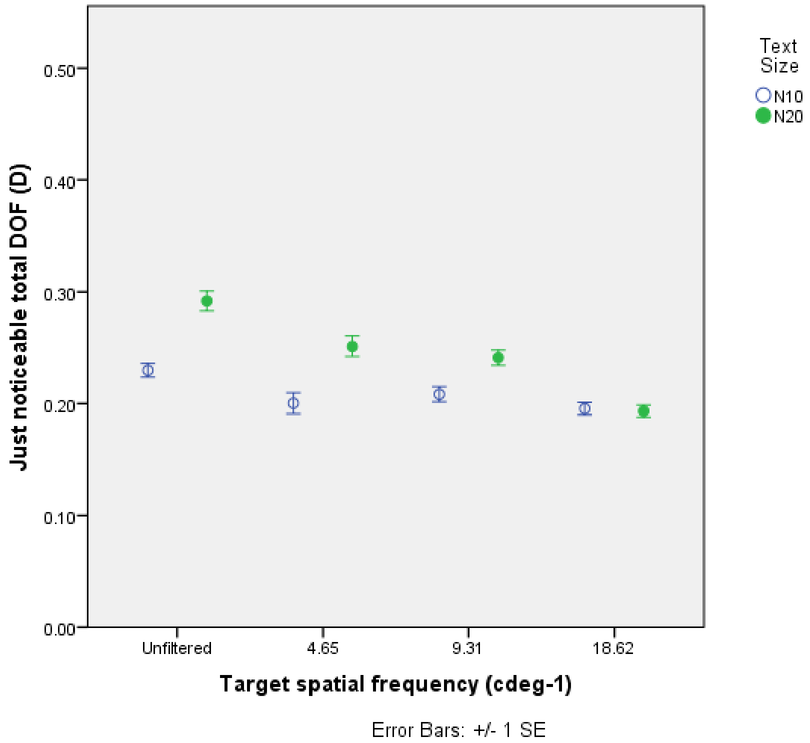

Figure 4.5 Just noticeable total DOF for targets that could be compared. There was a significant effect of target size on just noticeable total DOF [$F(1,43)=79.19$, $p<0.001$]

Target size had a significant effect on just noticeable DOF [$F(1,45)=72.63$, $p<0.001$, $\eta^2=0.62$] with N20 targets eliciting a larger DOF when compared with N10 for unfiltered targets (0.292D compared with 0.230D respectively), for 4.65cdeg^{-1}(0.251D compared with 0.200D respectively) and for 9.31 cdeg^{-1} (0.241 compared with 0.208D respectively). There was little difference in the just noticeable DOF recorded with N20 compared with N10 target sizes for the highest spatial frequency filter; 18.62cdeg^{-1} (0.194D compared with 0.193D respectively).

Repeated measures ANOVA analysed the effect of target size on the non resolvable total DOF for three spatial frequency filtered text targets. The N10 4.65cdeg^{-1} and 37.28cdeg^{-1} targets, and N20 2.33cdeg^{-1} target could not be resolved so this data could not be obtained (Figure 4.6).

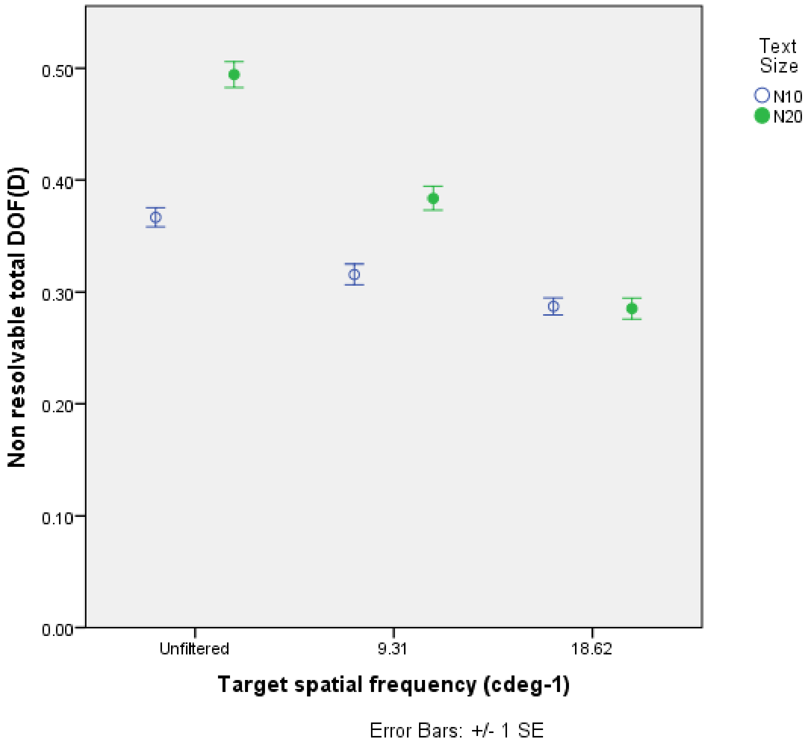

Figure 4.6 Non resolvable DOF for targets that could be compared. There was a significant effect of target size on non resolvable total DOF [$F(1,45)=135.95$, $p<0.001$]

Target size had a significant effect on non resolvable DOF [$F(1,45)=135.95$, $p<0.001$, $\eta^2=0.75$] with N20 eliciting a larger DOF when compared with N10 for unfiltered targets (0.494D compared with 0.367D respectively) and for 9.31cdeg^{-1} (0.384D compared with 0.316D respectively). There was little difference in the non resolvable DOF when viewing the N20 compared with N10 target sizes for the highest spatial frequency filter 18.62cdeg^{-1} (0.285D compared with 0.287D respectively).

4.3.2 Analysis of midpoints.

When conducting the subjective DOF experiment with the Badal lens set up, some subjects often reported that the starting position of the target was not at its optimum focus. Subjects reported that the target clarity improved as it was moved forwards. The midpoint of the subjective DOF was calculated to investigate whether the target viewed or refractive group affected the position.

Midpoints were calculated by taking half of the total DOF and subtracting this from the distal edge of the DOF. The dioptric value of this displacement could then be calculated by multiplying the linear measurement by 0.025D (the dioptric value of a millimetre in this Badal set up). The larger the dioptric value, the larger the proximal displacement of the midpoint from the starting position. It has been assumed that the midpoints of just noticeable and non resolvable DOF are the same and therefore only midpoints of just noticeable DOF have been analysed.

Z-scores identified no outliers. A mixed design repeated measures ANOVA was conducted as before (section 4.4). The two target sizes were considered separately. The dependent variable was the dioptric displacement of the subjective DOF midpoint from the starting position. Normality of the complete cohort for total DOF was found to follow a normal distribution (K-S test; $p>0.05$). Levene's test revealed that refractive group variances were homogenous for all repeated measures variables.

Midpoints recorded for just noticeable total DOF for N10 targets

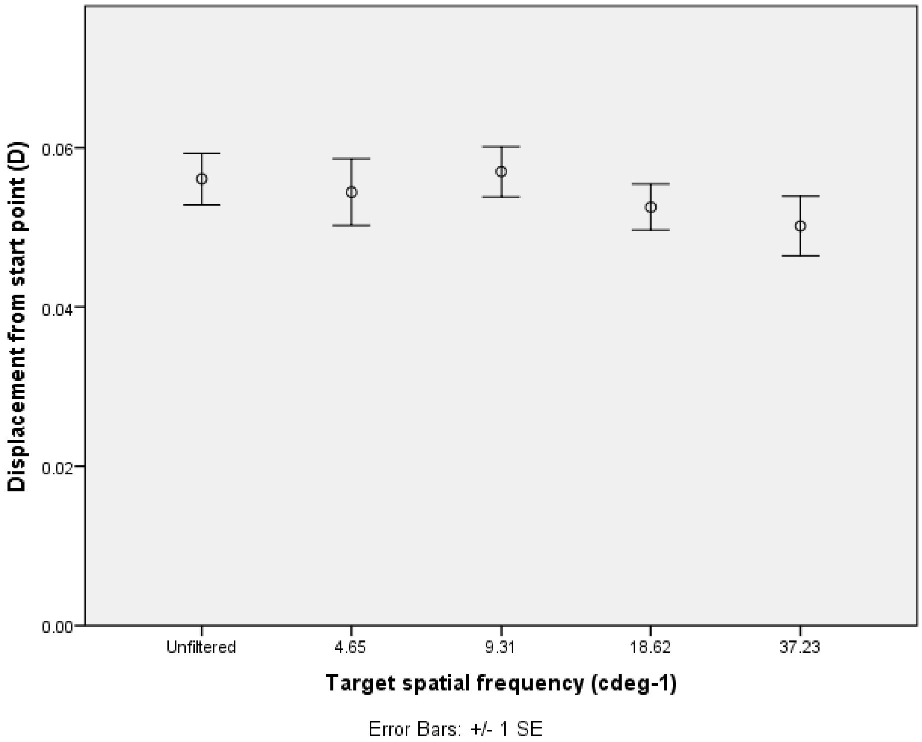

Figure 4.7 Dioptric displacement of the DOF midpoint from the original position when recording just noticeable DOF for N10 targets. There was no significant main effect of the spatial frequency filtered text on this midpoint [corrected using Greenhouse-Geisser; $F(2.68, 120.55)=2.08$, $p=0.11$]

There was no significant effect of refractive group on the midpoint of just noticeable DOF [$F(1,45)=0.17$, $p=0.69$]. There was no significant main effect of the spatial frequency filtered text on this midpoint [Figure 4.7; corrected using Greenhouse-Geisser; $F(2.68, 120.55)=2.08$, $p=0.11$].

Midpoints recorded for just noticeable total DOF for N20 targets

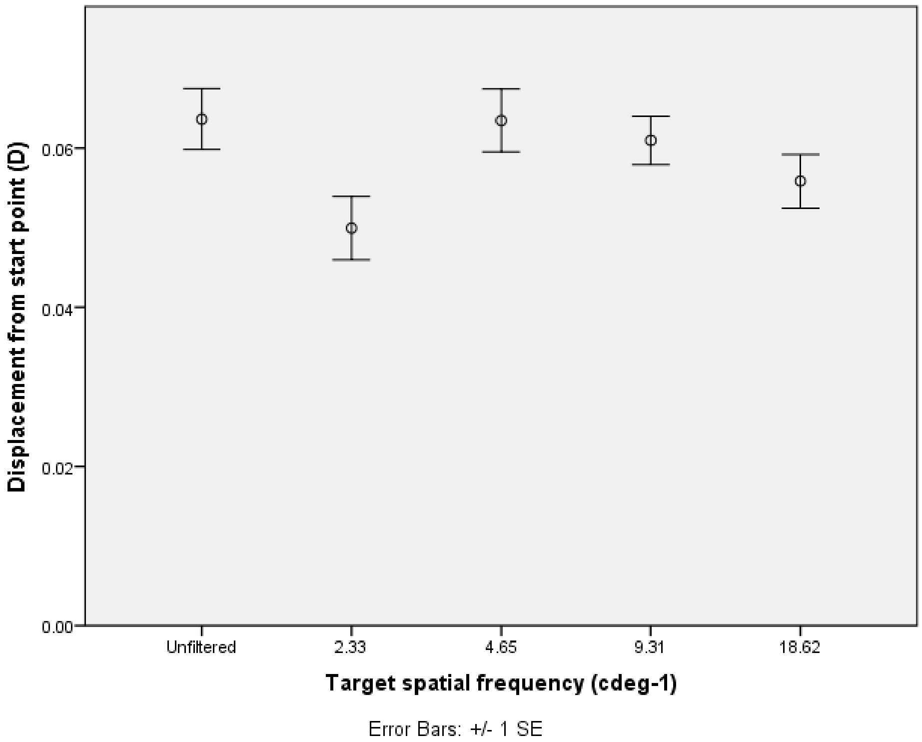

Figure 4.8 Dioptric displacement of the DOF midpoint from the original position when recording just noticeable DOF for N20 targets. There was a significant main effect of spatial frequency filtered text on this midpoint [corrected using Greenhouse-Geisser; $F(2.41, 108.58)=5.46$, $p<0.001$, $\eta^2=0.12$]

There was no significant effect of refractive group on the midpoint of just noticeable DOF [$F(1,45)=0.95$, $p=0.33$]. There was a significant main effect of spatial frequency filtered text on this midpoint [Figure 4.8; corrected using Greenhouse-Geisser; $F(2.41, 108.58)=5.46$, $p<0.001$, $\eta^2=0.12$]. Contrasts revealed that the unfiltered N20 target was displaced further forward when compared to the lowest spatial frequency filtered target, 2.33cdeg^{-1} [F(1,45)= 6.65, $p=0.01$ $\eta^2=0.13$] and the highest spatial frequency filtered target, 18.62cdeg^{-1} [$F(1,45)=10.65$, $p=0.002$, $\eta^2=0.19$]. The midpoint when viewing the peak text spatial frequency target (4.65cdeg^{-1}) was also displaced further forward when compared to the lowest spatial frequency filtered target; 2.33cdeg^{-1} [F(1,45)= 9.55, $p=0.003$ $\eta^2=0.18$] and the highest spatial frequency filtered target 18.62cdeg^{-1} [$F(1,45)=9.77$, $p=0.003$, $\eta^2=0.18$]. When repeated measures ANOVA were conducted on the emmetropes and myopes separately it was revealed that the significant main effect of spatial frequency filtered text was found in myopes [$F(4,112)=9.05$, $p<0.001$, $\eta^2=0.24$] but not in emmetropes [*F*(4,68)=1.22, *p*=0.31]. This would suggest that the myopes are responsible for the main effect of spatial frequency filtered text observed.

There was no significant interaction effect between refractive group and spatial frequency filtered text for the midpoint of just noticeable DOF [corrected using Greenhouse-Geisser; *F(*1.82, 80.02)=0.22, *p*=0.79].

Target size midpoints comparisons

A repeated measures ANOVA was conducted. The within subjects variable of spatial frequency filtered text included 4 levels; unfiltered, 4.65cdeg^{-1}, 9.31cdeg^{-1} and 18.62cdeg^{-1} (Figure 4.9). As the N10 2.33cdeg^{-1} and N20 37.23cdeg^{-1} targets could not be created, this data has not been included. The dependent variable was the dioptric displacement of the just noticeable DOF midpoint from the starting position.

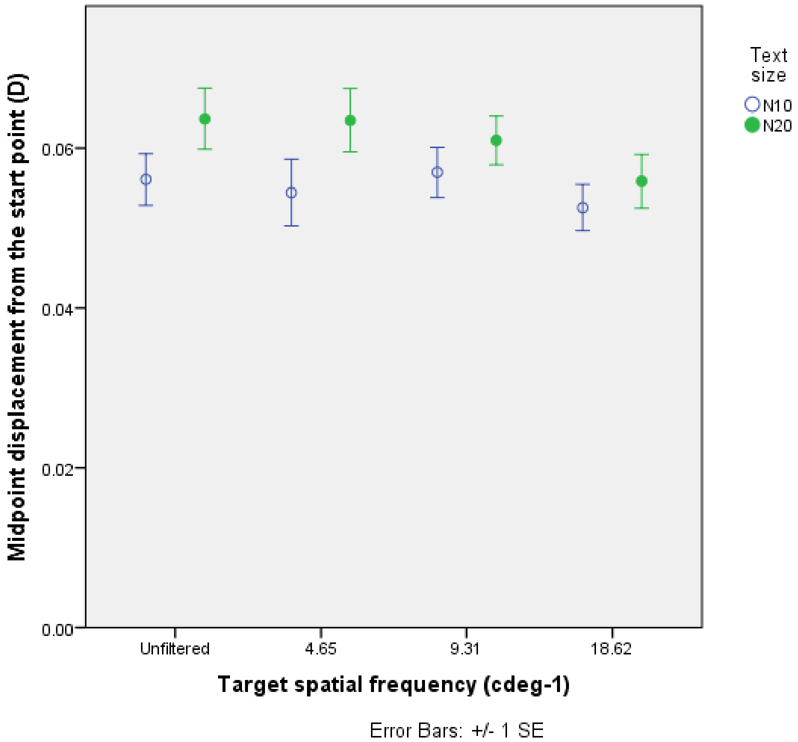

Figure 4.9 Midpoint displacement for all targets that could be compared.

Repeated measures ANOVA revealed a significant effect of target size on the midpoint of just noticeable DOF [F(1,45)=15.51, p<0.001, η^2=0.26] with N20 targets showing further displacement of midpoints when compared with N10 for unfiltered targets (0.064D compared with 0.056D respectively), for 4.65cdeg^{-1}(0.063D compared with 0.054D respectively), for 9.31 cdeg^{-1} (0.061D compared with 0.057D respectively) and for 18.62cdeg^{-1}(0.056D compared with 0.053D respectively) .

4.4 Discussion

Levels of subjective DOF

For an unfiltered N10 text target, just noticeable and non resolvable subjective DOF levels were found to be 0.220D±0.042 and 0.347D±0.046 respectively in emmetropes and 0.236D±0.041 and 0.379D±0.063 respectively in myopes. The current study used cycloplegia and 6mm artificial pupils. It had been assumed that the reaction times of myopes and emmetropes were the same. Yao *et al.* (2010) found levels of subjective DOF to be ±0.52D±0.30 in 12 emmetropes without cycloplegia and an average pupil size of 5.42mm±1.49. Vasudevan, Ciuffreda and Bin (2007) recorded subjective DOF using cycloplegia and a 5mm artificial pupil in 10 subjects (subjective refractions ranging from +1 to -3D) and found levels of ±0.63D±0.22. Although larger DOF would be expected with smaller pupils (Campbell, 1957; Charman and Whitefoot, 1977; Atchison, Charman and Woods, 1997) it is unlikely this is the only reason for smaller levels of subjective DOF in the current study. It is likely that subject instruction and the target used also affected results. Yao *et al.* (2010) used a square wave grating and did not use cycloplegia. They compared a moving target to a static one and subjects' were instructed to maintain focus. Just noticeable blur was recorded only in one direction by reducing target vergence. The set up of the study by Vasudevan, Ciuffreda and Bin (2007) was closer to that of the current study using cycloplegia and a Badal system although used a Maltese cross. Marcos, Moreno and Navarro (1999) used different criteria to the current study, defining subjective as the range over which 95% of 10-20 measurements of the far point were found with a 6mm pupil. However, they recorded a total subjective DOF of 0.21D, similar to levels of DOF found in the current study.

The current study recorded values of subjective focus asking subjects to report 'first noticeable blur' and for the point at which the target 'first became unresolvable'. Atchison, Charman and Woods (1997) highlighted the importance of subject instruction and also reported a change in subject blur criterion with letter size. They suggested that blurring of small sized letters was based on contrast changes whilst larger letters defocus criterion was based on edge sharpness. This does suggest that the target under observation would alter the subjective DOF magnitudes found. Atchison *et al.* (2005) also reported that the magnitudes of "troublesome" and "objectionable" limits were 1.6-1.8X and 2.1-2.5X relative to "noticeable" limits. This also explains differences found with different subject instruction and also explains larger values for the unresolvable compared to the just noticeable DOF in the current study.

The effect of refractive groups on the subjective DOF

Schmid *et al.* (2002) found no difference in blur detection between myopic and emmetropic children, using stationary targets (text and scenes). The current study found no significant difference in the just noticeable DOF of myopes and emmetropes regardless of which spatial frequency filtered text was viewed. Rosenfield and Abraham-Cohen (1999) showed myopes to have poorer blur sensitivity compared to emmetropes, however their task was different. They used a blur discrimination task where their subjects viewed a bipartite letter target and compared moving to stationary text, using cycloplegia and a 2mm artificial pupil. The measurements of just noticeable DOF in the current study consisted of blur detection tasks. Rosenfield and Abraham-Cohen (1999) also used a 2mm artificial pupil which may have increased blur discrimination threshold differences between myopes and emmetropes, enough to demonstrate significance.

It has been previously reported that myopes show improved visual acuity on removal of their spectacles or in other words have the ability to adapt to blur (Rosenfield, Hong and George, 2004). Non resolvable DOF was recorded in this study which examines the ability to resolve blurry letters. Myopes showed significantly larger non resolvable DOF when compared to emmetropes for both N10 and N20 targets suggesting that myopes tolerate more blur before they decide that text cannot be resolved. If the accommodation system is linked to the perception of text resolution then larger levels of retinal blur might be tolerated in myopes before they initiate corrective accommodative responses. If myopes can resolve blurry text they may adapt to the blurred image reducing the need to alter accommodation to improve the target focus.

The current study used cycloplegia to eliminate accommodation responses. Differences in myopes and emmetropes are therefore limited to perceptual differences. Whether differences in accommodation responses between myopes and emmetropes are structural (Mutti *et al.*, 1998) or neural (Gwiazda, Thorn and Held, 2005) in origin has been debated. If blur perception is found to be linked with accommodation responses then the differences in accommodation responses between myopes and emmetropes are likely to have at least some neural element.

The effect of spatial frequency filtered text on subjective DOF

The way in which the visual system interprets spatial frequency filtered text for text recognition is an important consideration when analysing the way we perceive blur in the spatial frequency filtered text targets. Legge *et al.* (2010) commented on the neurons in the primary visual cortex consisting of spatially localised receptive fields which are orientation selective. They stated that image detection and recognition required local pooling between neurons tuned to the same orientation, spatial frequency and phase. It has long been suggested that spatial frequency selective channels exist but it has been debated how these different channels contribute to text recognition. Majaj *et al.* (2002) reported that the spatial frequency channel used to identify letters increased as stroke frequency increased. When a letter target was filtered for different spatial frequencies, the channel frequency employed increased less than proportionally to the frequency of the target. They concluded that large letters are identified by the edges and small letters by the gross strokes.

Legge *et al.* (1985) measured reading speed whilst subjects viewed low-pass spatial frequency filtered text (using defocus blur) of differing bandwidths. They found that reading speed was maintained when the bandwidth extended at least one octave in spatial frequency above the fundamental frequency of the text (cycles/letter divided by letter size). It is likely that text recognition would be required for improved reading speeds.

These studies suggest that text recognition and reading speed are not only dependent on high spatial frequency information. The current study used band-pass filters, one octave in width. The very lowest spatial frequency filtered N10 and N20 text and the very highest spatial frequency filtered N10 text could not be resolved by the subjects (Figure 2.4). This may be explained by the findings of Legge *et al.* (1985) reporting that reading relied on the spatial frequencies within one octave of the peak spatial frequency of the text.

The largest DOF were seen with the target containing the peak spatial frequency of the text (unfiltered and peak spatial frequency filter). This might be expected as it is known text recognition is dependent on the peak text spatial frequency. Reduced blur sensitivity to these spatial frequencies may be beneficial to the visual system as it would maximise the range at which text could be resolved.

The Badal system used when recording subjective DOF maintains target size as the target moves but the target suffers defocus blur as it moves towards or away from the subject. A reduction of contrast sensitivity has been shown with defocus blur resulting in oscillations or “notches” in the contrast sensitivity function between the peak spatial frequency and the cut off spatial frequency (section 1.7.4). Therefore it might be expected the higher spatial frequency filtered targets would show the smallest DOF. The current study found higher spatial frequency filtered text targets elicited a smaller subjective DOF.

Legge *et al.* (1987b) measured effects of defocus blur on grating targets and reported that low spatial frequency targets would be less affected by defocus than high spatial frequency targets. Based on the findings of Legge *et al.* (1987b) it might be expected that the low spatial frequency filtered text targets would be less affected by defocus blur and elicit larger DOF. However, low spatial frequency filtered text targets also elicited a smaller subjective DOF. This might be because the ability to detect changes in target defocus is known to improve where the target has an increased level of defocus initially (Jacobs, Smith and Chan, 1989; Cufflin, Mankowska and Mallen, 2007). Low band-pass spatial frequency filters eliminate higher spatial frequencies, similar to the effect of defocus blur. The low band-pass filtered text targets could be considered to be blurry initially.

The effect of target size on subjective DOF

Atchison, Charman and Woods (1997) found that subjective DOF increased for larger targets and hypothesized this was due to the subjects applying different blur criterion to larger targets. Small changes in the focus of small targets have a more significant effect on the target spatial form but with larger more recognizable targets the blur criterion might be shifted towards changes in contrast. As targets become even larger, smaller focus errors have little effect on image contrast and it may be due to changes in edge sharpness which define the DOF. The current study has found target size to have a significant effect on subjective DOF. The smaller unfiltered N10 text contained more high spatial frequency information compared to the N20 target and studies have suggested that as target detail increases the DOF decreases (Ogle and Schwartz, 1959; Tucker and Charman, 1975; Legge *et al.*, 1987b; Atchison, Charman and Woods, 1997).

The current study has found that even when the two target sizes have been filtered for the same spatial frequencies the larger N20 targets still elicit a larger DOF compared to the N10 targets, except with the highest (18.62cdeg^{-1}) spatial frequency filtered text. This may be expected as the 4.65cdeg^{-1} band-pass filter applied to the N20 text contained the peak N20 text spatial frequency but the same filter applied to the N10 text was below the N10 peak text spatial frequency (9.31cdeg^{-1}). The N10 text has therefore suffered more image blur and it is known that the ability to detect changes in target defocus improves where the target is defocused initially (Cufflin, Mankowska and Mallen, 2007; Jacobs, Smith and Chan, 1989).

When viewing the highest spatial frequency filtered text targets the difference in DOF when viewing the N10 and N20 targets is negligible. The highest (18.62cdeg^{-1}) band-pass filter is within one octave of the N10 peak text spatial frequency but more than one octave from the N20 peak text spatial frequency. The high spatial frequency filtered N20 target will therefore be close to the limits of resolution and have suffered more image blur. Increased levels of blur applied to a target may improve the ability to detect blur and reduce the DOF found with the N20 text. This may explain the small differences between subjective DOF found when viewing the N10 and N20 high spatial frequency filtered text targets.

The 9.31cdeg^{-1} target contains the peak spatial frequency of the N10 text target but the N20 9.31cdeg^{-1} text target elicits a larger subjective DOF. This may be explained as larger DOF found with larger targets may also be due to the extent of the retina over which the target image forms. Ciuffreda, Wang and Wong (2005) stated that DOF increases at a rate of 0.11D/degree.

Midpoint of DOF

The midpoint of the subjective DOF was found to be further forward (more myopic) than the initial fixation point. This agrees with the findings of Ogle and Schwartz (1959). Wang and Kenneth (2006) reported that this was due to hyperfocal refraction, in which the distal edge of the DOF is made conjugate with optical infinity rather than the eye’s far point in order to maximise the range of clear vision. When subjective refraction is conducted at six metres this is achieved by maximising plus as conducted in the current study.

Midpoints of subjective DOF were found to be displaced further towards the Badal lens for the targets containing the peak spatial frequency of the text. By moving the target towards the Badal lens the effective power of the Badal lens is reduced and more myopic. The midpoints when viewing the N20 targets were found to be more myopic for the unfiltered and the peak text spatial frequency target compared to the lowest (2.33cdeg^{-1}) and highest (18.62cdeg^{-1}) spatial frequency filtered targets. The midpoints when viewing N10 targets showed a similar pattern to the N20 targets but the effect of spatial frequency filter did not quite reach significance (*p*=0.11). Green and Campbell (1965) reported that the optimum focus was more myopic for low and medium spatial frequency relative to high spatial frequency targets due to spherical aberration. The current study suggested that optimum focus is dependent on the peak text spatial frequency.

Radhakrishnan *et al.* (2004) reported that intermediate spatial frequency gratings (3cdeg^{-1}) had a more myopic optimum focus for myopes when compared to non-myopes. The current study found no significant differences in subjective DOF midpoints between myopes and emmetropes when viewing text targets.

4.5 Conclusion

The current study found that refractive error group differences in subjective DOF are dependent on the blur criterion (just noticeable or non resolvable). Myopes were not found to be worse at blur detection compared with emmetropes, but tolerated higher levels of blur when viewing text before they declared it unresolvable, regardless of text spatial frequency content.

If the perception and legibility of text is linked to accommodative responses, then myopes may tolerate more blur when viewing text before they initiate a corrective response. Myopes would then experience more hyperopic blur when reading, which has been suggested in animal studies as a potential myopigenic stimulus (Smith and Hung, 1999). Whether the poorer non resolvable blur found in myopes is a precursor or consequence of myopia requires longitudinal studies.

Blur detection and text resolution is dependent on the peak text spatial frequency and text detail rather than the specific spatial frequency band-pass filter. The largest levels of blur are tolerated for the unfiltered compared to filtered targets. Of the filtered targets the largest DOF was found when viewing the target containing the peak text spatial frequency (9.31cdeg^{-1} N10 and 4.65cdeg^{-1} N20 targets). This may benefit the visual system by maximizing the range over which text can be read.

Subjective DOF midpoints are more myopic when viewing the unfiltered targets and the targets containing the peak text spatial frequency. The possibility that the optimum focus is the result of increased levels of spherical aberration will be examined later in chapter 7.

Chapter 5: Experiment 3 Dynamic accommodation in myopes and emmetropes

5.1 Introduction

Dynamic accommodation is usually defined by the accommodative latency and accommodative RT (section 1.3.4; Cufflin and Mallen, 2008). Culhane and Winn (1999) and Seidel, Gray and Heron (2005) found no significant difference in accommodative latency between myopes and emmetropes but did find myopes to have longer RT. O'Leary and Allen (2001) found positive RT (far to near) were more often longer in myopes compared to emmetropes. Radhakrishnan, Allen and Charman (2007) investigated the dynamics of accommodative facility in myopes and emmetropes using +/- flippers at working distances of 40cm and 6m. Whilst viewing a near target accommodation velocity was similar in the two groups but relaxation of accommodation, and therefore RT, were slower in myopes. Whilst viewing a distance target the velocity of accommodation and relaxation was slower in myopes. It might have been expected that the current study would find myopes have no difference in accommodative latencies but slower RTs when compared to emmetropes.

Accommodation is thought to be primarily driven by retinal blur (Fincham, 1951; Campbell and Westheimer, 1960; Phillips and Stark, 1977; Tucker and Charman, 1979; Kruger and Pola, 1986; Morgan, 1986; Kruger and Pola, 1987; Ciuffreda, 1991) followed by disparity cues (Fincham and Walton, 1957). It has been reported that in the absence of disparity and retinal blur cues, proximal cues play a much larger role (Hung, Ciuffreda and Rosenfield, 1996; Thiagarajan, Lakshminarayanan and Bobier, 2008). In this study dynamic accommodation methods provide large proximal cues whereas objective DOF methods provide more subtle proximal cues (a gradual change in target vergence) and rely more on retinal blur cues. This study considered the effects of spatial frequency filtered text on proximal and retinal blur cues.

Mid-range spatial frequencies are thought to best drive accommodation (Owens, 1980; Bour, 1981; Ward, 1987). The CSF of the human eye also suggests that peak sensitivity of gratings is around 4-6cdeg^{-1} (Figure 5.1). This would suggest that a blurred retinal image would be best detected at the peak spatial frequency and may be most likely to initiate an appropriate corrective accommodative response.

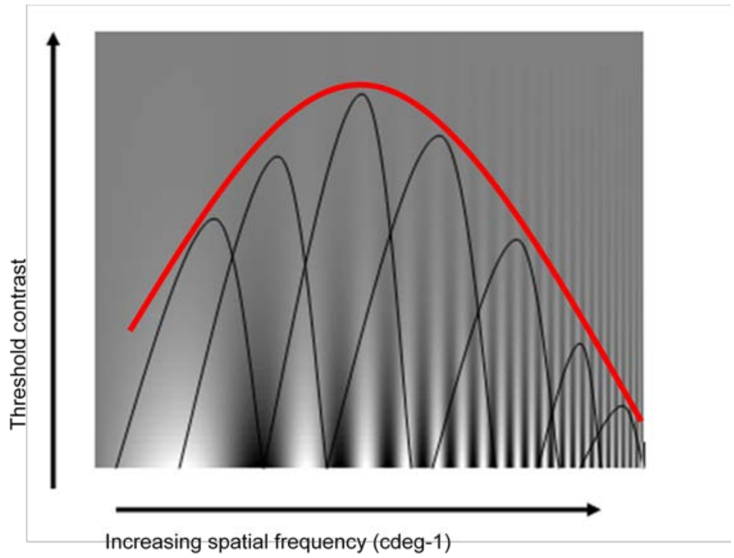

Figure 5.1 Contrast sensitivity function of the human eye shown in red. Black arches show the sensitivity of single channels. The peak spatial frequency lies between 4-6cdeg^{-1}

The previous experiments showed that non resolvable subjective DOF was larger in myopes and for targets containing the peak text spatial frequency. As peak text spatial frequency targets provided the poorest blur cues, it may be that dynamic accommodation responses are also poorer with peak text spatial frequency targets.

5.2 Methods

Subjects

43 subjects were recruited from the staff and students of Anglia Ruskin University.

Table 5.1 Refractive error range of each group

Refractive Error Group	n	Refractive error (mean ± SD; range)
Emmetropes	17	0.20DS ± 0.24; +0.50 to -0.37
Myopes	26	-3.89DS ± 1.62; -1.11 to -6.99

Procedure

Full methodology has been described in the methods section 2.6 but a summary follows here:

- Dynamic accommodation measurements were taken with the PRII from the right eye fully corrected in a trial frame and the left eye occluded. This was due to the refraction limits of the PRII (+5D to -7D).
- A stop watch and the PRII recording were started simultaneously, whilst the subject viewed the distance target
- The subject altered their focus of attention when requested from distance 6/9 Snellen letter (2m) to the near text target (40cm) and back again three times in each direction at 10s intervals
- Data was exported and cleaned using a MATLAB program written for this task
- The MATLAB program identified the start and end of accommodation changes as specified in a predetermined protocol, in order to calculate the accommodative latency and RT
- All the above measurements were taken for each text size and spatial frequency filtered text and were presented in a randomised order

5.3 Results

The experiment conducted was of mixed design with one independent (between subjects) variable; refractive group and two repeated measures (within subjects) variables; target size with two levels (N10 and N20) and spatial frequency filter with six levels (unfiltered, 2.33cdeg^{-1}, 4.65cdeg^{-1}, 9.31cdeg^{-1}, 18.62cdeg^{-1} and 37.25cdeg^{-1}). The N10 2.33cdeg^{-1} target had been excluded from the study and the N20 37.25cdeg^{-1} target could not be created (explained in section 2.4.5). For this reason initial analysis considered the results for the two target sizes separately. The dependent variables were positive (distance to near) and negative (near to distance) accommodative latency and positive and negative

RTs. Calculation of latency and RT are fully described in section 2.6.4. Standard deviations for individuals' positive and negative recordings were also considered.

Z-scores were calculated to identify outliers (section 2.5.3) and where z-scores were more than 3.29 values were replaced by the mean plus 3 times the standard deviation. This was applied to seventeen individual entries (<5% of the data).

Normality of the complete cohort was investigated using Kolmogorov-Smirnov test of normality for all positive and negative latency and RT for each target viewed. There were mixed results where K-S values were non-significant (p>0.05) and the null hypothesis could not be rejected. Non parametric tests were therefore required but there is no non parametric alternative to the mixed design repeated measures ANOVA. Mann-Whitney, a non parametric alternative to one-way ANOVA, was used to analyse differences between refractive error groups and each target was analysed separately. Non parametric Friedman's ANOVA, based on ranks, was used as an alternative to repeated measures ANOVA with only one repeated measure; spatial frequency filter. Parametric repeated measures ANOVA with LSD correction for multiple comparisons were also conducted to support any non parametric results found.

5.3.1 Latency and response times

Average positive latencies were longer than negative latencies and average positive RTs were longer than negative RTs for N10 and N20 unfiltered targets (Table 5.2).

Table 5.2 Dynamic accommodation measurements for the N10 and N20 unfiltered targets

	Unfiltered N10		Unfiltered N20	
	Positive	Negative	Positive	Negative
Latency (s)	0.24s±0.16	0.18s±0.13	0.21s±0.14	0.17s±0.14
Response times (s)	1.06s±0.50	0.99s±0.49	1.16s±0.62	0.89s±0.38

Positive accommodative latency

No significant difference in the positive latencies or the standard deviations were found in myopes and emmetropes for any target (Figures 5.2-5.5; Mann-Whitney; *p*>0.05). Friedman's ANOVA found no significant effect of the spatial frequency filtered text on the positive latency for N10 targets [$X^2(4)=1.32$, *p*=0.86] or N20 targets [$X^2(4)=1.74$, *p*=0.78].

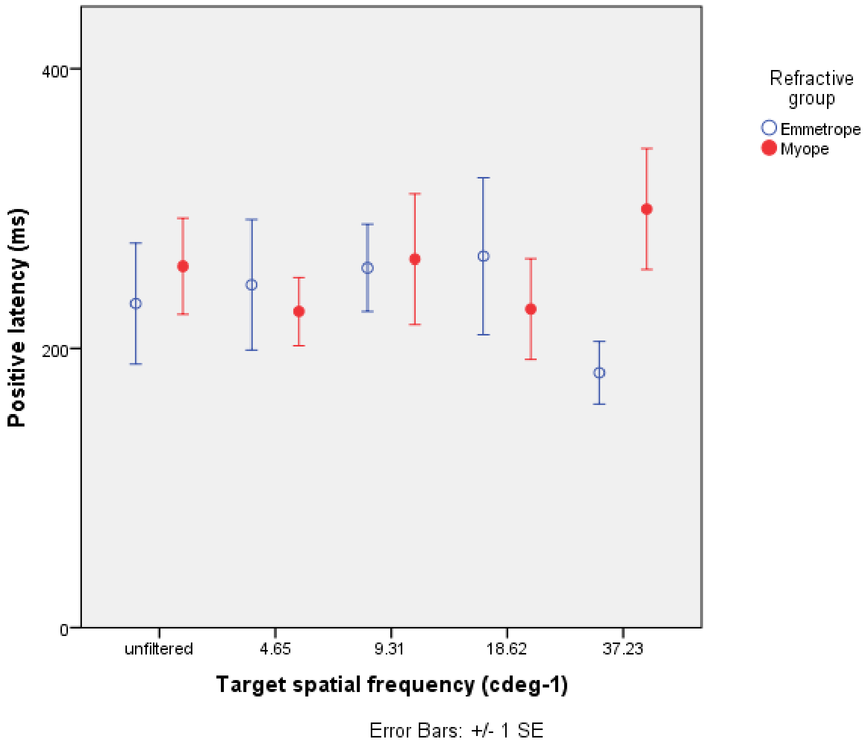

Figure 5.2 Positive dynamic latency observed for all the N10 targets for both myopes and emmetropes. There was no significant effect of refractive group on positive latency for any target (Mann-Whitney; *p*>0.05)

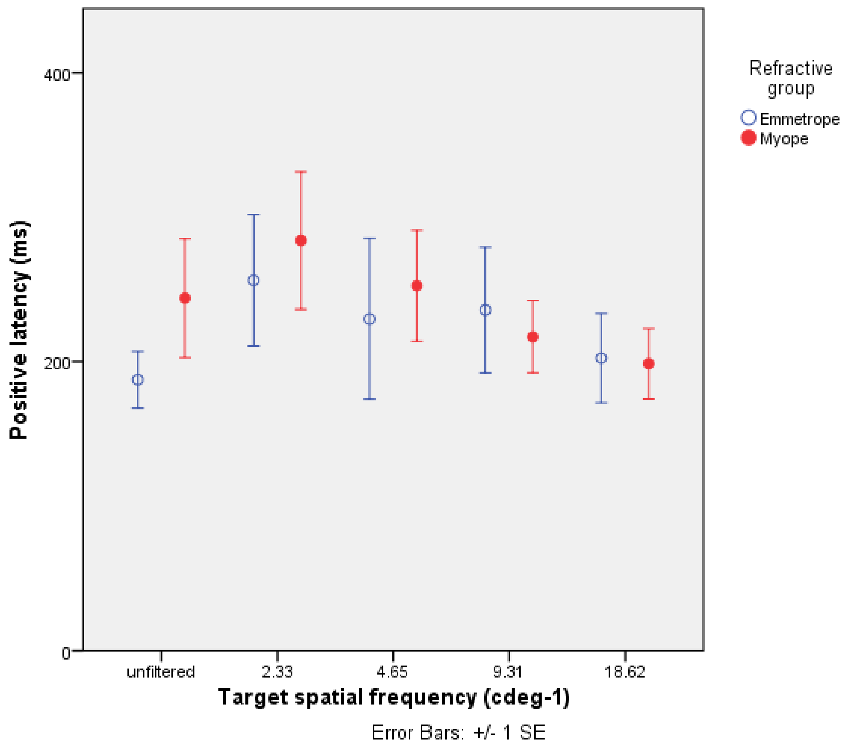

Figure 5.3 Positive dynamic latency observed for all the N20 targets for both myopes and emmetropes. There was no significant effect of refractive group on positive latency (Mann-Whitney; p>0.05)

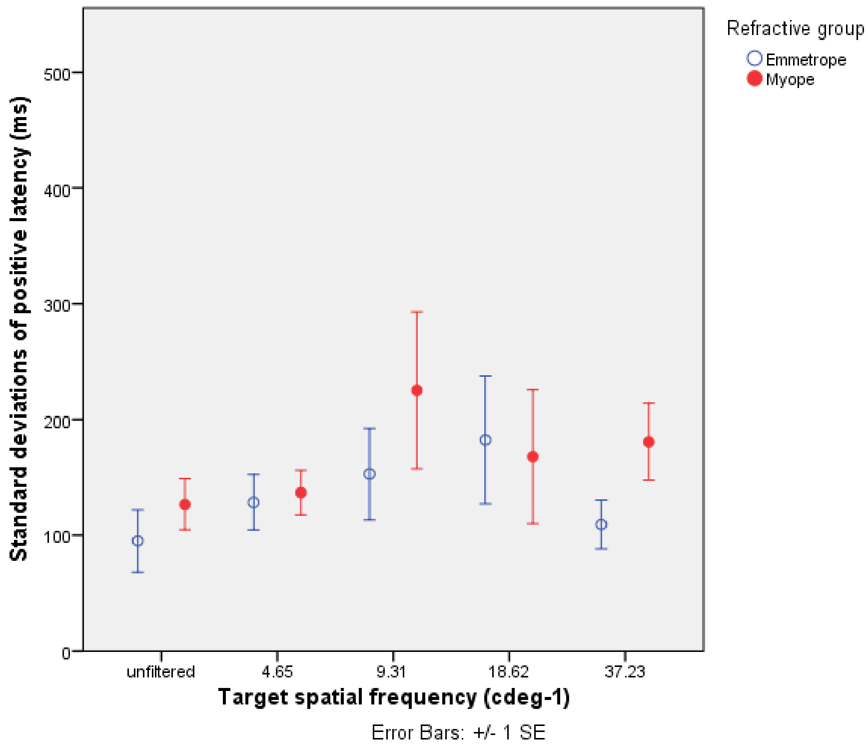

Figure 5.4 Standard deviations of positive dynamic latency observed for all the N10 targets for both myopes and emmetropes. There was no significant effect of refractive group on standard deviations of positive latency (Mann-Whitney; p>0.05)

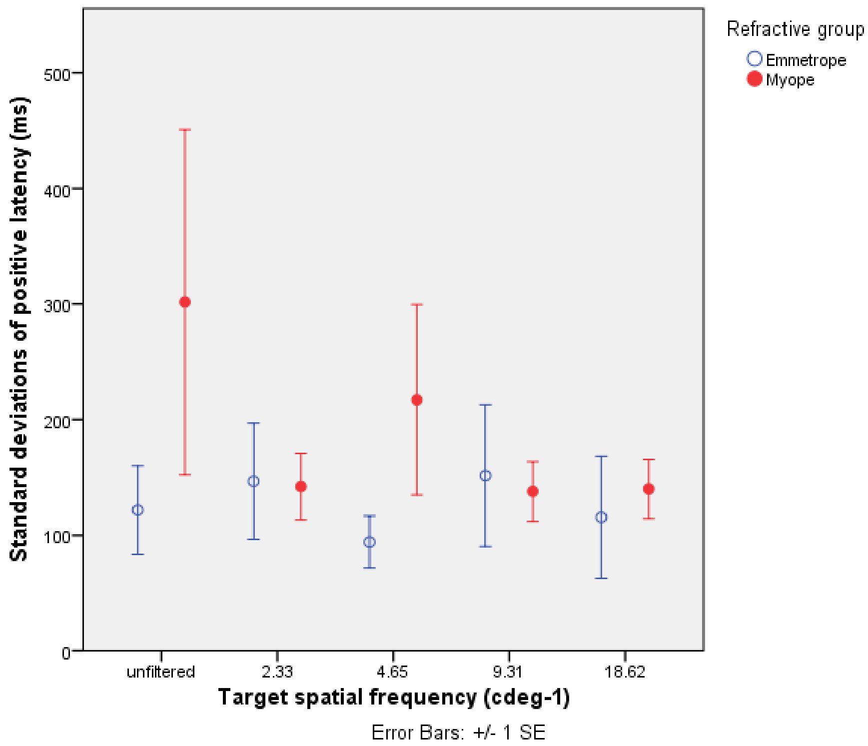

Figure 5.5 Standard deviations of positive dynamic latency observed for all the N20 targets for both myopes and emmetropes. There was no significant effect of refractive group on standard deviations of positive latency (Mann-Whitney; $p>0.05$)

Repeated measures ANOVA found no significant effect of refractive error group on positive latency for either N10 targets [$F(1,31)=1.71$, $p=0.20$] or for N20 targets [$F(1,29)=0.10$, $p=0.76$]. There was no significant effect of the spatial frequency filtered text on positive latency for either N10 targets [$F(4,124)=0.27$, $p=0.90$] or for N20 targets [corrected using Greenhouse-Geisser; $F(2.97, 86.24)=1.69$, $p=0.18$]. There was no significant difference between subjects' individual standard deviations in the two refractive groups for positive latency with N10 targets [$F(1,30)=1.21$, $p=0.28$] or with N20 targets [$F(1,21)=1.17$, $p=0.29$]. These results support the findings of the non parametric statistical tests.

Negative accommodative latency

No significant difference in the negative latency or the standard deviations were found in myopes and emmetropes for any target (Figures 5.6-5.9; Mann-Whitney; $p>0.05$).

Friedman's ANOVA found no significant effect of spatial frequency filtered text on negative latency for N10 targets [$X^2(4)=3.29$, $p=0.51$] or N20 targets [$X^2(4)=0.79$, $p=0.94$].

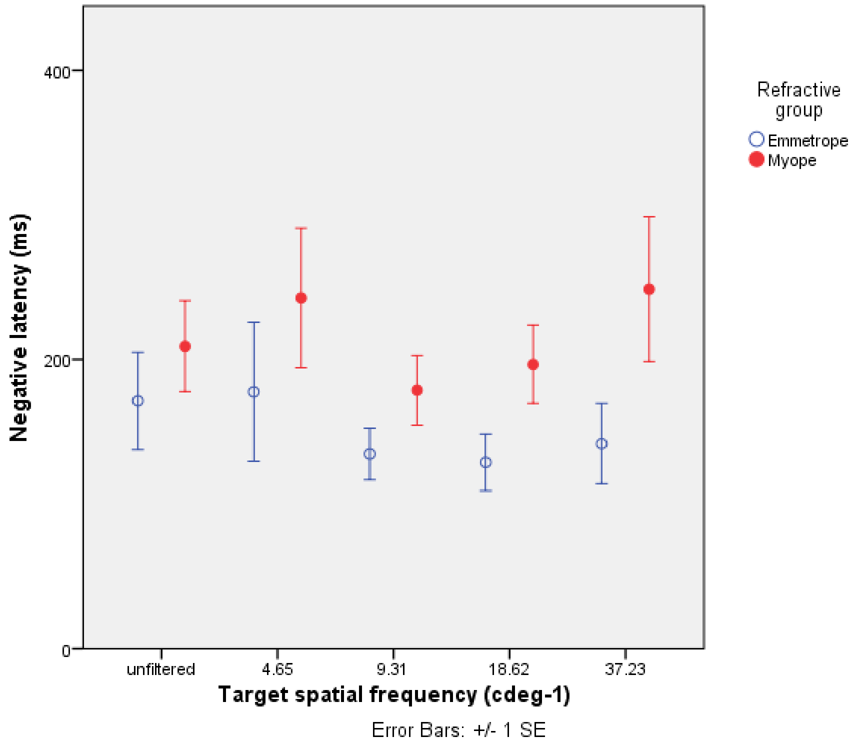

Figure 5.6 Negative dynamic latency observed for all the N10 targets for both myopes and emmetropes. There was no significant effect of refractive group on negative latency *(*Mann-Whitney*;* $p>0.05$)

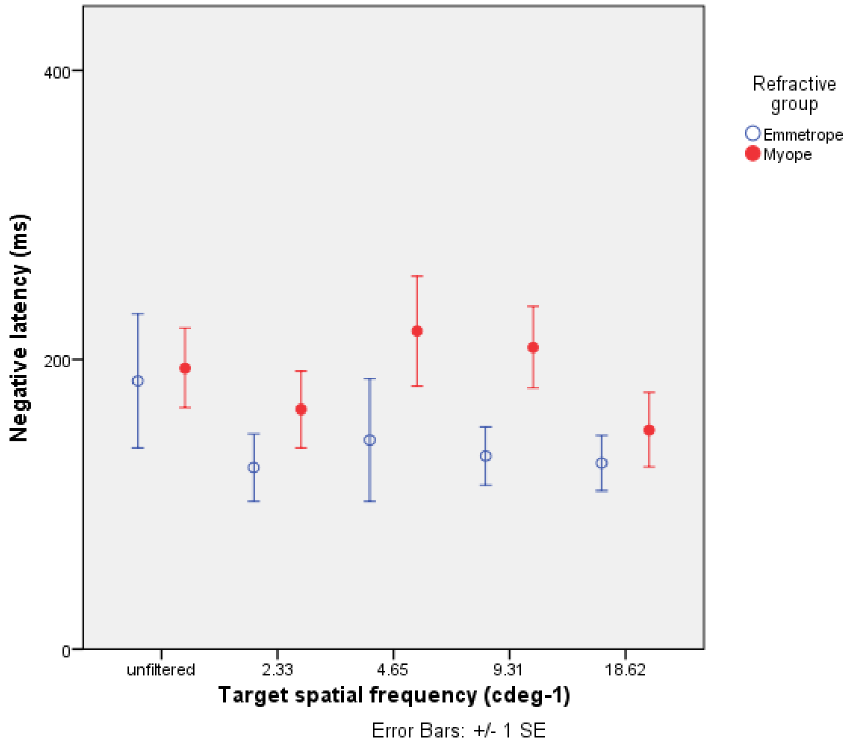

Figure 5.7 Negative dynamic latency observed for all the N20 targets for both myopes and emmetropes. There was no significant effect of refractive group on negative latency (Mann-Whitney*;* $p>0.05$)

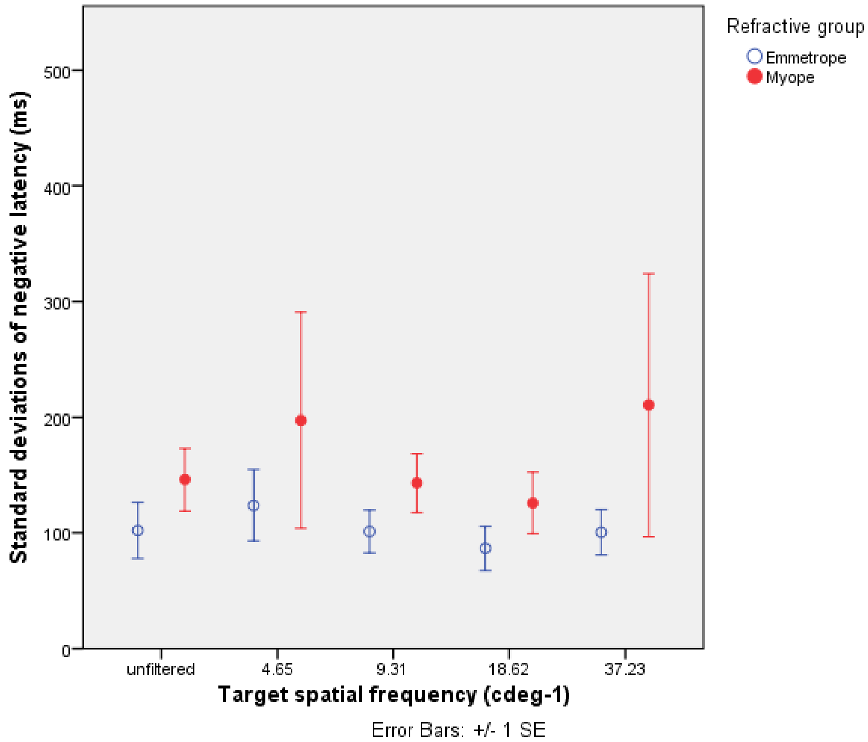

Figure 5.8 Standard deviations of negative dynamic latency observed for all the N10 targets for both myopes and emmetropes. There was no significant effect of refractive group on standard deviations of negative latency (Mann-Whitney; $p>0.05$)

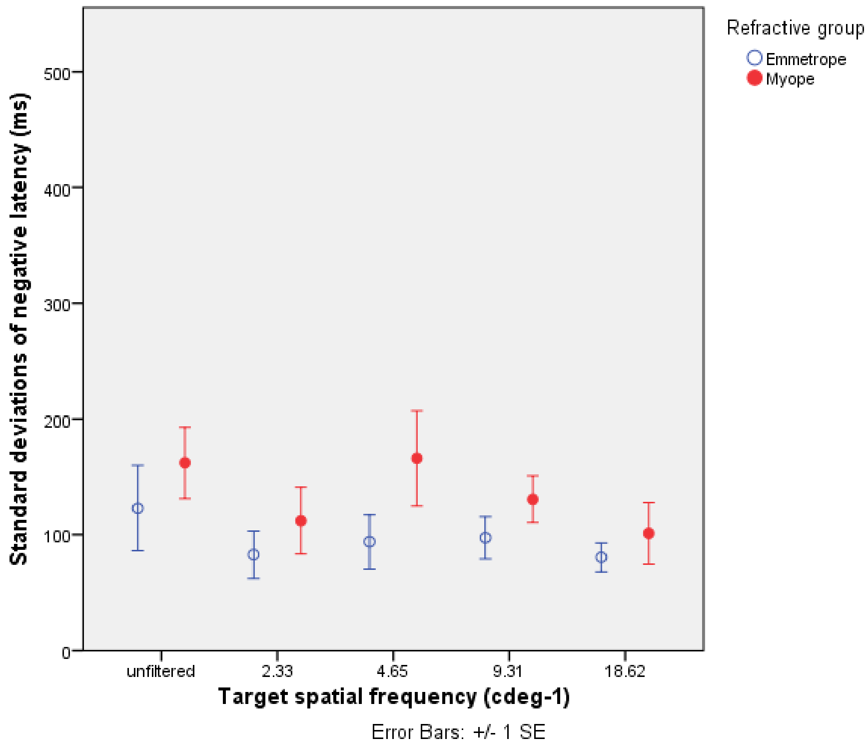

Figure 5.9 Standard deviations of negative dynamic latency observed for all the N20 targets for both myopes and emmetropes. There was no significant effect of refractive group on standard deviations of negative latency (Mann-Whitney; $p>0.05$)

Repeated measures ANOVA found no significant effect of refractive group on negative latency for either N10 targets [$F(1,30)=3.27$, $p=0.08$] or N20 targets [$F(1,29)=3.69$, $p=0.07$]. There was no significant effect of the spatial frequency filtered text on negative latency for either N10 targets [corrected using Greenhouse-Geisser; $F(3.22,96.58)=1.15$, $p=0.34$] or for N20 targets [$F(4,116)=1.05$, $p=0.39$]. Parametric results support the findings of the non parametric results which found no effect of refractive error group or spatial frequency filtered text on negative accommodative latency.

There was no significant difference between subjects' individual standard deviations in the two refractive groups for negative latency with N10 targets [$F(1,26)=3.08$, $p=0.09$] but a significant difference for N20 targets [$F(1,23)= 4.72$, $p=0.04$, $\eta^2=0.17$]. Standard deviations were larger in myopes compared to emmetropes but this difference was not large enough to reach significance in all parametric and non parametric test methods. Results might suggest that myopes do show more variable responses compared to emmetropes.

Positive response times

Mann-Whitney tests found significantly longer positive RTs in myopes compared to emmetropes for N10 targets (Figure 5.10): 9.31cdeg^{-1} ($U=99.00$, $z=-2.82$, $p=0.01$) and 18.62cdeg^{-1} ($U=74.5$, $z=-3.43$, $p=0.001$) and N20 targets (Figure 5.11): unfiltered ($U=107.50$, $z=-2.69$, $p=0.01$), 2.33cdeg^{-1} ($U=100.50$, $z=-2.30$, $p=0.02$), 9.31cdeg^{-1} ($U=136.00$, $z=-1.96$, $p=0.05$) and 18.62cdeg^{-1} ($U=110.00$, $z=-2.27$, $p=0.02$). Positive RTs were not significantly different between myopes and emmetropes for all other targets (Mann-Whitney; $p>0.05$). Standard deviations of individuals' positive RT (Figures 5.12-5.13) were found to be significantly different between myopes and emmetropes only for N10 target 9.31cdeg^{-1} ($U=260$, $z=2.31$, $p=0.02$) and the unfiltered N20 target ($U=232$, $z=2.73$, $p=0.01$). Friedman's ANOVA found no significant effect of the spatial frequency filtered text on the positive RT for N10 targets [$X^2(4)=5.27$, $p=0.26$] or N20 targets [$X^2(4)=4.87$, $p=0.30$].

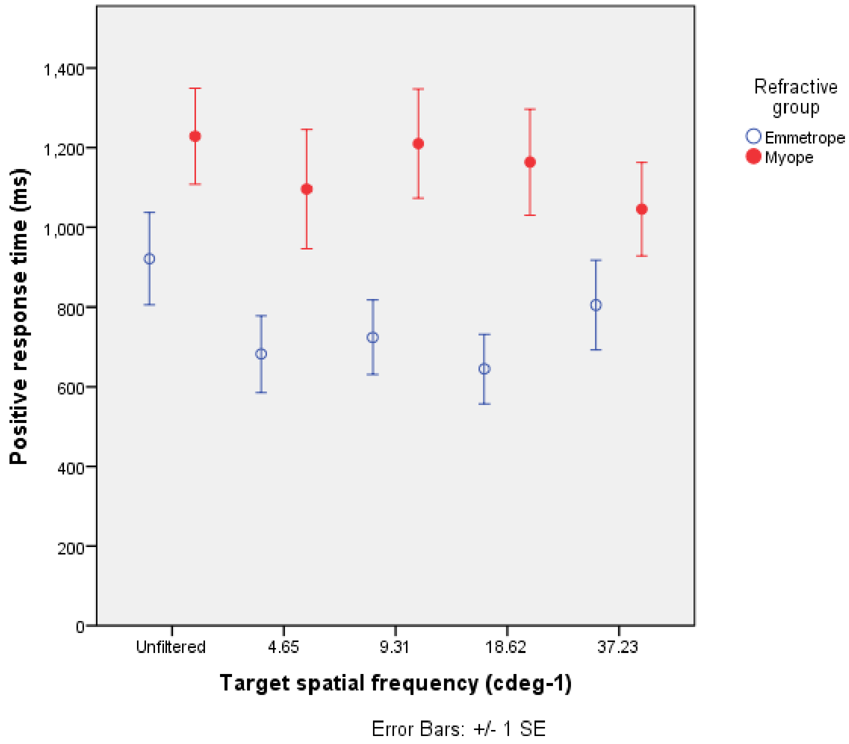

Figure 5.10 Positive dynamic RTs observed for all the N10 targets for both myopes and emmetropes. There was a significant effect of refractive group on positive RTs for N10 targets: 9.31cdeg^{-1} (*U*=99.00, *z*=-2.82, *p*=0.01) and 18.62cdeg^{-1} (*U*=74.5, *z*=-3.43, *p*=0.001)

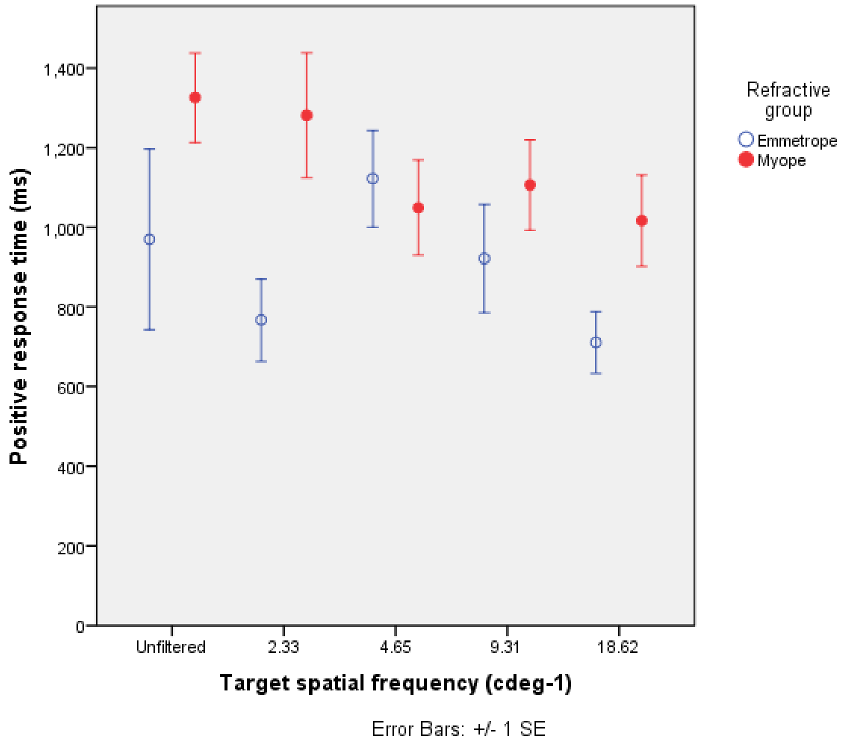

Figure 5.11 Positive dynamic RTs observed for all the N20 targets for both myopes and emmetropes. There was a significant effect of refractive group on positive RTs for N20 targets: unfiltered (*U*=107.50, *z*=-2.69, *p*=0.01), 2.33cdeg^{-1} (*U*=100.50, *z*=-2.30, *p*=0.02), 9.31cdeg^{-1} (*U*=136.00, *z*=-1.96, *p*=0.05) and 18.62cdeg^{-1} (*U*=110.00, *z*=-2.27, *p*=0.02)

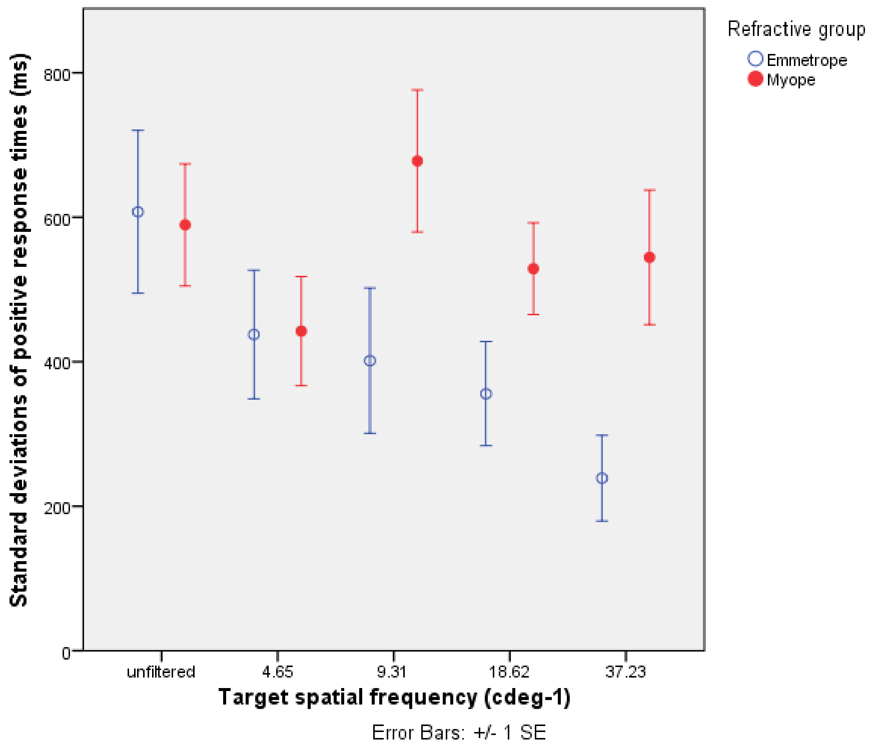

Figure 5.12 Standard deviations of positive dynamic RTs observed for all the N10 targets for both myopes and emmetropes. There was only a significant effect of refractive group on standard deviations of positive RTs for N10 9.31cdeg^{-1} target: (U=260, z=2.31, p=0.02)

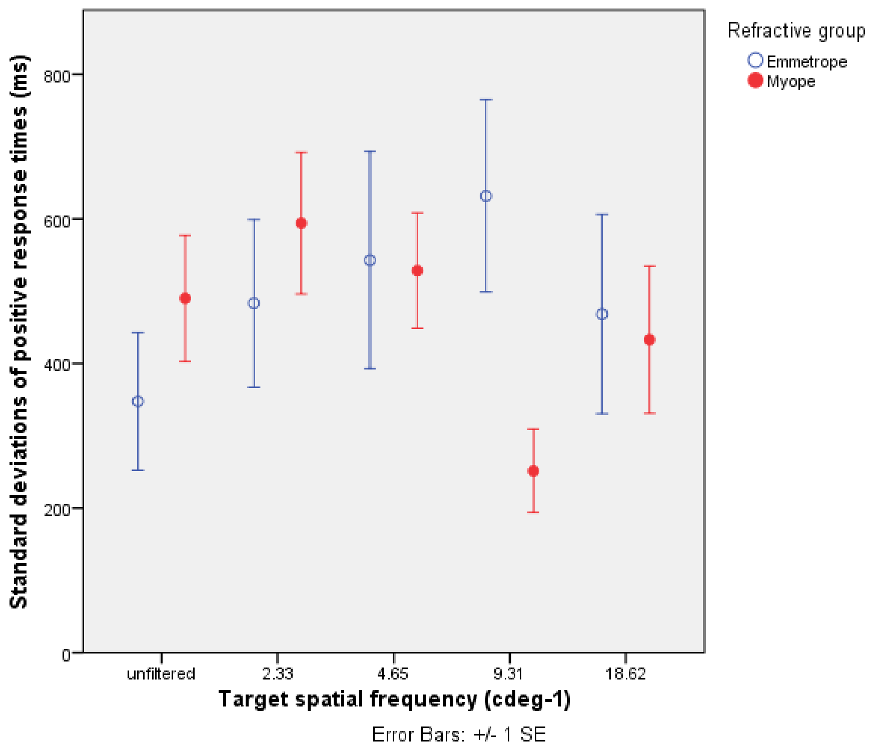

Figure 5.13 Standard deviations of positive dynamic RTs observed for all the N20 targets for both myopes and emmetropes. There was only a significant effect of refractive group on standard deviations of positive RTs for N20 unfiltered target: (U=232, z=2.73, p=0.01)

Repeated measures ANOVA found a significant effect of refractive group on positive RTs for N10 targets [F(1,32)=8.06, p=0.01, η^2=0.20]. Myopes showed significantly longer RTs when compared with emmetropes for all N10 targets: unfiltered (1197.04ms and 921.25ms respectively), 4.65cdeg^{-1} (1022.59ms and 682.08ms respectively), 9.31cdeg^{-1} (1129.26ms and 723.75ms respectively), 18.62cdeg^{-1} (1125.95ms and 644.17ms respectively) and 37.23cdeg^{-1} (987.41ms and 805.00ms respectively). There was also a significant effect of refractive group on positive RTs for N20 targets [$F(1,30)=4.35$, $p=0.04$, $\eta^2=0.13$] . Myopes showed significantly longer positive RTs when compared with emmetropes for N20 targets: unfiltered (1308.42ms and 969.74ms respectively), 2.33cdeg^{-1} (1193.68ms and 767.18ms respectively), 9.31cdeg^{-1} (1047.72ms and 921.54ms respectively) and 18.62cdeg^{-1} (969.47ms and 711.28ms respectively) but not for 4.65cdeg^{-1} (969.82ms and 1022.05ms respectively). There was no significant effect of the spatial frequency filtered text on positive RTs for either N10 targets [$F(4,128)=1.64$, $p=0.17$] or when viewing N20 targets [$F(4,120)=1.63$, $p=0.17$]. These results support the findings of the non parametric statistical tests.

Repeated measures ANOVA showed myopes to have significantly larger standard deviations for their positive RTs when compared to emmetropes with all filtered N10 targets [$F(1,29)= 6.02$, $p=0.02$, $\eta^2=0.17$]. There was no significant difference between standard deviations of refractive groups for positive RTs with N20 targets [$F(1,19)=0.28$, $p=0.60$]. The findings of the parametric and non parametric statistical tests are inconsistent although may suggest some increased variability in the responses of myopes compared to emmetropes.

As the positive RTs were longer in myopes compared to emmetropes, Pearson's correlation was conducted to investigate whether refractive error group differences were related to the level of refractive error. Significant negative correlations were found between the positive RTs and spherical equivalent refraction when viewing N10 targets: unfiltered ($r=-0.34$, $p=0.04$), 4.65cdeg-1 ($r=-0.40$, $p=0.01$), 9.31cdeg-1 ($r=0.33$, $p=0.04$) and 18.62cdeg-1 ($r=-0.53$, $p<0.001$) but not for 37.23cdeg-1 ($r=-0.27$, $p=0.09$). Significant negative correlations were found between the positive RTs and spherical equivalent refraction when viewing N20 targets: unfiltered ($r=-0.42$, $p=0.01$), 2.33cdeg-1 ($r=-0.42$, *p*=0.01) and 18.62cdeg-1 (*r*=-0.37, *p*=0.05) but not 4.65cdeg-1 (*r*=-0.07, *p*=0.67) and 9.31cdeg-1 (*r*=0.13, *p*=0.42). The negative correlations show that the more myopic the subject the longer their positive RTs.

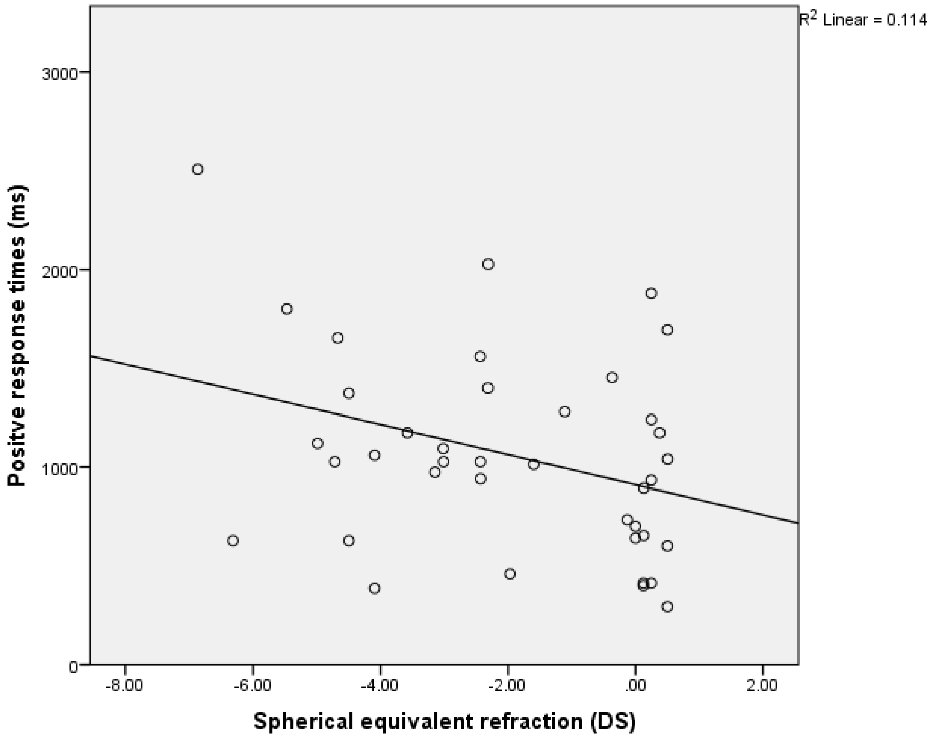

Figure 5.14 Correlation between positive RTs and spherical equivalent refraction for an unfiltered N10 text target

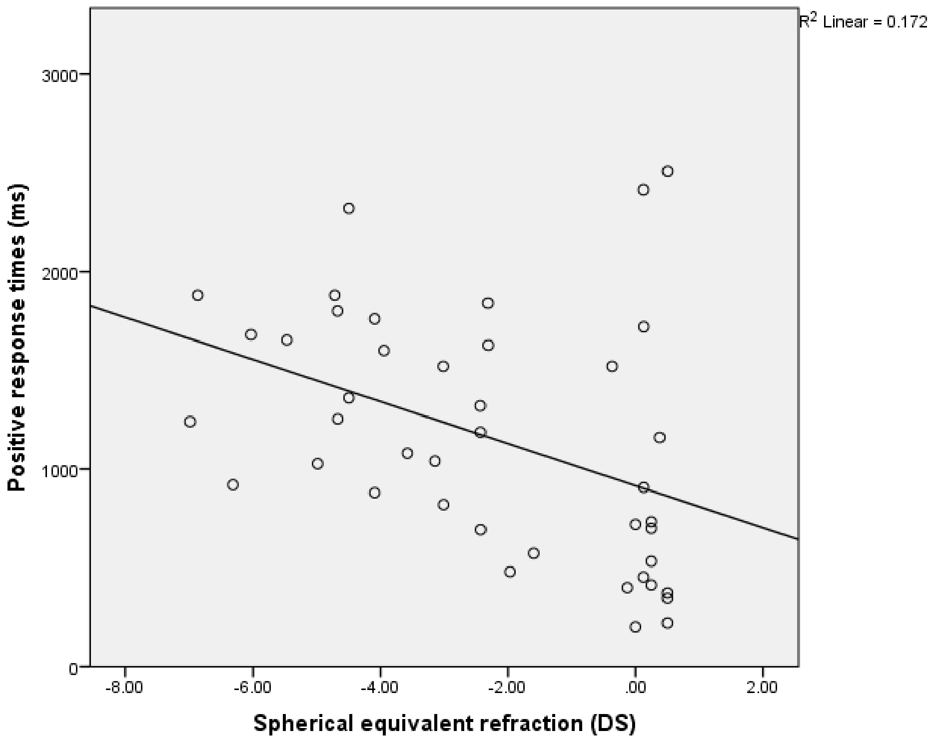

Figure 5.15 Correlation between positive RTs and spherical equivalent refraction for an unfiltered N20 text target

Negative response times

No significant difference in negative RTs or standard deviations were found between myopes compared to emmetropes for any target (Figures 5.16-5.19; Mann-Whitney; p>0.05). Friedman's ANOVA found no significant effect of the spatial frequency filtered text on the negative RTs for N10 targets [$X^2(4)=1.93$, $p=0.75$] or N20 targets [$X^2(4)=2.34$, $p=0.67$].

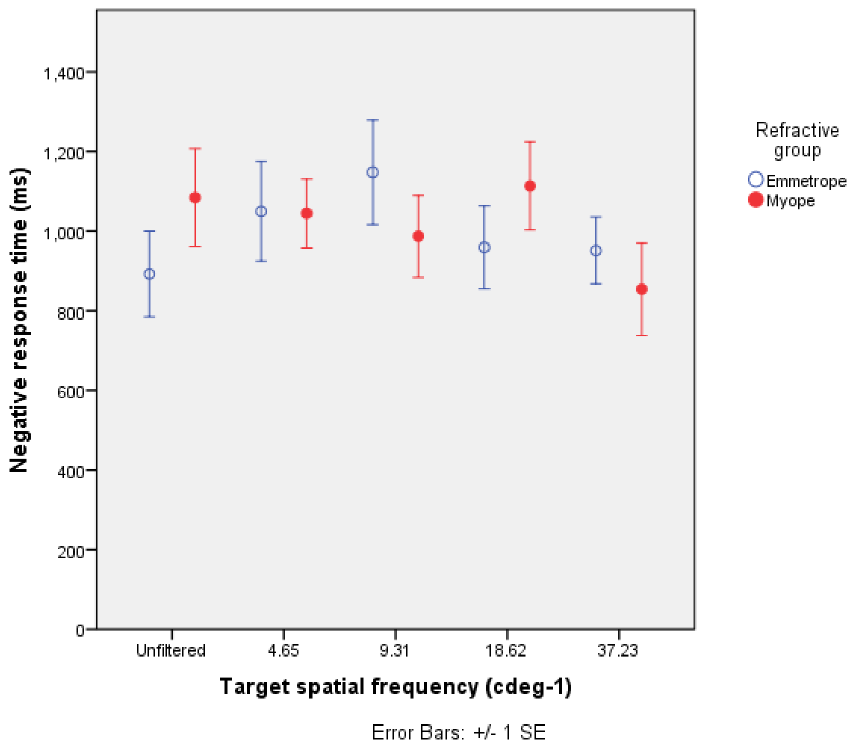

Figure 5.16 Negative dynamic RTs observed for all the N10 targets for both myopes and emmetropes. There was no significant effect of refractive group on negative RTs (Mann-Whitney; p>0.05)

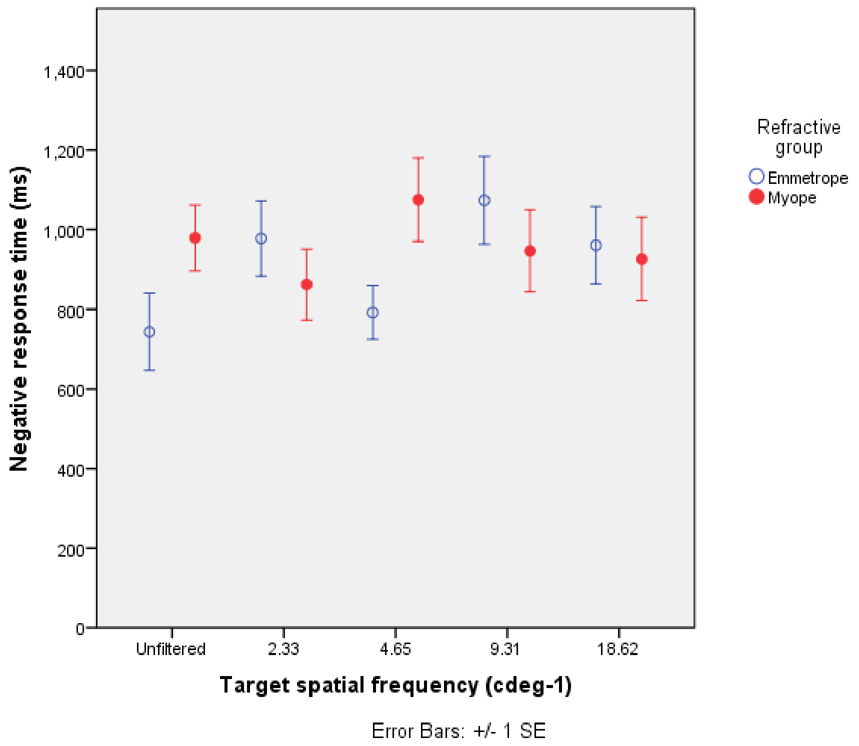

Figure 5.17 Negative dynamic RTs observed for all the N20 targets for both myopes and emmetropes. There was no significant effect of refractive group on negative RTs (Mann-Whitney; $p>0.05$)

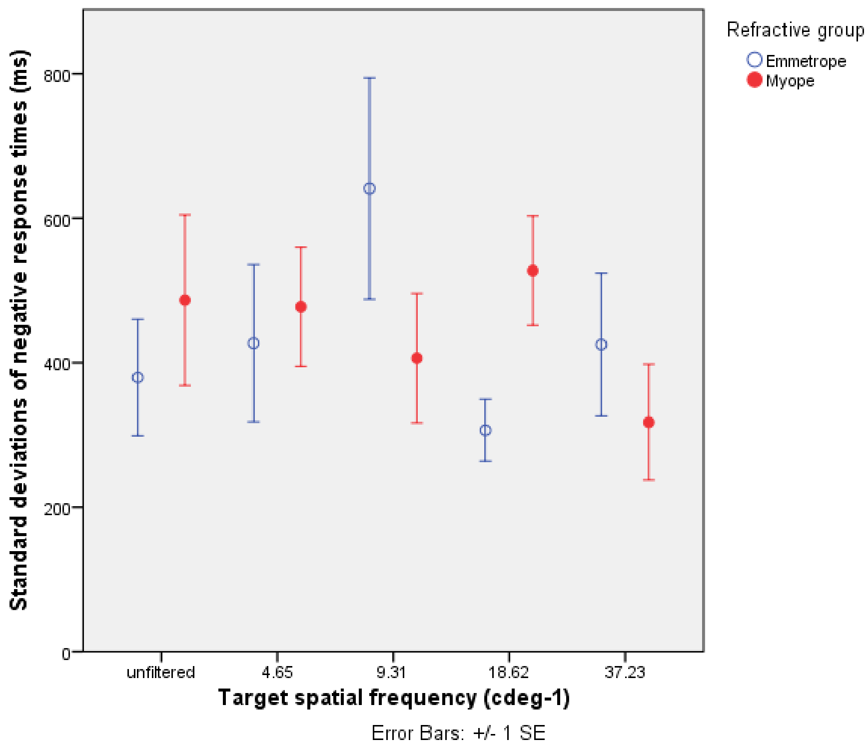

Figure 5.18 Standard deviations of negative dynamic RTs observed for all the N10 targets for both myopes and emmetropes. There was no significant effect of refractive group on standard deviations of negative RTs (Mann-Whitney; $p>0.05$)

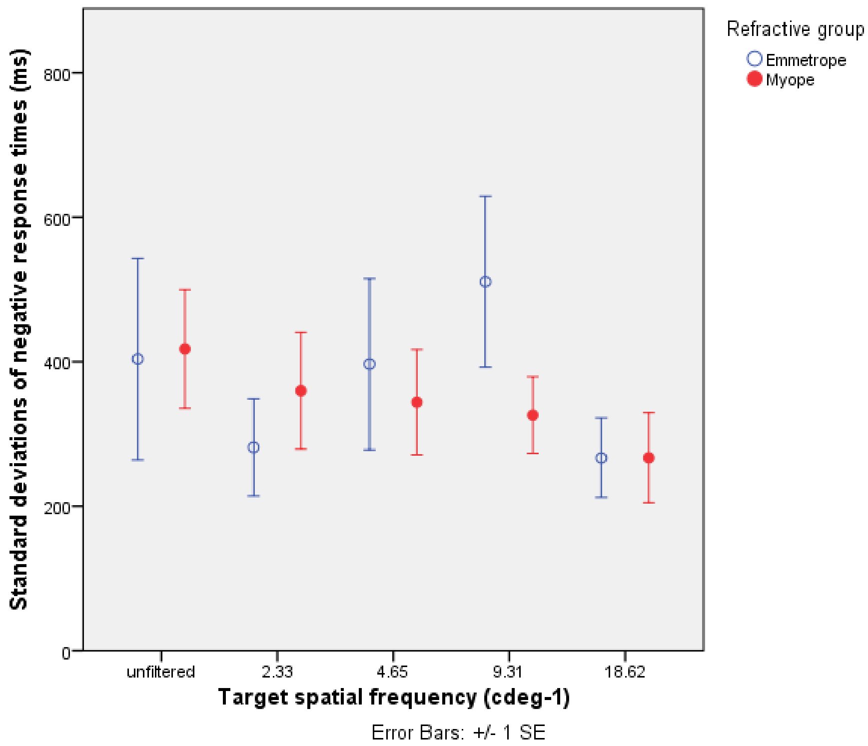

Figure 5.19 Standard deviations of negative dynamic RTs observed for all the N20 targets for both myopes and emmetropes. There was no significant effect of refractive group on standard deviations of negative RTs (Mann-Whitney; $p>0.05$)

Repeated measures ANOVA also found no significant effect of refractive group on negative RTs for either N10 targets [$F(1,31)=0.10$, $p=0.76$] or for N20 targets [$F(1,31)=0.50$, $p=0.48$]. No significant difference was found between individuals standard deviations of negative RTs between myopes and emmetropes with N10 targets [$F(1,25)=0.01$, $p=0.93$] or with N20 targets [$F(1,23)= 0.46$, $p=0.51$]. The parametric findings support those of the non parametric statistical tests.

5.3.2 Target size comparisons

Wilcoxon signed rank test, the non parametric alternative to a dependent t-test, was used to compare dynamic accommodation measurements made for the two target sizes N10 and N20. Each target spatial frequency filter had to be analysed separately. There was no significant difference between N20 and N10 targets for any target for positive and negative latency or positive and negative RTs ($p>0.05$).

Repeated measure ANOVA with two repeated measures variables; target size and spatial frequency filter, was also conducted. This revealed that the effect of target size on dynamic responses was not significant for positive latency [$F(1,24)=0.73$, $p=0.40$], negative latency [$F(1,25)=1.09$, $p=0.31$], positive RTs [$F(1,27)=1.35$, $p=0.26$] or negative RTs [$F(1,26)=3.34$, $p=0.08$]. The parametric findings support the results from the non parametric tests.

5.4 Discussion

Mean positive accommodative latencies and RTs were longer than negative latencies and RTs when viewing unfiltered N10 and N20 targets (Table 5.2). Latency values in the current study compared well to those of Culhane and Winn (1999) who reported similar accommodative latencies in their emmetropic subjects (0.25±0.05 positive and 0.22±0.22 negative) and RTs of about 1 second while subjects viewed a Maltese cross target. Strang *et al.* (2011) measured longer accommodative latencies (0.41s±0.13) although commented that this may have been as a result of using isolated spatial frequency targets when compared with other studies reporting shorter latencies which had used broader spatial frequency targets (Kasthurirangan, Vilupuru and Glasser, 2003; Seidel, Gray and Heron, 2003; Bharadwaj and Schor, 2005; Kasthurirangan and Glasser, 2005; Bharadwaj and Schor, 2006).

Accommodative latencies in myopes compared to emmetropes have been found to be longer (Seidel, Gray and Heron, 2003) and similar (Schaeffel, Wilhelm and Zrenner, 1993; Seidel, Gray and Heron, 2005; Strang *et al.*, 2011). Positive and negative latencies were not found to be significantly different between the two refractive error groups regardless of the target viewed.

Accommodative RTs have been found to be longer in myopes compared to emmetropes (Culhane and Winn, 1999; Seidel, Gray and Heron, 2005) and similar (Seidel, Gray and Heron, 2003). The current study found that the dynamic responses differed only in myopes and emmetropes when comparing their positive RTs. Positive RTs were related to the magnitude of refractive error. This suggested that myopes are no slower to initiate their accommodation responses compared to emmetropes but are slower to complete their inward accommodation response. Seidel, Gray and Heron (2005) and Culhane and Winn (1999) also found that myopes exhibited significantly longer RTs (beginning to end of accommodation response) but showed no difference in the accommodative latencies when compared to emmetropes.

In an experiment which used a Badal system to limit proximal cues Seidel, Gray and Heron (2003) found that late onset myopes had longer accommodative latencies. A later experiment (Seidel, Gray and Heron, 2005) used free space conditions, where proximal cues were available and showed that myopes had no difference in latencies but had longer RTs. The current experiment uses an open view system where the subject altered their attention between a distance and a near target thus providing large proximal cues. It may be proximal cues were used to initiate accommodative responses but retinal blur cues were used to refine accommodation. Strang *et al.* (2011) also commented in their study that where large accommodative step responses are required it is likely that perceived proximity is the primary stimulus for the accommodative response system whereas for smaller step responses it may be the retinal image blur which provides the primary stimulus. Myopes do not appear to have problems interpreting proximal cues but may be poorer at using retinal blur cues to fine tune the accommodation. The current study would support the theory that myopes are poorer at responding to blur cues (Rosenfield and Abraham-Cohen, 1999).

There is still speculation about whether poorer accommodation responses seen in myopes are neural in origin (Gwiazda *et al.*, 1993) or an innate structural problem (Mutti, 2010). Figures 5.20-5.21 are MATLAB outputs demonstrating examples of two subjects' (one emmetrope and one myope) positive accommodation responses. The myope shows greater variability during their accommodation response before reaching the final level which suggests a deficient neural accommodation response to a change in target vergence. If myopes had shown uninterrupted (straight) but slow positive accommodation changes, this may have been more indicative of a structural deficiency in myopes preventing efficient accommodation. This is more supportive of Gwiazda *et al.* (1993) who suggested that poorer accommodative responses in myopes are neural in origin.

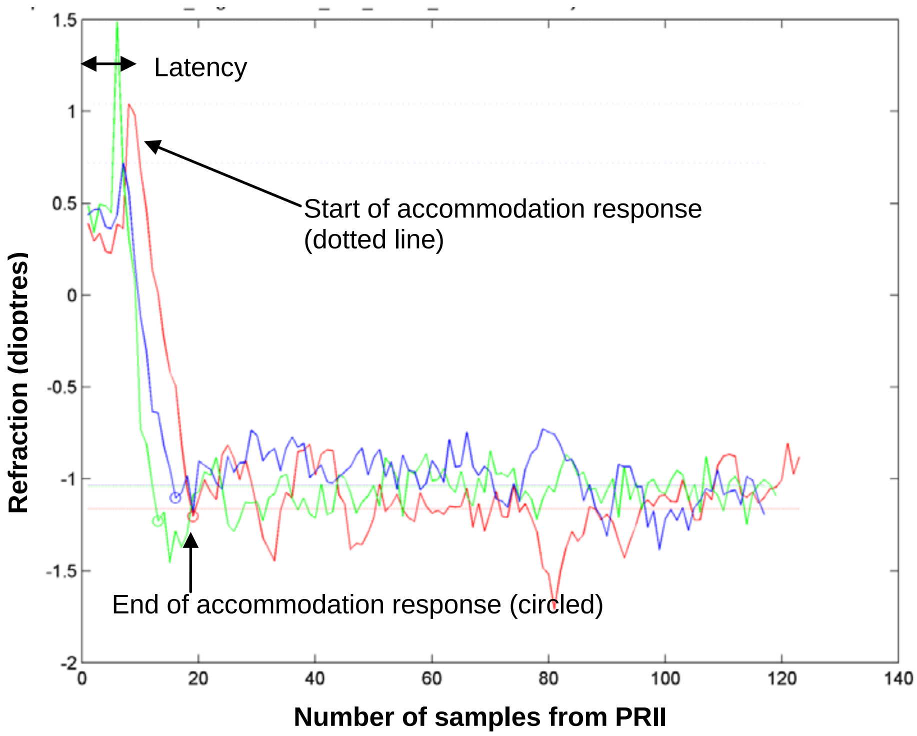

Figure 5.20 Three (red, blue and green) positive dynamic recordings from an emmetropic subject. Change of target vergence occurs at time 0 on the x-axis

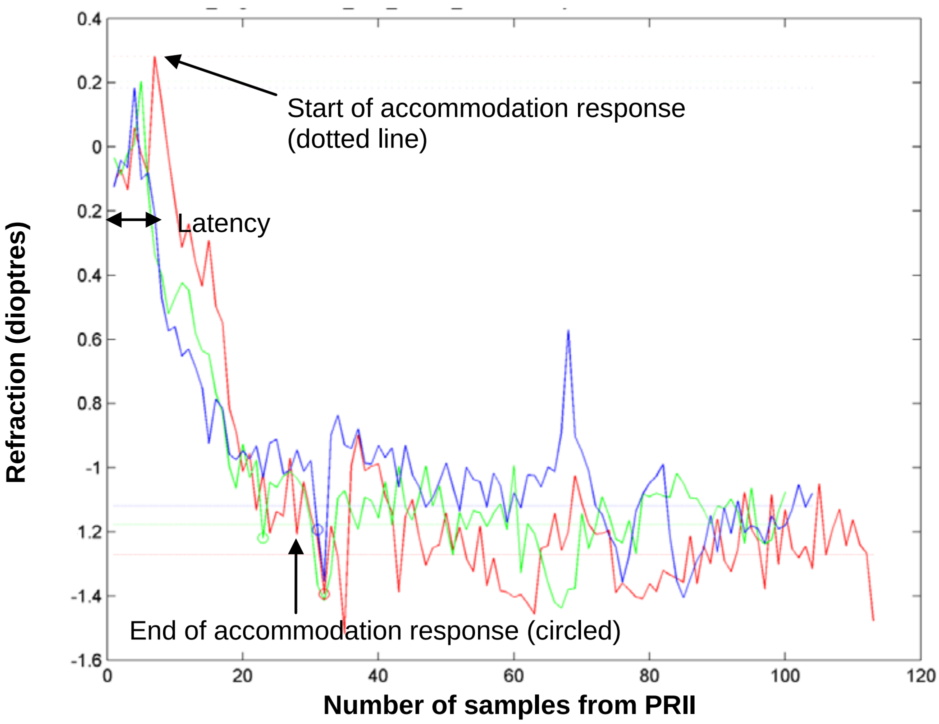

Figure 5.21 Three (red, blue and green) positive dynamic recordings from a myopic subject. Change of target vergence occurs at time 0 on the x-axis

The ‘fine focus theory’ of accommodation proposed by Charman and Heron (1979) suggested that accommodation responses are initiated by the lower spatial frequencies whilst higher spatial frequencies are used for accommodation refinement. This is thought to be due to lower spatial frequencies being less affected by defocus blur and therefore the only spatial frequencies available for the accommodation response system (Okada *et al.*, 2006). More recent studies have supported the theory that higher spatial frequencies aid accommodation refinement as the high spatial frequency information is unlikely to be perceived during a step response (Mucke *et al.*, 2008; Mucke *et al.*, 2010).

The current study suggests that dynamic accommodation responses (latencies and RTs) were independent of spatial frequency filtered text and size. Bour (1981) suggested that dynamic accommodation responses were optimal for intermediate spatial frequency gratings but only measured 2 subjects and used a Badal lens set up to limit proximal cues. Proximal cues available in the current study may improve dynamic accommodation responses and limit differences found with different spatial frequency filtered targets. Strang *et al.* (2011) found for small accommodative step responses (3/2D) spatial frequency of their grating targets had less effect on the size of the accommodative response. For larger step responses (4/1D) dynamic accommodation responses were dependent on the size of the accommodative stimulus demand and the target spatial frequency (with grating targets). They reported greater accommodative responses and an improved percentage of correct accommodation responses when viewing the mid spatial frequency grating (4cdeg^{-1}). The current study found that spatial frequency filtered text and text size did not influence the way subjects responded to proximal cues. The step response in the current study was 2.5/0.5D but it may be the differences found was due to the broad spatial frequencies available in the filtered text targets.

Strang *et al.* (2011) recorded a lower percentage of correct accommodation responses in myopes compared to emmetropes for the low (0.5cdeg^{-1}) and high (16cdeg^{-1}) grating targets for smaller step responses. However, they reported a similar accommodative dynamics to differing spatial frequency targets for myopes and emmetropes for larger accommodative step responses. The current study also found that with a larger step response (2.5/0.5D) the spatial frequency filtered text did not influence the differences seen in positive RTs between myopes and emmetropes. This suggests that even with broad spatial frequency targets, the effect on accommodation dynamics between myopes and emmetropes is limited for large step responses where large proximal cues are available.

5.5 Conclusion

In the presence of large proximal cues, myopes are no slower at initiating accommodative responses but may be poorer at utilizing retinal blur cues to refine their response when moving from a distance to near target compared to emmetropes.

Myopes' inability to respond well to blur has been previously reported (Rosenfield and Abraham-Cohen, 1999). The current study investigated subjective DOF using a Badal system to limit proximal cues allowing only retinal blur cues and myopes tolerated more blur before reporting a target was illegible. Clinically poorer accommodation responses in myopes have not been reported to be symptomatic. It may be that poorer blur sensitivity, seen in the subjective DOF experiments, demonstrates the development of a protective mechanism in myopes to ensure clarity in the event of inefficient accommodation.

Myopes were slower at reaching their final level of accommodation irrespective of the target under observation. Spatial frequency filtered text did affect subjective DOF in the absence of proximal cues. Where proximal cues are available, as in the dynamic experiments, spatial frequency filtered text did not appear to have significant effects on accommodation responses. This suggests that accommodation responses are driven by a range of spatial frequencies when viewing complex targets.

Chapter 6: Experiment 4 Objective depth of focus and accommodative microfluctuations in myopes and emmetropes

6.1 Introduction

A model of accommodation has been described previously (section 1.3.2) where defocus blur initiates an accommodative response. The DOF influences the detection of small changes in target vergence and refinement of accommodation responses. This influence may occur if someone were to adjust the position of a near task, perhaps whilst reading. DOF is known to be larger in myopes than emmetropes (Jiang, 1997; Vasudevan, Ciuffreda and Wang, 2006a).

Many studies have reported a link between myopia and near-work (Zadnik, 1997 for review; Angle and Wissmann, 1980; Kinge *et al.*, 2000) particularly for reading. Studies have also suggested that mid-range spatial frequency gratings best drive accommodation (Owens, 1980; Bour, 1981; Ward, 1987). Reading text contains a range of spatial frequencies which may affect accommodation responses differently. If mid-spatial frequencies elicit the most accurate accommodation responses it might have been expected that mid-spatial frequency filtered text targets would show a smaller DOF and the most accurate accommodation responses. However, the subjective DOF was larger with the text peak spatial frequency (different bands for two target sizes). If blur perception and accommodation responses are linked it might have been expected that these targets would also elicit the largest objective DOF.

Accommodative microfluctuations provide a feedback loop for the accommodation response system and have been found to be larger in myopes and with very high or very low spatial frequency sine wave targets (Day *et al.*, 2009a). Larger microfluctuations resulting from larger DOF will increase levels of accommodative inaccuracy. The current study used spatial frequency filtered text targets to examine the magnitude of microfluctuations in different refractive groups and investigate the influence of text detail and size.

6.2 Pilot Study

Refractive group differences

A pilot study was conducted to investigate DOF, test experimental design and make preliminary assessments of the differences between refractive groups. Objective DOF measurements were taken using the procedure described in section 2.7 but only tested the unfiltered N10 text target. 18 subjects were recruited; 7 emmetropes (0.09D±0.31; range 0.50 to -0.50D) and 11 myopes (-3.76D±2.24; range -0.62D to -8.03D). This preliminary data was used in the production of the MATLAB program designed to standardize the definition of the point of accommodation change. Figure 6.1 shows an example of a PRII recording. This pilot study noted the accommodation change manually. Two unmasked observers compared their results.

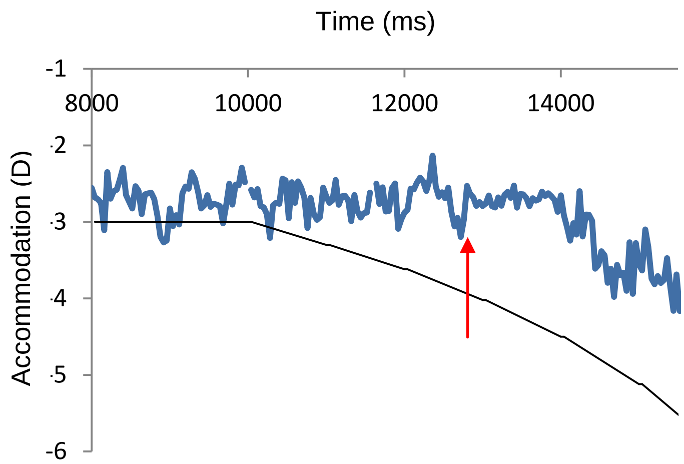

Figure 6.1 Example of an accommodation trace from PRII. Black line shows stimulus vergence in dioptres. The red arrow indicated the point where the accommodation change was identified

Table 6.1 Mean proximal, distal and total DOF for all emmetropes and myopes whilst viewing the unfiltered target

Refractive group		Proximal DOF(D)	Distal DOF(D)	Total DOF(D)
Emmetrope	Mean	0.402	0.383	0.784
	Std. Deviation	0.200	0.236	0.426
Myope	Mean	0.477	0.468	0.859
	Std. Deviation	0.220	.179	0.332
Total	Mean	0.446	0.433	0.830
	Std. Deviation	0.209	0.202	0.361

Although results showed a larger DOF in myopes compared to emmetropes, one-way ANOVA revealed this was not significant for proximal [$F(1,16)=0.52$, $p=0.48$], distal [$F(1,16)=0.72$, $p=0.41$] or total DOF [$F(1,17)=0.17$, $p=0.68$].

The same recordings for each subject were analysed by two observers. Paired sample t-tests were used to investigate inter-observer variation. There was no significant difference between the observations of proximal DOF [$t(15)=0.08$, $p=0.94$] but there was a significant difference in the distal DOF recorded by the two observers [$t(15)=-2.29$, $p=0.04$]. This pilot study highlighted the need for a protocol and an automated way of determining the point of accommodation change to ensure uniform analysis. This initiated the design of the MATLAB program enabling this task to be conducted more efficiently and accurately (described fully in sections 2.6.3 and 2.7.3).

Investigating the effects of spatial frequency filtered text on objective DOF

The pilot study further considered the effect of spatial frequency filtered text. Target design underwent refinement (section 2.4.5) following this initial study. The preliminary filtered targets had peak spatial frequencies of: 3, 11, 20 and 28cdeg^{-1}.

For this pilot study, 14 subjects were recruited; 5 emmetropes (0.13D±0.45; range +0.50 to -0.63D) and 9 myopes (-4.82D±2.99D; range -1.88 to -11.00D).

Table 6.2 Proximal, distal and total DOF values for all spatial frequency filtered targets

Target		Proximal DOF	Distal DOF	Total DOF
Unfiltered	Mean	1.395	0.310	1.705
	Std. Deviation	0.776	0.121	0.768
3cdeg^{-1}	Mean	1.082	0.290	1.359
	Std. Deviation	0.526	0.1460	0.534
11cdeg^{-1}	Mean	1.061	0.360	1.421
	Std. Deviation	0.285	0.138	0.307
20cdeg^{-1}	Mean	1.131	0.385	1.516
	Std. Deviation	0.626	0.153	0.682
28cdeg^{-1}	Mean	1.086	0.330	1.415
	Std. Deviation	0.608	0.081	0.613

These values show larger proximal DOF compared to distal DOF which may be as a result of the target on the motorised track moving at a constant speed which would move at a faster speed in Ds^{-1} proximally compared to distally. The point of accommodation change was identified manually. This data was not included in the final results as later experiments had improved subjects instruction to reduce this effect, automated MATLAB programs designed to clean the data and identify the point of accommodation change and redesigned spatial frequency filtered targets.

Repeated measures ANOVA found no significant difference in the total objective DOF between myopes and emmetropes [$F(1,13)=0.30$, $p=0.60$]. No significant effect of the target spatial frequency filter was found on either proximal [corrected for Greenhouse Geisser; $F(1.74, 22.66)=1.41$, $p=0.26$], distal [$F(2.34, 30.36)=1.48$, $p=0.24$] or total DOF [$F(1.72, 22.41)=0.93$, $p=0.40$]. Due to small subject numbers one-way ANOVA was conducted for each target separately to confirm the results of refractive error group differences. No significant difference was found between myopes and emmetropes in the proximal, distal or total objective DOF for any target ($p>0.05$).

Proximal DOF was found to be larger than distal DOF suggesting small inward changes in target vergence would be slower to elicit corrective accommodation responses.

6.3 Main experiment

6.3.1Subjects

46 subjects were recruited from the staff and students of Anglia Ruskin University.

Table 6.3 Refractive error range of each group

Refractive Error Group	n	Refractive error (mean ± SD; range)
Emmetropes	**18**	**0.15DS ± 0.31; +0.50 to -0.63**
Myopes	**28**	**-4.46DS ± 2.60; -1.11 to -12.44**

6.3.2 Procedure

Full methodology has been described in the methodology section 2.7 but a summary follows here.

- Objective DOF was measured using the PRII which recorded accommodation changes from the right eye while the left eye was occluded. The PRII limits on the maximum refraction (+5 to -7DS) meant that with accommodative effort, it was necessary to fully correct the right eye with a trial frame
- Times roman text targets were band-pass filtered for different spatial frequencies. The band-pass filters were one octave in width and based around the peak spatial frequency of the limb width of the text; N10 calculated to be 9.31cdeg^{-1} and N20 4.65cdeg^{-1}. Other band-pass filters applied were one octave away from the peak text spatial frequencies; 2.33cdeg^{-1}, 18.62cdeg^{-1} and 37.23cdeg^{-1} (section 2.4.5)
- Two text sizes; N10 and N20; allowed consideration as to whether it was the specific spatial frequency band or a feature of text detail which affected blur sensitivity

- A stop watch and the PRII recording were simultaneously and a measurement of accommodation whilst the subject viewed the static target at 40cm was taken for a period of 10 seconds. After 10s the motorised track was started and as the motor displaced the target at 2.1cms^{-1}, the linear and dioptric DOF could be calculated
- The target was moved from 40cm proximally and then distally four times at a speed of 2.1cms^{-1}. Vasudevan, Ciuffreda and Wang (2006b) used a target moving at an approximate speed (0.1-0.15Ds^{-1}). The current study used a motorised track which moved at 2.1cms^{-1} from a 40cm starting point, which if assuming a DOF of 1D, 0.5D either side of the starting point, approximated a similar speed and allowed the target position to be time linked with the refraction recording
- The subject was asked to maintain target clarity
- A MATLAB program written for the purpose was used to clean the data and identify the point at which accommodation changed (section 2.7.3). This defined the proximal and distal edge of the DOF
- Microfluctuations were recorded using the PRII whilst the subject was asked to maintain clarity of each target at 40cm for 60s. A MATLAB program written for the purpose cleaned the data, calculated the RMS values of the 60s recording, plotted an FFT of the recording and calculated the low, medium and high frequency components from power spectrum analysis
- As adaptation to spatial frequencies has been reported (section 1.7.4) all the above measurements were taken for each spatial frequency filtered text target, presented in a randomised order, in order to limit any potential effects of adaptation

Targets were positioned at 40cm from the subject's right eye slightly nasal to the line of sight so as not to obstruct the PRII. The gaze position was examined for the first 10 subjects to ensure minimal deviation from the line of sight. Assuming a DOF of 1D, the shift in gaze deviation was an average of 1.35±0.57degrees proximally and -1.03±0.53degrees distally. The PRII states that the recording is valid within 10° of gaze deviation and reports suggest that there is a maximum of 0.25D off axis error introduced for a 10° eccentricity (Schaeffel, Wilhelm and Zrenner, 1993).

The PRII simultaneously records refraction and pupil diameter (between 4 and 8mm). Although DOF is known to change with pupil diameter (Atchison, Charman and Woods, 1997) the DOF is not significantly affected until the pupil size is less than 3mm (Campbell, 1957; Charman and Whitefoot, 1977). The MATLAB cleaning program removed any accommodation data where the pupil measurement was less than 4mm.

6.4 Results

6.4.1 Objective DOF

A mixed design experiment was conducted with refractive group as an independent variable and target size and spatial frequency filter as within subject variables. Target size had two levels (N10 and N20) and spatial frequency filter had six levels (unfiltered, 2.33cdeg^{-1}, 4.65cdeg^{-1}, 9.31cdeg^{-1}, 18.62cdeg^{-1} and 37.25cdeg^{-1}). The N10 2.33cdeg^{-1} target had been excluded from the study and the N20 37.25cdeg^{-1} target could not be created (explained in section 2.4.5). For this reason initial analysis consider the results for the two target sizes separately. The dependent variables measured in this experiment were objective proximal and distal DOF (in dioptres) and the standard deviations of the subjects' recordings.

Z-scores were used to identify outliers (section 2.5.3) and those with z-scores >3.29 were replaced by the mean plus three times the standard deviation. This was applied to six individual entries only (<1% data).

Normality of the complete cohort was investigated using Kolmogorov-Smirnov test of normality for all proximal and distal DOF values for each target viewed. All K-S values were non significant (p>0.05) except for the values of proximal DOF for the N10 9.31cdeg^{-1} (p=0.04) and 18.62cdeg^{-1} (p=0.03) and N20 18.62cdeg^{-1} (p=0.04) targets, therefore the null hypothesis could not be rejected. Non parametric tests were therefore required but there is no non parametric alternative to the mixed design repeated measures ANOVA. Mann-Whitney, a non parametric alternative to one-way ANOVA, was used to analyse differences between refractive error groups but each target had to be analysed separately. Non parametric Friedman's ANOVA, based on ranks, was used as an alternative to repeated measures ANOVA but only allowed one repeated measures variable; spatial frequency filter. Parametric Repeated measures ANOVA were also conducted to support any non parametric results found.

Objective DOF when viewing N10 targets

The Mann-Whitney test found proximal objective DOF to be significantly larger in myopes compared to emmetropes (Figure 6.2) but only for the unfiltered target (U=134.00, z=-2.06, p=0.04). Distal objective DOF was significantly larger in myopes compared to emmetropes (Figure 6.3) for the 9.31cdeg^{-1} target (U=149.00, z=-2.18, p=0.03) and 37.23cdeg^{-1} target (U=101.00, z=-3.29, p=0.002).

Myopes showed larger total objective DOF when compared with emmetropes (Figure 6.4) for the unfiltered target (0.18D and 0.12D respectively) and for filtered targets; 4.65cdeg^{-1} (0.18D and 0.13D respectively), 9.31cdeg^{-1} (0.17D and 0.12D respectively) and 37.23cdeg^{-1} (0.19D and 0.09D respectively) but not with target 18.62cdeg^{-1} (0.13D and 0.14D respectively). However the Mann-Whitney test only found this difference to be significant when viewing the unfiltered target (U=129.00, z=-2.05, p=0.04) and filtered targets: 9.31cdeg^{-1} (U=109.00, z=-2.43, p=0.02) and 37.23cdeg^{-1} (U=77.00, z=-3.93, p=0.001). These differences may be statistically significant but may demonstrate limited clinical significance due to individual variation. Total objective DOF individual data for the unfiltered and 9.31cdeg^{-1} filtered N10 targets can be found in Appendix E.

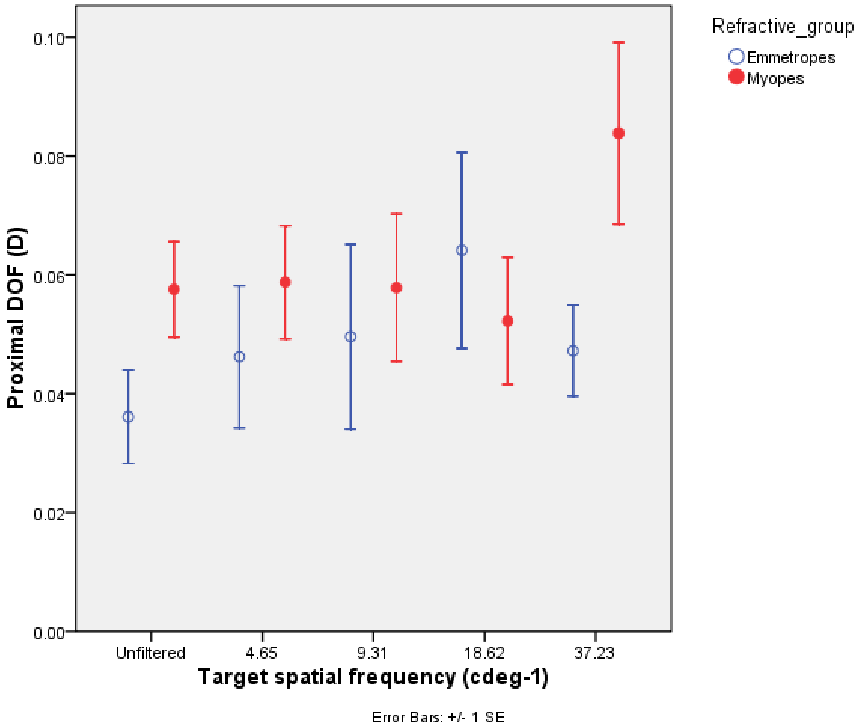

Figure 6.2 Proximal DOF for the N10 targets for myopes and emmetropes. Proximal DOF was found to be significantly larger in myopes but only for the unfiltered target (U=134.00, z=-2.06, p=0.04)

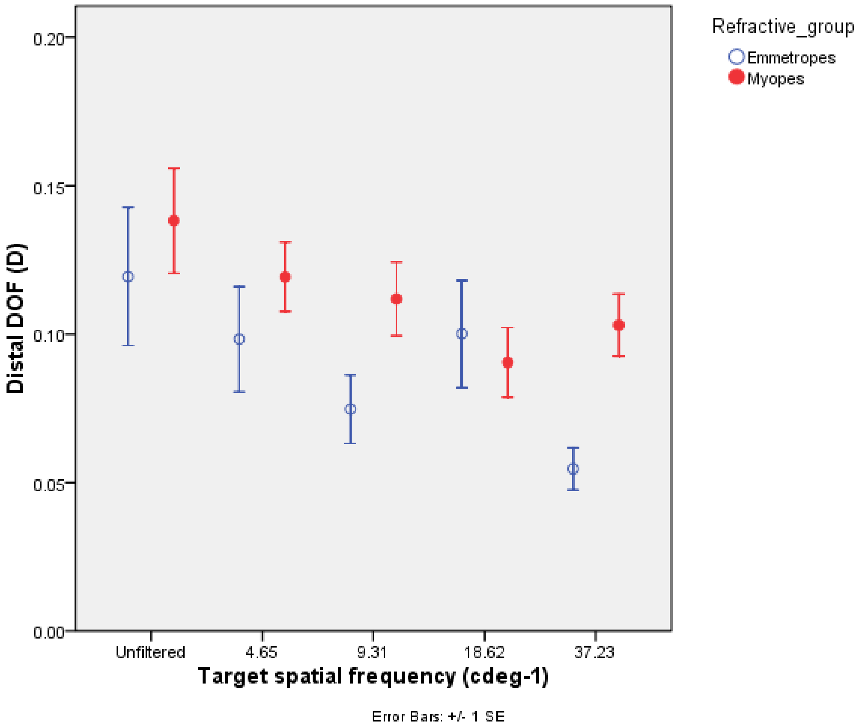

Figure 6.3 Distal DOF for the N10 targets for myopes and emmetropes. Distal objective DOF was significantly larger in myopes compared to emmetropes when viewing filtered spatial frequency targets 9.31cdeg^{-1} (U=149.00, z=-2.18, p=0.03) and 37.23cdeg^{-1} (U=101.00, z=-3.29, p=0.002)

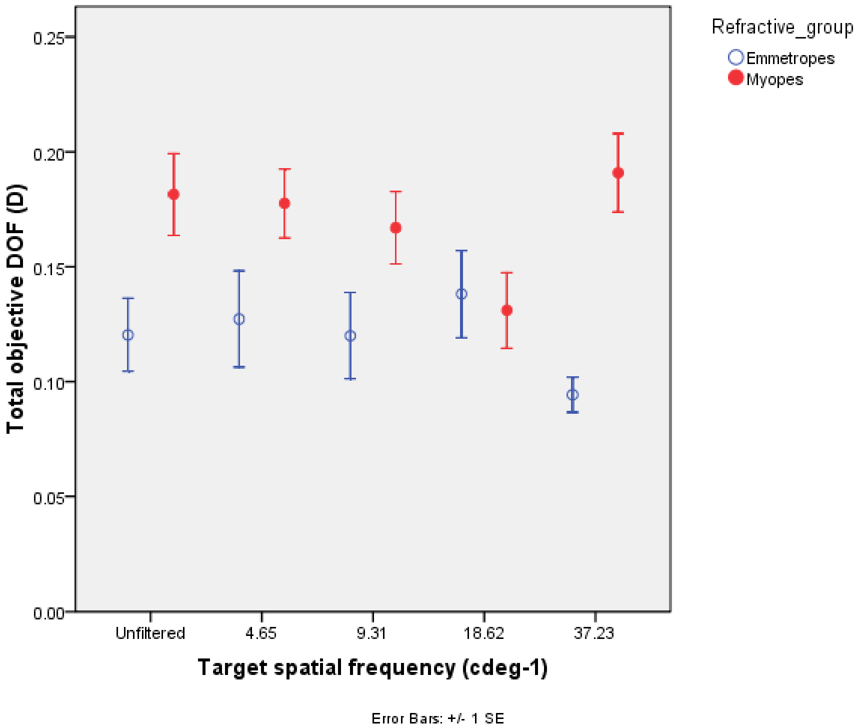

Figure 6.4 Total DOF for the N10 targets for myopes and emmetropes. Total objective DOF was significantly larger for myopes than emmetropes when viewing the unfiltered target (*U*=129.00, *z*=-2.05, *p*=0.04) and filtered targets: 9.31cdeg^{-1} (*U*=109.00, *z*=-2.43, *p*=0.02) and 37.23cdeg^{-1} (*U*=77.00, *z*=-3.93, *p*=0.001)

The Mann-Whitney test found no significant differences in the standard deviations of the proximal or distal objective DOF measurements between myopes and emmetropes (Figure 6.5-6.6; *p*>0.05) except for proximal measurements when viewing the unfiltered N10 text where emmetropes had larger standard deviations compared to myopes (*U*=69.5, *z*=-2.82, *p*=0.004).

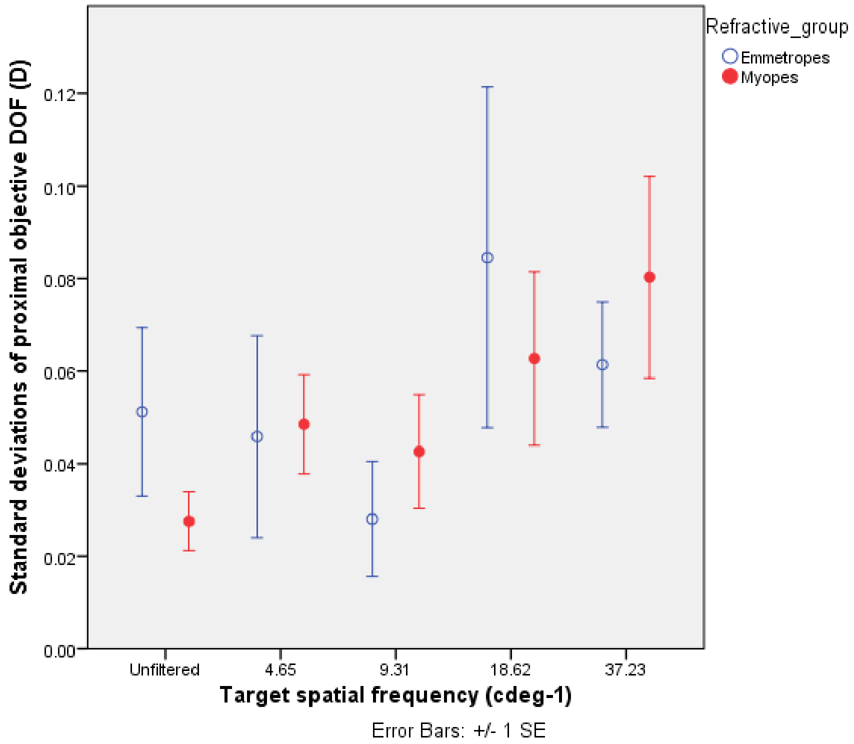

Figure 6.5 Standard deviations of proximal objective DOF for N10 targets for myopes and emmetropes. The Mann Whitney test found no significant difference between myopes and emmetropes for any target (p>0.05) except for the unfiltered N10 text where emmetropes had larger standard deviations compared to myopes (U=69.5, z=-2.82, p=0.004)

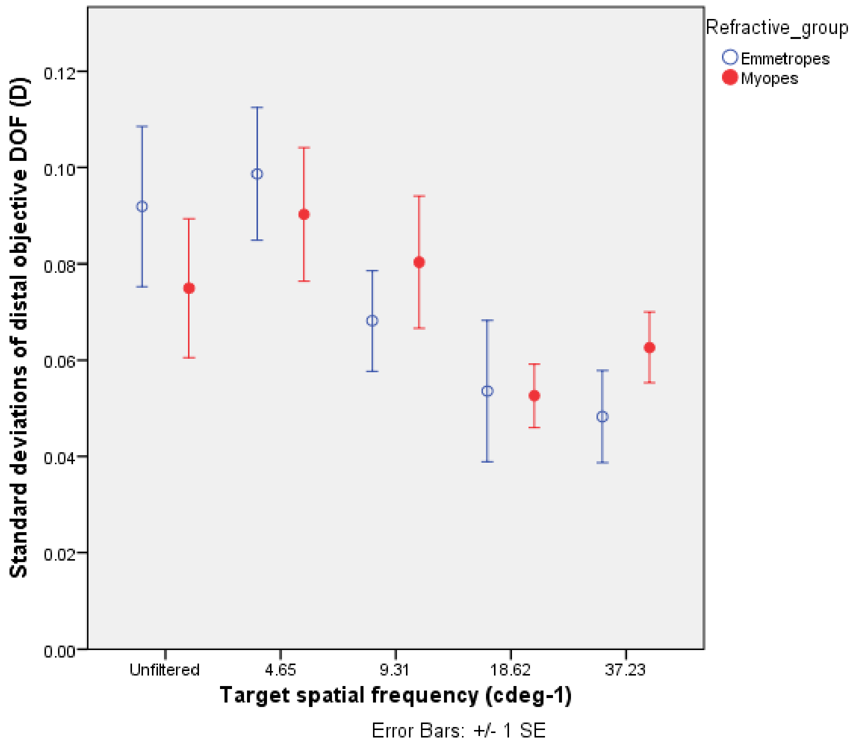

Figure 6.6 Standard deviations of distal objective DOF for N10 targets for myopes and emmetropes. No significant difference was found between myopes and emmetropes for any target (Mann- Whitney; p>0.05)

Friedman's ANOVA found no significant effect of the spatial frequency filtered text on the proximal DOF [$X^2(4)=2.68$, $p=0.61$], distal DOF [$X^2(4)=7.53$, $p=0.11$] or total objective DOF [$X^2(4)=2.38$, $p=0.67$].

Parametric Repeated measures ANOVA found no significant effect of refractive error group on proximal DOF [$F(1,35)=1.72$, $p=0.20$] or distal DOF [$F(1,42)=3.26$, $p=0.08$] but did find a significant effect on the total objective DOF [$F(1,35)=9.22$, $p=0.01$, $\eta^2=0.21$]. There was no significant difference between standard deviations of refractive groups for proximal [$F(1,24)=0.02$, $p=0.90$] or distal recordings [$F(1,33)=0.08$, $p=0.77$]. Due to the strict criteria of the parametric repeated measures ANOVA these statistics did lose power, however, results largely support the findings of the non parametric tests which found that total objective DOF was larger in myopes compared to emmetropes.

Repeated measures ANOVA found no significant effect of the spatial frequency filtered text on the proximal DOF [corrected using Greenhouse-Geisser; $F(3.23, 113.02)=0.70$, $p=0.57$], but there was a significant effect on distal DOF [$F(2.99, 125.42)=4.17$, $p=0.01$]. Contrasts revealed that the distal DOF was larger with the unfiltered text target when compared to the filtered targets (Figure 6.3); 9.31cdeg-1[$F(1,42)=6.89$, $p=0.01$, $\eta^2=0.14$], 18.62cdeg^{-1} [$F(1,42)=7.13$, $p=0.01$, $\eta^2=0.15$] and 37.23cdeg^{-1} [$F(1,42)=8.72$, $p=0.01$, $\eta^2=0.17$]. There was no significant difference of distal DOF of the unfiltered target when compared to the lowest spatial frequency filtered text; 4.65cdeg^{-1} [$F(1,42)=1.52$, $p=0.22$]. There was no significant effect of the spatial frequency filtered text on the total DOF [$F(4,140)=0.38$, $p=0.82$]. No significant interaction effect was found between refractive error group and spatial frequency filtered text for proximal [corrected using Greenhouse-Geisser; $F(3.23, 113.02)=1.13$, $p=0.34$] or distal DOF [$F(2.99, 125.42)=1.42$, $p=0.24$].

No effect of spatial frequency filtered text on proximal or total DOF was found with either parametric or non parametric statistical methods. The difference found in the distal DOF when viewing different spatial frequency filtered targets found with parametric statistical methods is unsupported by the non parametric Friedman's test.

Objective DOF when viewing N20 targets

The Mann-Whitney test found significantly larger proximal DOF in myopes compared to emmetropes (Figure 6.7) but only for the filtered target 4.65cdeg^{-1} (U=116.00, z=-2.38, p=0.02). There was no significant difference in distal DOF between refractive groups for any target (Figure 6.8; p>0.05). Myopes had a larger total objective DOF than emmetropes (Figure 6.9) when viewing the unfiltered targets (0.20D and 0.15D respectively) and for filtered targets 2.33cdeg^{-1} (0.19D and 0.17D respectively), 4.65cdeg^{-1} (0.22D and 0.15D respectively) and 9.31cdeg^{-1} (0.20D and 0.14D respectively) but not the very high spatial frequency filtered text; 18.62cdeg^{-1}. However, the Mann-Whitney test only found this difference to be significant when viewing the filtered target 4.65cdeg^{-1} (U=110.00, z=-2.54, p=0.01). Total objective DOF individual data for the unfiltered and 4.65cdeg^{-1} filtered N20 targets can be found in Appendix E.

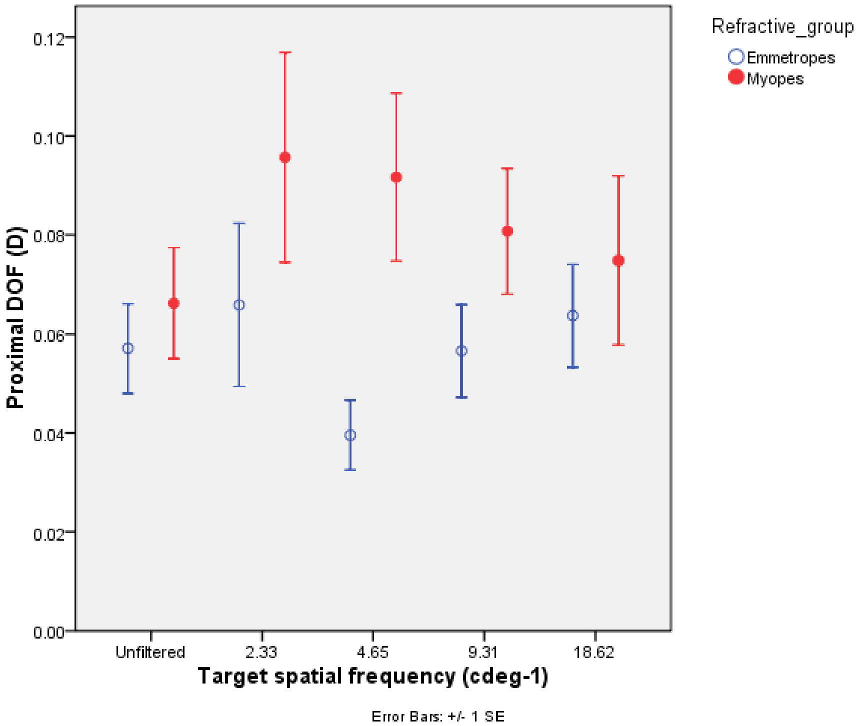

Figure 6.7 Proximal DOF for the N20 targets for myopes and emmetropes. Significantly larger proximal DOF were found in myopes but only for the 4.65cdeg^{-1} filtered target (Mann-Whitney; U=116.00, z=-2.38, p=0.02)

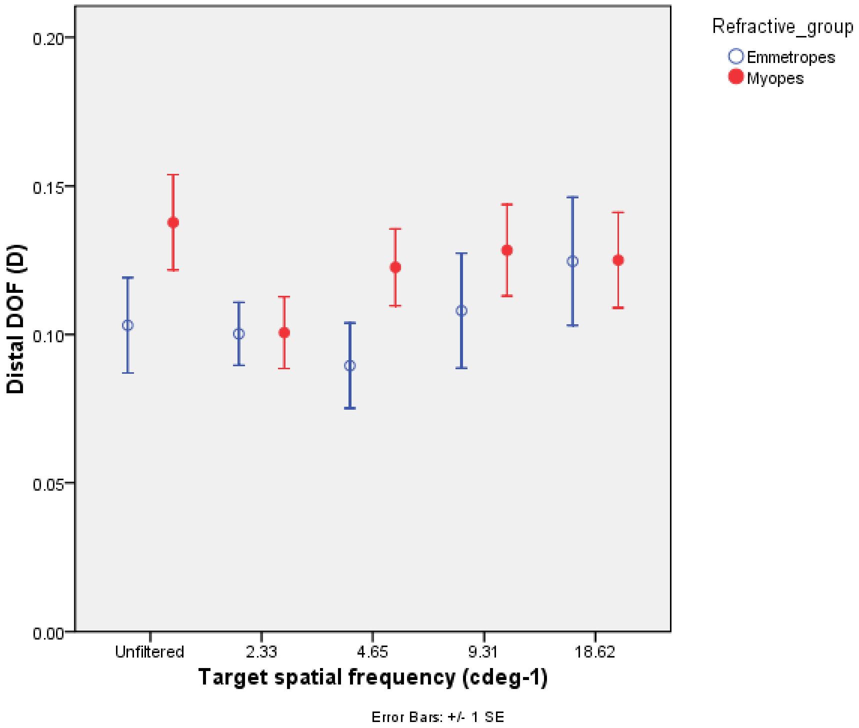

Figure 6.8 Distal DOF for the N20 targets for myopes and emmetropes. There was no significant effect of refractive group on distal DOF *(*Mann-Whitney*; p*>0.05)

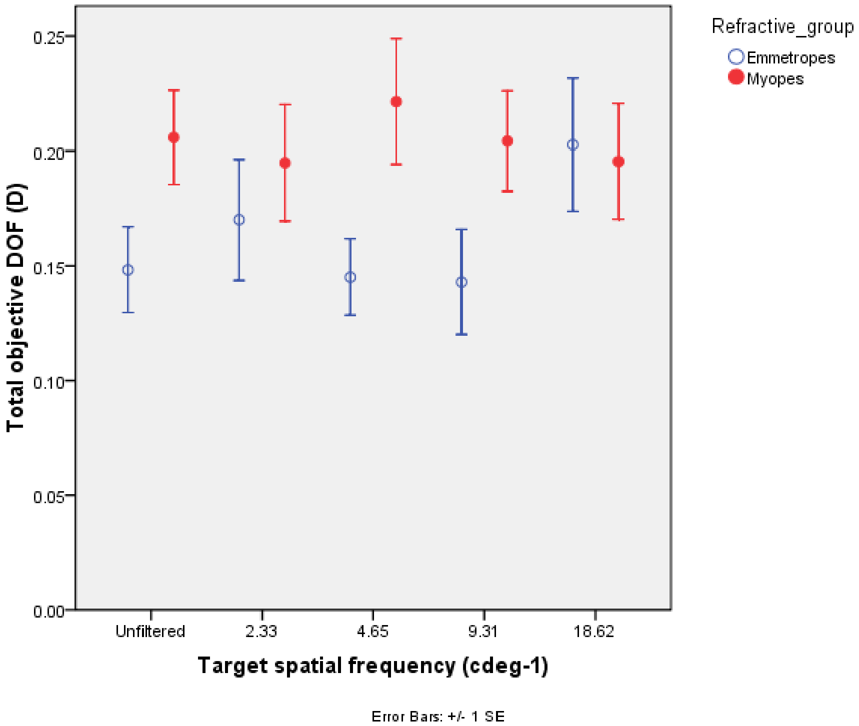

Figure 6.9 Total DOF for the N20 targets for myopes and emmetropes. Total objective DOF was found to be significantly larger for myopes than emmetropes but only when viewing the 4.65cdeg^{-1} filtered target (Mann-Whitney; U=110.00, z=-2.54, p=0.01)

The Mann-Whitney test found no significant difference in the standard deviations of proximal or distal DOF measurements between myopes and emmetropes (Figures 6.10-6.11; p>0.05), except for distal measurements when viewing the unfiltered N20 target (U=294.00, z=2.23, p=0.03). Examination of the standard deviations of individual subjects did reveal one emmetropic subject to have more variable responses to the 2.33 and 4.65cdeg^{-1} filtered N20 text targets.

Friedman's ANOVA found no significant effect of the spatial frequency filtered text on the proximal DOF [X^2(4)=1.45, p=0.84], distal DOF [X^2(4)=1.35, p=0.85] or total objective DOF [X^2(4)=3.41, p=0.49].

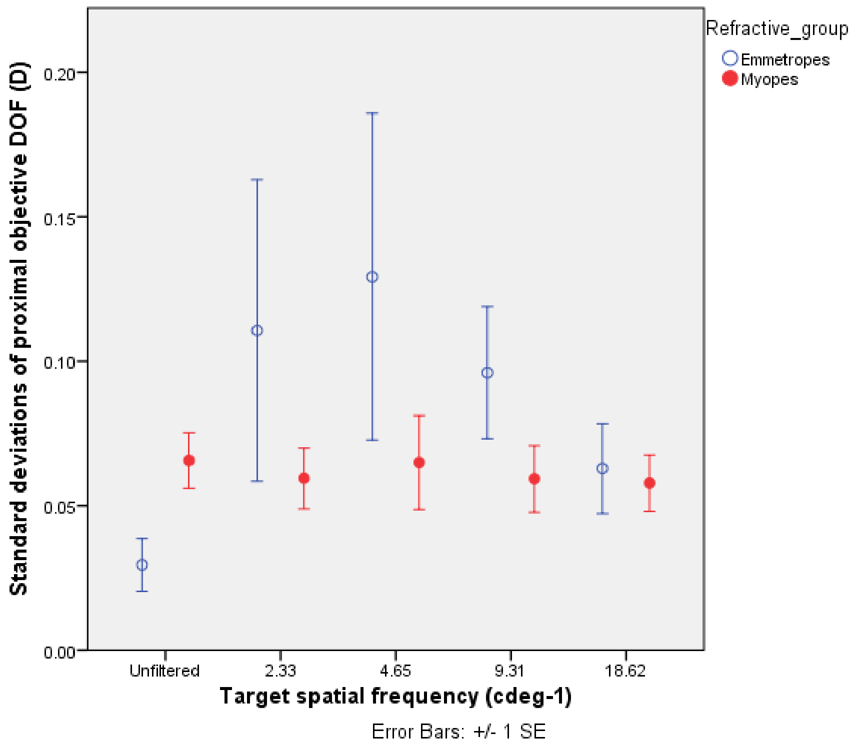

Figure 6.10 Standard deviations of proximal objective DOF for N20 targets for myopes and emmetropes. No significant difference was found between myopes and emmetropes for any target (Mann- Whitney; p>0.05)

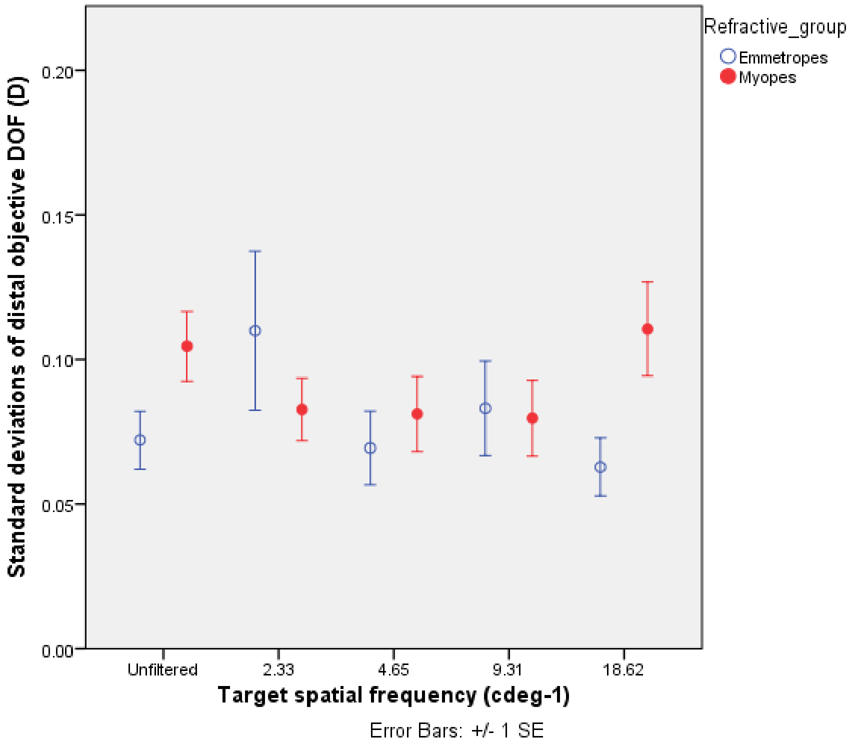

Figure 6.11 Standard deviations of distal objective DOF for N20 targets for myopes and emmetropes. The Mann-Whitney test found no significant difference between myopes and emmetropes for any target (p>0.05) except for the unfiltered target (U=294.00, z=2.23, p=0.03)

Parametric Repeated measures ANOVA found no significant effect of refractive group on proximal DOF [F(1,33)=3.66, p=0.06], distal DOF [F(1,41)=2.51, p=0.12] or total objective DOF [F(1,33)=3.34, p=0.08] seen with N20 targets. There was no significant interaction effect between refractive group and spatial frequency filtered text for proximal DOF [corrected using Greenhouse-Geisser; F(3.08, 101.75)=0.70, p=0.56] or distal DOF [F(3.20,131.15)=0.59, p=0.64]. There was no significant difference between standard deviations of refractive groups for proximal [F(1,30)=1.74, p=0.20] or distal recordings [F(1,37)=0.93, p=0.34]. Due to strict criteria of repeated measures ANOVA these results lost power and may be the reason that refractive error group differences in objective DOF did not quite reach significance.

Repeated measures ANOVA found no significant effect of the spatial frequency filtered text on the proximal DOF [corrected using Greenhouse-Geisser; F(3.03, 101.75)=0.47, p=0.71], the distal DOF [F(3.20,131.15)=0.88, p=0.46] or total DOF [F(4,132)=0.37, p=0.83]. These results support those found with non parametric statistical tests.

Target size comparisons

Repeated measure ANOVA examined the effects of target size on total objective DOF. The two repeated measures (within subjects) variables included target size and spatial frequency filter with 4 levels; unfiltered, 4.65cdeg^{-1}, 9.31cdeg^{-1} and 18.62cdeg^{-1} (Figure 6.12).

Target size had a significant effect on total objective DOF [$F(1,31)=15.99$, $p<0.001$, $\eta^2=0.34$] with N20 targets eliciting a larger DOF when compared with N10 for unfiltered targets (0.189D compared with 0.165D respectively), for 4.65cdeg^{-1} (0.195D compared with 0.166D respectively), for 9.31 cdeg^{-1} (0.184 compared with 0.159D respectively) and for 18.62cdeg^{-1} (0.198D compared with 0.132D respectively).

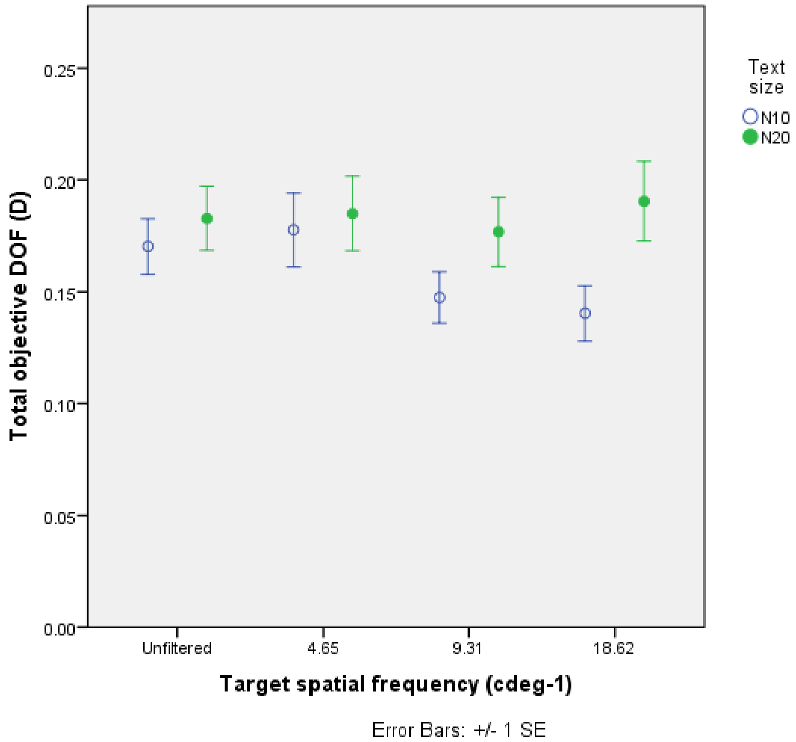

Figure 6.12 Objective DOF for all targets that could be compared. There was a significant effect of target size on total objective DOF [$F(1,43)=79.19$, $p<0.001$]

6.4.2 Accommodative microfluctuations and refractive group differences

The experiment conducted was of mixed design as for the objective DOF. The dependent variables measured in this experiment were RMS of accommodative microfluctuations, low frequency components (<0.6Hz), medium frequency component (0.6Hz-1Hz) and high frequency components (1-2.1Hz).

Z-scores (section 2.5.3) were used to identify outliers and values >3.29 were replaced with the mean plus three times the standard deviation. This applied to only eight entries (<1% data).

Normality of the complete cohort was investigated using Kolmogorov-Smirnov test of normality for all RMS, LFC, MFC and HFC values for each target viewed. There were mixed results with some K-S values showing significance. This meant the null hypothesis could not be rejected. Non parametric tests were therefore required but there was no non parametric alternative to the mixed design repeated measures ANOVA. The non parametric Mann-Whitney test was used to analyse differences between refractive error groups but each target had to be analysed separately. Non parametric Friedman's ANOVA, based on ranks, was used as an alternative to repeated measures ANOVA with only one repeated measure; spatial frequency filter. Parametric repeated measures ANOVA was also conducted to support any non parametric results found.

RMS of accommodative microfluctuations and refractive group differences

Myopes showed larger RMS values compared with emmetropes for all targets (Table 6.4). Figure 6.13-6.14 plot the accommodative microfluctuations for an emmetrope and a myope. The Mann-Whitney test only found refractive error group differences to be significant when viewing the N10 targets (Figure 6.15); unfiltered (U=316, z=2.78, p=0.01), 4.65cdeg^{-1} (U=312, z=2.55, p=0.01), 9.31cdeg^{-1} (U=299, z=2.22, p=0.03) and for N20 targets (Figure 6.16); unfiltered (U=308, z=2.75, p=0.01), 2.33cdeg^{-1} (U=298, z=2.75, *p*=0.03), 4.65cdeg^{-1} (*U*=305, *z*=2.09, *p*=0.04). Friedman's ANOVA found no significant effect of the any of spatial frequency filtered text targets on RMS values (p>0.05).

Parametric Repeated measures ANOVA also found a significant effect of refractive group on RMS for N10 targets [$F(1,34)=5.85$, $p=0.02$, $\eta^2=0.15$] and for N20 targets [$F(1,36)=7.35$, $p=0.01$, $\eta^2=0.17$]. There was no significant effect of the spatial frequency filtered text on the RMS values when viewing N10 targets [corrected using Greenhouse-Geisser; $F(2.86, 97.27)=0.25$, $p=0.85$] or when viewing N20 targets [$F(2.52, 90.83)=2.22$, $p=0.10$]. These results support the findings of the non parametric statistical tests.

Table 6.4 Average RMS values for all emmetropes and myopes whilst viewing the unfiltered and spatial frequency filtered N10 and N20 text targets

RMS	**N10**					**N20**				
Target spatial frequency(cdeg^{-1})	**UF**	**4.65**	**9.31**	**18.62**	**37.23**	**UF**	**2.33**	**4.65**	**9.31**	**18.62**
Emmetropes	0.22	0.25	0.24	0.23	0.25	0.23	0.25	0.24	0.24	0.23
Myopes	0.37	0.35	0.35	0.35	0.31	0.39	0.39	0.32	0.31	0.28

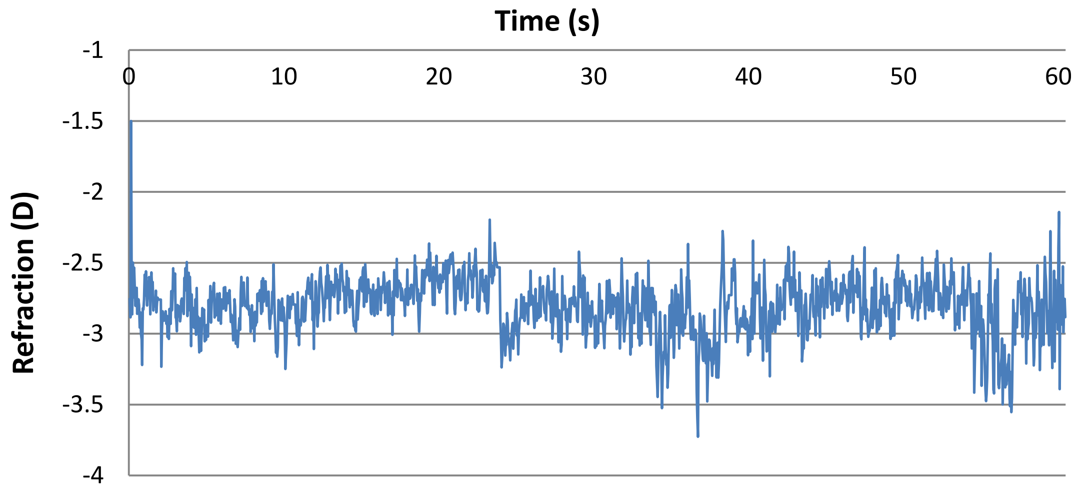

Figure 6.13 A typical microfluctuation recording of an emmetropic subject

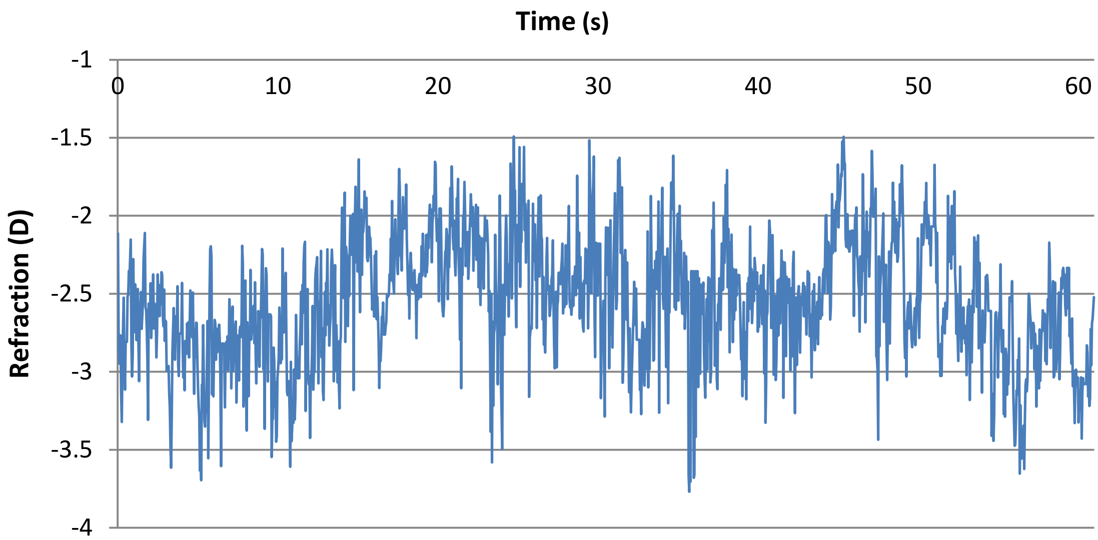

Figure 6.14 A typical microfluctuation recording of a myopic subject

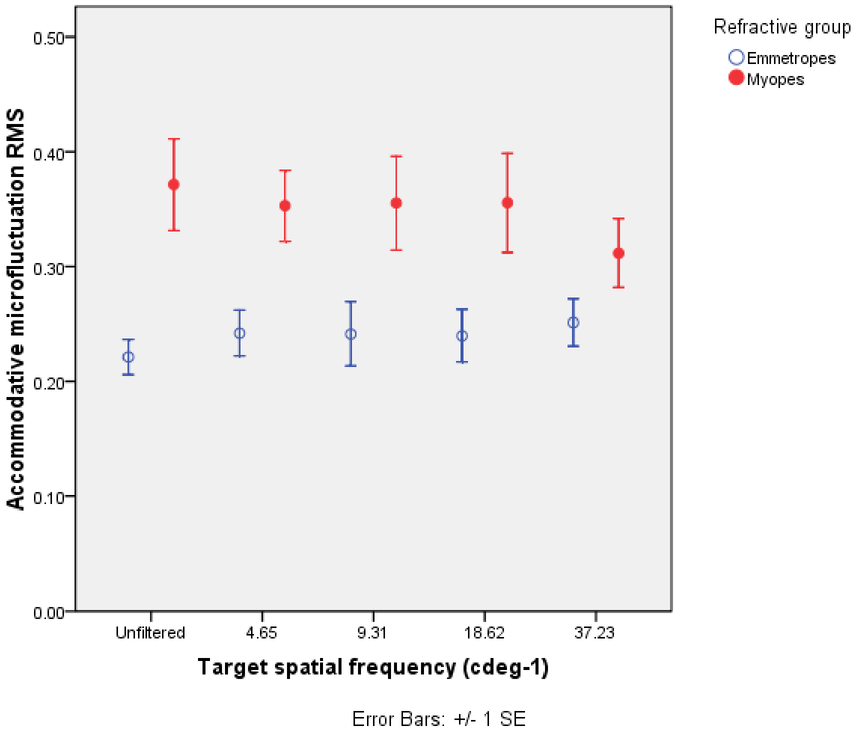

Figure 6.15 Accommodative microfluctuation RMS for the N10 targets for myopes and emmetropes. The Mann-Whitney test found RMS to be significantly larger in myopes for the targets; unfiltered; (U=316, z=2.78, p=0.01), 4.65cdeg^{-1} (U=312, z=2.55, p=0.01) and 9.31cdeg^{-1} (U=299, z=2.22, p=0.03)

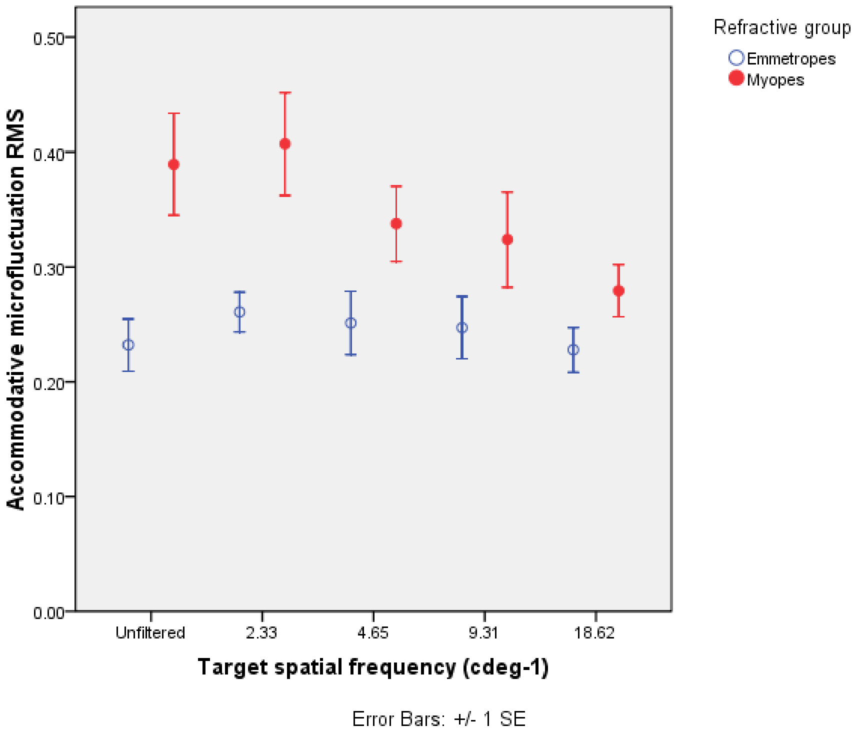

Figure 6.16 Accommodative microfluctuation RMS for the N20 targets for myopes and emmetropes. The Mann-Whitney test found RMS to be significantly larger in myopes for targets; unfiltered (U=308, z=2.75, p=0.01), 2.33cdeg^{-1} (U=298, z=2.75, p=0.03) and 4.65cdeg^{-1} (U=305, z=2.09, p=0.04)

Low frequency components of accommodative microfluctuations and refractive group differences

The Mann-Whitney test found no significant difference between LFC in myopes and emmetropes for any N10 (Figure 6.17; $p>0.05$) or N20 targets (Figure 6.18; $p>0.05$). Friedman's ANOVA found no significant effect of the spatial frequency filtered text on RMS values for any target ($p>0.05$).

Parametric repeated measures ANOVA also found no significant effect of refractive group on the LFC when viewing N10 [$F(1,36)=0.17$, $p=0.68$] or N20 targets [$F(1,36)=3.54$, $p=0.07$]. Spatial frequency filtered text did not show a significant effect on the LFC for the N10 [$F(4,144)=1.09$, $p=0.36$] or N20 targets [corrected using Greenhouse-Geisser; $F(2.47, 88.76)=1.33$, $p=0.27$]. These results support the findings of the non parametric statistical tests.

Table 6.5 Average LFC values for emmetropes and myopes for the unfiltered and spatial frequency filtered N10 and N20 text targets

LFC	**N10**					**N20**				
Target spatial frequency(cdeg^{-1})	**UF**	**4.65**	**9.31**	**18.62**	**37.23**	**UF**	**2.33**	**4.65**	**9.31**	**18.62**
Emmetropes	0.032	0.031	0.033	0.032	0.034	0.031	0.029	0.029	0.029	0.027
Myopes	0.031	0.033	0.035	0.033	0.034	0.034	0.032	0.032	0.032	0.032

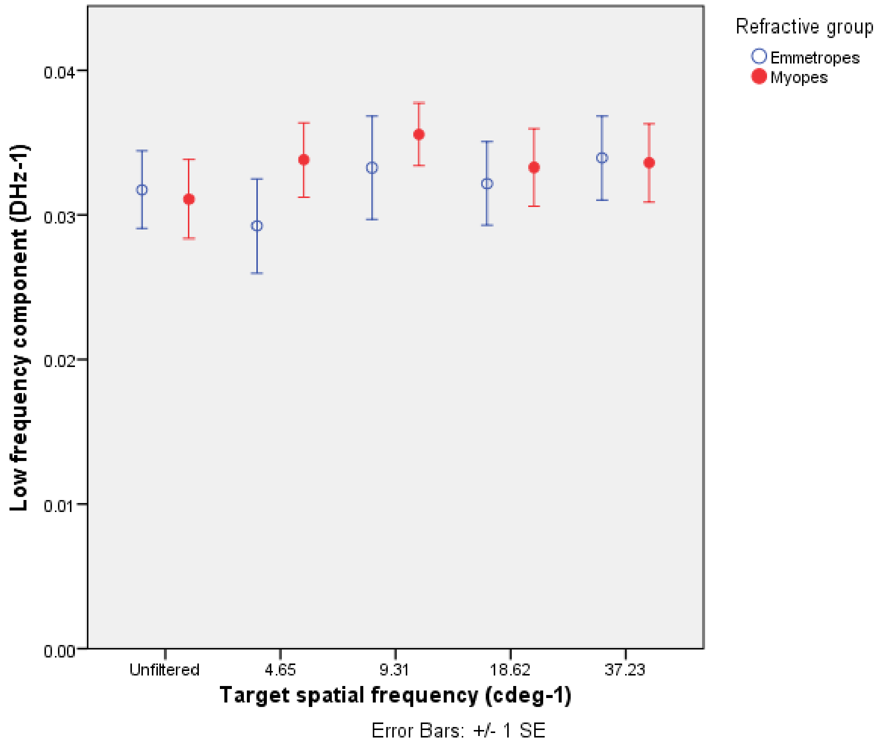

Figure 6.17 Accommodative microfluctuation LFC for the N10 targets for myopes and emmetropes. There was no significant effect of refractive group on LFC (Mann-Whitney; p>0.05)

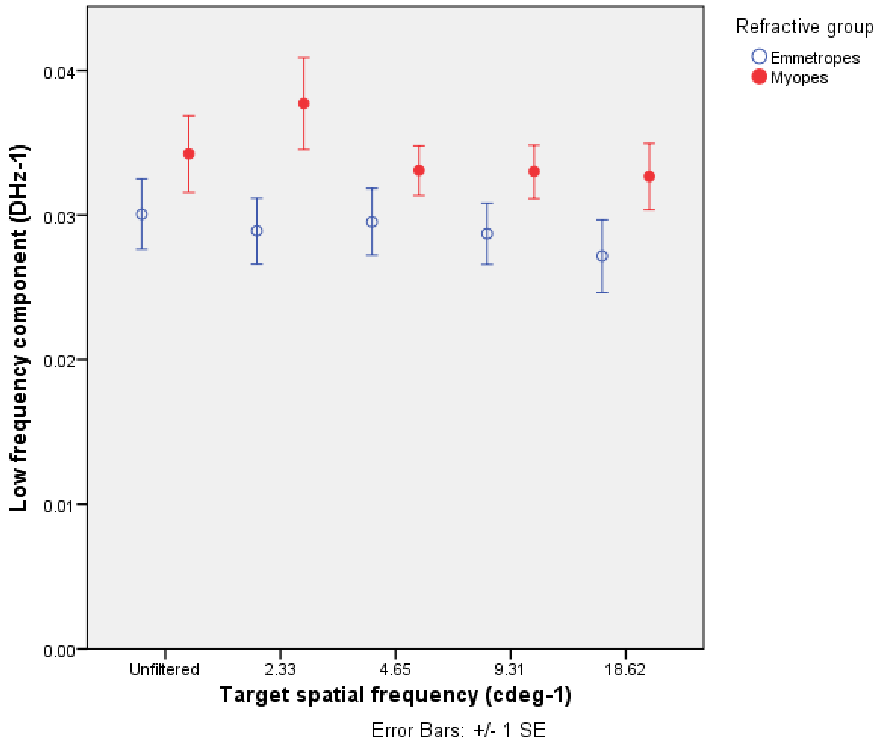

Figure 6.18 Accommodative microfluctuation LFC for the N20 targets for myopes and emmetropes. There was no significant effect of refractive group on LFC (Mann-Whitney; p>0.05)

Medium frequency components of accommodative microfluctuations and refractive group differences

Myopes showed larger MFC values when compared with emmetropes for all targets (Table 6.6). The Mann-Whitney test found the MFC was significantly larger in myopes when viewing the N10 targets (Figure 6.19); unfiltered (U=294, z=2.51, p=0.01) and 4.65cdeg^{-1} (U=321, z=2.78, p=0.01) and N20 targets (Figure 6.20); unfiltered (U=305, z=3.00, p=0.003) and 2.33cdeg^{-1} (U=293, z=2.06, p=0.04).

Friedman's ANOVA found the spatial frequency filtered text had a significant effect on the MFC for N10 targets [X^2(4)=9.62, p=0.04] and for N20 targets [X^2(4)=15.07, p=0.01]. This statistical test method is based on ranks, and showed the smallest mean value of MFC for the highest spatial frequency filtered N10 (37.23cdeg^{-1}) and N20 (18.62cdeg^{-1}) targets. This may suggest that MFC are of smaller magnitude when viewing high spatial frequency filtered text.

Repeated measures ANOVA found a significant effect of refractive group on MFC when viewing N10 [F(1,34)=6.36, p=0.02, η^2=0.16] and N20 targets [F(1,36)=10.27, p=0.003, η^2=0.22]. These results largely support the findings of the non parametric statistical tests where the MFC are larger in myopes than emmetropes. No significant effect of the spatial frequency filtered text on the MFC values was found when viewing N10 targets [F(4,136)=0.78, p=0.54]. Spatial frequency filtered text was found to have a significant effect on the MFC for N20 targets [corrected using Greenhouse-Geisser; F(2.48, 89.11)=3.93, p=0.02, η^2=0.10]. Contrasts revealed that MFC was only significantly larger for the unfiltered text target compared to the spatial frequency filtered text; 18.62cdeg^{-1} [F(1,36)=5.65, p=0.02, η^2=0.14]. The results of the parametric tests also might suggest that MFC values are smaller when viewing the higher spatial frequency filtered targets.

Table 6.6 Average MFC values for emmetropes and myopes for the unfiltered and spatial frequency filtered N10 and N20 text targets

MFC	N10					N20				
Target spatial frequency(cdeg^{-1})	**UF**	**4.65**	**9.31**	**18.62**	**37.23**	**UF**	**2.33**	**4.65**	**9.31**	**18.62**
Emmetropes	0.0033	0.0036	0.0034	0.0033	0.0039	0.0031	0.0038	0.0037	0.0033	0.0034
Myopes	0.0048	0.0056	0.0047	0.0047	0.0044	0.0055	0.0054	0.0049	0.0043	0.0039

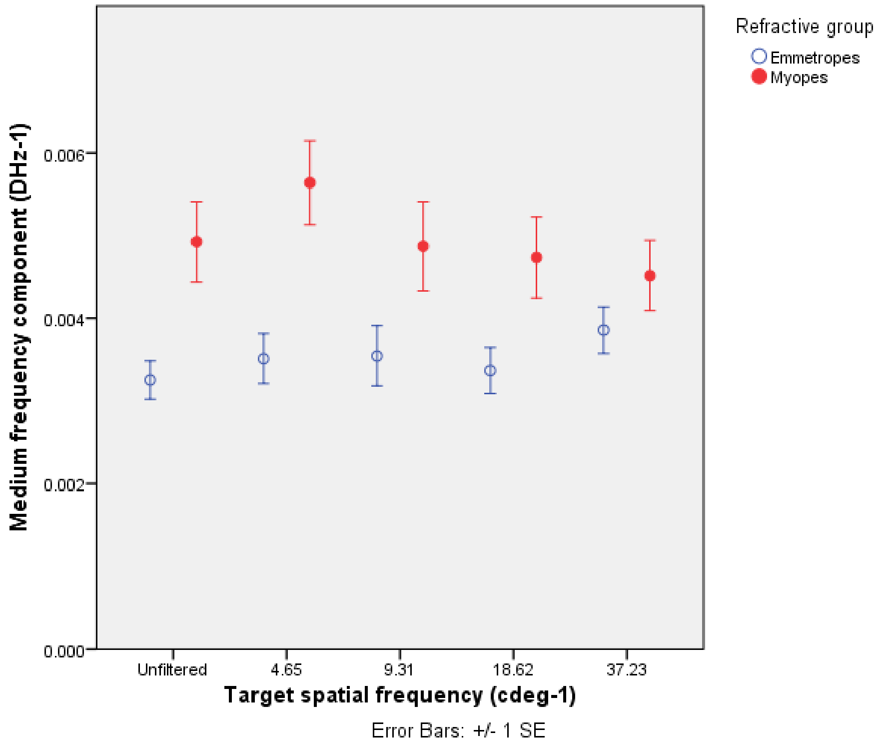

Figure 6.19 Accommodative microfluctuation MFC for the N10 targets for myopes and emmetropes. The Mann-Whitney test found the MFC was significantly larger in myopes for the N10 targets; unfiltered (U=294, z=2.51, p=0.01) and 4.65cdeg^{-1} (U=321, z=2.78, p=0.01)

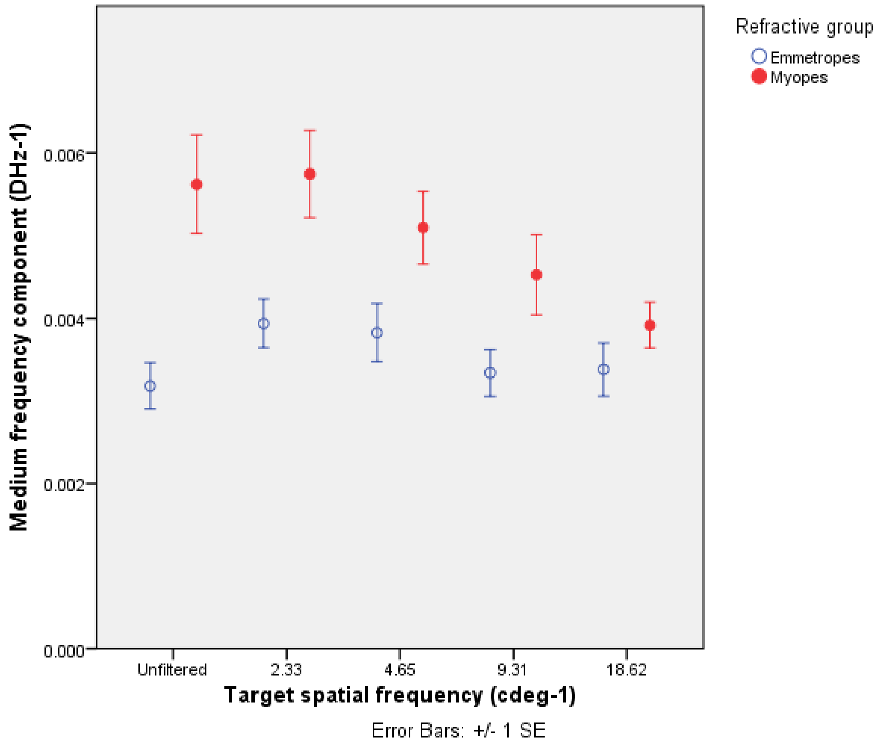

Figure 6.20 Accommodative microfluctuation MFC for the N20 targets for myopes and emmetropes. The Mann-Whitney test found the MFC was significantly larger in myopes for the N20 targets; unfiltered (U=305, z=3.00, p=0.003) and 2.33cdeg^{-1} (U=293, z=2.06, p=0.04)

High frequency components of accommodative microfluctuations and refractive group differences

Myopes showed larger HFC values compared to emmetropes for all targets (Table 5.7). The Mann-Whitney test found these differences to be significant when viewing the N10 targets (Figure 6.17); unfiltered (U=309, z=2.51, p=0.004) and 4.65cdeg^{-1} (U=294, z=2.09, p=0.04) and N20 targets (Figure 6.18): unfiltered (U=309, z=3.11, p=0.002) and 2.33cdeg^{-1} (U=307, z=2.42, p=0.02). Friedman's ANOVA found no significant effect of the spatial frequency filtered text on HFC values for N10 targets [X^2(4)=1.31, p=0.86] but a significant effect of spatial frequency filtered text on HFC was found for N20 targets [X^2(4)=11.77, p=0.04]. This statistical test method is based on ranks and showed the smallest mean value of HFC when viewing the highest spatial frequency filtered (18.62cdeg^{-1}) target.

Parametric Repeated measures ANOVA found a significant effect of refractive group on HFC for the N10 targets [F(1,35)=6.34, p=0.02, η^2=0.15] and for the N20 targets [F(1,36)=9.70, p=0.004, η^2=0.21]. No significant effect of the spatial frequency filtered text on the HFC values was found when viewing N10 targets [*F*(4,140)=0.62, *p*=0.65]. A significant effect of spatial frequency filtered text on the HFC was found when viewing N20 targets [corrected using Greenhouse-Geisser; *F*(2.93, 105.56)=3.40, *p*=0.02, η^2=0.09]. Contrasts revealed that HFC was only significantly larger with the unfiltered text target when compared with the spatial frequency filtered text; 18.62cdeg-^{1} [*F*(1,36)=6.23, *p*=0.02, η^2=0.15]. These results support the non parametric findings suggesting HFC are smaller when viewing higher spatial frequency filtered text.

Table 6.7 Average HFC values for emmetropes and myopes for the unfiltered and spatial frequency filtered N10 and N20 text targets

HFC	**N10**					**N20**				
Target spatial frequency(cdeg^{-1})	**UF**	**4.65**	**9.31**	**18.62**	**37.23**	**UF**	**2.33**	**4.65**	**9.31**	**18.62**
Emmetropes	0.0064	0.0075	0.0072	0.0070	0.0077	0.0063	0.0071	0.0069	0.0064	0.0066
Myopes	0.0095	0.0098	0.0095	0.0090	0.0084	0.0106	0.0105	0.0092	0.0087	0.0074

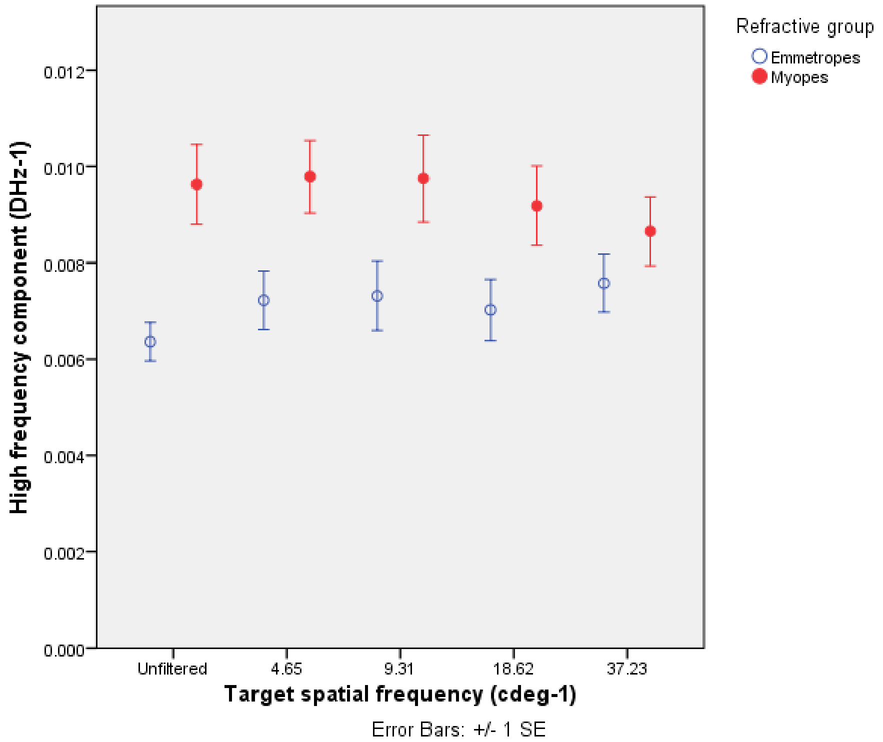

Figure 6.21 Accommodative microfluctuation HFC for the N10 targets for myopes and emmetropes. The Mann-Whitney test found the HFC to be significantly larger in myopes for the N10 targets; unfiltered (*U*=309, *z*=2.51, *p*=0.004) and 4.65cdeg^{-1} (*U*=294, *z*=2.09, *p*=0.04)

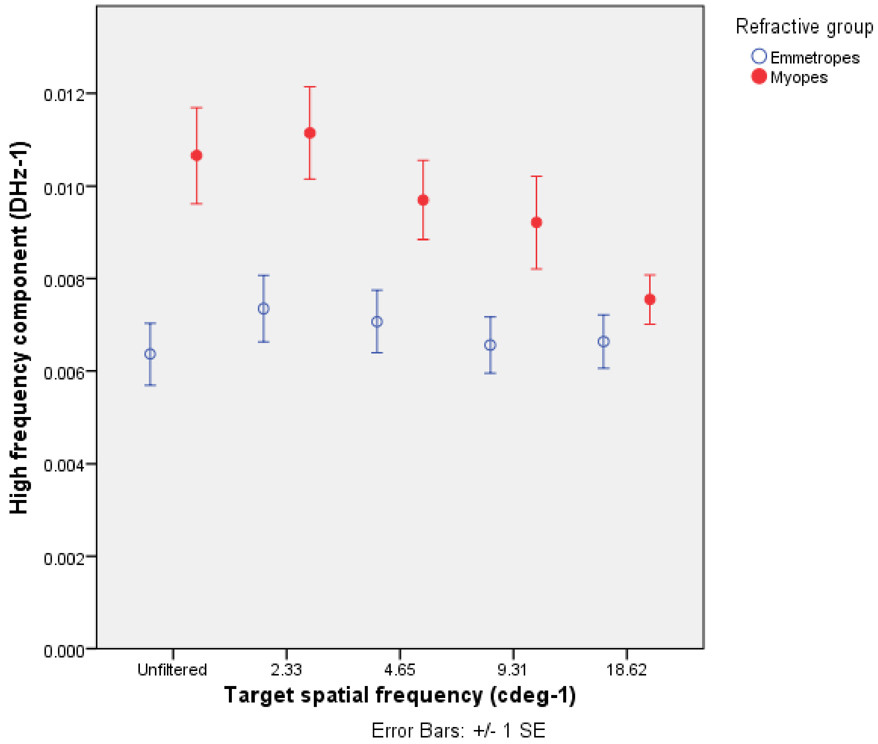

Figure 6.22 Accommodative microfluctuation HFC for the N20 targets for myopes and emmetropes. The Mann-Whitney test found the HFC to be significantly larger in myopes for the N20 targets; unfiltered (U=309, z=3.11, p=0.002) and 2.33cdeg^{-1} (U=307, z=2.42, p=0.02)

6.5 Discussion

Levels of objective DOF

For an unfiltered text target, total objective DOF was found to be 0.170D±0.08 for N10 text and 0.182D±0.09 for N20 text. Vasudevan, Ciuffreda and Bin (2007) conducted measurements of objective DOF in a similar open view experimental set up and found objective DOF to be ±0.59D±0.1D when viewing a Maltese cross target. Their values were much larger than the current study, although may be explained by their target which may have larger blur thresholds. They also applied a different protocol to determine the end point of accommodation change where the accommodative response amplitude was 0.25D or greater for at least two seconds. Their protocol was attempted in the current study, but it was found that this did not allow for accommodative microfluctuations and took longer to reach an end point. A refined protocol has been explained in chapter 3, section 2.7.3.

The effect of refractive error groups on the objective DOF and accommodative microfluctuations

Vasudevan, Ciuffreda and Wang (2006a) found that myopes had a larger objective DOF compared to emmetropes. The current study was the first to date to consider the effect of spatial frequency filtered text on the objective DOF in refractive error groups. Our data showed small but statistically significant differences in the objective DOF of myopes and emmetropes. The results showed that the objective DOF and RMS of microfluctuations, based on neural accommodation responses were larger in myopes than emmetropes particularly for peak text spatial frequencies (spatial frequency bands which included the spatial frequency of the main limb of the text). This suggests a link between microfluctuations and objective DOF. Neural accommodative response differences in myopes and emmetropes to text targets may be influenced by the detail contained within the text, rather than the specific spatial frequency band. In normal reading the accommodative inaccuracies may be increased in myopes compared with emmetropes due to a reduced ability to respond to the peak text spatial frequency and to maintain accurate accommodation to these targets. Larger objective DOF in myopes may be explained by their poorer blur sensitivity (subjective DOF) which was also found in the current study.

Although previous studies have found myopes to have larger MFC and HFC of microfluctuations, they have suggested that larger magnitudes of microfluctuations in myopes compared to emmetropes are mediated by the LFC (Day *et al.*, 2006; Harb, Thorn and Troilo, 2006). The current study found no difference between refractive error groups in the LFC but larger MFC and HFC of accommodative microfluctuations. Winn *et al.* (1990) commented that the neurologically controlled LFC might be dependent on the systemically controlled HFC and that an increase in the magnitude of the HFC could swamp the accommodation control offered by the LFC. It may then be possible that the increased magnitude of MFC and HFC in myopes is enough to swamp the LFC reducing the benefits this provides to the accommodation control system and contributing to poorer accommodation responses in myopes.

The effect of target size and spatial frequency filtered text on the objective DOF and accommodative microfluctuations

The accommodation system has been thought to respond best to mid-range spatial frequency gratings (section 1.7.3; Owens, 1980; Bour, 1981; Ward, 1987). These studies examine levels of accommodation responses to gratings in a small number of subjects with mixed refractive errors but might suggest that mid-range spatial frequencies would give rise to the smallest DOF and best blur sensitivity. However, other studies have stated that as spatial frequencies increase DOF is expected to decrease (Tucker, Charman and Ward, 1986; Legge *et al.*, 1987a; Marcos, Moreno and Navarro, 1999).

The current study was the first to examine the DOF and accommodative microfluctuations using different spatial frequency filtered text rather than gratings. Spatial frequencies contained within text appear to have little effect on the objective DOF or the accommodative microfluctuations which suggest that the responses which might be expected from the human CSF do not apply when viewing mixed spatial frequency complex targets. Myopes showed larger objective DOF and accommodative microfluctuations when viewing the peak text spatial frequencies. The refractive error group differences were small but statistically significant but the study suggests that these differences may be exaggerated when viewing peak text spatial frequencies, even though these are not the same as the peak spatial frequencies of the CSF.

Taylor *et al.* (2009) examined the accommodation response/stimulus curves with grating targets and found no significant difference in accommodative behaviour between myopes and emmetropes for all spatial frequencies. The current study showed myopes and emmetropes to have similar patterns of accommodative behaviour to the different spatial frequency filtered text targets. However, the study suggests that refractive error group differences in accommodative behaviour may be dependent on text detail rather than a specific spatial frequency band.

The current study found that the larger target size resulted in larger objective DOF regardless of spatial frequency filter. Studies which have found DOF increases with target size have based findings on subjective end points (Atchison, Charman and Woods, 1997; Ciuffreda, Wang and Wong, 2005). The current study measures objective endpoints and supported findings that DOF increases with increasing target size. Smaller DOF when viewing smaller letter targets has been thought to be due to an increased high spatial frequency content of smaller letters (section 4.5; Ciuffreda, Wang and Wong, 2005; Wang and Kenneth, 2006). The larger DOF seen with larger targets could be because the larger targets extend further over the retina (Ciuffreda, Wang and Wong, 2005). Larger targets may therefore, give rise to poorer accommodation responses.

Few studies comment on the variability of accommodation responses to targets of different spatial frequencies. Bour (1981) did consider the RMS of accommodation responses and found the RMS to be larger when viewing the high spatial frequency grating (16cdeg^{-1}) compared to mid-spatial frequency (4cdeg^{-1}). Ward (1987) supported this finding although considered the variability of the accommodation responses across their eight subjects rather than the variability of accommodation of the individual subjects. The current study found no difference in the RMS, regardless of which spatial frequency filtered text was under observation.

6.6 Conclusion

Myopes may have reduced accommodative responses compared to emmetropes when viewing text targets containing the peak spatial frequency. Myopes have been shown in the current study to have similar accommodative latencies to emmetropes but poorer RTs (Chapter 5). This suggests large proximal blur cues available in the dynamic experimental set up may be used to initiate accommodation changes, whilst retinal blur cues are used to refine accommodation responses, a theory supported by Strang *et al.* (2011). Myopes also demonstrated larger objective DOF compared to emmetropes and although differences were small, this might suggest that myopes respond poorly to retinal blur cues.

Myopes may be poorer at utilising blur cues when compared to emmetropes particularly when viewing text targets containing peak text spatial frequencies. Myopes may then suffer increased levels of hyperopic blur when reading compared to emmetropes, regardless of text size. It has been previously suggested that hyperopic blur may provide a myopigenic stimulus. Small adjustments in the distance of a near text target may not be enough to extend beyond the DOF of myopes, resulting in inaccurate accommodation responses. Strang *et al.* (2011) also suggested that myopes may have more trouble accommodating accurately to small changes in defocus. Small target vergence changes, for example changing attention from a computer screen to written work, may cause more of a problem than with larger step changes (far distance to near task).

Chapter 7: Higher order aberrations and their relationship to depth of focus

7.1 Introduction

Higher order aberrations are distortions of the wavefront of light as it passes through the eye, as the eye is not a perfect optical system. As these aberrations affect the quality of the image formed on the retina, they may affect the accommodation response. Any reduction in accommodative response would lead to hyperopic retinal defocus, a stimulus to ocular growth.

Previous studies have investigated how the level of higher order aberrations might affect the accommodation response (section 1.6.3). Fernandez and Artal (2005) found that accommodation response times increased when higher order aberrations were corrected. Other studies have found that inducing spherical aberration has increased subjective DOF (Rocha *et al.*, 2009; Benard, Lopez-Gil and Legras, 2011) and accommodative microfluctuations (Gambra *et al.*, 2009).

Spherical aberration occurs in an imperfect optical system where peripheral rays are focussed in front (positive spherical aberration) or behind (negative spherical aberration) the paraxial focal point. This has the effect of a longitudinal displacement of the image from the point of optimal focus, resulting in a larger depth of field when an object lies in front of the plane of best focus (in the case of positive spherical aberration) and when an object lies behind the plane of best focus (in the case of negative spherical aberration). It may be that increased levels of spherical aberration are positively correlated with larger subjective and objective DOF and larger levels of accommodative microfluctuations. If individuals have larger levels of positive spherical aberration, which shifts the optimal focus of an object in front of the retina, they may have larger levels of accommodative lag in order improve the optimum focus of the image. The current study investigated possible correlations between the higher order aberration levels in individuals and their DOF, microfluctuations and dynamic accommodation.

Previous studies have reported that myopes do not have larger levels of spherical aberration compared to emmetropes (Cheng *et al.*, 2004; Charman, 2005). However, a study by Hartwig and Atchison (2012) on a database of 24,000 subjects suggested that 12% of spherical aberration recorded could be explained by spherical equivalent refraction. Therefore, the possibility that higher order aberrations particularly levels of spherical aberration might influence refractive error group differences in objective and subjective DOF cannot be ignored.

7.2 Methods

Subjects

Higher order aberrations were measured in all subjects participating in the objective and subjective DOF experiments. 47 subjects were recruited for the subjective DOF and 46 subjects for the objective DOF experiments from the staff and students of Anglia Ruskin University (Table 4.1 and 6.3).

Procedure

Full methodology has been described in the methodology section 2.8 but a summary follows here.

- The COAS-HD (Complete Ophthalmic Analysis System; Wavefront Sciences) wavefront aberrometer was used to take measurements for all subjects
- Three aberrometry measurements were taken whilst the left eye observed the near N10 unfiltered text target placed at 40cm. Full subjective refractive correction and base out prism were placed in front of the left eye to align the visual axis of the right eye with the internal target. The analysis diameter was based on the average pupil diameter taken from the objective DOF measurements taken with the PRII

- Aberrometry measurements were also taken from all subjects for the subjective DOF study with the patient dilated and a 6mm analysis diameter applied to results. This was the artificial pupil size used in the subjective DOF experiments
- Averages of each wavefront term were calculated along with RMS values

7.3 Results

7.3.1 Higher order aberrations, refractive groups and subjective DOF

Higher order aberrations were measured after cycloplegia of each subject. An analysis diameter of 6mm was used as this was the artificial pupil size used for the subjective DOF measurements. Outliers were identified using z-scores (section 2.5.3) and values replaced with the mean plus three times the standard deviation. Only 1 entry was identified as an outlier from 423 entries in total.

No significant difference was found in higher order aberration RMS values between myopes and emmetropes [independent t-test; $t(45)=-0.80$, $p=0.59$]. No significant difference was found between myopes and emmetropes for any of the higher order aberration terms (Figure 7.1); trefoil, spherical aberration, secondary astigmatism, coma or quadrafoil ($p>0.05$).

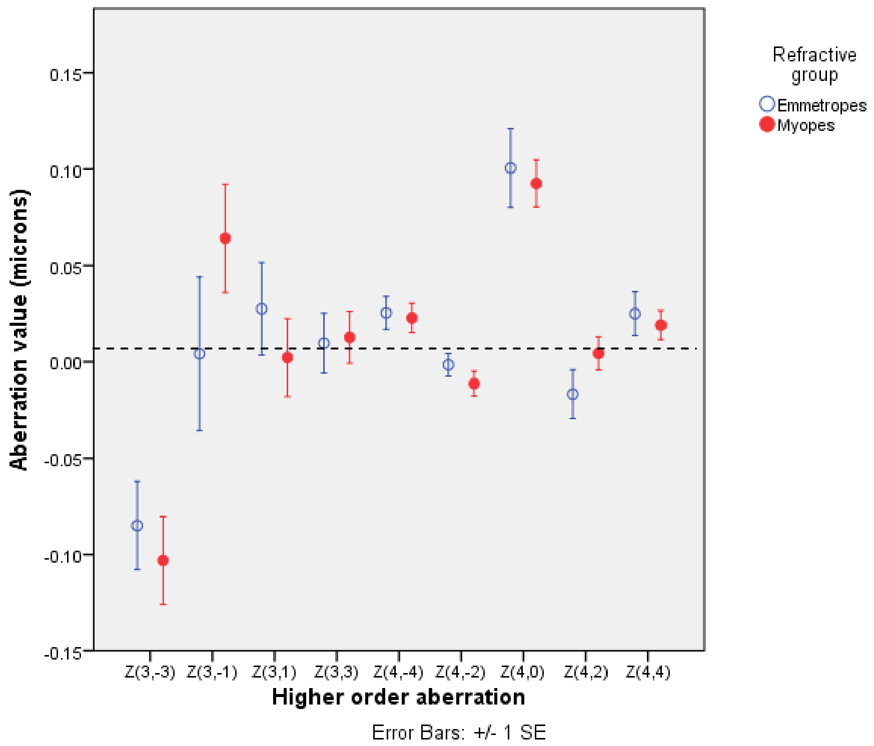

Figure 7.1 Higher order aberration values taken whilst the subject's pupils were dilated for both myopes and emmetropes. There was no significant difference between refractive groups for any term (*p*>0.05). The dashed line denotes zero aberration

No correlation was found between higher order RMS values with a 6mm pupil and spherical equivalent refraction (Pearson's correlation; *r*=-0.19, *p*=0.20). Pearson's correlation found vertical coma (Z_3^{-1}) and spherical equivalent refraction to be significantly negatively correlated (Figure 7.2; *r*=-0.35, *p*=0.02). No correlation was found between any other higher order aberration term and spherical equivalent refraction (Table 7.1, *p*>0.05).

Table 7.1 Pearson correlation between spherical equivalent refractions and higher order aberrations

		Z_3^{-3}	Z_3^{-1}	Z_3^{1}	Z_3^{3}	Z_4^{-4}	Z_4^{-2}	Z_4^{0}	Z_4^{2}	Z_4^{4}	RMS
Spherical equivalent refraction	Pearson Correlation	0.142	-0.346*	0.038	-0.208	-0.052	0.130	-0.061	-0.088	0.047	-0.192
	Sig. (2-tailed)	0.340	0.017	0.801	0.160	0.729	0.383	0.685	0.558	0.756	0.197

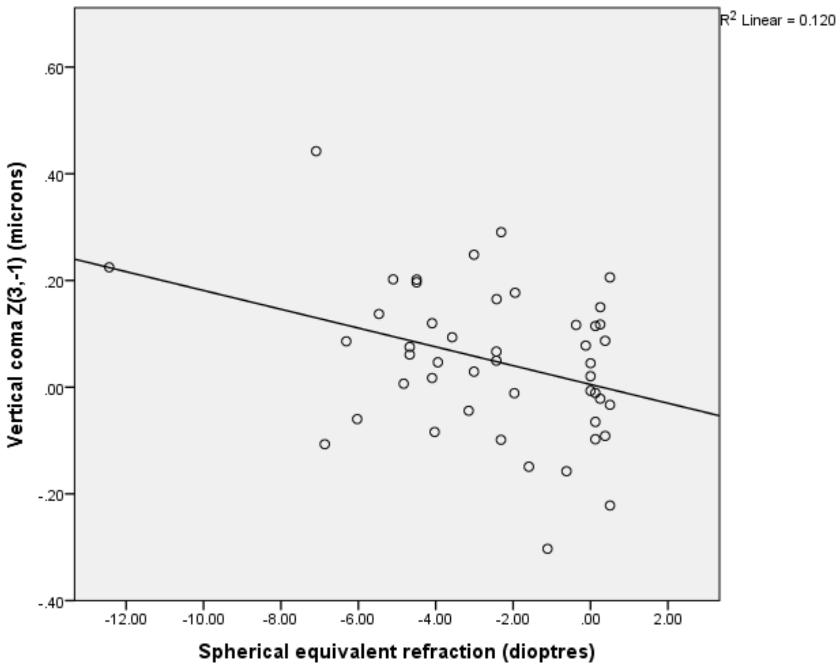

Figure 7.2 Vertical coma (Z_3^{-1}) taken whilst the subject's pupils were dilated (analysis diameter 6mm) compared to their spherical equivalent subjective refraction. A significant negative correlation was found between coma (Z_3^{-1}) and spherical equivalent refraction; Pearson's correlation (r=-0.35, p=0.02)

Effects of higher order aberrations on subjective DOF with different spatial frequency filtered text targets

The effect of higher order aberration on the subjective DOF was investigated using Pearson's correlations (Tables 7.2-7.3). No correlation was found between the RMS and subjective DOF when viewing an unfiltered N10 target (just noticeable DOF; r=0.22, p=0.13 or non resolvable DOF; r=0.19, p=0.20). For an unfiltered N20 target, no correlation was found between the RMS and the just noticeable subjective DOF (r=0.23, p=0.12) but a significant positive correlation was seen between the RMS value and the subjective non resolvable DOF (Figure 7.3, r=0.34, p=0.02).

A significant correlation between the RMS of higher order aberrations and just noticeable DOF was seen only when viewing the N20 18.62cdeg^{-1} target (r=0.36, p=0.01). A significant correlation between the RMS of higher order aberrations and non resolvable DOF was seen when viewing an N10 filtered target; 9.31cdeg^{-1} (r=0.36, p=0.01) and 18.62cdeg^{-1} (r=0.31, p=0.04).

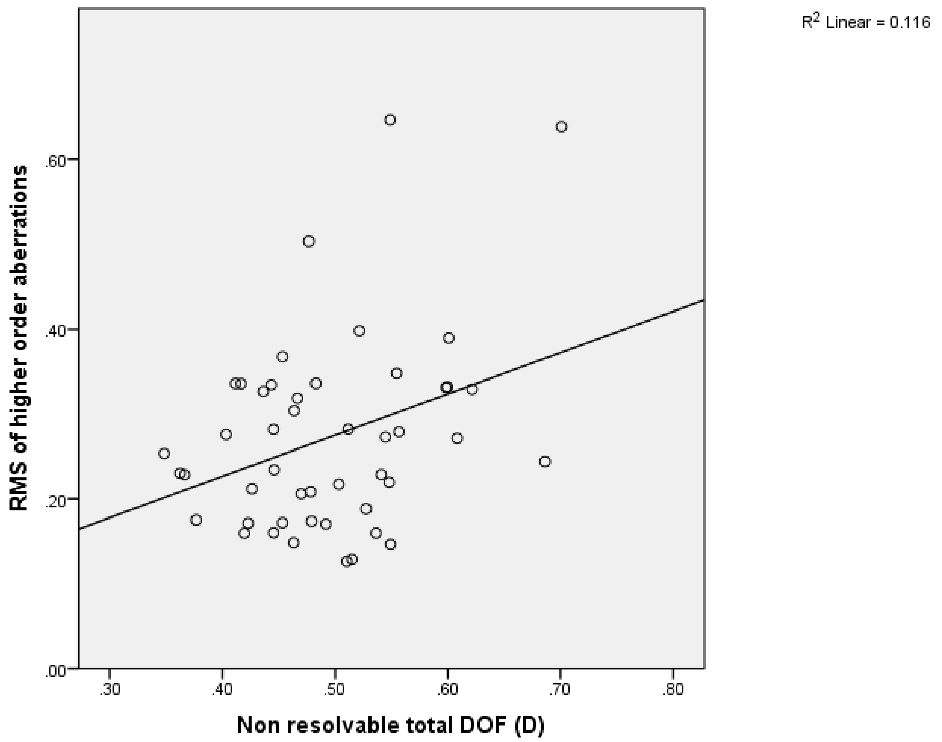

Figure 7.3 Correlation between the RMS of the higher order aberrations and the total non resolvable subjective DOF when viewing an unfiltered N20 target. This shows a significant positive correlation (Pearson's correlation; *r*=0.34, *p*=0.02)

Table 7.2 Pearson's correlation between RMS values of the higher order aberrations and the just noticeable subjective DOF recorded whilst viewing all spatial frequency filtered targets

Target size		N10					N20				
Target spatial frequency (cdeg-1)		Un-filtered	4.65	9.31	18.62	37.23	Un-filtered	2.33	4.65	9.31	18.62
RMS	Pearson Correlation	0.224	0.093	0.285	0.183	0.162	0.231	-0.204	0.082	0.216	0.364*
	Sig. (2-tailed)	0.131	0.532	0.052	0.219	0.277	0.118	0.170	0.585	0.144	0.012

Table 7.3 Pearson's correlation between RMS values of the higher order aberrations and the non resolvable subjective DOF recorded whilst viewing all spatial frequency filtered targets

Target size		N10			N20			
Target spatial frequency (cdeg-1)		Unfiltered	9.31	18.62	Unfiltered	4.65	9.31	18.62
RMS	Pearson Correlation	0.193	0.356*	0.305*	0.340*	0.079	0.189	0.059
	Sig. (2-tailed)	0.195	0.014	0.037	0.019	0.595	0.204	0.696

Some correlations between the higher order aberrations and the subjective DOF were found with different spatial frequency filtered targets (Tables 7.4-7.5). Correlations were found between oblique trefoil (Z_3^{-3}) and the just noticeable subjective DOF recorded for the filtered N10 targets; 9.31cdeg^{-1} (*r*=-0.33, *p*=0.02) and 18.62cdeg^{-1}(*r*=-0.32, *p*=0.03) and the non resolvable subjective DOF recorded for the N10 target; 18.62cdeg^{-1} (*r*=-0.34, *p*=0.02). Significant correlations were also seen between horizontal trefoil (Z_3^{3}) and just noticeable DOF recorded for the N10 18.62cdeg^{-1} target (*r*=-0.32, *p*=0.03) and for the N20 2.33cdeg^{-1} target (*r*=-0.44, *p*=0.002).

Table 7.4 Correlations of higher order aberrations with the total just noticeable subjective DOF when viewing the different spatial frequency filtered text targets

Target size and spatial frequency (cdeg-1)		N10					N20				
Higher order aberrations		Un-filtered	4.65	9.31	18.62	37.23	Un-filtered	2.33	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	-0.258	0.023	-0.330*	-0.316*	-0.022	-0.138	0.197	-0.136	-0.085	-0.190
	Sig. (2-tailed)	0.080	0.879	0.024	0.030	0.883	0.355	0.184	0.361	0.568	0.200
(Z_3^{-1})	Pearson Correlation	-0.012	0.005	0.120	0.074	-0.029	0.031	-0.102	0.067	-0.100	0.096
	Sig. (2-tailed)	0.939	0.976	0.421	0.622	0.849	0.835	0.496	0.653	0.505	0.522
(Z_3^{1})	Pearson Correlation	-0.014	-0.082	-0.181	-0.037	-0.054	0.072	-0.002	-0.072	0.285	0.088
	Sig. (2-tailed)	0.928	0.582	0.223	0.803	0.719	0.631	0.989	0.628	0.052	0.558
(Z_3^{3})	Pearson Correlation	-0.277	-0.143	-0.078	-.0321*	-0.118	-0.183	-.0439**	-0.261	-0.160	-0.148
	Sig. (2-tailed)	0.059	0.336	0.601	0.028	0.431	0.217	0.002	0.076	0.283	0.320
(Z_4^{-4})	Pearson Correlation	-0.105	0.068	-0.174	-0.150	0.127	0.064	0.113	-0.123	-0.095	0.027
	Sig. (2-tailed)	0.484	0.650	0.243	0.314	0.394	0.669	0.449	0.412	0.527	0.855
(Z_4^{-2})	Pearson Correlation	0.065	-0.065	0.098	0.092	0.019	0.012	0.061	0.093	0.041	-0.001
	Sig. (2-tailed)	0.666	0.664	0.512	0.537	0.899	0.937	0.683	0.532	0.785	0.993
(Z_4^{0})	Pearson Correlation	0.224	0.089	0.271	0.114	0.176	0.183	-0.078	0.143	-0.033	0.168
	Sig. (2-tailed)	0.130	0.554	0.066	0.447	0.238	0.217	0.601	0.339	0.825	0.259
(Z_4^{2})	Pearson Correlation	0.135	0.256	0.059	-0.061	0.149	0.055	0.228	0.106	0.060	0.035
	Sig. (2-tailed)	0.366	0.082	0.693	0.682	0.317	0.712	0.124	0.479	0.690	0.816
(Z_4^{4})	Pearson Correlation	-0.016	-0.205	0.031	0.148	-0.078	0.193	-.0295*	-0.147	0.085	0.153
	Sig. (2-tailed)	0.914	0.167	0.836	0.320	0.604	0.194	0.044	0.325	0.571	0.305

Table 7.5 Correlations of higher order aberrations with the total non resolvable subjective DOF when viewing the different spatial frequency filtered text targets. The N10 4.65cdeg^{-1} and 37.23cdeg^{-1} and N20 2.33cdeg^{-1} could not be resolved and so data could not be obtained

Target size and spatial frequency (cdeg-1)		N10			N20			
Higher order aberrations		Unfiltered	9.31	18.62	Unfiltered	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	-0.234	-0.232	-0.340*	-0.255	-0.160	-0.091	-0.177
	Sig. (2-tailed)	0.113	0.116	0.019	0.084	0.282	0.545	0.233
(Z_3^{-1})	Pearson Correlation	0.028	0.164	0.117	0.097	-0.035	-0.034	0.023
	Sig. (2-tailed)	0.849	0.270	0.432	0.515	0.816	0.819	0.878
(Z_3^{1})	Pearson Correlation	-0.093	-0.187	-0.127	0.028	-0.249	0.206	-0.007
	Sig. (2-tailed)	0.533	0.208	0.396	0.852	0.092	0.164	0.965
(Z_3^{3})	Pearson Correlation	-0.246	-0.061	-0.172	-0.255	0.004	-0.184	-0.094
	Sig. (2-tailed)	0.095	0.685	0.249	0.084	0.981	0.216	0.528
(Z_4^{-4})	Pearson Correlation	-0.132	-0.173	-0.186	-0.033	-0.158	-0.258	-0.144
	Sig. (2-tailed)	0.377	0.244	0.211	0.823	0.290	0.080	0.335
(Z_4^{-2})	Pearson Correlation	0.086	-0.108	0.013	-0.036	0.031	-0.034	0.101
	Sig. (2-tailed)	0.568	0.470	0.929	0.809	0.838	0.820	0.501
(Z_4^{0})	Pearson Correlation	0.096	0.238	0.180	0.091	0.090	-0.048	0.088
	Sig. (2-tailed)	0.521	0.107	0.227	0.543	0.546	0.747	0.557
(Z_4^{2})	Pearson Correlation	0.081	-0.090	0.000	0.071	0.033	-0.082	-0.046
	Sig. (2-tailed)	0.587	0.545	0.998	0.637	0.826	0.584	0.760
(Z_4^{4})	Pearson Correlation	0.018	0.119	0.090	0.148	0.033	0.200	0.080
	Sig. (2-tailed)	0.906	0.426	0.547	0.319	0.824	0.179	0.592

Effects of higher order aberrations on subjective DOF midpoints

The subjective DOF experiments found that the text spatial frequency filter had a significant effect on the subjective DOF midpoints (section 4.4.7). The unfiltered targets and those containing the peak text spatial frequencies gave rise to midpoints which were further displaced towards the subject. By moving the target towards the Badal lens the effective power of the Badal lens is reduced. The focus of the unfiltered and peak text spatial frequency targets is therefore initially more myopic. Whether this midpoint displacement was as a result of the higher order aberrations was investigated.

Pearson's correlations between higher order aberrations and midpoints of just noticeable subjective DOF were conducted (Table 7.6). A significant positive correlation was found between RMS values of higher order aberrations and the just noticeable subjective DOF midpoints for all N10 targets and N20 targets; 9.31cdeg^{-1} and 18.62cdeg^{-1}. It was assumed that the just noticeable and non resolvable subjective DOF midpoints were the same and therefore only just noticeable subjective DOF midpoints were considered.

Table 7.6 Correlations between higher order aberrations and the dioptric midpoints of the total just noticeable subjective DOF for the spatial frequency filtered text targets

Target size		N10					N20				
Target spatial frequency (cdeg-1)		Unfiltered	4.65	9.31	18.62	37.23	Unfiltered	2.33	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	-0.102	-0.252	-0.206	-0.125	-0.011	-0.129	0.202	-0.169	-0.186	-0.143
	Sig. (2-tailed)	0.494	0.087	0.165	0.404	0.939	0.387	0.172	0.256	0.209	0.337
(Z_3^{-1})	Pearson Correlation	0.088	0.195	0.217	0.154	0.124	0.217	0.112	0.189	0.181	0.212
	Sig. (2-tailed)	0.557	0.189	0.143	0.302	0.408	0.142	0.453	0.204	0.223	0.152
(Z_3^{1})	Pearson Correlation	-0.017	-0.015	-0.080	-0.020	-0.063	-0.040	0.010	-0.158	0.110	0.085
	Sig. (2-tailed)	0.912	0.922	0.592	0.896	0.673	0.787	0.947	0.287	0.462	0.569
(Z_3^{3})	Pearson Correlation	-0.007	0.011	0.040	-0.025	0.004	0.079	-0.301*	0.044	-0.074	-0.085
	Sig. (2-tailed)	0.962	0.942	0.788	0.869	0.981	0.599	0.040	0.769	0.620	0.571
(Z_4^{-4})	Pearson Correlation	-0.132	0.115	-0.068	-0.164	-0.061	-0.053	0.117	-0.012	-0.245	-0.099
	Sig. (2-tailed)	0.376	0.441	0.649	0.271	0.684	0.725	0.433	0.934	0.097	0.509
(Z_4^{-2})	Pearson Correlation	-0.179	-0.170	-0.141	-0.215	-0.114	-0.255	-0.204	-0.082	-0.217	-0.237
	Sig. (2-tailed)	0.230	0.253	0.344	0.148	0.447	0.084	0.169	0.585	0.143	0.108
(Z_4^{0})	Pearson Correlation	0.362*	0.369*	0.459**	0.394**	0.365*	0.310*	0.082	0.392**	0.314*	0.285
	Sig. (2-tailed)	0.013	0.011	0.001	0.006	0.012	0.034	0.585	0.006	0.032	0.052
(Z_4^{2})	Pearson Correlation	0.006	-0.043	0.016	-0.064	0.077	-0.006	0.054	0.038	-0.057	-0.115
	Sig. (2-tailed)	0.969	0.773	0.916	0.668	0.608	0.971	0.719	0.799	0.705	0.441
(Z_4^{4})	Pearson Correlation	0.161	-0.050	0.058	0.153	-0.020	0.095	-0.269	-0.067	0.156	0.114
	Sig. (2-tailed)	0.279	0.739	0.697	0.306	0.892	0.525	0.067	0.656	0.295	0.447
RMS	Pearson Correlation	0.311*	0.391**	0.428**	0.388**	0.325*	0.264	0.044	0.198	0.357*	0.343*
	Sig. (2-tailed)	0.033	0.007	0.003	0.007	0.026	0.073	0.767	0.182	0.014	0.018

A significant positive correlation was found between spherical aberration (Z_4^0) and the midpoints seen with all N10 targets and with the N20 targets; unfiltered, 4.65cdeg^{-1} and

9.31cdeg^{-1}. Examples of subjects with small and larger levels of spherical aberration and their midpoint displacements are shown in Figure 7.4.

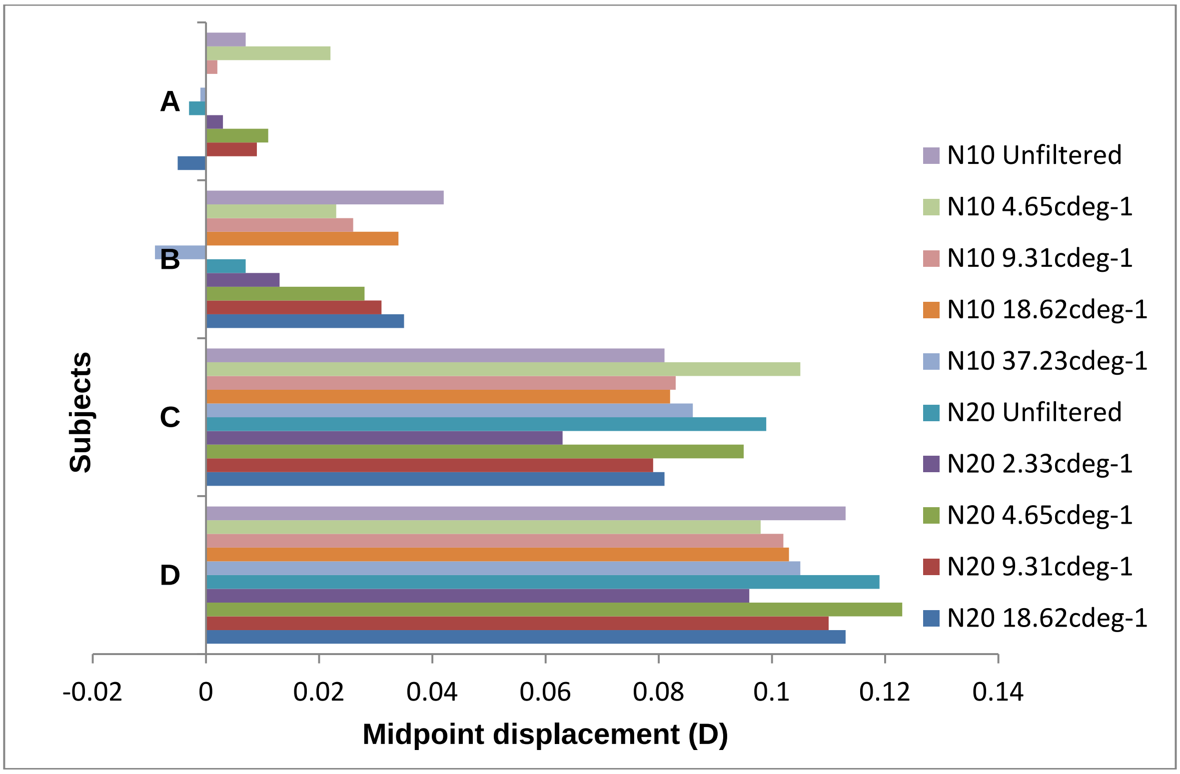

Figure 7.4 Examples of subjects' subjective just noticeable DOF midpoints when viewing different spatial frequency filtered targets. The larger the dioptric value of the midpoint, the further forward and more myopic the displacement of the DOF midpoint. Subjects A and B demonstrate two subjects with low levels of spherical aberration (0.02 and 0.01µm respectively). Subjects C and D demonstrate two subjects with higher levels of spherical aberration (0.21 and 0.17µm respectively). These subjects have varied spherical equivalent refractions (A -6.31D; B 0.13D; C -3.02D; D -12.44D)

7.3.2 Higher order aberrations, refractive groups and objective DOF

Correlations between higher order aberrations and objective DOF were only conducted where the pupils measured with the PRII and the wavefront aberrometer were within 1mm of each other. Therefore correlations were conducted on 33 subjects rather than the 46 subjects that completed all of the experiments.

Levene's test revealed that equality of variances between myopic and emmetropic refractive groups for all higher order aberrations could be assumed (p>0.05). Outliers were identified using z-scores (section 2.5.3) and values replaced with the mean plus three times the standard deviation. Only 4 individual entries were identified as outliers from 330 entries in total.

Independent t-tests were used to examine differences between refractive groups (Figure 7.5). No significant difference was found between the RMS values of higher order aberration between myopes and emmetropes [$t(31)=1.42$, $p=0.17$]. No significant differences were found between myopes and emmetropes for any of the higher order aberration terms (trefoil, spherical aberration, secondary astigmatism or quadrafoil; $p>0.05$). A significant difference was found between the vertical coma (Z_3^{-1}) seen in myopes and emmetropes [$t(31)=-2.16$, $p=0.04$]. Average values of vertical coma (Z_3^{-1}) were -0.02±0.10microns in myopes and -0.11±0.13microns in emmetropes. Differences between myopes and emmetropes could not be explained by any differences in pupil size. No significant difference was found between the pupil sizes of the two refractive groups [independent t-test: $t(40)=0.77$, $p=0.45$].

Correlations between higher order aberrations and spherical equivalent refraction were also investigated. No correlation was found between RMS values and spherical equivalent refraction (Figure 7.6, $r= 0.19$, $p=0.29$). No correlation was found between any higher order aberration term and spherical equivalent refraction ($p>0.05$) except for vertical coma (Z_3^{-1}) (Table 7.7). Pearson's correlation found vertical coma (Z_3^{-1}) and spherical equivalent refraction to be significantly negatively correlated ($r=-0.48$, $p=0.005$).

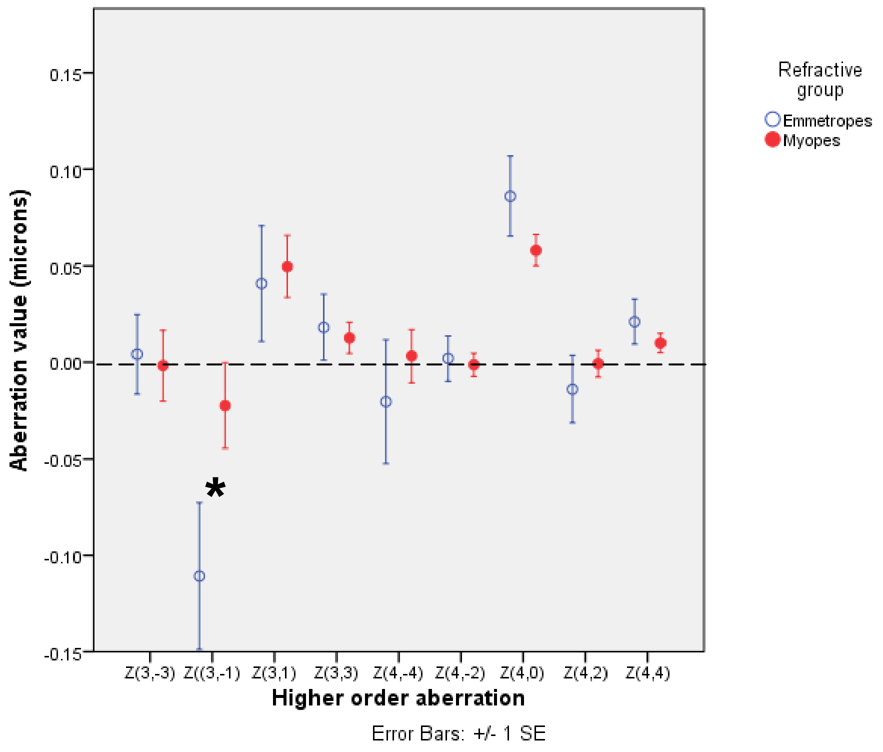

Figure 7.5 Higher order aberration values taken whilst viewing a near target at 40cm for both myopes and emmetropes. There was no significant difference between refractive error groups for any term (*p*>0.05) except vertical coma (Z_3^{-1}) (*p*= 0.04) shown with *. The dashed line denotes zero aberration

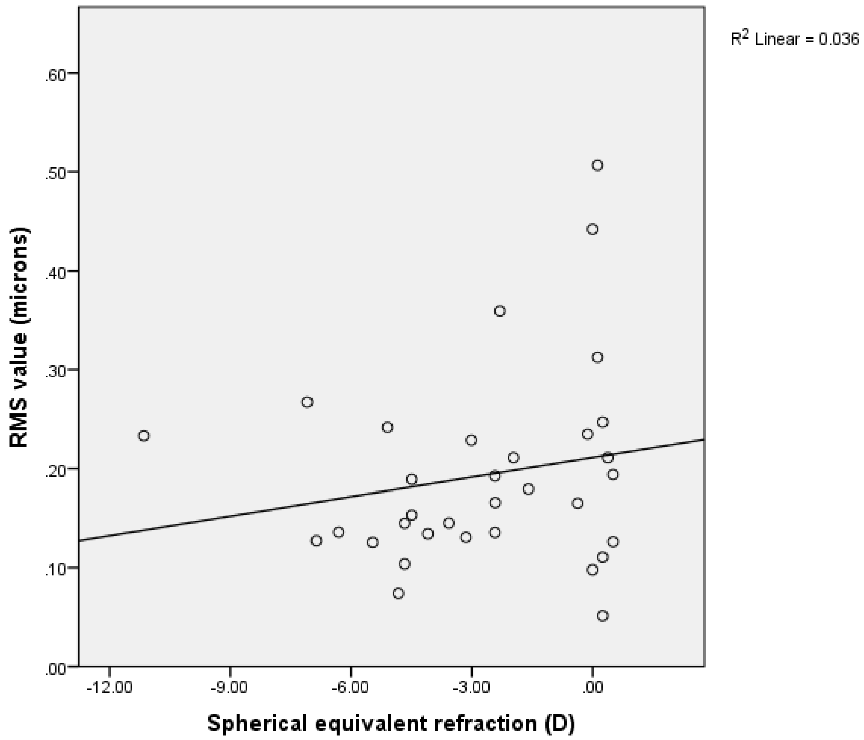

Figure 7.6 The RMS values of higher order aberrations taken whilst viewing a near target at 40cm for each subject compared to their spherical equivalent subjective refraction. No correlation was seen between RMS and spherical equivalent refraction (Pearson's correlation; *p*=0.29)

Table 7.7 Correlations between higher order aberration terms and the spherical equivalent refraction

		Z_3^{-3}	Z_3^{-1}	Z_3^{1}	Z_3^{3}	Z_4^{-4}	Z_4^{-2}	Z_4^{0}	Z_4^{2}	Z_4^{4}	RMS
Spherical equivalent refraction	Pearson Correlation	0.217	-0.475**	0.238	0.079	-0.173	0.008	0.187	0.047	0.172	0.189
	Sig. (2-tailed)	0.224	0.005	0.182	0.661	0.337	0.967	0.297	0.795	0.338	0.292

Effects of higher order aberrations on objective DOF with different spatial frequency filtered text targets

The effect of higher order aberrations on the objective DOF was investigated. When viewing an unfiltered target, there was no correlation between the RMS of the higher order aberrations and the objective DOF when viewing an N10 target (*r*=0.18, *p*=0.31) or an N20 target (*r*=0.03, *p*=0.88) (Table 7.8).

Table 7.8 Correlations between higher order aberrations and the total objective DOF for the spatial frequency filtered text targets

Target size and spatial frequency (cdeg-1)		N10					N20				
Higher order aberrations		Un-filtered	4.65	9.31	18.62	37.23	Un-filtered	2.33	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	-0.043	0.184	0.266	-0.036	0.167	0.078	-0.074	0.201	-0.216	0.048
	Sig. (2-tailed)	0.810	0.313	0.148	0.852	0.368	0.671	0.686	0.269	0.251	0.789
(Z_3^{-1})	Pearson Correlation	0.302	0.072	0.296	0.243	0.480**	0.016	0.284	0.051	0.513**	0.144
	Sig. (2-tailed)	0.087	0.694	0.106	0.203	0.006	0.930	0.115	0.783	0.004	0.426
(Z_3^{1})	Pearson Correlation	0.153	0.587**	0.079	-0.016	0.102	-0.044	0.021	-0.093	0.098	-0.063
	Sig. (2-tailed)	0.396	0.000	0.672	0.936	0.585	0.811	0.909	0.613	0.605	0.726
(Z_3^{3})	Pearson Correlation	0.162	-0.268	-0.042	-0.336	-0.254	0.284	-0.258	0.068	-0.269	0.012
	Sig. (2-tailed)	0.367	0.137	0.821	0.074	0.168	0.116	0.154	0.711	0.150	0.946
(Z_4^{-4})	Pearson Correlation	-0.046	-0.356*	-0.308	-0.134	-0.087	-0.067	-0.213	-0.034	0.228	0.006
	Sig. (2-tailed)	0.798	0.046	0.092	0.490	0.641	0.714	0.242	0.854	0.225	0.974
(Z_4^{-2})	Pearson Correlation	0.099	0.414*	-0.067	0.028	-0.027	0.009	0.165	-0.021	-0.078	0.149
	Sig. (2-tailed)	0.585	0.019	0.722	0.887	0.887	0.959	0.367	0.909	0.683	0.409
(Z_4^{0})	Pearson Correlation	-0.005	0.439*	0.260	0.111	-0.142	-0.091	0.298	0.137	-0.219	0.014
	Sig. (2-tailed)	0.978	0.012	0.157	0.568	0.444	0.621	0.098	0.455	0.245	0.938
(Z_4^{2})	Pearson Correlation	-0.359*	0.135	-0.190	-0.148	0.037	-0.275	-0.060	-0.098	-0.049	-0.095
	Sig. (2-tailed)	0.040	0.463	0.306	0.442	0.843	0.127	0.743	0.593	0.799	0.598
(Z_4^{4})	Pearson Correlation	0.050	-0.156	0.077	0.022	0.027	0.006	-0.160	0.043	0.178	-0.062
	Sig. (2-tailed)	0.784	0.392	0.680	0.911	0.884	0.976	0.382	0.815	0.346	0.731
RMS	Pearson Correlation	0.181	0.218	0.079	-0.228	-0.135	0.027	-0.075	0.004	-0.065	-0.155
	Sig. (2-tailed)	0.314	0.231	0.673	0.233	0.468	0.882	0.685	0.981	0.733	0.389

There were some significant correlations between higher order aberrations and the objective DOF although these correlations seemed to be less consistent than those found with the subjective DOF and higher order aberrations. Notably there may be evidence to suggest that there was some influence of coma on the objective DOF as significant positive correlations were found between vertical coma (Z_3^{-1}) and the objective DOF recorded whilst viewing the N10 37.23cdeg^{-1} target and the N20 9.33cdeg^{-1} target and horizontal coma (Z_3^{1}) and objective DOF when viewing the N10 4.65cdeg^{-1} target.

7.3.3 Effects of higher order aberrations on dynamic accommodation with different spatial frequency filtered text targets

The effect of higher order aberrations on the dynamic accommodation was investigated (Tables 7.9-7.12). For an N10 unfiltered target, there was no correlation between the RMS of the higher order aberrations and positive latency (r=-0.14, p=0.46), negative latency (r=-0.26, p=0.17), positive RTs (r=0.01, p=0.95) or negative RTs (r=-0.20, p=0.30). For an N20 unfiltered target, there was no correlation between the RMS of the higher order aberrations and positive latency (r=-0.17, p=0.35), negative latency (r=-0.25, p=0.18) or positive RTs (r=-0.27, p=0.13) although significant negative correlation was found for negative RTs (r=-0.52, p=0.003). No correlations were found for the N20 unfiltered target between negative RT and higher order aberration terms (p>0.05) except for spherical aberration (r=-0.43, p=0.02).

No correlations were found between RMS and positive or negative latencies for any N10 or N20 target. No correlations were found between the RMS and positive and negative RTs for any N10 or N20 filtered targets (p>0.05) except the negative RT for the N10 4.65cdeg^{-1} target (r=-0.47, p=0.01) and for the N20 9.31cdeg^{-1} target (r=0.41, p=0.02).

Table 7.9 Correlations between higher order aberrations and dynamic latencies for all N10 spatial frequency filtered targets

		Positive latencies					Negative latencies				
Higher order aberrations		Un-filtered	4.65	9.31	18.62	37.23	Un-filtered	4.65	9.31	18.62	37.23
(Z_3^{-3})	Pearson Correlation	0.052	0.143	-0.003	0.188	0.206	0.080	0.115	0.048	0.244	0.076
	Sig. (2-tailed)	0.780	0.452	0.985	0.319	0.267	0.673	0.545	0.798	0.194	0.686
(Z_3^{-1})	Pearson Correlation	-0.045	-0.157	0.202	0.059	-0.250	-0.193	-0.026	0.031	-0.154	0.162
	Sig. (2-tailed)	0.811	0.409	0.276	0.755	0.175	0.308	0.893	0.868	0.417	0.384
(Z_3^{1})	Pearson Correlation	-0.207	-0.349	-0.029	0.235	-0.228	-0.208	-0.209	-0.249	0.071	0.023
	Sig. (2-tailed)	0.264	0.059	0.877	0.211	0.217	0.270	0.268	0.176	0.710	0.903
(Z_3^{3})	Pearson Correlation	-0.204	0.049	0.144	-0.497**	-0.032	0.088	-0.129	0.079	0.075	0.002
	Sig. (2-tailed)	0.272	0.796	0.440	0.005	0.864	0.644	0.498	0.672	0.696	0.992
(Z_4^{-4})	Pearson Correlation	0.477*	0.240	-0.076	0.229	0.193	.0398*	0.091	0.232	0.252	-0.102
	Sig. (2-tailed)	0.007	0.202	0.683	0.223	0.299	0.029	0.633	0.209	0.179	0.586
(Z_4^{-2})	Pearson Correlation	0.014	0.040	-0.009	0.114	0.159	0.133	-0.010	0.044	-0.090	-0.008
	Sig. (2-tailed)	0.941	0.835	0.962	0.549	0.394	0.483	0.958	0.815	0.636	0.967
(Z_4^{0})	Pearson Correlation	-0.221	-0.081	0.074	0.150	-0.349	-0.170	-0.368*	-0.205	-0.050	-0.150
	Sig. (2-tailed)	0.233	0.669	0.691	0.428	0.054	0.370	0.045	0.268	0.794	0.420
(Z_4^{2})	Pearson Correlation	0.128	-0.107	-0.334	0.071	0.056	0.080	0.149	0.093	0.054	-0.265
	Sig. (2-tailed)	0.494	0.573	0.067	0.708	0.765	0.674	0.431	0.617	0.775	0.149
(Z_4^{4})	Pearson Correlation	0.077	0.017	0.390*	-0.031	-0.027	0.058	0.042	-0.018	0.109	0.125
	Sig. (2-tailed)	0.680	0.930	0.030	0.873	0.886	0.762	0.827	0.923	0.565	0.503
RMS	Pearson Correlation	-0.138	-0.169	0.130	0.036	-0.324	-0.257	-0.184	-0.182	0.004	0.063
	Sig. (2-tailed)	0.460	0.371	0.485	0.848	0.076	0.170	0.329	0.328	0.984	0.734

Table 7.10 Correlations between higher order aberrations and dynamic RTs for all N10 spatial frequency filtered targets

		Positive response times					Negative Response times				
Higher order aberrations		Un-filtered	4.65	9.31	18.62	37.23	Un-filtered	4.65	9.31	18.62	37.23
(Z_3^{-3})	Pearson Correlation	0.140	0.020	-0.024	0.182	-0.121	0.032	0.007	-0.212	0.130	-0.245
	Sig. (2-tailed)	0.460	0.917	0.898	0.336	0.516	0.868	0.971	0.252	0.493	0.184
(Z_3^{-1})	Pearson Correlation	0.163	0.089	0.258	0.128	0.386*	-0.141	-0.133	0.057	-0.141	0.204
	Sig. (2-tailed)	0.390	0.639	0.160	0.502	0.032	0.458	0.483	0.759	0.457	0.270
(Z_3^{1})	Pearson Correlation	0.118	-0.006	-0.097	-0.065	-0.117	-0.345	-0.499**	-0.222	-0.221	-0.285
	Sig. (2-tailed)	0.536	0.975	0.605	0.731	0.532	0.062	0.005	0.229	0.240	0.120
(Z_3^{3})	Pearson Correlation	-0.105	-0.049	-0.281	-0.013	0.095	0.310	0.055	0.041	-0.102	0.279
	Sig. (2-tailed)	0.580	0.795	0.125	0.946	0.612	0.095	0.774	0.825	0.592	0.129
(Z_4^{-4})	Pearson Correlation	0.265	0.122	0.384*	0.186	0.098	0.123	0.197	0.194	0.180	0.038
	Sig. (2-tailed)	0.157	0.521	0.033	0.325	0.601	0.519	0.298	0.296	0.340	0.838
(Z_4^{-2})	Pearson Correlation	-0.462*	-0.163	-0.166	-0.346	-0.501**	0.076	-0.028	0.047	0.195	-0.130
	Sig. (2-tailed)	0.010	0.390	0.372	0.061	0.004	0.689	0.884	0.801	0.302	0.486
(Z_4^{0})	Pearson Correlation	0.083	-0.107	-0.015	-0.035	0.157	-0.257	-0.275	0.042	-0.400*	0.165
	Sig. (2-tailed)	0.661	0.573	0.934	0.852	0.398	0.171	0.142	0.825	0.028	0.375
(Z_4^{2})	Pearson Correlation	-0.175	-0.006	-0.062	-0.182	-0.259	-0.092	0.132	0.046	0.169	-0.081
	Sig. (2-tailed)	0.355	0.974	0.741	0.334	0.160	0.630	0.488	0.807	0.372	0.665
(Z_4^{4})	Pearson Correlation	0.152	-0.100	0.060	0.040	0.059	-0.046	-0.347	-0.224	0.013	0.048
	Sig. (2-tailed)	0.422	0.598	0.750	0.833	0.754	0.808	0.060	0.226	0.946	0.798
RMS	Pearson Correlation	0.011	-0.090	-0.056	-0.083	0.096	-0.196	-0.465**	-0.163	-0.287	0.054
	Sig. (2-tailed)	0.952	0.635	0.766	0.664	0.607	0.300	0.010	0.381	0.124	0.772

Table 7.11 Correlations between higher order aberrations and dynamic latencies for all N20 spatial frequency filtered targets

		Positive latencies					Negative latencies				
Higher order aberrations		Un-filtered	2.33	4.65	9.31	18.62	Un-filtered	2.33	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	0.283	-0.076	0.009	-0.023	-0.165	-0.207	0.219	0.357	0.076	-0.101
	Sig. (2-tailed)	0.117	0.688	0.964	0.902	0.383	0.264	0.236	0.053	0.686	0.597
(Z_3^{-1})	Pearson Correlation	-0.039	0.055	0.061	0.174	0.273	-0.108	-0.023	-0.283	0.154	-0.133
	Sig. (2-tailed)	0.833	0.771	0.754	0.340	0.144	0.563	0.904	0.129	0.410	0.482
(Z_3^{1})	Pearson Correlation	-0.102	-0.081	-0.013	-0.040	0.162	-0.363*	0.000	0.010	0.066	-0.187
	Sig. (2-tailed)	0.578	0.670	0.947	0.827	0.394	0.045	0.999	0.957	0.723	0.322
(Z_3^{3})	Pearson Correlation	-0.036	0.167	-0.102	-0.011	0.097	0.362*	0.059	0.019	0.039	0.303
	Sig. (2-tailed)	0.843	0.377	0.599	0.952	0.610	0.045	0.752	0.922	0.836	0.103
(Z_4^{-4})	Pearson Correlation	0.264	0.266	0.318	0.225	0.027	0.043	0.103	0.006	0.036	0.247
	Sig. (2-tailed)	0.144	0.155	0.093	0.216	0.886	0.820	0.580	0.974	0.847	0.188
(Z_4^{-2})	Pearson Correlation	-0.139	0.411*	0.135	-0.170	0.044	0.256	0.040	0.132	0.104	0.186
	Sig. (2-tailed)	0.447	0.024	0.487	0.353	0.818	0.164	0.831	0.488	0.579	0.324
(Z_4^{0})	Pearson Correlation	0.105	0.157	0.142	0.266	0.238	-0.203	-0.140	-0.289	-0.176	-0.182
	Sig. (2-tailed)	0.567	0.407	0.461	0.142	0.205	0.274	0.452	0.122	0.343	0.335
(Z_4^{2})	Pearson Correlation	-0.068	0.109	0.239	-0.335	-0.112	0.141	0.012	0.205	0.134	0.021
	Sig. (2-tailed)	0.710	0.567	0.211	0.061	0.556	0.449	0.949	0.278	0.472	0.914
(Z_4^{4})	Pearson Correlation	-0.082	-0.112	-0.381*	0.185	-0.019	-0.086	0.064	-0.135	-0.200	-0.004
	Sig. (2-tailed)	0.654	0.555	0.042	0.310	0.923	0.645	0.733	0.476	0.281	0.983
RMS	Pearson Correlation	-0.170	0.048	0.059	-0.094	0.057	0.245	-0.336	-0.343	-0.093	0.052
	Sig. (2-tailed)	0.351	0.803	0.759	0.610	0.765	0.184	0.064	0.064	0.619	0.784

Table 7.12 Correlations between higher order aberrations and dynamic RTs for all N20 spatial frequency filtered targets

		Positive response times					Negative Response times				
Higher order aberrations		Un-filtered	2.33	4.65	9.31	18.62	Un-filtered	2.33	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	0.051	0.006	-0.162	-0.199	0.033	0.223	-0.385*	0.326	-0.226	-0.192
	Sig. (2-tailed)	0.783	0.975	0.402	0.275	0.862	0.227	0.032	0.079	0.221	0.310
(Z_3^{-1})	Pearson Correlation	0.105	0.077	-0.035	0.495**	-0.071	-0.051	-0.235	-0.079	-0.143	0.107
	Sig. (2-tailed)	0.566	0.686	0.856	0.004	0.709	0.786	0.203	0.676	0.444	0.574
(Z_3^{1})	Pearson Correlation	-0.129	-0.109	0.092	0.422*	-0.025	0.090	-0.388*	0.117	-0.114	-0.139
	Sig. (2-tailed)	0.480	0.565	0.635	0.016	0.894	0.630	0.031	0.537	0.540	0.463
(Z_3^{3})	Pearson Correlation	0.254	0.295	0.000	-0.103	-0.017	-0.286	0.250	-0.186	0.219	0.219
	Sig. (2-tailed)	0.160	0.114	0.999	0.574	0.929	0.118	0.175	0.325	0.236	0.245
(Z_4^{-4})	Pearson Correlation	-0.081	-0.073	0.119	0.425*	0.251	0.160	0.048	-0.003	0.038	0.205
	Sig. (2-tailed)	0.658	0.703	0.538	0.015	0.181	0.391	0.798	0.989	0.837	0.277
(Z_4^{-2})	Pearson Correlation	-0.217	0.045	-0.320	-0.330	-0.098	-0.022	0.365*	-0.198	0.144	-0.294
	Sig. (2-tailed)	0.233	0.812	0.091	0.065	0.606	0.905	0.044	0.295	0.438	0.115
(Z_4^{0})	Pearson Correlation	-0.221	0.027	-0.012	0.170	-0.115	-0.429*	-0.166	-0.087	-0.069	0.039
	Sig. (2-tailed)	0.223	0.888	0.952	0.351	0.544	0.016	0.373	0.647	0.712	0.839
(Z_4^{2})	Pearson Correlation	-0.037	-0.160	-0.155	-0.215	0.053	0.027	0.174	0.107	-0.060	-0.075
	Sig. (2-tailed)	0.842	0.400	0.422	0.238	0.780	0.887	0.349	0.573	0.749	0.693
(Z_4^{4})	Pearson Correlation	-0.008	0.024	0.002	0.374*	0.108	0.050	-0.162	-0.076	-0.237	0.044
	Sig. (2-tailed)	0.967	0.902	0.992	0.035	0.571	0.789	0.385	0.691	0.199	0.819
RMS	Pearson Correlation	-0.272	-0.184	0.071	0.409*	-0.092	-0.520**	0.001	-0.227	0.006	-0.018
	Sig. (2-tailed)	0.132	0.332	0.714	0.020	0.627	0.003	0.997	0.229	0.976	0.923

As correlations were calculated for all higher order aberration terms with ten targets this produced 400 different statistics. 5% of these correlations occurred by chance (type 1 error) and therefore some significant correlations found between higher order aberrations and dynamic accommodation could be explained by chance.

7.3.4 Effects of higher order aberrations on accommodative microfluctuations with different spatial frequency filtered text targets

Correlations were conducted between higher order aberrations and the RMS values of accommodative microfluctuations (Table 7.13). Few significant results were found between higher order aberrations and the RMS of accommodative microfluctuations although some significant correlations were found between spherical aberration (Z_4^0) and the RMS for the N10 targets: 4.65cdeg^{-1} (r=0.37, p=0.04) and 18.62cdeg^{-1} (r=0.39, p=0.04) and the N20 4.65cdeg^{-1} target (r=0.37, p=0.04). This might suggest that the larger the magnitude of spherical aberration, the larger the accommodative microfluctuations when viewing certain targets.

Table 7.13 Correlations between higher order aberrations and RMS of accommodative microfluctuations for the spatial frequency filtered targets (cdeg^{-1})

		RMS for N10 targets					RMS for N20 targets				
Higher order aberrations		Unfiltered	4.65	9.31	18.62	37.23	Unfiltered	2.33	4.65	9.31	18.62
(Z_3^{-3})	Pearson Correlation	0.149	0.309	0.285	0.257	0.083	0.103	0.053	0.157	0.127	-0.039
	Sig. (2-tailed)	0.424	0.091	0.121	0.171	0.650	0.581	0.777	0.392	0.496	0.835
(Z_3^{-1})	Pearson Correlation	0.060	-0.124	-0.010	-0.348	-0.108	-0.046	0.132	-0.202	-0.233	-0.101
	Sig. (2-tailed)	0.750	0.507	0.958	0.060	0.556	0.804	0.479	0.267	0.207	0.589
(Z_3^{1})	Pearson Correlation	-0.121	0.014	-0.089	-0.115	-0.114	-0.088	-0.074	-0.189	-0.044	-0.040
	Sig. (2-tailed)	0.517	0.941	0.633	0.546	0.536	0.638	0.691	0.300	0.814	0.831
(Z_3^{3})	Pearson Correlation	-0.332	-0.241	-0.169	-0.161	-0.118	-0.070	-0.393*	-0.084	-0.141	0.083
	Sig. (2-tailed)	0.068	0.192	0.364	0.395	0.520	0.708	0.029	0.647	0.450	0.659
(Z_4^{-4})	Pearson Correlation	-0.037	-0.191	-0.200	-0.294	-0.289	-0.163	0.000	-0.217	-0.028	-0.124
	Sig. (2-tailed)	0.845	0.303	0.282	0.115	0.109	0.380	0.999	0.232	0.881	0.508
(Z_4^{-2})	Pearson Correlation	-0.051	0.132	-0.172	0.033	0.069	-0.047	0.005	-0.036	0.090	-0.050
	Sig. (2-tailed)	0.786	0.478	0.355	0.864	0.708	0.801	0.979	0.847	0.629	0.789
(Z_4^{0})	Pearson Correlation	-0.286	0.370*	-0.239	0.387*	-0.176	-0.213	-0.343	0.366*	-0.294	-0.335
	Sig. (2-tailed)	0.119	0.040	0.195	0.035	0.335	0.249	0.059	0.040	0.109	0.065
(Z_4^{2})	Pearson Correlation	0.047	0.005	-0.056	0.042	-0.123	0.002	0.341	0.060	-0.059	-0.055
	Sig. (2-tailed)	0.802	0.978	0.764	0.827	0.503	0.992	0.061	0.743	0.753	0.768
(Z_4^{4})	Pearson Correlation	0.145	0.082	0.105	-0.056	0.041	0.012	0.001	0.000	0.071	0.001
	Sig. (2-tailed)	0.437	0.659	0.574	0.770	0.822	0.950	0.998	0.998	0.704	0.996
RMS	Pearson Correlation	-0.070	-0.280	-0.205	-0.319	-0.066	-0.261	-0.408*	0.404*	-0.331	0.401*
	Sig. (2-tailed)	0.708	0.128	0.270	0.086	0.719	0.156	0.023	0.022	0.069	0.025

7.4 Discussion

Previous studies have suggested that spherical aberration may provide a stimulus for myopia development (Thorn *et al.*, 2000; Marcos, Barbero and Llorente, 2002). Spherical aberration causes longitudinal displacement of an image from the point of optimal focus and therefore, it has been suggested this may provide another stimulus for ocular elongation and myopia development. Larger levels of spherical aberration in myopes compared to emmetropes have not been found (Cheng *et al.*, 2004; see Charman, 2005 for a review). However, a study by Hartwig and Atchison (2012) suggested that spherical aberration might be influenced by refractive error. The current study finds that myopes do not show significantly larger levels of spherical aberration compared to emmetropes with 6mm pupils or with natural pupils whilst accommodating. A significant negative correlation is found between vertical coma (Z_3^{-1}) and spherical equivalent refraction both when measured with natural pupils and accommodation and with dilated 6mm pupils. Coma may therefore have more potential to influence accommodation differences in refractive error groups rather than spherical aberrations.

Benard, Lopez-Gil and Legras (2011) found that with a 6mm pupil the addition of 0.3 and 0.6 microns of spherical aberration caused an increase in the subjective DOF. This suggests that larger levels of spherical aberration would lead to larger subjective DOF. Significant positive correlations were found between RMS values and just noticeable subjective DOF when viewing the N20 18.62cdeg^{-1} target. Significant positive correlations were also found between RMS values and non resolvable subjective DOF when viewing N10 9.31cdeg^{-1} and 18.62 cdeg^{-1} targets and N20 unfiltered target. However, no correlations existed between spherical aberration and subjective DOF. The current study found average magnitudes of spherical aberration with a 6mm pupil to be 0.10μm±0.07, much smaller than the values used in the study by Benard, Lopez-Gil and Legras (2011) and therefore unlikely to be large enough to bring about changes in the DOF.

Some significant negative correlations were found between oblique and horizontal trefoil (Z_3^{-3}, Z_3^{3}) and just noticeable DOF (for the N10 9.31cdeg^{-1} and 18.62cdeg^{-1} targets) and non resolvable DOF (for the N10 2.33 cdeg^{-1} and 18.62cdeg^{-1} targets). This suggests some influence of trefoil (Z_3^{3} and Z_3^{-3}) on subjective DOF. Although simulating trefoil in a study by Rocha *et al.* (2009) did not affect DOF it may depend on the target size and spatial frequencies under observation.

It has been suggested that neural adaptation occurs for familiar aberrations which means they do not affect target clarity whereas the introduction of induced, unfamiliar aberrations have more effect on apparent blur of the target (Artal *et al.*, 2004; Chen *et al.*, 2007). This suggests that levels of aberrations found in the natural eye will have less effect on blur perception than induced unfamiliar aberrations. The current study found that the magnitude of subjective DOF was dependent on the spatial frequency filtered text target under observation. Results suggested that oblique and horizontal trefoil were more likely to influence subjective DOF compared to other higher order aberration terms. There may be some interplay between higher order aberrations and the spatial frequency filtered target under observation on the levels of subjective DOF.

Charman and Jennings (1976) found more myopic focus for intermediate compared to high spatial frequency gratings in myopes. This study found a more myopic focus for the unfiltered and peak spatial frequency filtered text targets. However, optimum focus was not found to be dependent upon refractive error group unlike the findings of Radhakrishnan *et al.* (2004). Significant positive correlations were found between levels of spherical aberration (Z_4^0) and the subjective DOF midpoints for unfiltered text and for most filtered targets. Larger magnitudes of spherical aberration gave rise to more myopic midpoints of subjective DOF. Green and Campbell (1965) reported a more myopic focus for low to moderate compared to high spatial frequency gratings and attributed this to spherical aberration. The current study suggests that spherical aberration affects the midpoint of subjective DOF.

Rocha *et al.* (2009) found inducing trefoil or coma with an adaptive optics visual simulator had no effect on overall DOF but inducing spherical aberration increased DOF. The current study found no consistent correlations between spherical aberration and the objective DOF or dynamic accommodation (latency or RTs) for any target, although there may be some influence of the magnitude of spherical aberration on the magnitude of microfluctuations. Magnitudes of spherical aberration (mean: 0.07μm ±0.05) recorded with natural pupils and accommodating eyes were unlikely to be large enough to influence DOF.

Hofer *et al.* (2001) found that fluctuations in wavefront aberrations were not only limited to defocus (accommodative microfluctuations) but also higher order aberrations. However, Hofer *et al.* (2001) reported that accommodative microfluctuations are not of sufficient magnitude to produce the fluctuations in higher order aberrations, given that higher order aberrations are known to change with accommodation. Zhu, Collins and Robert Iskander, 2004), unlike Hofer *et al.* (2001) did find some correlation between the fluctuations of higher order aberrations and defocus. Winn *et al.* (1990) reported a link between the magnitude of accommodative microfluctuations and the arterial pulse and Zhu, Collins and Robert Iskander (2004) also reported an association between the pulse and most wavefront aberration fluctuations (including spherical aberration). These studies suggest at least an association between the accommodative microfluctuations and higher order aberrations and the results of the current study do support this finding suggesting some association between spherical aberration and the magnitude of accommodative microfluctuations.

7.5 Conclusion

This study found no difference in the spherical aberration or RMS values between myopes and emmetropes with either dilated pupils or whilst accommodating. This would suggest differences found in accommodation responses between myopes and emmetropes are unlikely to be attributable to spherical aberration. Spherical aberration levels recorded for naturalistic near viewing conditions were unlikely to be large enough to enhance DOF. However, vertical coma (Z_3^{-1}) was correlated with spherical equivalent refraction. Some correlations were also found between trefoil (Z_3^3 and Z_3^{-3}) and subjective DOF. This study suggested that third order aberrations (coma and trefoil) were more likely to influence accommodation responses than fourth order aberrations (spherical, quadrafoil and secondary astigmatism.

This study found that levels of spherical aberration are correlated with the displacement of the subjective DOF midpoint. This showed that although spherical aberration did not affect the magnitude of subjective DOF it could affect the position of DOF depending on target spatial frequency content.

This study found spherical aberration was unlikely to explain differences in the subjective and objective DOF and dynamic accommodation and accommodative microfluctuations found in myopes and emmetropes. However, third order higher aberration terms (coma and trefoil) were found to have more potential to influence accommodation differences. This highlighted the importance of considering all higher order aberration terms (rather than just spherical aberration) when considering optical influences on DOF in future studies considering accommodation response system and perceptual differences in myopes and emmetropes.

Chapter 8: Discussion and conclusions

8.1 Study objectives and gaps in the knowledge

Increasing prevalence of myopia (discussed in section 1.1) means that investigation into the causes and possible treatments is becoming ever more important. It has been suggested that at least a portion of myopia is not genetic and therefore preventable (Angle and Wissmann, 1980). Myopia is due to axial elongation thought to be caused by hyperopic retinal defocus. Accommodation inaccuracies have been widely thought to provide a source of this hyperopic defocus but reasons why myopes have poorer accommodation is still unknown. Extended levels of near work, particularly reading, are also linked with increased levels of myopia progression. This study examined whether different features of text lead to poor blur sensitivity and inaccurate accommodation responses. Knowledge of what features of text are poorly responded to by myopes compared to emmetropes will be important in designs of future treatment strategies for myopia such as blur training to improve blur sensitivity.

8.1.1 The effect of accommodative inaccuracy on peripheral retinal blur

Hyperopic peripheral refraction has been found in myopes in various studies (section 1.4.3) but to date no study has investigated the effect of accommodative lag on the peripheral blur experienced for near tasks. Mutti *et al.* (2011) refined conclusions from their previous study and were more conservative about stating the risk of peripheral hyperopia on myopia development, however, consideration may need to be given to the combined accommodative lag and peripheral refraction. The current study found that accommodative lag was not different in myopes and emmetropes. However, accommodative lag shifted the near plano relative peripheral refraction in low and moderate myopes into hyperopic blur and exaggerated the relative peripheral hyperopia in high myopes for near viewing. Peripheral refraction in conjunction with accommodative lag may therefore, increase or decrease the risk of suffering hyperopic blur. Accommodative lag still needs to be considered in conjunction with peripheral refraction in order to assess the peripheral blur experienced in different refractive groups for near tasks.

Figure 8.1 shows a diagrammatic representation of skiagrams created from the results in the current study. Hoogerheide, Rempt and Hoogenboom (1971) reported that those subjects with at least a portion of the tangential and sagittal image shell providing hyperopic defocus were more at risk of developing myopia. The current study did not find that all myopes had a portion of the tangential and sagittal image shells provided hyperopic defocus. However, with the addition of accommodative lag at least a portion of tangential and sagittal image shells were shifted so that they provided hyperopic defocus and this may also suggest that accommodative lag increases the risk of further myopia development.

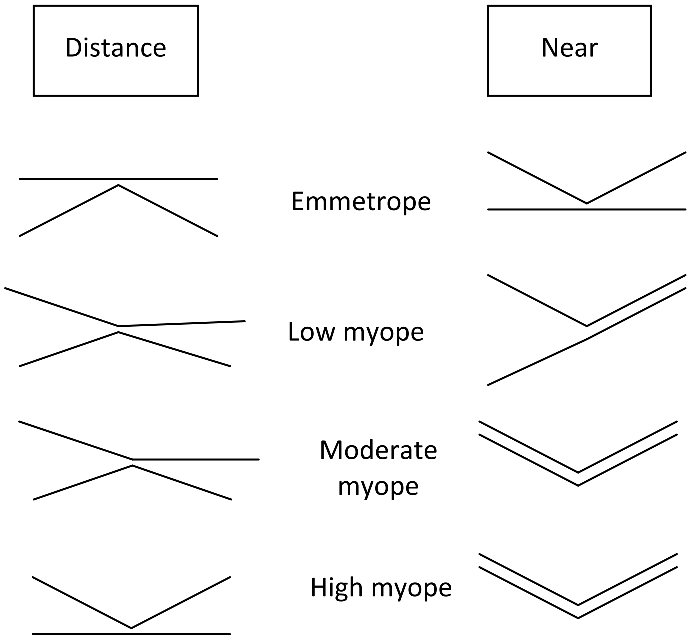

Figure 8.1 Skiagrams representing the findings of peripheral refraction in the current study. Lines moving in an upward direction demonstrate hyperopic defocus whilst straight lines represent refraction near emmetropia. The two lines in each case represent the tangential and sagittal image shells. The distance plots (left) represent the findings for distance viewing and the near plots (right) represent the findings for near viewing

Treatment strategies manipulating the peripheral blur (Holden *et al.*, 2010; Sankaridurg *et al.*, 2011) experienced by myopes in order to reduce myopia progression have had statistically significant but clinically very small effects. These studies may need to consider the influence of accommodative lag on peripheral hyperopic blur experienced for near viewing tasks and the possibility of correcting peripheral hyperopic blur for each individual depending on their levels of near work in order to improve treatment effects.

8.1.2 The effect of text spatial frequency filter and size on the subjective DOF in myopes and emmetropes

Treatment strategies for myopia prevention have considered manipulating blur sensitivity using blur training methods to improve accommodation responses (Cufflin, Mankowska and Mallen, 2007; Cufflin and Mallen, 2008). Myopes have been shown to have poorer blur sensitivity (Rosenfield and Abraham-Cohen, 1999). As increased levels of near work have been linked with myopia development, the current study attempted to consider if different features of text contribute to poor blur sensitivity. If certain elements of text detail can be isolated as having more effect on the poor blur sensitivity in myopes then these could be targeted in blur training strategies. No difference was found in just noticeable blur between myopes and emmetropes but myopes were better at resolving blurry letters regardless of the text spatial frequency filter or size.

Watson and Ahumada (2011) reviewed many studies investigating blur discrimination and detection and described a simple model of the pattern of blur detection thresholds which they stated was a direct consequence of the CSF. However, none of the studies they reviewed used complex text targets. The peak spatial frequency of the human CSF is between 4-6cdeg^{-1} based on grating targets.

The peak text spatial frequency was calculated using the limb width of a letter (1 dark line and 1 light line equivalent to 1 cycle). This meant that the same spatial frequency filter resulted in a different appearance of the two text sizes. The peak spatial frequencies of the N10 and N20 text were found to be 9.31cdeg^{-1} and 4.65cdeg^{-1} respectively. Larger subjective DOF were found for the peak text spatial frequency targets and the larger N20 text targets. Subjective DOF was dependent on the text detail rather than the specific spatial frequency filter that might be predicted from the human CSF. In the absence of the peak text spatial frequency blur was less well tolerated.

Previous studies found letter recognition was reliant on the object detail (cycles per letter) rather than specific spatial frequencies (Chung, Legge and Tjan, 2002). The current study suggested that subjective DOF, relying on blur perception, was also related to the object detail.

8.1.3 The effect of text spatial frequency filter and size on the dynamic accommodation responses in myopes and emmetropes

Strang *et al.* (2011) found myopes were poorer at responding to blur signals and speculated whether this was due to the initiation or fine tuning of the accommodation response. The current study found that myopes were not poorer at initiating accommodation (latencies) but were poorer at refining their accommodation response (positive RTs). This suggests that large proximal cues may drive the initial accommodation response. Retinal blur cues appeared to drive accommodation refinement and the myopes were poorer at using these cues when altering attention towards a near target.

Dynamic accommodation has been found to be optimal for mid-range spatial frequency gratings (Bour, 1981) in an experiment where proximal cues were limited. Strang *et al.* (2011) reported greater accommodative responses and an improved percentage of correct accommodation responses to mid spatial frequency gratings (4cdeg-1) for large accommodative step responses (4/1D). Dynamic accommodation responses in the current study were found to be unaffected by text spatial frequency filter or size. The difference in findings may be due to the broad spatial frequency content of the text targets used in the current study.

Myopes exhibited slower positive RTs regardless of text spatial frequency filter or size. As the spatial frequency filter applied to the text had no effect on dynamic accommodation responses, this suggested that the accommodation system may be driven by a variety of spatial frequencies when viewing complex targets.

Dynamic responses and subjective DOF are affected differently by the spatial frequency filtered text targets. This would suggest that studies investigating accommodative facility training (velocity of accommodation to plus/ minus flippers) should base their end points on changes in accommodation responses rather than just subjective perception of blur.

8.1.4 The effect of text spatial frequency filter and size on the objective DOF and accommodative microfluctuations in myopes and emmetropes

Larger objective DOF found in myopes would lead to larger levels of accommodative inaccuracy. Larger objective DOF may be explained by larger accommodative microfluctuations and poorer blur sensitivity also found in this study and supported in other studies (Jiang, 1997; Day *et al.*, 2006; Vasudevan, Ciuffreda and Wang, 2006a).

Spatial frequencies of complex text targets were not shown to affect accommodation responses although the differences in objective DOF of myopes and emmetropes were found when viewing the peak text spatial frequency (the spatial frequency of the limb width of the letter). The current study has suggested that with complex text targets it may not just be the mid-spatial frequencies which best drive accommodation as previously reported in studies using gratings (Owens, 1980; Bour, 1981; Ward, 1987). Future attempts to improve blur sensitivity and accommodation responses using blur training may consider concentrating on the peak spatial frequency of text targets rather than specific spatial frequency band filters.

Spatial frequency filters applied to text have a significant effect on subjective DOF but not on objective DOF which suggest that the accommodation responses rely on more than just subjective blur perception. Attempts to alter blur sensitivity in order to improve accommodation responses should base improvements on measurements of accommodation response rather than subjective perception of blur.

8.1.5 The effect of higher order aberrations on blur sensitivity and accommodation responses

This study aimed to investigate any possible optical contributions to blur sensitivity and accommodation responses. It was expected based on previous findings (section 1.6.3) that increased levels of spherical aberration would lead to larger DOF, accommodative microfluctuations and poorer dynamic accommodation. Due to image degradation it was expected that higher order aberrations would have more effect on the higher spatial frequency filtered text targets. However, myopes showed lower levels of spherical aberration compared to emmetropes with dilated 6mm pupils (although not significant) and showed no difference with natural pupils. Levels of spherical aberration were not correlated with larger subjective DOF, objective DOF or dynamic accommodation (latency or RTs) although the results might suggest some association between spherical aberration and the magnitude of accommodative microfluctuations.

Theories that spherical aberration may be a cause of accommodative lag are not supported by this study. Levels of spherical aberration in natural accommodating eyes, found in the current study, were unlikely to be large enough to enhance DOF.

A significant negative correlation was found between vertical coma (Z_3^{-1}) and spherical equivalent refraction both when measured with natural pupils and accommodation and with dilated 6mm pupils. Examination of correlations between higher order aberrations and objective DOF seemed to suggest that third order terms (coma and trefoil) may have more effect on accommodation responses. However, it is unlikely that correction of natural levels of higher order aberrations would affect accommodation responses.

8.2 Accommodation Control

The accommodation control model developed by Hung and Semmlow (1980) described a dual feedback mechanism consisting of input from both the accommodative stimulus and vergence elements with some contribution from proximal cues. Hung, Ciuffreda and

Rosenfield (1996) considered this model and the contribution of proximal cues to accommodation with accommodative and vergence control under a combination of open and closed loop conditions. Under open loop conditions the accommodative or vergence cues are eliminated. In closed loop, more naturalistic viewing conditions, accommodative or vergence cues have significant contributions and in this situation, proximal cues contribute very little (~4%).

In the current study objective and dynamic accommodation measurements were taken monocularly, eliminating vergence cues. Targets were viewed in free space, where accommodative cues and proximal cues were available. Hung, Ciuffreda et al. (1996) suggested that when vergence cues are eliminated but accommodative cues are still available the influence of proximal cues was still small (~4%).

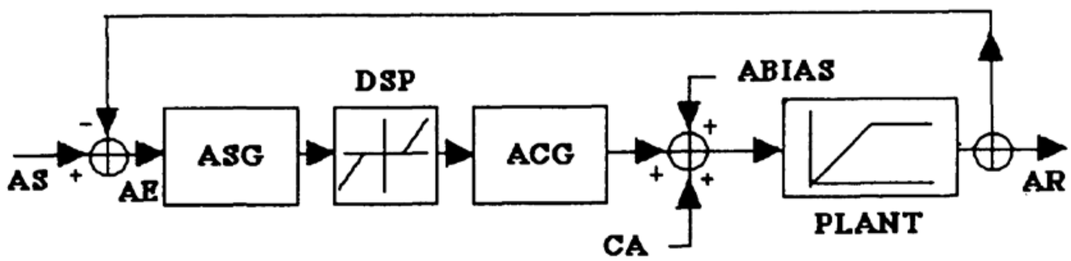

Figure 8.2 Diagram taken from Jiang (1997) showing a model of accommodation control. Accommodative stimulus (AS) forms the blur signal and results in an accommodative response (AR). The difference between AR and AS results in accommodative error (AE) as an input to the system. Degradation of the blur signal in the sensory part of the system is represented by accommodative sensory gain (ASG). The threshold for oculomotor control is represented by deadspace (DSP) or the depth of focus. The resulting signal goes into the accommodative controller, a linear operator with gain, the accommodative controller gain (ACG). Output from here is summed with vergence accommodation (CA) (not applicable in the current study) and tonic accommodation (ABIAS) to drive the accommodative plant which results in the accommodation response

Jiang (1997) used an accommodation control model to analyse accommodative behaviour (Figure 8.2). This model helped to consider influences on the accommodation control system and the current study aimed to investigate what might contribute to reduced accommodation responses in myopes compared to emmetropes.

8.2.1 Refractive group differences in accommodation

Accommodative lag was not found to differ between myopes and emmetropes in the current study (section 3.3). However, it has already been suggested that static accommodation needs to be considered alongside the variability in accommodation to fully investigate refractive error group differences (Seidel, Gray and Heron, 2003; Seidel, Gray and Heron, 2005; Day *et al.*, 2006; Radhakrishnan, Allen and Charman, 2007; Langaas *et al.*, 2008). The current study aimed to investigate the perceptual (subjective DOF), neural (objective DOF) and optical (higher order aberrations) influences on accommodation and refractive error group differences.

Differences in blur perception found in the subjective DOF experiments suggest that myopes have higher blur thresholds which may contribute to poorer accommodation responses. Myopes were found to have larger subjective and objective DOF compared to emmetropes. It may be that myopes have developed poorer blur sensitivity as a protective mechanism to limit symptoms of poorer objective DOF. Larger objective DOF in myopes compared to emmetropes may suggest poorer neural responses to retinal blur cues. In the accommodation control model (Figure 8.2) the current study considered the deadspace (DSP) where the DOF component plays a role.

In real world situations, where large step responses are made, it may be the proximal cues that provide most influence in initiating accommodative responses (accommodation stimulus (AS) in the Jiang (1997) model). In real near work situations, such as altering ones reading position, proximal cues would be small and retinal blur cues and DOF would play a larger role in refining accommodation responses. Accommodative latency in this study relied on large proximal cues and was not different in the refractive error groups. Poorer positive accommodative RTs in myopes were likely to depend on retinal blur cues, also suggesting differences in the neural accommodation control system between myopes and emmetropes. This conclusion is one supported by Strang *et al.* (2011) who also suggested myopes were poorer at interpreting small changes in defocus to fine tune accommodation responses.

8.2.2 Effects of text target spatial frequency content

Previous findings suggest mid-spatial frequency gratings best drive accommodation (Owens, 1980; Bour, 1981; Ward, 1987). From the data in the current study it was shown that mid-range spatial frequency text targets do not have the smallest blur thresholds (subjective DOF).The current study suggests that resolution and optimum focus of text targets is dependent on text detail rather than specific spatial frequency bands. The poorest blur sensitivity and more myopic optimum focus was observed with the peak text spatial frequency (N10: 9.31cdeg^{-1} and N20: 4.65cdeg^{-1}). Spatial frequency filtered text was not found to affect accommodation responses (dynamic or objective DOF). However, differences in objective DOF in myopes and emmetropes were seen when viewing the peak text spatial frequency detail.

As studies have suggested that spherical aberration affects the contrast sensitivity of particularly intermediate spatial frequencies (Charman and Jennings, 1976; Jansonius and Kooijman, 1998), other studies have considered the possibility that the source of poorer accommodation in myopes is due to optical differences (Radhakrishnan *et al.*, 2004). Radhakrishnan *et al.* (2004) reported that differences in the CSF between myopes and emmetropes might be due to differences in aberrations, which although not found to be significantly different may still affect accommodation responses. Further studies have considered the possibility of correcting or inducing aberrations to improve accommodation responses. However, the current study aimed to consider the effect of spatial frequencies in real world text targets on accommodation. If the text detail rather than specific spatial frequency band affects accommodation differences in myopes, then treatment strategies aimed at altering aberrations to improve the CSF in myopes to intermediate spatial frequencies, are unlikely to improve accommodation responses to text targets.

8.2.3 Optical influences

Little difference has been found in the higher order aberrations in myopes and emmetropes (Cheng *et al.*, 2004; Hartwig and Atchison, 2012). The current study found a significant negative correlation between vertical coma (Z_3^{-1}) and spherical equivalent refraction. Studies have induced aberrations to investigate the effects on DOF (Rocha *et al.*, 2009; Benard, Lopez-Gil and Legras, 2011) and accommodation responses (Theagarayan *et al.*, 2009). However, Artal *et al.* (2004) and Chen *et al.* (2007) suggested that neural adaptation occurs to familiar aberrations so induced unfamiliar aberrations would have more impact on the apparent blur of the target. The levels of natural and familiar aberrations found in the current study would suggest that aberrations in the natural accommodating eye are unlikely to be large enough to enhance DOF. This also supports the conclusion in section 8.2.2 that optical treatment strategies aimed at correcting aberrations in order to improve accommodation responses are unlikely to be successful.

8.3 Study limitations

Although this research answered all objectives there were some limitations to the study.

The mixed designs of the experiments with multiple between subjects variables, meant that Repeated measures ANOVA was used. Strict criteria of this test meant that any missing data affected the power of the final result. The difficulty in using the PRII, requiring full subject attention and certain pupil sizes meant complete data sets were almost impossible. This limited the conclusions that could be made although trends were still found. As no non parametric statistical test was available offering an alternative to the Repeated measures ANOVA, this had to be used to support non parametric statistics where data did not conform to normality.

The population of subjects were not separated into late onset and early onset myopes as this would require a longitudinal study. This meant it was difficult to consider the environmental and genetic component of any refractive error group differences. It was also not known whether the subjects were stable or progressing myopes which also would require further longitudinal studies.

8.4 Recommendations for further research

This study took measurements from individuals in order to examine the differences in accommodation responses and blur sensitivity. Although differences between myopes and emmetropes have been found, conclusions about whether these differences are a cause or consequence of myopia are limited without further longitudinal studies. The investigation of particularly the subjective DOF, objective DOF and microfluctuations over time would be of interest to clarify whether these differences are found prior to myopia development.

Treatment strategies aimed at correcting peripheral hyperopia should assess accommodative lag in conjunction with peripheral refraction to fully assess the peripheral blur experienced. Although it would be difficult to design contact lenses to correct the peripheral hyperopic blur experienced for near, for each subject individually, having knowledge of their accommodative lag and the levels of peripheral refraction corrected may reveal which subjects are most likely to benefit from the treatment.

Where blur adaptation is used to improve blur sensitivity and accommodation, recording only perceptual responses would not be sufficient to draw conclusions about accommodation response changes. Vera-Diaz *et al.* (2004) considered whether blur adaptation improved the accommodation response but measured only static accommodation responses rather than DOF or dynamic accommodation. As no differences were found in static accommodative lag between myopes and emmetropes, further study examining blur adaptation effects on dynamic accommodation responses and DOF would be of significance. As myopes have larger objective DOF when viewing the peak text spatial frequencies, future research could investigate whether adaptation to these particular text targets could close the gap between accommodation response differences in myopes and emmetropes.

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Appendix A

Participant Information Leaflet

Title of the project: The optical, neural and perceptual basis of blur sensitivity differences in myopes and emmetropes

Main investigator and contact details: Mrs Heather Shorrock
Rackham Room 202
Anglia Ruskin University,
East Road, Cambridge, CB1 1PT
Heather.shorrock@anglia.ac.uk
0845 196 2106 (ext.2106)

Members of the research team: Dr Sheila Rae, Professor Shahina Pardhan, Dr Ian van der Linde

Thank you for volunteering to participate in this study.

We are studying how different factors such as the size and shape of your eyes relate to your ability to notice when objects become blurred. This helps us to understand why people become myopic (short-sighted) and will help us to finds ways to prevent myopia developing in the future.

The research is being done by the Vision and Eye Research Unit at the Department of Optometry and Ophthalmic Dispensing at Anglia Ruskin University and is funded by Anglia Ruskin University.

We have invited you to take part as we need to compare people with normal sight to those who are already myopic.

We will take measurements of the size, shape and focusing of your eyes.

We will take a series of measurements of the size and shape of your eyes and your ability to focus your eyes which will involve you looking at a series of fixation targets whilst we measure your eyes. .

We will then assess how sensitive your eyes are to blurred objects. In order to carry out these measurements an eye drop (Cyclopentolate) will be used to relax the accommodation of the eyes. This drop has been used routinely in eye examinations, especially for examining children. The eye drop will dilate your pupil and will make your near vision blurry for the remainder of the day and you may be more sensitive to bright lights. A slight blurring of your distance vision may also be noticed, especially in bright light and we would recommend that you do not drive, ride a bicycle or operate heavy machinery for the remainder of the day. The eye drop will take around 30 minutes to work and up to 24 hours to fully wear off.

There is also a very small risk of a side effect to the drops which is a condition called *closed angle glaucoma*. The signs and symptoms of this are a painful red eye and seeing haloes around lights. The initial part of the examination will include tests to highlight those people who may be at risk of this condition, in which case we would not use the eye drops or include you in the study. If, however, you do experience the above signs and symptoms then contact us immediately or attend a hospital accident and emergency department.

Any information obtained during this study and identified with you will remain confidential and will be disclosed only with your permission. If the results of the study are published you will not be identified by name.

Your decision to take part will not affect your current or future relationship with Anglia Ruskin University. You may withdraw from the study, without explanation, at any time.

If you have any further queries you can contact Heather Shorrock, Department of Optometry and Ophthalmic Dispensing, Room Rackham 202 at Anglia Ruskin University in Cambridge, by e-mail to heather.shorrock@anglia.ac.uk or on 0845 196 2106.

Appendix B

Anglia Ruskin University
Cambridge & Chelmsford

NAME OF PARTICIPANT:

Title of the project: The Optical, neural and perceptual basis of blur sensitivity and interpretation differences in myopes and emmetropes.

Main investigator and contact details: Mrs Heather Shorrock
Rackham Room 202
Anglia Ruskin University,
East Road, Cambridge, CB1 1PT
Heather.shorrock@anglia.ac.uk
0845 196 2106

Members of the research team: Dr Sheila Rae, Professor Shahina Pardhan, Dr Ian van der Linde

1. I agree to take part in the above research. I have read the Participant Information Sheet which is attached to this form. I understand what my role will be in this research, and all my questions have been answered to my satisfaction.

2. I understand that I am free to withdraw from the research at any time, for any reason and without prejudice.

3. I have been informed that the confidentiality of the information I provide will be safeguarded.

4. I am free to ask any questions at any time before and during the study.

5. I have been provided with a copy of this form and the Participant Information Sheet.

Data Protection: I agree to the University[1] processing personal data which I have supplied. I agree to the processing of such data for any purposes connected with the Research Project as outlined to me

Name of participant (print)……………………….Signed………………..….Date………………

Name of witness (print)…………………………..Signed………………..….Date………………

YOU WILL BE GIVEN A COPY OF THIS FORM TO KEEP

If you wish to withdraw from the research, please complete the form below and return to the main investigator named above.

Title of Project:

I WISH TO WITHDRAW FROM THIS STUDY

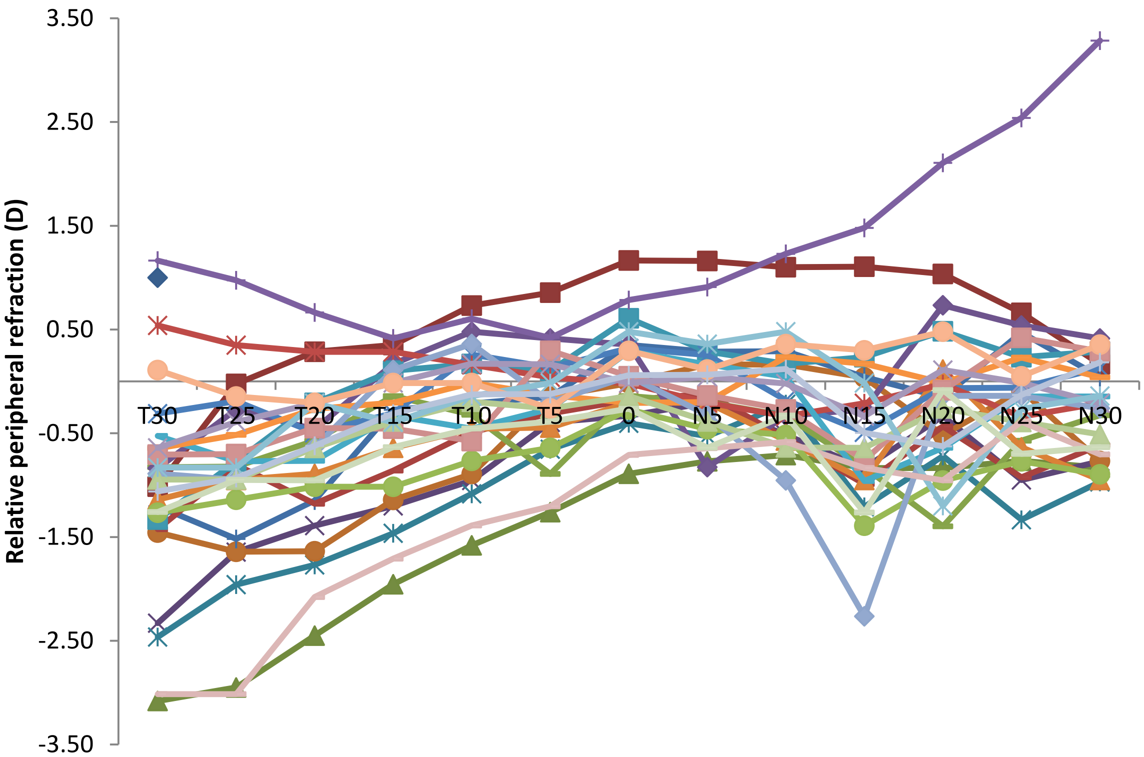
Signed: ___________________________________ Date: ______________________

[1] "The University" includes Anglia Ruskin University and its partner colleges

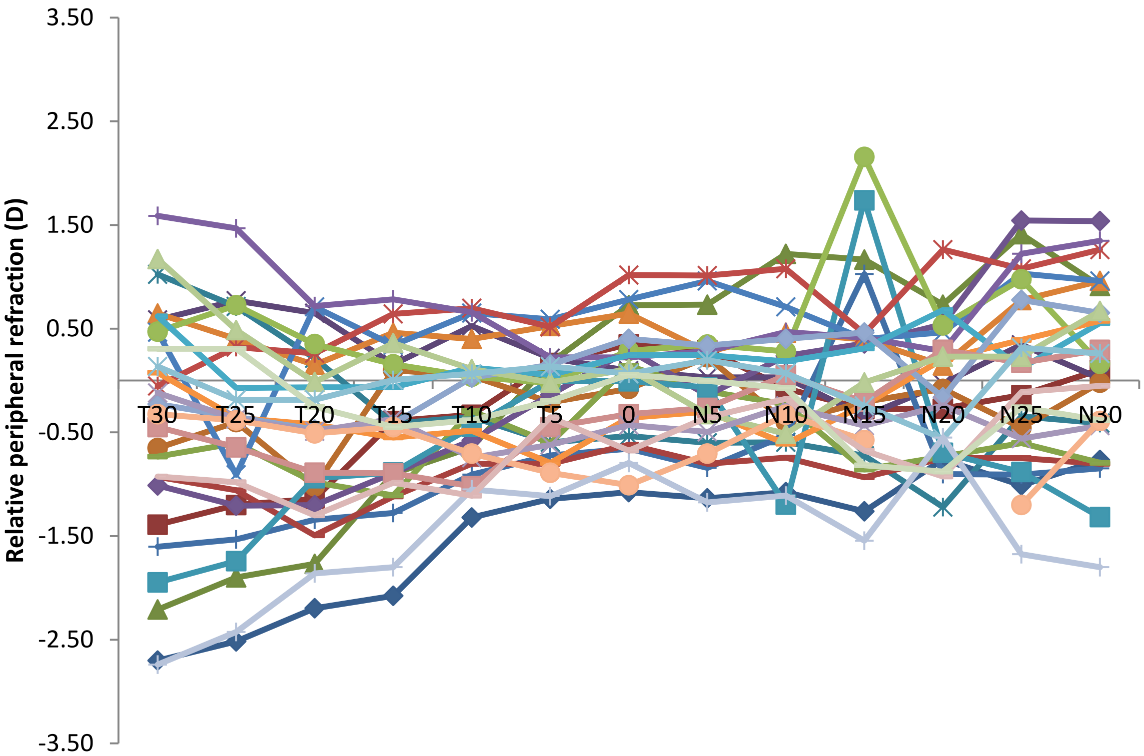
Appendix C

Relative peripheral refraction individual data

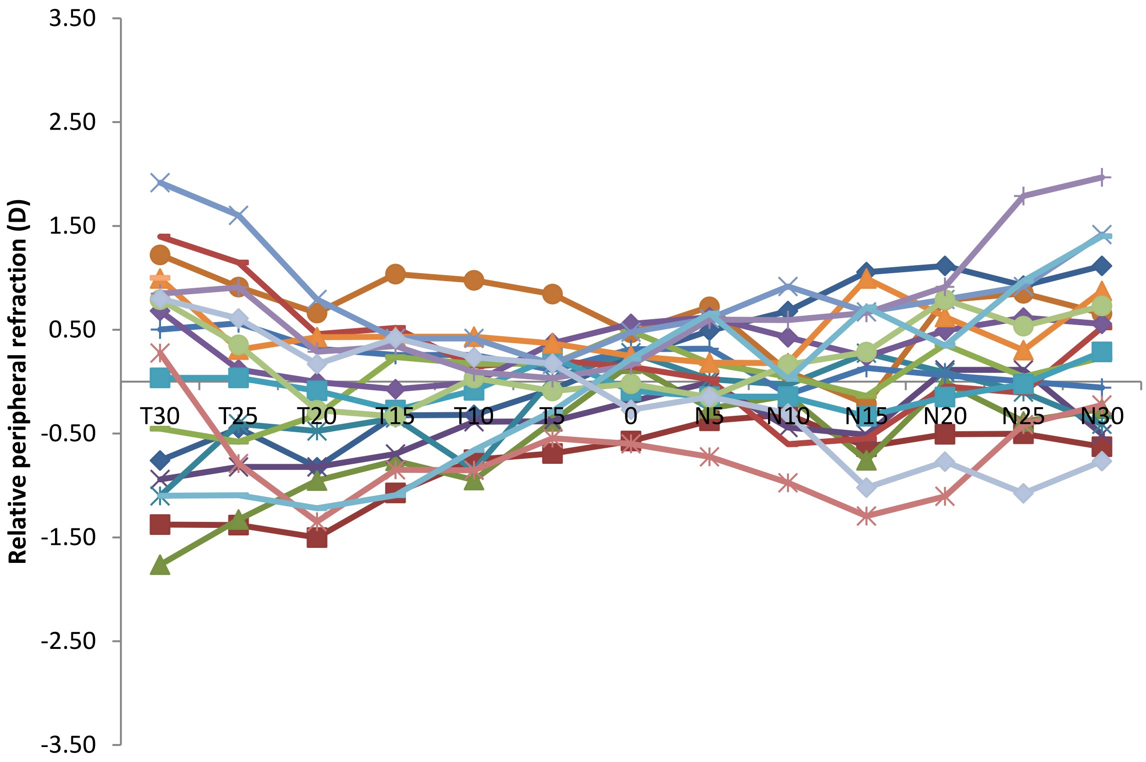
Emmetropes:



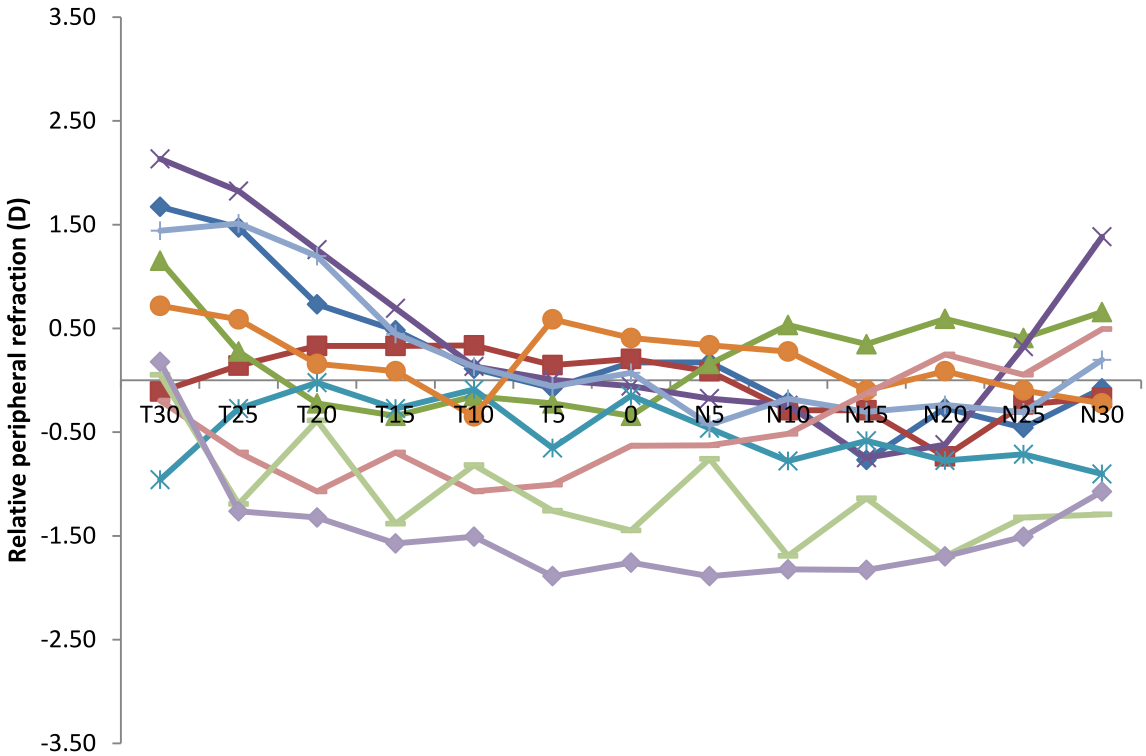
Low myopes:



Moderate myopes:

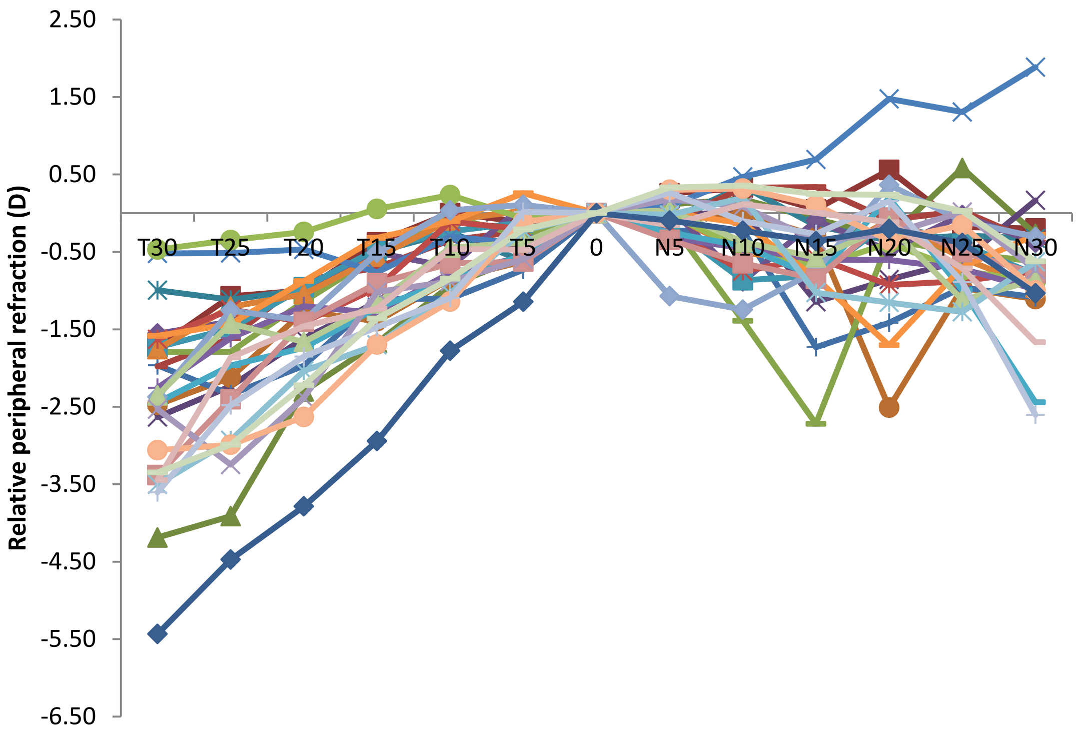


High myopes:

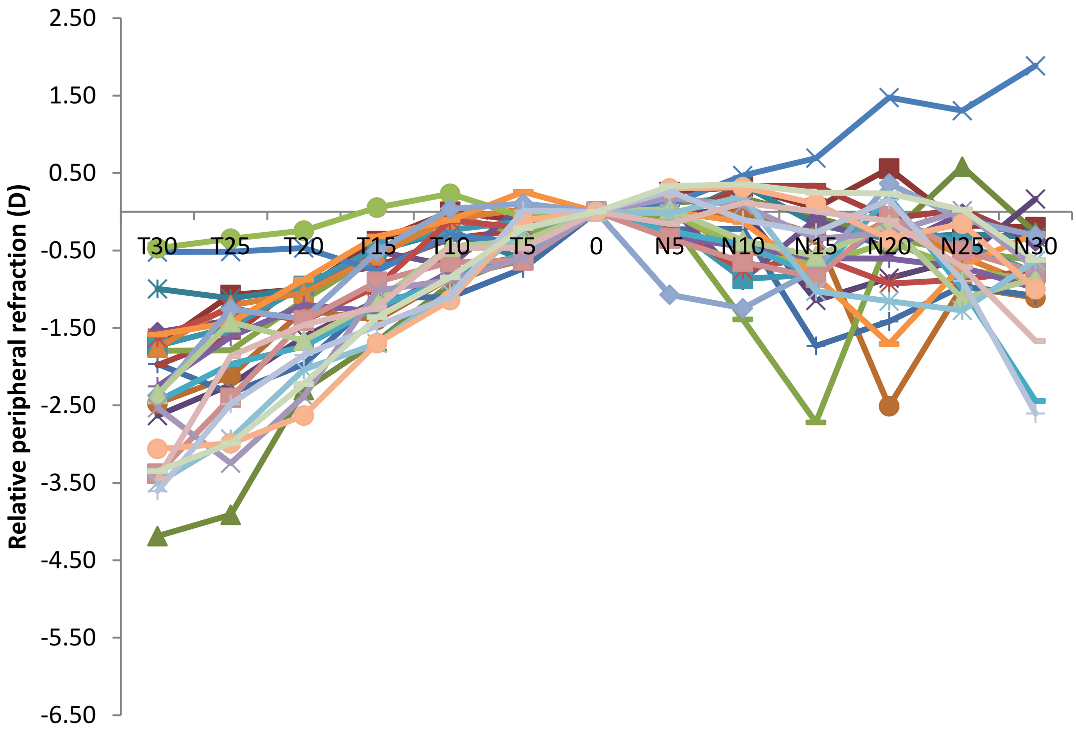


Individual data for tangential astigmatism normalised around centre

Emmetropes:



Low myopes:



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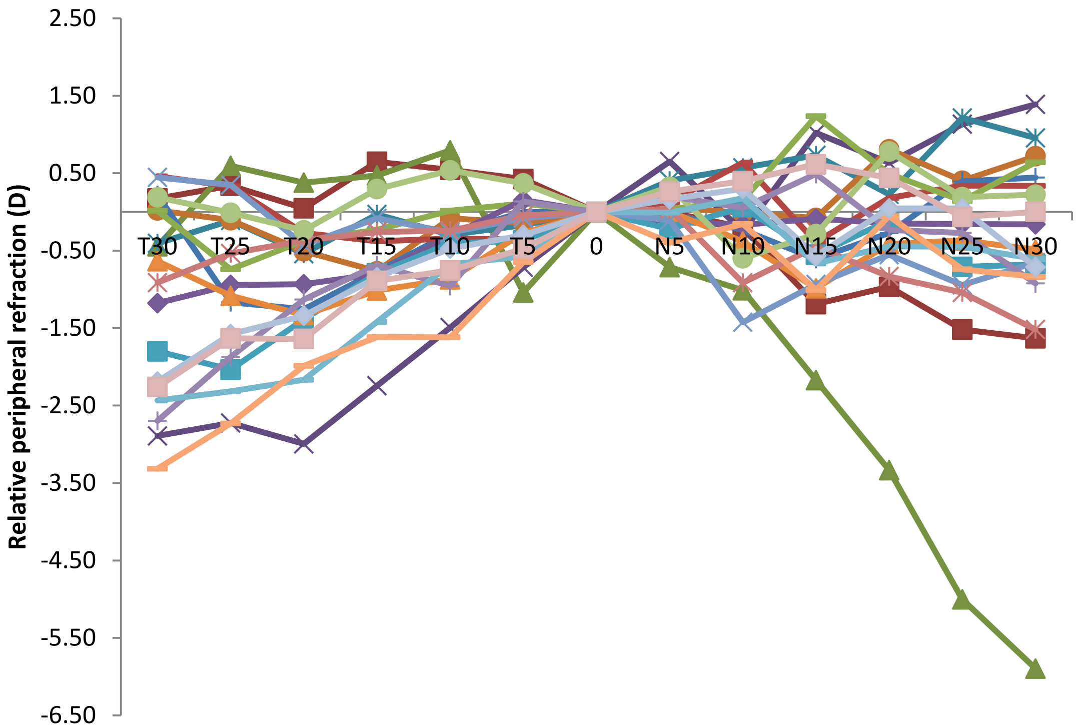
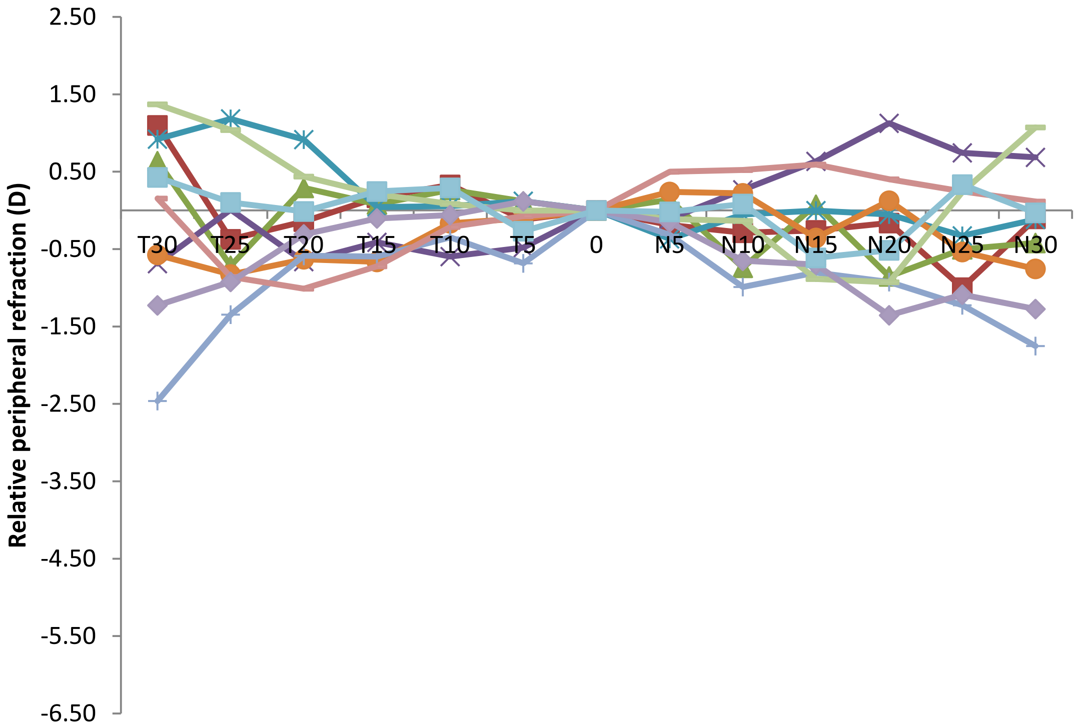
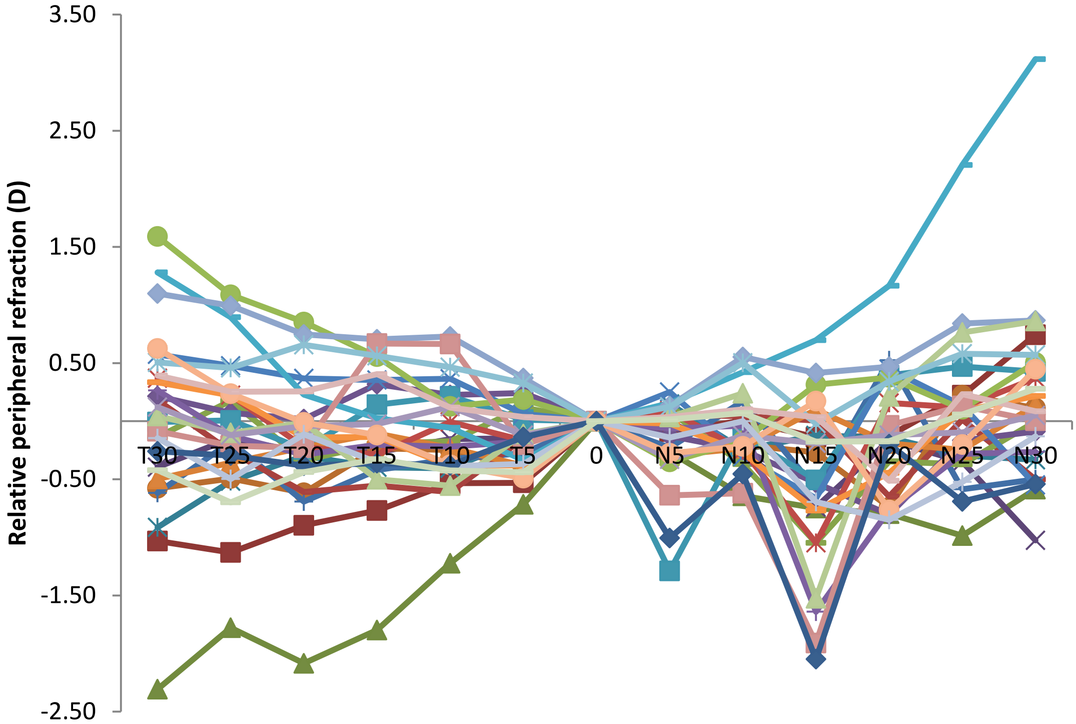


High myopes:

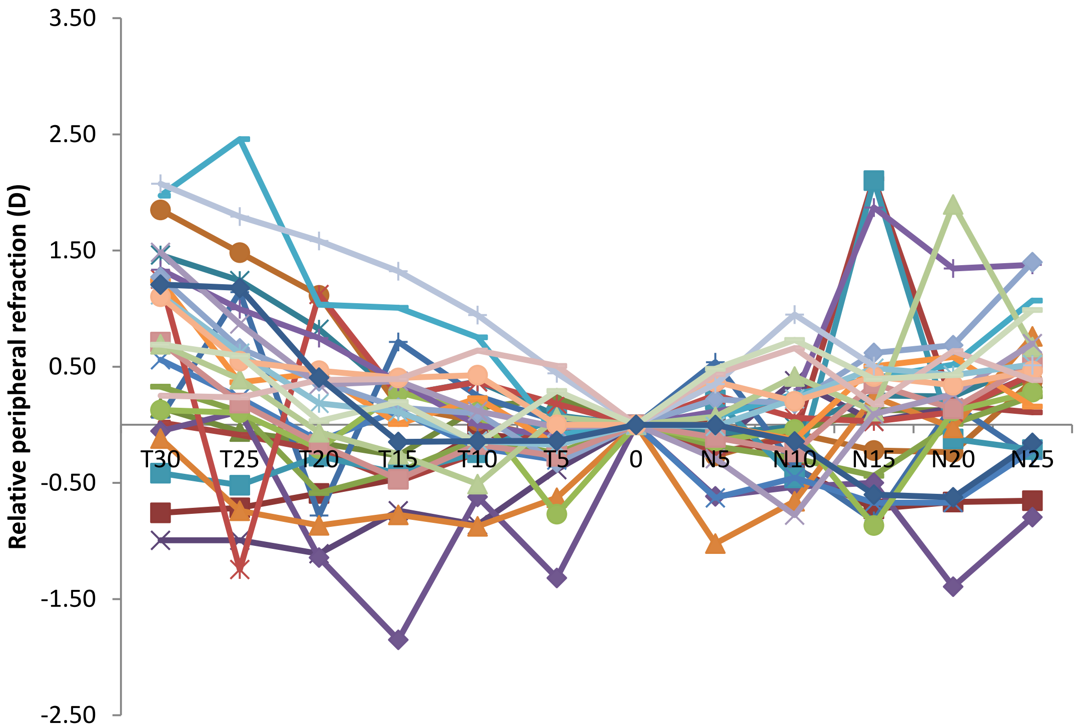


Individual data for sagittal astigmatism normalised around centre

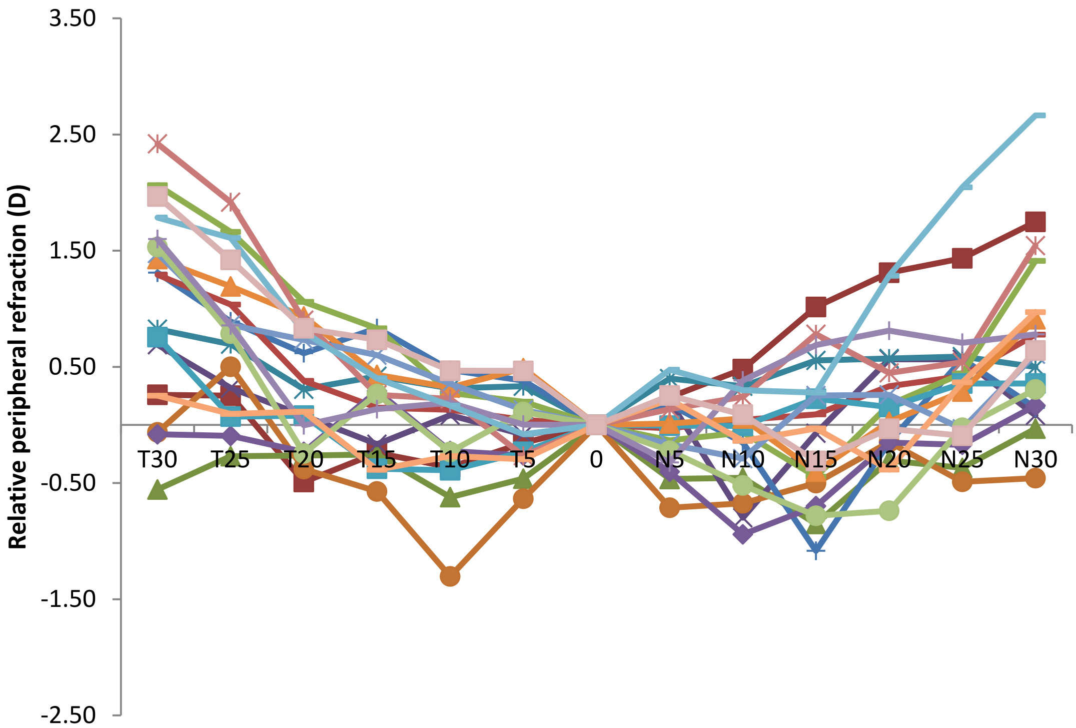
Emmetropes:



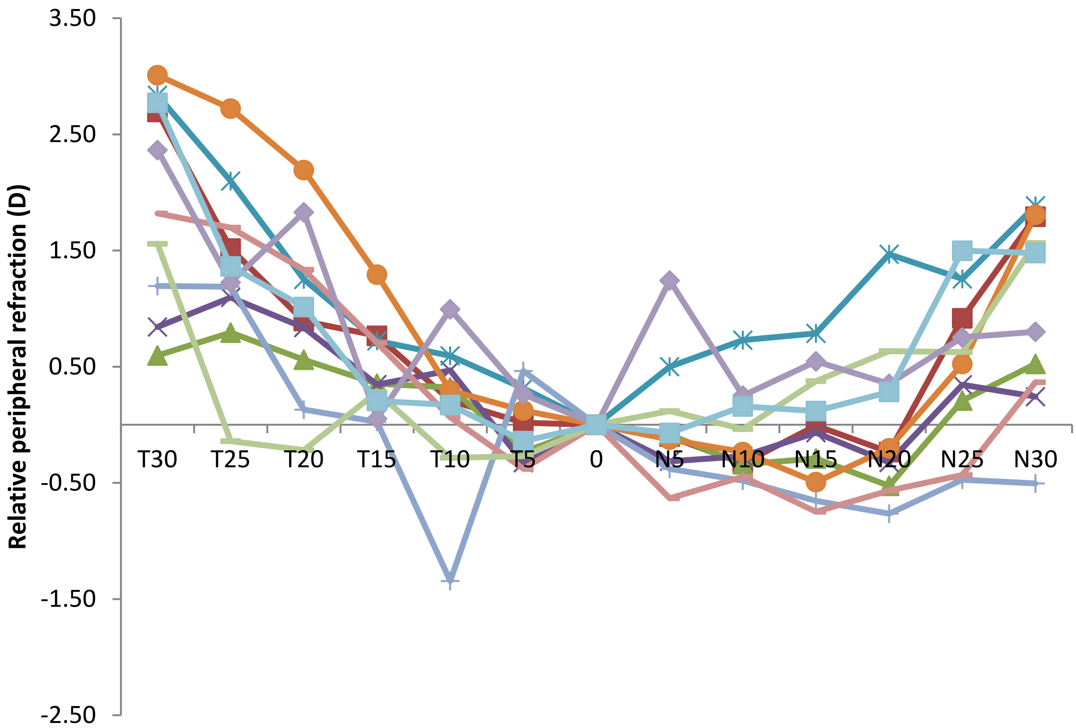
Low myopes



Moderate myopes



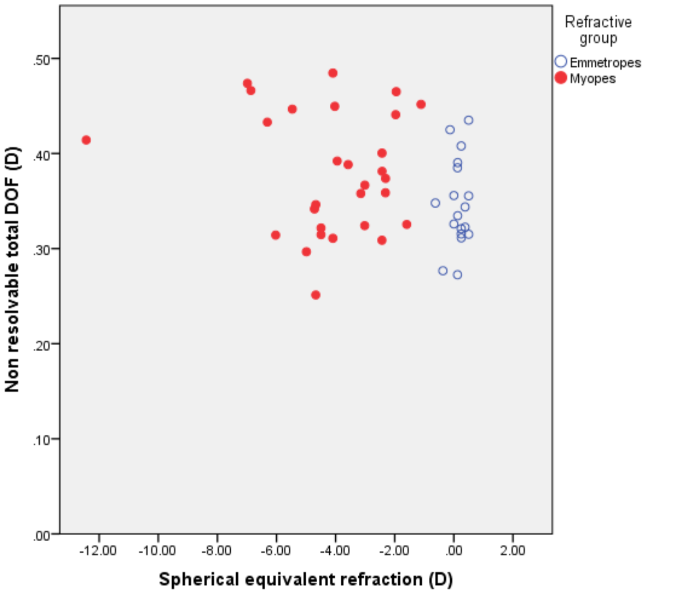
High myopes:



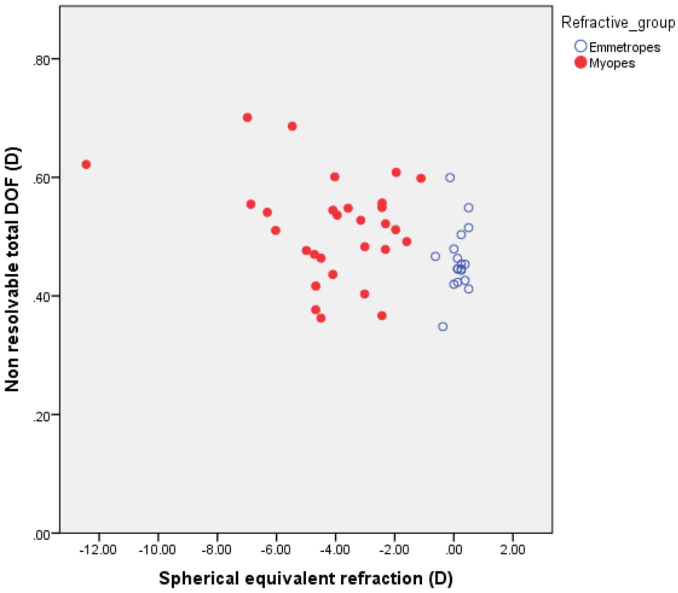
Appendix D

Subjective DOF individual data

Total non resolvable DOF whilst viewing an N10 target



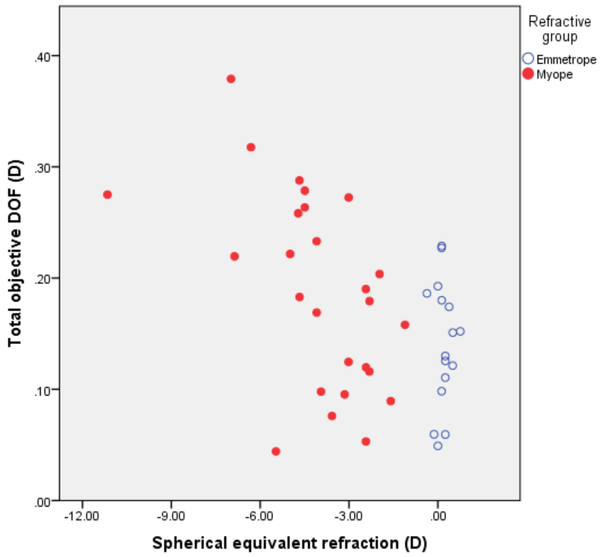
Total non resolvable DOF whilst viewing an N20 target



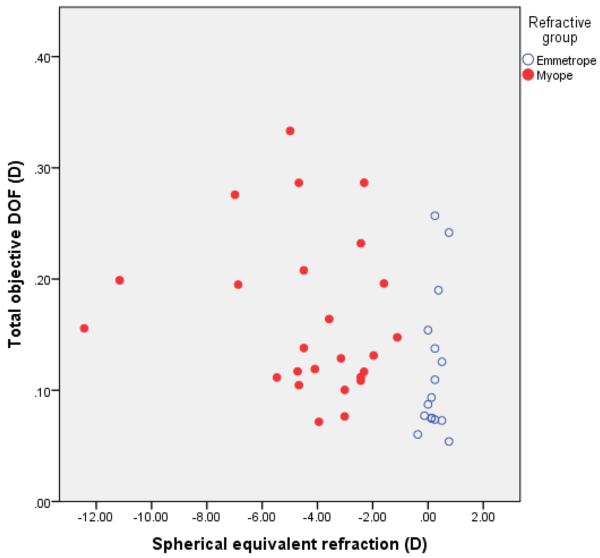
Appendix E

Objective DOF individual data

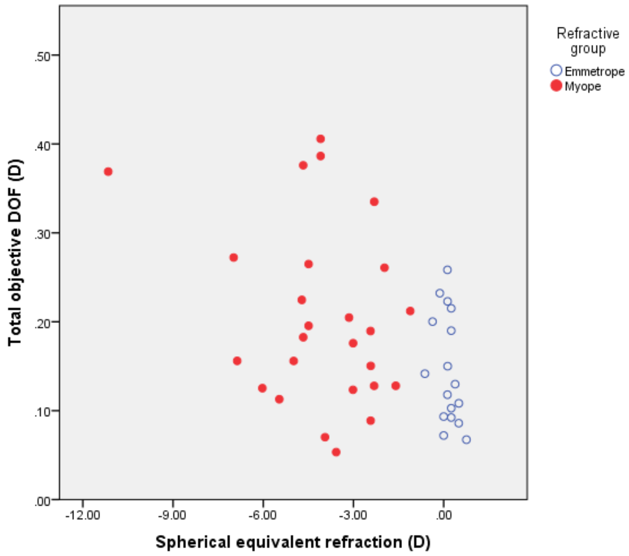
Total objective DOF for N10 unfiltered target
Total objective DOF was significantly larger for myopes than emmetropes when viewing the unfiltered target (Mann-Whitney; U=129.00, z=-2.05, p=0.04)



Total objective DOF for N10 9.31cdeg^{-1} (peak spatial frequency) target
Total objective DOF was significantly larger for myopes than emmetropes when viewing the filtered target 9.31cdeg^{-1} (Mann-Whitney; U=109.00, z=-2.43, p=0.02)



Total objective DOF for N20 unfiltered target
Total objective DOF was larger for myopes than emmetropes but not found to be significant when viewing the unfiltered target (Mann-Whitney*; U*=293.00, *z*=1.91, *p*=0.06)



Total objective DOF for N20 4.65cdeg^{-1} (peak spatial frequency) target
Total objective DOF was significantly larger for myopes than emmetropes when viewing the filtered 4.65cdeg^{-1} target (Mann-Whitney; *U*=110.00, *z*=-2.54, *p*=0.01)