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**STRUCTURAL AND FUNCTIONAL ASPECTS OF
MYOPIA IN YOUNG ADULTS**

**An investigation of nearwork-induced transient myopia
and accommodation in relation to refractive stability**

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**Submitted for the degree
of Doctor of Philosophy**

Bradford School of Optometry and Vision Science

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Structural and Functional Aspects of Myopia in Young

Adults

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Orthokeratology**

SUMMARY

This thesis has investigated nearwork-induced transient myopia and accommodation responses in relation to refractive stability, multichromatic stimuli and orthokeratology. Five individual studies have been carried out. Initially an investigation into the temporal and dioptric aspects of nearwork-induced transient myopia was undertaken, suggesting that increased task duration does not increase the level, or slow the regression of post-task NITM, however an increase in the dioptric demand of the task does. In the second study, a longitudinal myopia progression study, these findings were related to short term myopia progression.

The third investigation demonstrates the feasibility of measuring the biometric correlates of nearwork-induced transient myopia using a low coherence reflectometry device (LenStar, Haag Streit Koeniz, Switzerland).

Fourthly, a comparison of the differences between static and dynamic accommodative responses, microfluctuations and nearwork-induced transient myopia produced when viewing a black/white target as oppose to a red/blue target has suggested the possibility of four accommodative responses to this multichromatic stimulus. Further investigation will be necessary to investigate if any of these response types are related to myopia progression.

The final study investigates the effect of two different designs of orthokeratology contact lenses (C5 and polynomial) on visual function. It appears to be the case that although the polynomial lens design has a larger refractive effect than the C5 lens it reduces both high and low contrast corrected visual acuity to a greater extent. The higher the baseline mean spherical equivalent refractive error the larger the detrimental effect.

CONTENTS

	PAGE
SUMMARY	1
CONTENTS	3
DEDICATION	15
ACKNOWLEDGEMENTS	16
LIST OF TABLES	17
LIST OF FIGURES	19
CHAPTER 1 MYOPIA	25
1.1 INTRODUCTION	25
1.2 PREVALENCE	25
1.3 IMPACT	26
1.4 EMMETROPIZATION	28
1.5 OCULAR COMPONENTS	30
1.6 RISK FACTORS	31
1.6.1 Genetics verses environment	31
1.6.2 Nearwork	33
1.6.1.1 Nearwork and early onset myopia	34
1.6.1.2 Nearwork and late onset myopia	34
1.6.3 Accommodation	35
1.6.4 Accommodative stimulus response function	36
1.6.5 Nearwork-induced transient myopia	37
1.6.6 High AC/A ratio	40
1.6.7 Sports and outdoor activities	40
1.6.8 Aberrations	41
1.6.9 Relative peripheral hypermetropia	43
1.7 MYOPIA CONTROL	44
1.7.1 Under-correction	44

1.7.2	Correction with plus power for near work	45
1.7.3	Pharmaceutical agents	46
1.7.4	Contact lenses	47
1.7.5	Orthokeratology	48
1.7.6	Correction of relative peripheral hypermetropia	49
1.8	CONCLUSION	50
CHAPTER 2	INSTRUMENTATION	52
2.1	MEASUREMENT OF REFRACTIVE ERROR	52
2.1.1	Shin-Nippon SRW-5000 autorefractor	52
2.1.1.1	Validity and repeatability of the Shin-Nippon SRW-5000	53
2.1.2	Shin-Nippon NVision-K autorefractor	55
	Validity and repeatability of the Shin-Nippon NVision-K	56
2.2	MEASUREMENT OF ACCOMMODATION	57
2.2.1	Shin-Nippon SRW-5000 for continuous recording of accommodation	57
2.2.1.1	Calibration of the Shin-Nippon SRW-5000 autorefractor for continuous recording of accommodation	59
2.2.1.2	Accommodation measurement	60
2.2.1.3	Precision of continuous recording	63
2.3	BADAL OPTOMETER	65
2.3.1	Presentation of accommodative stimulus during Shin-Nippon autorefractor measurements	66
2.3.2	Shin-Nippon SRW-5000 autorefractor in the measurement of the accommodative stimulus-response function (ASRF)	66
2.4	MEASUREMENT OF OCULAR PARAMETERS	68
2.4.1	IOLMaster	68
2.4.1.1	Measurement of corneal radius	68

2.4.1.2	Measurement of anterior chamber depth	67
2.4.1.3	Measurement of axial length	67
2.4.1.4	Validity and repeatability of the IOLMaster	69
2.4.2	LenStar	70
2.4.2.1	Validity and repeatability of the LenStar	71
2.5	MEASUREMENT OF MONOCHROMATIC ABERRATIONS	72
2.5.1	Shack-Hartmann aberrometer	72
2.5.1.1	Control panel of the Shack-Hartmann aberrometer	75
2.5.1.2	Presentation of accommodative stimuli within the Shack-Hartmann aberrometer	78
2.5.1.3	Calibration and verification of the Shack- Hartmann aberrometer	79
2.5.1.3.i	Artificial eye calibration	79
2.5.1.3.ii	Real eye calibration	80
2.6	MEASUREMENT OF VISUAL ACUITY	81
2.6.1	Bailey Lovie Chart	81
CHAPTER 3	TEMPORAL FACTORS AND DIOPTRIC DEMAND IN NEARWORK-INDUCED TRANSIENT MYOPIA	84
3.1	INTRODUCTION	84
3.1.1	Measurement of NITM	89
3.1.2	Refractive correction	90
3.1.3	Age of participants	91
3.1.4	Task paradigm	91
3.1.5	Comparison of results between NITM studies	92
3.1.6	Temporal factors and NITM	93
3.1.7	Dioptric value and NITM	94

3.1.8	Symptoms of NITM	95
3.1.9	Aim of the study	96
3.2	METHOD	97
3.2.1	Instrumentation	97
3.2.1.1	Refraction	97
3.2.1.2	Accommodation	97
3.2.1.3	The task	97
3.2.2	Procedure	100
3.2.2.1	Pre-task	100
3.2.2.2	Task	100
3.2.2.3	Post-task	101
3.2.3	Participants	101
3.2.4	Analysis	102
3.3	RESULTS	103
3.3.1	Experiment 1	103
3.3.1.1	Within-task accommodation	103
3.3.1.2	Post-task NITM values	104
3.3.1.3	Post-task group mean NITM values	105
3.3.1.4	Comparison between post-task NITM values of asymptomatic and symptomatic individuals	108
3.3.1.5	Regression	110
3.3.1.6	Post-task regression quotient for the whole cohort	111
3.3.1.7	Comparison between post-task NITM regression quotient for asymptomatic and symptomatic individuals	112
3.3.2	Experiment 2	114
3.3.2.1	Post-task group mean NITM values for the whole cohort	115

3.3.2.2	Comparison between post-task NITM values of asymptomatic and symptomatic individuals	116
3.3.2.3	Post-task regression quotient for the whole cohort	117
3.3.2.4	Comparison between post-task NITM regression quotient for asymptomatic and symptomatic individuals	118
3.4	DISCUSSION	120
3.4.1	Within-task accommodation values	120
3.4.2	Task duration and NITM	121
3.4.3	Dioptric demand and NITM	123
3.4.4	Sympathetic system and NITM	124
3.4.5	Experimental limitations	126
CHAPTER 4	MYOPIA PROGRESSION IN OPTOMETRY STUDENTS, OCULAR CORRELATES AND ASSOCIATION WITH NEARWORK-INDUCED TRANSIENT MYOPIA	127
4.1	INTRODUCTION	127
4.1.1	Prevalence of myopia in the general population	127
4.1.2	Prevalence of refractive errors in student populations	128
4.1.3	Difficulty in comparison of refractive error studies	129
4.1.3.1	Classification of refractive error	129
4.1.3.2	Measurement of refractive error	129
4.1.3.3	Age range	130
4.1.3.4	Analysis of data	130
4.1.4	Ocular correlates of myopia progression	130
4.1.5	Myopia progression	131
4.1.6	Myopia progression and nearwork-induced transient myopia	133
4.1.7	Aim of the study	134

4.2	METHOD	137
4.3	RESULTS	138
4.3.1	Participants	138
4.3.2	Analysis of initial data collection	139
4.3.2.1	Refractive error	139
4.3.2.2	Comparison of refractive error between males and females	140
4.3.2.3	Ocular components	141
4.3.2.4	Correlation of ocular components	142
4.3.2.5	Familial myopia	144
4.3.2.6	Nearwork and sport	145
4.3.2.7	Ethnic origin	146
4.3.3	Two year follow up data analysis	146
4.3.3.1	Refractive error	146
4.3.3.2	Myopia progression	147
4.3.3.2.i	Progression in all participants	147
4.3.3.2.ii	Myopia progression in refractive groups	148
4.3.3.2.iii	Myopia progression and association with AL/CR	149
4.3.3.2.iv	Myopia progression with nearwork and sporting activities	150
4.3.3.2.v	Myopia progression and ethnic origin	151
4.3.3.2.vi	Myopia progression and spectacle wear for nearwork	151
4.3.3.2.vii	Subjectively reported nearwork-induced transient myopia and myopia progression	151
4.3.3.2.viii	Myopia progression and objective measurement of NITM	154
4.4	DISCUSSION	156
4.4.1	Myopia prevalence in a student population	157
4.4.2	Ocular biometric correlates of myopia	158

4.4.3	Familial myopia	159
4.4.4	Myopia, nearwork and sporting activities	159
4.4.5	Ethnic origin and myopia	159
4.4.6	Myopia progression in a student population	160
4.4.7	Myopia progression and subjectively reported nearwork-induced transient myopia	161
4.4.8	Myopia progression and objective measurements of nearwork-induced transient myopia	162
4.4.9	Experimental limitations	162
CHAPTER 5	A BIOMETRIC INVESTIGATION OF NEARWORK-INDUCED TRANSIENT MYOPIA	164
5.1	INTRODUCTION	164
5.1.1	Accommodation	164
5.1.2	Biometric assessment of the accommodating eye	164
5.1.2.1	A-scan ultrasonography	165
5.1.2.2	Partial coherence interferometry	165
5.1.2.3	Scheimpflug technique	166
5.1.2.4	Magnetic resonance imaging	166
5.1.2.5	Optical coherence tomography	167
5.1.3	Change in axial length with accommodation	167
5.1.4	Change in anterior chamber depth with accommodation	168
5.1.5	Change in lens thickness with accommodation	168
5.1.6	Change in the position of the lens with accommodation	169
5.1.7	Structural changes of the eye during accommodation and the relation to myopia	169

5.1.8	Changes in ocular structure associated with nearwork-induced transient myopia	171
5.1.9	Aim of the study	171
5.2	INSTRUMENTATION	172
5.2.1	Measurement of refractive error	172
5.2.2	Ocular biometry	172
5.2.2.1	LenStar	172
5.2.2.2	IOLMaster	172
5.2.3	The task	172
5.2.4	The procedure	175
5.2.5	NITM measurements	176
5.2.6	Participants	177
5.3	RESULTS	177
5.3.1	Comparison between IOLMaster and LenStar	177
5.3.2	Comparison of biometry measurements with and without the accommodation stimulus system in place	179
5.3.3	Comparison of AL, ACD and LT for 0 D accommodation and 5 D accommodation	180
5.3.4	Average time to take measurements	184
5.3.5	Dynamic results	186
5.3.6	Lens thickness and associated NITM	188
5.4	DISCUSSION	189
5.4.1	Experimental limitations	191
CHAPTER 6	THE EFFECT OF A MULTICHROMATIC STIMULUS ON THE ACCOMMODATIVE RESPONSE OF THE EYE	193
6.1	INTRODUCTION	193

6.1.1	Longitudinal chromatic aberration of the eye	193
6.1.2	Longitudinal chromatic aberration and emmetropization	194
6.1.3	Accommodative response to monochromatic targets	195
6.1.4	Accommodative response to multichromatic targets	195
6.1.5	Subjective symptoms associated with viewing coloured targets	196
6.1.6	Accommodative microfluctuations	197
6.1.6.1	The properties of accommodative microfluctuations	197
6.1.6.2	Significance of accommodative microfluctuations	198
6.1.6.3	The effect of accommodation on microfluctuations	200
6.1.6.4	The effect of colour on microfluctuations	200
6.1.7	Nearwork-induced transient myopia and coloured targets	201
6.1.8	Aim of the study	201
6.2	METHOD	202
6.1.6	Instrumentation	202
6.1.6.1	Refraction	202
6.1.6.2	Accommodation	202
6.1.6.3	The target	202
6.1.6.4	The task	205
6.1.7	Experiment 1. Steady state accommodation	206
6.1.8	Experiment 2. Dynamic accommodation	206
6.1.9	Experiment 3. NITM measurements	206
6.1.10	Procedure	208
6.1.11	Participants	209
6.1.12	Analysis	210
6.1.12.1	Accommodative response	210
6.1.12.2	Microfluctuations	211
6.1.12.3	Squarewaves	213

6.1.12.4	Sinewaves	214
6.1.12.5	NITM	115
6.1.12.6	Statistics	216
6.2	RESULTS	216
6.2.1	Accommodative response	216
6.2.2	Microfluctuations	218
6.2.3	Squarewaves	220
6.2.4	Sinewaves	225
6.2.5	NITM	227
6.3	DISCUSSION	229
6.3.1	Accommodative response	229
6.3.2	Microfluctuations	231
6.3.3	Dynamic accommodation	232
6.3.4	Experimental limitations	233
CHAPTER 7	THE EFFECT OF TWO DIFFERENT DESIGNS OF ORTHOKERATOLOGY LENSES ON VISUAL FUNCTION	235
7.1	INTRODUCTION	235
7.1.1	History of orthokeratology	235
7.1.2	Orthokeratology lens design	236
7.1.3	Myopia reduction	239
7.1.4	Corneal response	240
7.1.5	Contrast sensitivity	242
7.1.6	Aberrations	243
7.1.7	Aim of the study	246
7.2	METHOD	247
7.2.1	Recruitment	247

7.2.2	Initial fitting assessment	247
7.2.2.1	Measurement of vision	247
7.2.2.2	Refraction	248
7.2.2.3	Measurement of high and low contrast VA	248
7.2.2.4	Measurement of heterophoria	248
7.2.2.5	Accommodation measurement	248
7.2.2.6	Aberration measurements	248
7.2.2.7	Accommodative stimulus response function	249
7.2.2.8	Nearwork-induced transient myopia	250
7.2.2.9	Post-lens fitting assessment	251
7.2.2.10	Analysis	251
7.3	RESULTS	252
7.3.1	Participants	252
7.3.2	Baseline data	252
7.3.3	Six month data	253
7.3.4	Aberrations	259
7.3.5	Accommodative stimulus response function	261
7.3.6	Nearwork-induced transient myopia	263
7.4	DISCUSSION	265
7.4.1	The effect of orthok on visual function	265
7.4.2	The effect of two different orthok lens designs on visual function	267
7.4.3	Experimental limitations	2679
CHAPTER 8	CONCLUSIONS AND FUTURE WORK	269
8.1	Conclusions	270
8.2	Future work	264

REFERENCES		274
APPENDICES		305
Appendix 1	Acronyms and abbreviations	305
Appendix 2	Aberrations	308
Appendix 3	Aberrometer calibration and varification	324
Appendix 4	Laser safety	337
Appendix 5	Subject information sheets questionnaires	339
Appendix 6	Individual NITM and regression quotient plots	354
Appendix 7	Static accommodative response graphs	362
SUPPORTING PUBLICATIONS		364

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LIST OF TABLES

	PAGE
3.1 A comparison of recent studies involving NITM.	86
3.2 Average mean spherical equivalent and age of the cohort.	102
3.3 Group mean within-task accommodation responses for Experiment 1.	103
3.4 Calculation of post-task NITM values.	105
3.5 Group mean level of NITM for each task duration.	106
3.6 Group mean within-task accommodation responses for Experiment 2.	114
3.7 Group mean level of NITM for each dioptric stimulus.	115
3.8 Table of p -values to compare the level of NITM to different dioptric stimuli.	116
4.1 Table showing the repeatability of refractive measurement.	132
4.2 Comparison of refractive studies on student populations.	135
4.3 Comparison of myopia progression studies in student populations.	136
4.4 Ocular components of first year optometry students.	142
4.5 Index of familial myopia in each refractive group.	144
4.6 Hours of nearwork, computer work and sporting activity undertaken.	145
4.7 Number of myopes and non-myopes from Asian and Caucasian backgrounds.	146
4.8 Ocular parameters at the initial and year two data points.	147
4.9 Comparison of changes in ocular components over a two year period.	149
4.10 Comparison of changes in refractive components over a two year period.	149
4.11 Number and percentage of participants not aware and aware of NITM.	152
4.12 Comparison between ocular parameters in the non-NITM and NITM groups.	152
4.13 Change in ocular parameters for the non-NITM and NITM groups over two years.	153
4.14 Change in ocular parameters in association with wearing glasses for nearwork.	153

5.1	Group mean AL and ACD measurements for the IOLMaster and the LenStar.	177
5.2	Group mean values for the AL, ACD and LT with and without th80 beamsplitter.	180
5.3	Measurements of AL, ACD and LT for both the 0 D and 5 D stimuli.	181
5.4	Group mean LenStar values for AL, ACD and LT for both the 0 D and 5 D stimuli.	181
6.1	Distance and near targets presented during NITM experiments.	207
6.2	Group mean normalised accommodative responses for the whole cohort.	217
6.3	Results of Friedman's ANOVA.	220
6.4	Results of Wilcoxon signed-rank tests.	220
6.5	Group mean reaction and response times.	221
6.6	Difference between individual accommodative responses for peaks and troughs of the squarewave stimuli.	222
6.7	Group mean peak and trough responses for the squarewave stimuli.	224
6.8	Group mean gain and phase lag for the sinewave stimuli.	225
6.9	Difference between individual accommodative responses for the peaks and troughs of the sinewave stimuli.	226
6.10	Group mean peak and trough responses for the sinewave stimuli.	227
7.1	Studies investigating change in aberrations after orthok.	245
7.2	Reasons for participant discontinuation.	253
7.3	Baseline parameters for the whole cohort.	253
7.4	Individual baseline and six month visions.	254
7.5	Individual baseline and six month MSE refractive error.	255
7.6	Individual baseline and six month high contrast visual acuities.	255
7.7	Individual baseline and six month low contrast visual acuities.	256
7.8	Individual baseline and six month amplitudes of accommodation.	257

7.9	Individual baseline and six month distance and near phoria measurements.	257
7.10	Average spherical aberration pre and post-orthok lens fitting.	259
7.11	Average W_{RMS} aberration pre and post-orthok lens fitting.	260
A2.1	Zernicke polynomials up to the fourth-order	312
A3.1	Mean induced cylinder power and axis orientation	330

LIST OF FIGURES

	PAGE	
1.1	Diagram illustrating myopia prevalence.	27
1.2	Example of an accommodative stimulus response function.	36
2.1	External view of the Shin-Nippon SRW-5000.	53
2.2	High contrast measurement ring.	58
2.3	Binary ring image.	59
2.4	Control panel for continuous recording of accommodation.	62
2.5	Raw accommodation data.	63
2.6	Filtered accommodation data.	63
2.7	Graphs to show precision of continuous recording system.	65
2.8	Design of Badal system.	66
2.9	Example of an accommodative stimulus response function.	68
2.10	Principle of partial coherence interferometry.	71
2.11	Diagram of a custom built Shack-Hartmann aberrometer.	76
2.12	Comparison of the homogeneity of the Shack-Hartmann spots.	77
2.13	Control panel for Shack-Hartmann aberrometer.	78
2.14	Comparison of the visibility of the Shack-Hartmann spots.	79
2.15	Search blocks centred on the Shack-Hartmann spots.	80
3.1	Experimental design used to investigate NITM.	98

3.2	Diagram to illustrate the use of the mirror in the experimental design.	99
3.3	Group mean level of NITM per second for each task duration.	106
3.4	Group mean level of NITM for each task duration.	106
3.5	Mean level of NITM per second for non-NITM and NITM groups for each task duration.	108
3.6	Mean level of NITM for non-NITM and NITM groups for each task duration.	109
3.7	Graph illustrating calculation of regression quotient.	110
3.8	Group mean regression quotient for each task duration.	111
3.9	Mean regression quotient for non-NITM and NITM groups for each task duration.	113
3.10	Group mean level of NITM for each dioptric demand.	115
3.11	Mean level of NITM for non-NITM and NITM groups for each dioptric demand.	117
3.12	Group mean regression quotient for each dioptric demand.	118
3.13	Mean regression quotient for non-NITM and NITM groups for each dioptric demand.	119
4.1	Initial data showing spread of MSE refractive error in optometry students.	140
4.2	Spread of MSE in male and female optometry students.	141
4.3	Axial length vs. MSE.	142
4.4	AL/CR vs. MSE.	143
4.5	Anterior chamber depth vs. MSE.	143
4.6	Mean corneal radius vs. MSE.	143
4.7	Change in axial length vs. change in MSE.	148
4.8	Change in mean corneal radius vs. change in MSE.	148
4.9	AL/CR vs. change in MSE.	150
4.10	AL/CR vs. change in axial length.	150
4.11	Objective level of NITM vs. change in MSE.	155

4.12	Regression quotient vs. change in MSE.	155
4.13	Objective level of NITM vs. change in axial length.	156
4.14	Regression quotient vs. change in axial length.	156
5.1	Photograph of experimental design to investigate structural changes during disaccommodation.	174
5.2	Diagram showing the system used to stimulate accommodation.	175
5.3	Bland Altman plot to show the difference in AL measurement vs. the average AL.	178
5.4	Bland Altman plot to show the difference in ACD measurement vs. the average ACD.	179
5.5	Correlation between AL and change in AL, ACD and LT with 5 D of accommodation.	183
5.6	Correlation between MSE and change in AL, ACD and LT with 5 D of accommodation.	184
5.7	Graph illustrating measurement time.	185
5.8	LT change vs. time for participant EM.	186
5.9	Individual plots of change in ACD and LT vs. time.	187
5.10	LT vs time during the period 60s post-task for participant EM.	189
5.11	Accommodation vs. time during the period 60s post-task for participant EM.	189
6.1	Chromatic aberration of the eye.	194
6.2	Graph to illustrate a power spectrum.	197
6.3	Targets used during accommodation and colour experiment.	203
6.4	Graphs to illustrate the average wavelengths reflected from the targets.	204
6.5	Photograph illustrating experimental design.	205
6.6	Diagram showing experimental design.	207
6.7	Circuit diagram to show control of target movement in NITM experiment.	208

6.8	Examples of data before and after filtering for blinks.	211
6.9	Illustration of reaction and response times for squarewave data.	214
6.10	Illustration of phase lag and gain for sinewave data.	215
6.11	Graphs to illustrate the four groups of static accommodative response.	217
6.12	Graph to illustrate group mean static accommodative response data.	218
6.13	Graphs illustrating microfluctuation data.	219
6.14	Graph illustrating accommodation trace from subject MB.	220
6.15	Graphs illustrating peaks and troughs of squarewave data.	221
6.16	Graphs illustrating the difference in squarewave response to a 0 – 3 D stimulus for B/W and R/B targets.	223
6.17	Graphs illustrating the difference in squarewave response to a 2 - 4 D stimulus for B/W and R/B targets.	224
6.18	Graphs illustrating peaks and troughs of sinewave data.	226
6.19	Graph to show group mean levels of NITM.	227
6.20	Graph to show group mean regression quotient of NITM.	228
6.21	Effects of chromatic aberration with the eye focused for different wavelengths.	231
7.1	Post-orthok high contrast uncorrected VAR score vs. baseline MSE.	258
7.2	Post-orthok high contrast corrected VAR score vs. baseline MSE.	258
7.3	Post-orthok low contrast corrected VAR score vs. baseline MSE.	258
7.4	Change in W_{RMS} and spherical aberration (Z12) vs. baseline MSE.	261
7.5	Graphs illustrating ASRF for each participant pre and post-orthok lens fitting.	262
7.6	Graph illustrating group mean ASRF before and after the orthok procedure.	263
7.7	Group mean level of NITM pre and post-orthok.	264
7.8	Group mean regression quotient pre and post-orthok.	264

A2.1	A perfect optical system.	308
A2.2	An aberrated optical system.	308
A2.3	Wavefront aberrations.	309
A2.4	Representation of $((\rho, \theta)$ in the pupil plane.	310
A2.5	Zernicke pyramid.	312
A2.6	Shack-Hartmann sensor.	318
A3.1	Measured spherical error vs. actual lens power.	327
A3.2	Bland Altman plot comparing power of trial lenses to measured spherical error.	327
A3.3	Spherical aberration vs. actual lens power.	328
A3.4	W_{RMS} vs. actual lens power.	329
A3.5	Corrected MSE, J_0 and J_{45} vs. actual MSE.	331
A3.6	Effect of changing lens power on measured spherical aberration.	332
A3.7	Effect of changing lens power on measured W_{RMS} .	332
A3.8	Spherical aberration Vs. participant number.	333
A3.9	Bland Altman plot comparing spherical aberration for data 1 and data 2.	333
A3.10	W_{RMS} vs. participant number.	334
A3.11	Bland Altman plot comparing W_{RMS} for data 1 and data 2.	334
A6.1	Individual post-task NITM values for asymptomatic group (Experiment 1).	354
A6.2	Individual post-task NITM values for symptomatic group (Experiment 2).	355
A6.3	Individual post-task regression quotient values for asymptomatic group (Experiment 1).	356
A6.4	Individual post-task regression quotient values for symptomatic group (Experiment 1).	357
A6.5	Individual post-task NITM values for asymptomatic group (Experiment 2).	358
A6.6	Individual post-task NITM values for symptomatic group (Experiment 2).	359
A6.7	Individual post-task regression quotient values for asymptomatic group (Experiment 2).	360

A6.8	Individual post-task regression quotient values for symptomatic group (Experiment 2).	361
A7.1	Individual normalised accommodative responses.	362

Chapter 1

Myopia

1.1 Introduction

Myopia is the state where in a relaxed eye, images are focused in front of the photoreceptor plane. Literature suggests that myopia is becoming more prevalent, particularly in certain areas of the world. The reason for this is uncertain and appears to be multifactorial. A vast amount of research has been conducted in this area; however, due to the number of variables involved, no definitive conclusions on myopia development have been reached at present.

1.2 Prevalence

Myopia appears to be becoming more prevalent worldwide [1-4] and affects at least 20% of adults in the United States [5-9], Australia [2, 10], Europe [11-15] and the Middle East [1, 16], and from 20% to over 70% in some Asian countries [17-22] (Figure 1). Urban areas tend to be more affected than rural ones [23].

The onset of myopia is rare before school age and increases in prevalence during the school years and into early adulthood [18, 24-29], however there seems to be a trend towards a greater number of children with early onset myopia, and higher refractive errors [3]. Females generally tend to have a slightly higher prevalence of myopia than males [30, 31] however this has not always been found to be the case [18].

Longitudinal studies show that the prevalence of myopia declines after the age of 40 years until about the age of 70 years [32, 33]. These changes seem to occur regardless of gender, education and refractive status. There are still questions as to whether this hyperopic shift in refractive error with age is due to a true longitudinal change in prescription or whether it is due to a cohort effect [34]. For this reason, when determining the prevalence of myopia we must be careful not to confuse a longitudinal

decrease in myopia after the age of 40 years with an increase in prevalence of myopia in the general population. After the age of 70 years there tends to be a myopic shift, probably due to nuclear sclerosis of the crystalline lens.

1.3 Impact

The increasing prevalence of myopia has a worldwide public health impact. The correction of myopia with spectacles, contact lenses or refractive surgery contributes an economic burden to society [35]. In developing countries, uncorrected refractive error is a significant cause of visual impairment. Myopia in particular is a problem as it starts at a relatively young age unlike other forms of visual impairment such as the more common forms of cataract or age related macular degeneration. Left uncorrected, myopia can cause lifelong visual impairment with a substantial social, educational and economic impact [2, 36].

High myopia in particular, is associated with various ocular pathologies such as cataract, glaucoma, chorioretinal abnormalities and optic disc abnormalities [37]. Better understanding of the reasons behind its development, progression and risk factors would therefore greatly benefit public health.

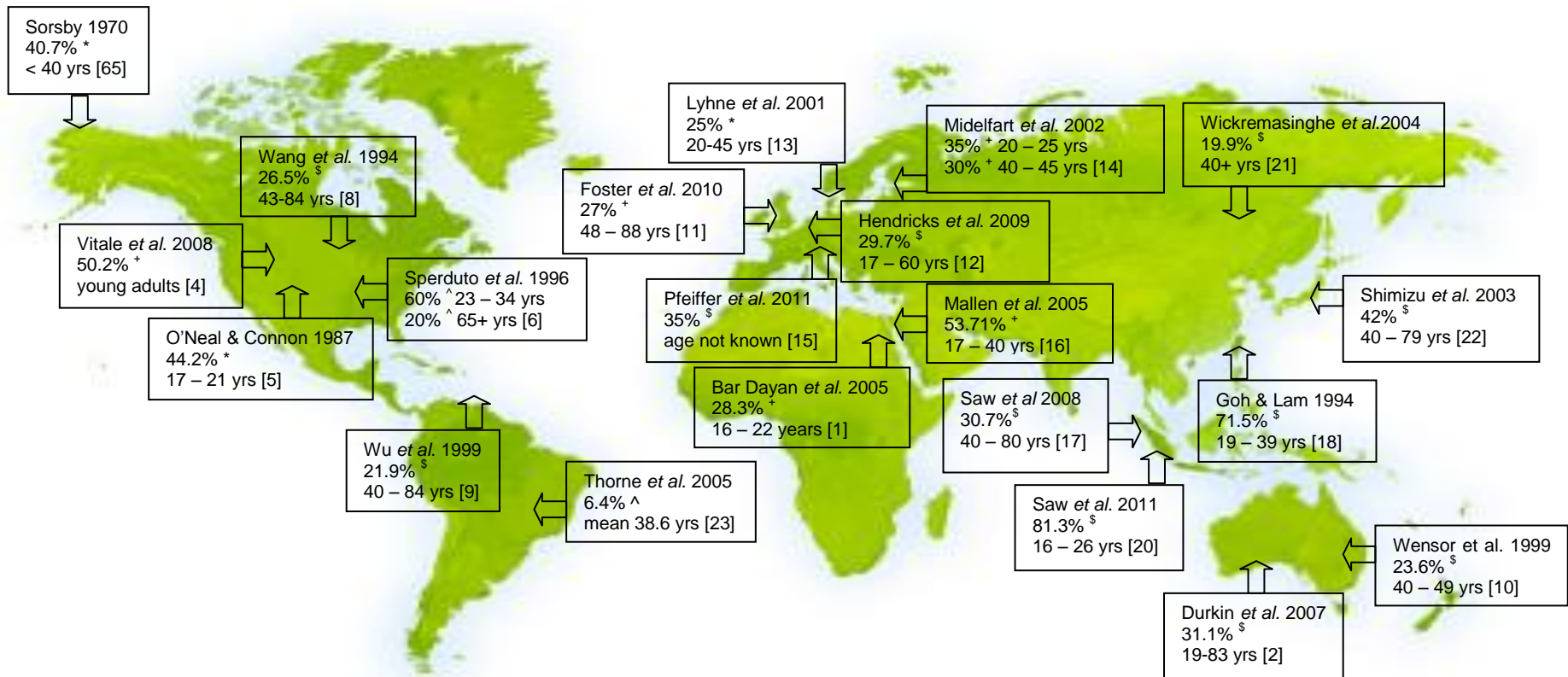


Figure 1.1. Diagram illustrating myopia prevalence in different areas around the world. (* myopia ≤ -0.25 D, + myopia ≤ -0.50 D, § myopia < -0.50 D, ^ myopia ≤ -1 D).

1.4 Emmetropization

It used to be thought that the growth of the human eye from birth to adult size was a passive process; however animal studies have shown that post-natal eye growth and emmetropization are hugely dependent on the visual input received by the eye. Young chicks are often studied as they have rapid eye growth, excellent optics, good central visual acuity and as their eyes function independently; binocular effects are minimized. Form deprivation in chicks has been shown to induce myopia due to axial length elongation [38, 39]. On termination of the treatment, the eyes seem to recover to various extents due to cessation of vitreous chamber growth and corneal flattening. The amount of induced myopia is less in older chicks, and the recovery has been found to be slower and less complete. A similar result has been found in marmosets although the timing seems more critical; the older animals showing a more variable response to form deprivation and less chance of recovery [40].

It has also been demonstrated in chick eyes that hyperopic blur causes a myopic shift in axial length and myopic blur causes a hyperopic shift. In chicks, -10 to +15 D of spectacle blur induced at hatching can be almost completely compensated for within a week [38]. Again this mechanism seems to become less effective as the chick ages. Experiments on guinea pigs show similar results, although the compensation is not so complete [41]. Infant monkeys have also been shown to compensate for, and recover from experimentally induced blur, again to a lesser extent (-3 to +6 DS) [42].

Much less literature is available regarding form deprivation and blur effects in humans. Dense vitreous haemorrhage, neonatal eyelid closure and congenital lens opacity have all been associated with axial myopia [43-45]. However, although visual deprivation seems to affect normal eye growth in humans it does not appear to be as predictable a result as in some animal studies [46].

The control of ocular growth due to visual input appears to be locally regulated within the eye. Form deprivation myopia still occurs when the action potentials of the retinal

ganglion cells have been blocked [47], and experimentally induced refractive errors occur even when the optic nerve has been severed [47, 48]. It also appears that visual input can affect areas of the eye selectively. Lower field myopia has been shown to be present in a variety of birds [49]. Rather than being an error in their visual development it has been suggested this is an active adaptation to their situation. It enables the birds to forage on the ground without having to accommodate, as this would make it difficult for them to see predators. Local retinal sensitivity has also been shown to occur to form deprivation in chick eyes [39] and to blur in monkey eyes [50].

It would be sensible to suggest that the fovea dominates the emmetropization process, as the visual resolution is highest at this point. However this does not seem to be the case. In monkeys who have had foveal ablation, normal ocular development occurs even without foveal input [51]. If the monkeys experience form deprivation, myopia occurs as it would if the fovea was intact. It therefore appears that visual signals from the peripheral retina can be used for axial length regulation.

Emmetropization, therefore, appears to be an active rather than passive process [52]. The axial length of the eye is matched to the optical properties of the cornea and lens so when eye growth stops, the image focuses clearly on the retina. The human eye shows a broad range of refractive errors at birth and moves towards emmetropia, initially quite rapidly, gradually slowing down. At about the age of five to six years there appears to be the smallest standard deviation in refractive errors [53]. It is believed that the eye reaches adult emmetropic size by the age of 13-14 years [54], although it has been suggested that some eyes continue natural growth up until the age of 18 years [55]. Emmetropization is also coordinated between the eyes so generally the prescription of the two eyes in an individual are matched.

Early onset myopia occurs during the period of physical growth, and is thought to occur up until the age of about 14 years [55], although this period could be slightly longer. It may be due to a failure of the emmetropization process in which the axial length of the

eye grows excessively, and is not compensated for by corneal or lenticular power. Alternatively, the emmetropization process may be functioning, but may produce an incorrect response due to an abnormal visual input. The younger a subject is when they become myopic the more myopic it appears they are likely to become [27]. Myopia has also been associated with against-the-rule astigmatism in infancy [53].

Late onset myopia occurs after physical growth has stopped, usually in the late teens and early twenties although it has been shown to occur in the thirties and forties, too [56]. Late onset myopia may be more related to environmental factors. Animal studies show that although the older eye is not as flexible to change as the younger one, visual experience can affect refractive state throughout life [39, 40]. Human studies have shown increases in the amount of myopia in young adults exposed to high educational demand and nearwork intensive occupations [5, 25, 56]. These changes occurred after theoretical emmetropization had taken place, suggesting other factors may be involved in myopia progression.

1.5 Ocular Components

In theory, myopia could be caused by either excessive axial length or excessive refractive power of the cornea or lens. Changes in the level of myopia have been shown to correlate directly to changes in axial length and vitreous chamber depth in both early and late onset myopia [25-27, 56]. There does not appear to be as strong a correlation between the amount of myopia and anterior chamber depth, lens thickness or corneal curvature. In myopes the crystalline lens seems to become slightly thinner as the myopia progresses [57]. This may be a compensatory mechanism to counteract axial length growth.

It has been suggested that emmetropic children with longer eyes are more likely to become myopic [28], however there has been found to be no significant difference in the ocular structures between eyes that remain emmetropic, and those that go on to

develop late onset myopia [56]. Older subjects appear to have shorter axial lengths and vitreous chamber depths than younger subjects, which correlates with the fact that older people have been found to be less myopic [33]. This could be due to a cohort effect whereby the older generation have shorter axial length due to poorer diet, general health or other environmental factors, or it may be a longitudinal change in eye shape with increased age.

In children it has been found that a steep cornea, and axial length/corneal radius (AL/CR) ratio greater than three is associated with future myopic development [58]. The highest values of sensitivity and specificity being in the horizontal corneal meridian. A study on adult myopia development showed slightly different results, with the AL/CR ratio at the beginning of the study being no different for emmetropes who became myopic during the study to those who did not [56]. Those who were already myopic had a higher AL/CR ratio: however there was no statistically significant difference between progressing myopes and those who were stable.

There also appears to be a relationship between astigmatism and myopia progression, with slower progression being observed in those subjects with with-the-rule astigmatism as opposed to those with against-the-rule or none at all [59].

Although the structural cause of early onset and late onset myopia has been shown to be the same, the actual stimulus for their onset may be different.

1.6 Risk factors

1.6.1 Genetics verses environment

Twin studies have shown that up to 86% of spherical equivalent ametropia, be it myopia or hyperopia, may be genetic [13, 60]. Several chromosomal localisations have been reported for high myopia but this only accounts for a very small proportion of subjects. It has been more difficult to find genes linked to low or moderate myopia [3].

Children with a parent who is myopic have more chance of becoming myopic than children with emmetropic or hyperopic parents. If both parents are myopic there is an even greater risk [27]. Having two myopic parents has been found to be one of the best non-ocular predictors of future myopia in eight to nine year olds [61]. There have been various reports on heritability of astigmatism [60, 62, 63]. As yet there does not appear to be any consensus on its cause although studies have suggested it is associated with myopia and does not appear to change significantly over time [25, 64, 65].

Twin studies could underestimate the environmental impact on myopia due to the shared environment. Research on siblings suggests variance in refractive error can be explained largely by familial factors, however it is difficult to determine whether these are environmental or genetic [66]. A child's environment during development is likely to be more similar to their siblings than their parents, however a parent's attitude to work and education will affect the way they bring up their child. There is a strong association between education and myopia both in the length of time spent in education and level achieved [8]. Higher socio-economic status is associated with a higher prevalence of myopia [28].

Lower correlations in myopia have been reported where parents have had a very different developmental environment to their children or there is a large age difference between siblings [3, 67]. A twin study in Denmark determined that although there appeared to be a high heritability for ocular refraction there was evidence of a gene-environment interaction with more myopia being found in those who spent more time in education [13]. This suggests environmental factors may be involved in myopia development. A study which showed a higher prevalence of myopia in Jewish boys (81.3%) attending an orthodox school with a very high and unusual near vision demand suggests an environmental cause for the myopia, as the prevalence at the female orthodox school with a lower near work demand was much less (36.2%) [31]. It could

be expected that if the cause of myopia was mainly genetic the prevalence should have been similar. However it is possible that inherited factors include a susceptibility to adaptive myopia which may explain why some people can be highly educated, do large amounts of near work but not become myopic [13, 60].

1.6.2 Nearwork

Although inherited factors may contribute greatly to the prevalence of spherical equivalent ametropia in the general population, there does appear to have been an increase in myopia prevalence as society has moved towards spending larger amounts of time undertaking close tasks. There has always been the suggestion of an association between myopia and nearwork, and a substantial amount of research has been carried out on this subject, however a direct relationship has been difficult to establish due to all other possible associated factors.

Different generations of genetically related family members show a different prevalence to myopia [67]. In Barrow, Alaska, the schooling system changed in the late 1940s from voluntary, ungraded schooling to compulsory, graded schooling. Sorsby *et al.* found a lower prevalence of myopia in those schooled before these changes (13.8%) than those schooled after (43.4%), with little correlation between parental refractive error and that of their offspring. Conversely, Wu and Edwards [68] found that having myopic parents increased the chance of myopia development in offspring. However, over two generations, the odds of a child with no myopic parents developing myopia increased, suggesting an environmental influence seems to be having more effect.

Populations living in rural environments as opposed to city dwellers in the same country show lower myopia prevalence. In Brazil the indigenous people of the upper Amazon basin who are illiterate have a 2.7% prevalence of myopia whereas in the younger, slightly educated Brazilians who live in the city nearby the prevalence is 11.3% [23].

1.6.2.1 Nearwork and early onset myopia

A study of Singapore school children has shown that the strongest risk factor for high myopia (-3.00 DS or more) in six to nine year olds is the number of books read per week [28]. This was corroborated by a study of children in Finland [69], where the degree and progression of myopia were associated with both the amount of nearwork and reading distance. Temporal variations have been observed in myopia progression in children during the academic year with a greater progression following end of year exams [29] and a slower progression during the summer vacation [70]. This suggests intense periods of nearwork stimulate myopia progression in children.

It is hard to quantify the extent to which nearwork actually influences myopia onset and progression, as ascertaining the amount and type of nearwork a subject has done throughout their life is difficult. Jones *et al.* [61] found no significant relationship between the amount of nearwork undertaken at the age of eight and future myopia development, and Rose *et al.* [71], in a large scale study of six and twelve year olds, found very little association between near or intermediate work carried out and myopia. There also appear to be other variables to consider such as intelligence. Non verbal IQ has been shown to be a totally independent risk factor for myopia [72]. If there was a genetic link between myopia and intelligence, it may be that nearwork has very little effect on myopia progression. It is possible that cerebral and ocular growth are both genetically determined with similar genes determining both eye and neocortical size.

1.6.3.1 Nearwork and late onset myopia

Late onset myopia has also been shown to be associated with nearwork. Eighty percent of workers undertaking quality control in a Norwegian textile factory started wearing a myopic correction six months or more after employment [73] whereas none of the controls working in the same factory at different jobs were myopic. The work undertaken did not need particularly accurate accommodation but the moving textiles

meant the images on the retina were changing constantly. In animal studies blur has been shown to cause recalibration of the axial length of the eye leading to myopia development. The experimental group did, however, have a higher prevalence of familial myopia than the controls which may have skewed the results.

In a study in the UK [74] 71% percent of clinical microscopists were found to be myopic. This is a graduate entry profession but this figure is high compared to that for European student populations [75, 76], suggesting the working environment may stimulate myopia onset and progression. As the population is slightly older (median age 29.7 years) than an undergraduate population a slightly higher myopia prevalence may be expected.

1.6.3 Accommodation

When a presbyopic subject is presented with a near target, or when minus lenses are placed in front of their eyes, accommodation takes place to focus the image clearly on the retina. There are four components to the accommodative response – blur accommodation, proximal accommodation, vergence accommodation and tonic accommodation [77]. Blur-driven accommodation is the automatic change in the refractive state of the eye in response to blur to create a clear image on the retina [78]. It is limited by the depth of focus of the eye as the larger the eyes depth of focus the less accommodative response will be necessary to produce a clear image. Proximal accommodation occurs due to the knowledge that an object is close. This tends to be the case with instrument myopia [79]. Vergence accommodation is due to there being a neural link between the accommodative and vergence systems [80]. Changes in vergence within the ocular system produce corresponding changes in accommodation. Tonic accommodation is the resting state of the eye when there is no visual feedback [81]. In this situation the other three accommodative components are absent. In everyday circumstances these components work in unison.

1.6.4 Accommodative stimulus response function (ASRF)

This is produced by measuring the actual accommodative response of a subject to stimuli of varying dioptric demands. These dioptric stimuli can be produced either by varying the distance of a target in real space, changing the position of a target within a Badal system or presenting a series of negative lenses when fixating a distance target or positive lenses when fixating a near target. A typical curve is shown in Figure 1.2.

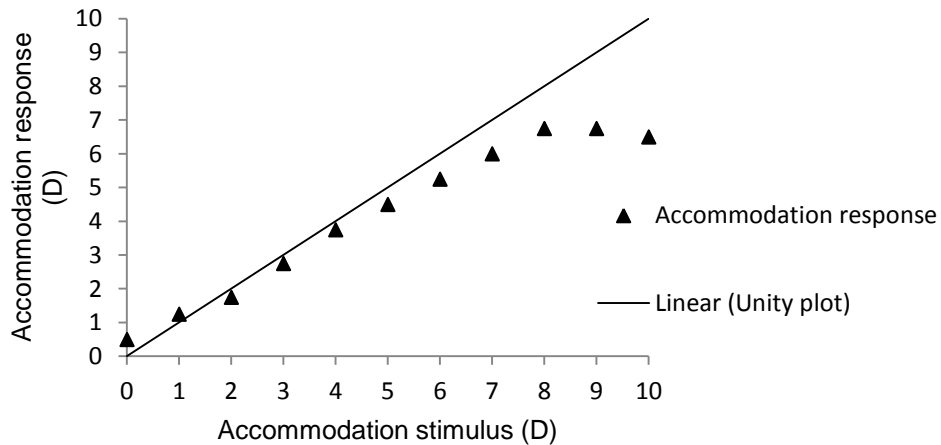


Figure 1.2. A typical accommodative stimulus response function (ASRF) shown by the red symbols. The solid black line indicates how the function would look if the accommodation response was equal to the accommodation stimulus.

Initially the curve demonstrates a slight lead in accommodation to very low dioptric stimuli (approximately 0 – 1.5 D). This is followed by a linear lag in accommodation where a change in accommodative stimulus causes a proportional change in accommodative response; however it is less than the stimulus. The third phase of the accommodation response profile is characterised by a zone of reducing response per unit increase in demand, which continues until it plateaus at the amplitude of accommodation. Once the amplitude of accommodation has been exceeded and the retinal image is blurred the accommodation response starts to decline towards the tonic accommodative level.

A lag of accommodation means the accommodative response measured is less than the accommodative stimulus presented. Under real target viewing conditions there

appears to be no relationship in adults or children between the ASRF and refractive error [82, 83]. Blur-only driven accommodative stimuli, such as minus lenses, produce shallower ASRFs in all refractive groups but more so in progressing myopes [82, 83]. Larger accommodative lags have been associated with more recent onset myopia, myopia progression and higher levels of myopia in early and late onset myopes [34, 35, 84]. They do not seem to be associated with long-term stable myopia and there have been reports that there is no increase in lag to indicate myopia onset [82, 85]. Other investigations however, have shown reduced accommodation in children up to two years prior to myopia onset [86].

An increased lag of accommodation at near would cause hyperopic retinal blur to be present, and animal studies have shown that this type of blur can stimulate axial length growth. However, as increased lag of accommodation does not always appear to be associated with the onset of myopia, it may be possible that although the accommodative response appears to be altered in myopes it may not necessarily be the cause of myopia onset.

1.6.5 Nearwork-induced transient myopia

When a step input of blur is presented to a subject, there is a latency of about 0.37 seconds before the accommodation system responds, and it takes just over one second from stimulus presentation for the response to become steady [87]. When the stimulus is removed after a period of nearwork, many individuals show a slight transient myopic shift in their prescription. The size of this transient shift has been found to be between 0.14 – 1.30 D and the decay has been reported to take from 30 seconds to a few hours to return to baseline [88-101]. For asymptomatic individuals this shift is within the depth of focus of their eye so blur is not subjectively detected. For susceptible individuals the myopic shift is greater and becomes apparent as distance vision blur. This is classed as nearwork-induced transient myopia (NITM).

In a comparison of a number of studies on NITM [88], longer task durations seem to demonstrate larger amounts of NITM and also longer decay times. Closed-loop adaptive shifts using normal blur feedback are consistently less than open-loop ones, probably due to the accommodative system being able to use blur feedback and depth of focus cues to return back to baseline more efficiently. The cognitive demand of the near task does not seem to affect the amount or decay time of the NITM [96], however a high cognitive near task followed by a passive distance task does appear to make the myopic shift more demonstrable [101]. NITM has also been shown to be blur driven as it does not seem to be affected by disparity vergence [97]. After a period of nearwork, subjects who have reported NITM symptoms show large initial myopic shifts, slowed initial response decay and an increase in overall variability of the accommodative response [91].

The accommodation response characteristics seem to differ in some myopes compared to emmetropes and hyperopes. As discussed previously, myopes tend to show a greater accommodative lag to high dioptric stimuli, they have also in some cases shown an increased lead of accommodation for distance [99]. Both early onset [100] and late onset myopes [90, 93, 98, 99] have been shown to be more susceptible to NITM than emmetropes. Progressing myopes seem more susceptible to nearwork after-effects than stable myopes or emmetropes, and the rate of decay of the after effects is slower [99]. Recent research has shown progressing myopes also show additivity of NITM following consecutive, one hour near tasks [98], however, ten minute near tasks with five minute distance vision breaks in between produced no additivity in any refractive group [102]. Is NITM a side effect of myopia progression or is it the cause? Although the main innervation to the ciliary muscle controlling accommodation is via the parasympathetic nervous system there is also sympathetic innervation present [103]. The parasympathetic system causes excitation and a rapid (one to two second) accommodation response, while the sympathetic system is inhibitory and

produces a smaller (up to -2 D), slower response (onset of action 10 to 40 s) which is directly related to the level of activity of the parasympathetic system [103].

Two theories linking autonomic innervation and myopia development have been put forward [104]. The first is that a deficit in sympathetic innervation to the ciliary muscle increases the level and decay time of NITM following a period of prolonged nearwork. The second is that there is a deficit in parasympathetic innervation which would in turn reduce sympathetic innervation as the two are linked. In this case reduced accommodation may cause blur for nearwork while reduced inhibition may cause prolonged NITM. Both cases could possibly cause chronic retinal blur over a period of time.

Recent research [105] has shown that only around 30% of individuals have access to this sympathetic innervation, and when it is blocked an increase in NITM is demonstrated. However, what is unclear at present, is whether this is then linked to myopia development or progression.

If NITM is persistently present cumulative distance vision blur could be the cause of axial elongation and myopia. As already discussed, blur causes myopia in animal models. However the distance vision blur induced with NITM is myopic and animal studies have shown myopic blur causes hyperopic axial length growth.

Hung and Ciuffreda [106] have put forward an incremental retinal-defocus theory of myopia development. It suggests that axial length regulation is controlled by change in retinal blur rather than just the presence of blur alone which gives no directional cue. An increase in the area of retinal defocus may retard axial length growth while a decrease in retinal defocus area may increase growth. NITM induces the equivalent of a slight plus lens at near which may gradually increase over time as the NITM builds up. This would reduce retinal blur at near causing axial length growth and myopia progression.

1.6.6 High AC/A ratio

Myopic children and young adults with late onset myopia have been shown to have high response AC/A ratios before, during and after the onset of myopia [86, 107-109]. A shift in heterophoria towards esophoria whilst wearing full correction has also been found to occur during myopia onset [110]. The increased accommodation associated with the near esophoria causes the high AC/A ratio. This may be a measurement which can be a useful indicator of those susceptible to myopia. Stimulus AC/A, which tends to be measured in practice, has been shown to be the same between all refractive groups and would therefore be no use as an indicator. Surprisingly, there appears to be no difference in AC/A ratio with the level of myopia [107].

Is this raised AC/A ratio just a predictor of myopia or is it somehow a cause? It has been suggested that the high AC/A ratio, low tonic accommodation and larger accommodative lag associated with myopia may be due to a mechanical pseudocycloplegia caused by increased tension on the crystalline lens as the eye enlarges [107]. Alternatively it is possible that subjects with a raised AC/A ratio accommodate less to keep their heterophoria compensated during nearwork which then causes a lag of accommodation. Both these scenarios would cause prolonged retinal hyperopic blur. This may then lead to axial length growth.

1.6.7 Sports and outdoor activities

Sports and outdoor activities have been shown to have a preventative effect against myopia development in children [61, 71, 111], particularly boys. Jones *et al.* [61] classed sports and outdoor activities together in their questionnaire and found that more hours spent engaged in these activities as an eight year old lead to a significantly lower chance of becoming myopic five years later. Rose *et al.* [71] classed indoor and outdoor sport separately and found that in 12 year old children indoor sport had no significant relationship to refractive error, however, myopes did significantly less

outdoor activity. Non-myopic medical students were found to have undertaken more outdoor activity before the age of seven than their myopic colleagues [112]. A similar result was found in young adults [75] where over a two year period, physical activity was found to be protective against myopia development and progression. It is possibly the case, however, that physical activity is not actually preventative, but myopes choose to participate in less sport due to their spectacles or they have a nature whereby they prefer studious activities to physical activity. It is also difficult to separate sporting activity from outdoor activity. Is it the actual physical activity which may be preventative or is it just being outdoors and looking in the distance?

1.6.8 Aberrations

Refractive error development is known to be influenced by retinal image quality in a number of species ranging from chickens to monkeys [38, 40, 42]. Higher-order aberrations in the human eye are known to degrade retinal image quality [113]. It may therefore be possible that high levels of axial or peripheral aberrations can cause myopic progression in some individuals, as with defocus models in animals. There are conflicting reports in the literature regarding potential links between higher-order aberrations and myopia. A number of studies have found no evidence to suggest that myopes have higher root mean squared wavefront aberration (W_{RMS}) values than emmetropes in adults [114-116] or children [117]. Conversely, He *et al.* [118] found emmetropes had significantly lower W_{RMS} than myopes in both children and young adults, although there was only a low correlation between mean spherical equivalent (MSE) refractive error and aberration values, again suggesting no real link between level of myopia and level of aberrations. Paquin *et al.* [119] linked higher W_{RMS} values to increased myopia in 27 young adult myopes at both 5 mm and 9 mm pupil diameters. Carkeet *et al.* [116] did, however, find statistically less fourth-order spherical aberration in their group of lower myopes (-3.00 to -0.50 D) than the high myopes or emmetropes.

Collins *et al.* [120] also found lower fourth-order aberrations in young adults who were myopic as opposed to emmetropic. They used a crossed cylinder aberroscope technique, and at least a third of the myopic eyes initially registered in this study were not analysed as the grid was too distorted to give an image. It is therefore possible that aberration levels in the myopic participants may have been higher than those actually found. In a recent study, Kwan *et al.* [121] found similar results. Their group of high myopes were found to have significantly lower total fourth-order and fourth-order spherical wavefront aberrations. They also compared the aberration values between the right and left eyes of 26 anisometropes. They found that in agreement with their previous results, the more myopic eye had significantly lower total third and fourth-order W_{RMS} aberrations and lower fourth-order spherical aberration than the eye with no myopia. Llorente *et al.* [122] showed that hypermetropes have significantly higher fourth-order spherical and total third and higher order W_{RMS} values than myopes. There was no significant difference between the internal spherical aberration of the two groups suggesting that the higher levels of spherical aberration found in hypermetropic eyes may be corneal in origin.

Buehren *et al.* [123] found significantly higher fourth, fifth and sixth-order W_{RMS} aberrations in young adult myopes compared to emmetropes. This appears to be the only study where progressing myopes have been selected which could possibly account for the higher levels of aberrations found, as in other studies all myopes both progressing and non-progressing have been placed together in one group. There is the possibility that progressing myopes have higher levels of aberrations than non-progressing myopes.

Vasudevan *et al.* [124] measured corneal wavefront aberrations on 10 myopic and nine emmetropic subjects. They measured corneal topography data using an Orbscan II (Bausch and Lomb, New York) and used it to calculate the corneal wavefront aberrations. This is therefore measuring a different parameter from previous studies

which have all measured total ocular wavefront aberrations of the eye. The study was small but results showed that the myopic group had corneal higher order wavefront aberrations of a greater magnitude than the emmetropic group. They also found myopes to have higher levels of fourth-order spherical aberration than emmetropes.

1.6.9 Relative peripheral retinal hypermetropia

Animal studies have shown that the peripheral retina appears to have an influence on regulating axial length growth, as emmetropization occurs even when the fovea has been ablated [51]. Literature suggests that myopes tend to have a less oblate eye shape than emmetropes and hypermetropes with a longer axial length and a larger height and width [125-127]. Measurements of horizontal peripheral refraction in both adults [128] and children [129] have suggested that in myopes the prescription becomes relatively hyperopic towards the periphery whereas the peripheral refraction of emmetropes and hypermetropes tends to be relatively more myopic in the periphery. There are, however, crossovers between the groups. There is some limited evidence that shows that in the vertical field both myopes and emmetropes appear to have a relatively myopic shift towards the periphery [128].

Animal studies have suggested that hypermetropic blur in the peripheral retina can cause axial elongation and myopia development [130, 131]. A study of pilots [132] found that those who had more relative peripheral hypermetropia became more myopic, suggesting that individuals with a less oblate eye shape and larger amounts of peripheral retinal hypermetropia may be more susceptible to myopia development. Mutti *et al.* [133] found that children who became myopic had greater relative peripheral hypermetropia two years before myopia onset than those who remained emmetropic. This was, however, preceded by a reduction in hypermetropia and an increase in axial length and therefore could possibly be a consequence of changing eye shape rather than a causative factor in myopia development. Their results also suggested that

relative peripheral hypermetropia is not a significant risk factor for myopia development in children and is only slightly associated with myopia progression [134].

1.7 Myopia control

1.7.1 Under-correction

Animal studies have shown that myopic defocus causes a reduction in axial length growth leading to emmetropization [38, 41, 42]. If this model is valid for human eyes, then in theory, under-correction of a myopic subject should slow or halt the progression of the myopia. However, if this is the case, why does myopia occur in the first place? The main difference between the animal and human studies is that in the case of animals the myopia is experimentally induced, whereas in humans myopia occurs naturally. Two studies comparing myopia progression in under corrected human subjects as opposed to fully corrected subjects have shown that rather than halting myopia progression, under-correction appears to increase it slightly [135, 136]. A study by Ong *et al.* [137] which compared myopia progression in children who wore their spectacles constantly with those who wore them occasionally and those who did not wear them at all found no significant difference between the groups.

A surprising result was found in a study by Phillips [138]. Thirteen children were corrected with monovision spectacles to see if it would reduce accommodative demand and therefore slow myopia progression. All 13 subjects were found to use their dominant distance vision eye for both distance and nearwork meaning that the eye corrected for near had constant myopic defocus. Myopic progression was found to be slower in the eye corrected for nearwork than the one corrected for distance vision suggesting that constant myopic blur may slow myopic progression.

1.7.2 Correction with plus power for near work

There appears to be some association between the development and progression of myopia and the amount or type of nearwork a person undertakes. If this link between myopia development and nearwork is due to accommodation, and the near visual input is modified using a bifocal or varifocal correction, could this reduce the rate of myopia progression? A number of studies have been undertaken to investigate this theory with mixed results [59, 69, 139-142]. An early study in the USA [59] found no reduction in myopia progression over three years when children wearing bifocals were compared to those wearing a single vision correction. Similar results were found in Finland [69], and a study on Hong Kong school children found no significant difference in myopia progression or axial length growth between a control group wearing single vision correction and another group wearing progressive addition lenses over two years [139]. However, other studies have shown promising results, suggesting it may be possible to modify myopia development. In the USA a trial using +1.50 D addition bifocal lenses on esophoric children found a 0.25 D reduction in myopia progression over 30 months [142]. In the COMET study [140] a 0.20 D treatment effect was found using progressive addition lenses, although the majority of this occurred in the first year of the three year study. A study in Hong Kong found a 0.57 D reduction in progression over two years with +2.00 D addition progressive lenses [141].

In all the studies there is quite a large variation in results, with the treatment effect being larger in some subjects than others. It may be that correcting children with plus power for nearwork is more effective for certain groups, as the treatment effect has been shown to be greater in children with large accommodative lags associated with near esophoria [139, 143], lower initial levels of myopia, shorter reading distance and more time spent doing close work [140]. Although statistically significant, it is debatable whether the size of reduction in myopia would warrant this method being used in widespread clinical practice. It has however shown that to a certain extent, modifying

the visual input can affect refractive development in children.

1.7.3 Pharmaceutical agents

As it has been suggested that accommodation may be associated with myopia development and progression, a number of studies have been undertaken involving drugs which inhibit the accommodation response. Atropine is a nonselective, muscarinic antagonist and it inhibits the actions of acetylcholine on the iris sphincter muscle and the ciliary body, causing mydriasis and cycloplegia. In Hong Kong [144] 0.98 D less myopia progression and 0.37 mm less axial length growth occurred over 1.5 years in subjects using a combination of atropine and progressive lenses as opposed to controls wearing single vision spectacles with no atropine. Unfortunately the results are confounded by the use of progressive lenses as well as atropine, as it is possible they have an independent effect on myopia progression. A two year study in Singapore [145] where only one eye was treated with atropine and single vision lenses were used, found a similar result, with 0.92 D less progression and 0.40 mm less axial length growth in the treated eye.

The mechanism of action of atropine on axial length growth is still unclear, although there is evidence that the reduction of myopic progression is not related to the inhibition of accommodation alone. Pirenzepine, a relatively selective M1 muscarinic receptor antagonist, which is unlikely to cause significant mydriasis and cycloplegia, was found to reduce myopia progression by 0.37 D over one year [146]. Atropine has also been shown to eliminate experimentally induced myopia in chick eyes, the intraocular muscles of which contain nicotinic receptors which means atropine does not produce cycloplegia or pupil dilation. This suggests the slowing of myopia progression may be via a non-accommodative process [147].

1.7.4 Contact lenses

The notion that contact lens wear slows the progression of myopia has been of interest to researchers for a long time, and a number of studies have been carried out with varying results. Stone [148] fitted polymethyl methacrylate (PMMA) corneal lenses to 80 children and compared myopia progression over five years, to that of 40 control subjects wearing spectacles. The contact lenses caused 0.50 D corneal flattening and an increase in with-the-rule astigmatism of 0.50 D. Corneal flattening seemed to account for half the reduction in myopia progression and when this was taken in to account the myopic progression of the contact lens wearing group was 0.22 D less per year than the spectacle wearing group. Stone suggested this may have been due to reduced axial length growth although this was not measured. Work by Grosvenor *et al.* [149] supported these results with the use of rigid gas permeable (RGP) lenses. After two years they found 0.17 D per year less myopic progression in the contact lens wearing group, although most of this difference seemed to occur in the first year. In this study the axial length of the eye was also measured and was found to have increased by 0.1 mm in the RGP lens wearers and 0.6 mm in the control group. A study on myopia progression in Singaporean children [150] found 0.36 D less myopia progression per year with contact lens wear than spectacle wear. They actually found less than half of this to be due to corneal flattening and suggested this may be because children with higher degrees of myopia have less malleable corneas. All three studies did comment, however, that although these are average results and indicate a trend towards a reduction in myopia progression, there was a great variation in results between subjects and it did not seem possible to predict which participants would experience the greatest treatment effect.

More recent randomized studies [151, 152] show slightly different results. The first compared myopia progression in RGP lens wearers with that of spectacle wearers and found no difference in progression between the two groups over the 24 month trial

period. There did seem to be a problem with the amount of time the subjects were wearing their lenses per day with at least 35% wearing them less than 4 hours, however, no pattern of reduced progression with increased hours worn was found [151]. The second compared progression in RGP wearers with that of soft lens wearers. There was an average of 0.21 D per year less progression in the RGP lens wearing group [152]. However this appeared to be due to corneal steepening in the soft lens wearers as no significant difference was found in axial length change between the groups. As the subjects did not have a period without their lenses at the end of the trial it is impossible to tell whether the treatment was permanent or not.

1.7.5 Orthokeratology

With increasing incidence of myopia, particularly in East Asia, research is being undertaken to investigate whether orthokeratology (orthok) treatment can slow or even halt myopia progression. Because, by the nature of the treatment, refractive error is reduced or eliminated by the fitting of the lenses, it is difficult to report myopia progression by measuring prescription change alone. As axial length growth is associated with myopic progression this measurement can be used to assess longitudinal changes. One case study has reported that after two years of treatment with orthok in one eye only of an anisometropic patient, the axial length had increased by 0.21 mm more in the untreated eye compared to the treated one [153]. This was associated with a -0.75 D myopic shift in the prescription. Could this show that without intervention the eyes would have changed equally and that the orthok procedure had slowed the myopic progression, as generally the two eyes of a subject grow by similar amounts?

Three other studies, each carried out over a period of two years, showed that after orthok treatment there was a significant slowing of eye growth in the orthok lens wearing group as compared to a control group who wore spectacle correction [154, 155]

or soft contact lenses [156]. Axial length measurements after orthok treatment can be confounded by the fact that the treatment process causes the cornea to thin slightly [157-160]. Walline *et al.* [156], however, also measured vitreous chamber depth and found a significant difference between its growth in the treated and the control eyes. Kakita *et al.* [155] took their baseline axial length measurement three months after the orthok treatment began, eliminating the effect of corneal changes when comparing longitudinal data. However, as with the RGP studies above there were large differences in eye growth between subjects, and it would be difficult to predict on whom this sort of treatment would be most successful. Recent literature suggests this treatment effect may be due to the orthok procedure altering the pattern of the peripheral refraction by making it relatively more myopic as compared to the central refraction [161, 162].

1.7.6 Correction of relative peripheral hypermetropia

Literature has suggested that peripheral hyperopic blur in monkeys can cause myopia development, and that relative peripheral hypermetropia is possibly a risk factor for myopia onset and progression [132]. It has been shown that in both adults [163] and children [164] relative peripheral hypermetropia is greater whilst wearing corrective spectacle lenses than without, possibly exacerbating the problem. Specially designed spectacle lenses [163] and contact lenses [165] may possibly reduce relative peripheral hypermetropia therefore research is now being aimed at longitudinal progression studies comparing the effects of these interventions. A study investigating the effect of three different designs of myopia reducing spectacle lenses has found no significant reduction in myopia progression between these lenses and standard spectacle lenses in a cohort of 6 to 16 year olds over one year [166]. However, there was found to be a significant reduction in a group of younger children with a parental history of myopia. Further studies need to be carried out regarding this effect.

1.8 Conclusion

There is strong evidence to suggest that myopia development is due to a number of genetic and environmental factors. How these factors interact with each other remains unknown. Some individuals appear very susceptible to becoming myopic, but it is difficult to determine whether this is purely genetic or if there is some additional environmental input. Other individuals resist myopia development regardless of the environmental pressures imposed on them.

Until the cause of myopia is fully understood, treatment is difficult. Various methods of myopia control have been attempted with limited success. As myopia becomes more prevalent in certain areas of the world the search for a modality of prevention or treatment has intensified.

The aim of this thesis is to investigate a number of areas associated with NITM, accommodation and myopia development and progression which have not been previously addressed by the current literature. In an overview of studies investigating NITM, Ong [88] suggests that increasing the duration of a nearwork task increases the magnitude of NITM post-task and slows its regression. The same paper also suggests that increasing the dioptric value of a nearwork task has no effect on the magnitude of post-task NITM or the speed of its regression. However, as no single experiment has examined this theory, the aim of the present study is to carry out an experiment to address each situation.

Early onset, late onset and progressing myopes have been shown to be more susceptible to NITM than stable myopes or emmetropes [90, 93, 98, 99, 101]. These studies have, however, been carried out using retrospective refractive data. The aim of this study is to combine a prospective myopia progression study with a series of NITM-related experiments to determine whether any correlation is present between myopia progression, and either post-task NITM levels or post-task NITM regression.

Although NITM is presumed to be due to lenticular hysteresis, biometric measurements of the lens have not yet been taken in association with NITM measurements. This study aims to develop a method which enables tracking of changes in lens thickness during disaccommodation with the possibility of building a system to record NITM and ocular biometry simultaneously.

There is a substantial amount of literature investigating the effect of coloured targets on the accommodation system. The majority of these, however, have studied the effect of monochromatic stimuli on the static accommodative response [167-169]. In a real world situation many nearwork stimuli are multichromatic, especially with the advent of laptops and smart phones. We will therefore investigate the effects of multichromatic stimuli on various aspects of accommodation: steady state accommodation, dynamic accommodation and NITM.

Orthokeratology has been shown to possibly reduce myopia progression [154-156]. This may be due to changes in peripheral refraction, or alternatively, due to changes in near visual function. As little is known about how the orthok procedure affects near visual function, we aim to assess the effect of orthok on near-vision aberrations, NITM and ASRF.

Chapter 2

Instrumentation

2.1 Measurement of refractive error

2.1.1 Shin-Nippon SRW-5000 autorefractor (Shin-Nippon, Tokyo, Japan)

The Shin-Nippon SRW-5000 is an open view autorefractor which gives natural, binocular vision of the real world making it a useful instrument for accommodation research, as near stimuli can be placed at a range of distances from the eye under test. The instrument has been described and validated by Mallen, Wolffsohn *et al.* [170].

The optical layout of the Shin-Nippon SRW-5000 is shown in Figure 2.1. A built-in visual display screen provides an image of the pupil to aid alignment of the autorefractor along the subject's visual axis. Once the subject is aligned, a ring target of infra-red light (wavelength 850 nm) is imaged on the retina for 250 ms. Refractive error is calculated in two stages. For the initial measurement, a lens is moved rapidly on a motorized track to place the ring image approximately in focus on a charge-coupled device (CCD) camera chip. During this, and subsequent measurements, the image of the ring target is then analysed digitally in multiple meridians to calculate the sphero-cylindrical refractive error. The diameter of the measurement ring is larger in myopic eyes, smaller in hyperopic eyes and elliptical in astigmatism.

The SRW-5000 has a static measurement range of ± 22 DS and ± 10 DC in either 0.125 or 0.25 D steps for sphere and cylinder power, and 1-180° in one degree steps for cylindrical axis. Back vertex distances of 0, 10, 12, 13.5, 15 and 16.5 mm can be selected. Image analysis is performed in 0.15 seconds, however, only a maximum of 45 static readings can be taken in one minute as the initial measurement takes longer due to the motorized movement of the focusing lens. The refractive data is displayed on the visual display screen, and is printed using a built-in thermal printer. The minimum

pupil diameter which will allow measurement is given by the manufacturer as 2.9 mm and this was confirmed by Mallen *et al.* [170].

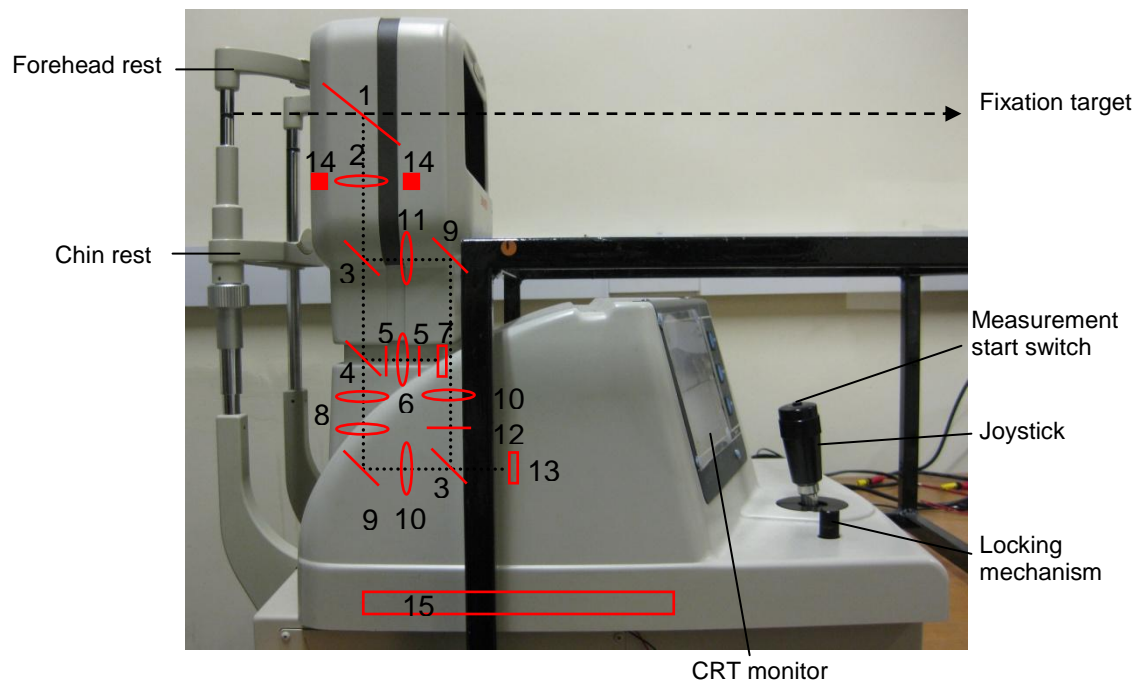


Figure 2.1. The external view of the Shin-Nippon SRW-5000 autorefractor incorporating the optical layout. 1. semi-silvered mirror; 2. view window lens; 3. semi-silvered viewing mirror; 4. perforated mirror; 5. masks; 6. lens; 7. infra-red light source for measuring; 8. relay lenses; 9. mirror; 10. focusing lenses; 11. field lens; 12. aperture; 13. CCD chip; 14. illuminating/alignment light sources; 15. power and external interface connectors (redrawn from Mallen *et al.* 2001).

2.1.1.1 Validity and repeatability of the Shin-Nippon SRW-5000 autorefractor

Mallen *et al.* [170] compared the autorefractive data (non-cycloplegic) obtained from 200 eyes of 100 adults using the SRW-5000 to that obtained by subjective refraction. A large distribution of prescriptions were measured ranging from -15.00 D to +6.50 D. The Shin-Nippon was found to give a slightly more positive mean spherical equivalent ($+0.16 \pm 0.44$ D, $p < 0.001$) and spherical component ($+0.15 \pm 0.46$ D, $p < 0.001$) than subjective refraction. The cylinder component was analysed in conventional clinical notation, and also converted into vector representation (Jackson crossed-cylinder at axis 0° with power J_0 and Jackson crossed-cylinder at axis 45° with power J_{45}) [171].

The cylindrical vectors were found to be slightly more negative than subjective refraction ($J_0 -0.10 \pm 0.19$ D, $p < 0.001$; $J_{45} -0.10 \pm 0.15$ D, $p < 0.001$) but there was no significant difference between the raw cylindrical component found by the autorefractor and subjective refraction. No bias in the measured spherical component or mean spherical equivalent (MSE) with higher prescriptions was evident, although for prescriptions more myopic than -10 D or more hyperopic than +2.50 D, the MSE measured by the autorefractor becomes more divergent from that of subjective refraction. The J_0 and J_{45} vectors again showed no bias for higher magnitudes of cylindrical error; however, there does appear to be a definite positive bias in the raw cylindrical component for higher cylindrical errors.

To test intra-session repeatability, seven autorefractor measurements were taken on each subject during the session [170]. The standard deviations of these measurements were found to be low (0.14 D spherical component; 0.13 D MSE; 0.16 D cylindrical component; 0.08 J_0 vector; 0.07 J_{45} vector). Inter-session repeatability was tested by repeating the measurements on 50 eyes at a further session. Ninety seven percent of the MSE and cylinder component measurements were within ± 0.50 D of the first set of measurements.

The SRW-5000 has also been evaluated in 44 young children age four to eight years with prescriptions ranging from -3.25 D to +4.75 D [172]. A subjective, cycloplegic refraction was taken as the gold standard and compared to cycloplegic and non-cycloplegic autorefraction. There was a good correlation between the gold standard and cycloplegic autorefraction with the subjective refraction giving slightly more positive spherical (+0.13 D) and cylindrical (+0.21 D) measurements. When compared to the non-cycloplegic autorefraction, there was a poorer correlation between the measurements, particularly for the spherical component (subjective refraction being +0.52 D more positive than autorefraction) and more variability (SD of spherical component being ± 0.29 D for the cycloplegic condition and ± 0.42 D for the non-

cycloplegic condition). Reliability and repeatability were found to be much better when cycloplegia was used, particularly in the more hyperopic children. This was probably due to the target used not controlling accommodation in such young children. Repeatability was found to be similar to that reported for the Canon R1 which has previously been the open view autorefractor of choice for experimental accommodation work [96, 99].

2.1.2 Shin-Nippon NVision-K 5001 autorefractor (Shin-Nippon, Tokyo, Japan)

The internal optics of the Shin-Nippon SRW-5000 autorefractor have been modified in the production of the NVision-K 5001. The infra red refractive error measurement ring has been segmented to avoid a patent infringement. Measurements can be taken on pupils ≥ 2.3 mm and refractive error and keratometry measurements can be taken simultaneously. The instrument has been described and validated by Davies *et al.* [173].

As with the SRW-5000, refractive error measurements are taken in a two-step process, however, during the second stage of measurement, the NVision K-5001 uses three arcs of infra red light rather than the complete measurement ring. These arcs have a smaller radius of curvature than the measurement ring allowing measurements to be taken on subjects with smaller pupil sizes. The distance between the ring segments is measured to calculate the sphero-cylindrical refractive prescription. The power range is the same as that for the SRW-5000; the differences being no 16 mm back vertex distance option, and up to 106 static readings can be taken in one minute.

To measure corneal curvature, a ring of infra red light is reflected from the cornea and analysed. The diameter of the reflected ring is measured in three meridians separated by 60° . Corneal parameters are expressed as radius of curvature (range 5 to 10 mm) in

0.01 mm steps and refractive power (range 33.75 to 67.50 D) in 0.12/0.25 D steps and 1-180° in one degree steps for principal meridian axes.

2.1.2.1 Validity and repeatability of the Shin-Nippon NVision-K5001 autorefractor

Davies *et al.* [173] compared the autorefractive data (non-cycloplegic) obtained from 198 eyes of 99 adults using the NVision-K to that obtained by subjective refraction, and the corneal radius measurements to those obtained by Javal-Schiotz keratometry. A large range of prescriptions were measured ranging from -8.25 D to +7.25 D and corneal curvatures ranged from 7.10 to 8.55 mm.

The NVision-K 5001 gave a similar MSE ($+0.14 \pm 0.35$ D, $p = 0.67$) and spherical component ($+0.18 \pm 0.35$ D, $P = 0.60$) to subjective refraction. Approximately 85 % of autorefractor measurements were within ± 0.50 D of the spherical component of the subjective refraction and 89 % were within ± 0.50 D of the cylindrical component.

No bias in the measured spherical component or MSE with higher refractive errors was shown. The J_0 and J_{45} vectors again revealed no bias for higher magnitudes of cylindrical error; however, there does appear to be a positive bias in the measured cylindrical component for cylindrical errors above -0.75 D.

Corneal curvature measured by the NVision-K 5001 was not significantly different to that found using the Javal-Schiotz keratometer in either vertical or horizontal meridians, and there appeared to be no bias with the magnitude of the radius.

To test intra-session repeatability, six autorefractor measurements were taken on each subject during the session. The standard deviations of these measurements were found to be low (0.11 D spherical component; 0.09 D MSE; 0.13 D cylindrical component; 0.07 J_0 vector; 0.06 J_{45} vector). Inter-session repeatability was tested by repeating the measurements on all 198 eyes at a further session. Ninety five percent of the MSE and cylinder component measurements were within ± 0.50 D of the first set of measurements. Inter-session repeatability was also good for the corneal radii

measurements with 95% of second visit measurements being within ± 0.10 mm for the horizontal meridian and ± 0.15 mm for the vertical.

Since the NVision-K 5001 is open view, different stimulus vergences can be achieved either in free space by manipulating target distance, or within a Badal optometer. Since the closeness of the Badal lens to the eye may induce proximal accommodation, the potential difference between this design and free-space viewing should be considered. Cleary *et al.* found no statistically significant difference between measurements taken by the NVision-K 5001 when viewing a target at distance compared to viewing a target at optical infinity through a +5 D Badal lens system [79] suggesting that the use of a Badal system does not induce proximal accommodation.

2.2 Measurement of accommodation

2.2.1 Shin-Nippon SRW-5000 autorefractor for continuous recording of accommodation

The Shin-Nippon autorefractor described above can be modified to record dynamic accommodation measurements [174]. When a measurement is taken using the SRW-5000 in static mode the infrared ring target is illuminated briefly, the image analysed and the refractive error displayed. To take dynamic measurements, the ring must be illuminated constantly by altering the 'sales mode' menu. This is achieved by holding down the button on top of the joystick when the SRW-5000 is initially switched on until a 'beep' is heard. 'Sales mode selected' can then be seen on the screen. A menu is displayed and under 'set system items' 'Ref. LED' can be altered from 'Auto' to 'On'. The infrared measurement ring is then constantly visible whenever the SRW-5000 is in line with the visual axis. A mask is placed on the instrument to remove most of the alignment circle leaving only two dots at the top and bottom of the circle visible, this is to reduce interference with image analysis (Figure 2.2).

The internal video image of the retinal reflection can be extracted via a Bayonet Neill-Concelman (BNC) cable connected to points TP5 and TP16 on the SRW-5000 circuit board. This means that the signal is extracted before the alignment, vertex distance and refractive information is added to the image, making it easier for the software to distinguish the infrared measurement ring. The video image is then captured by an IMAQ PCI-1409 image acquisition card (National Instruments, Texas, USA) installed in a personal computer (Pentium III 733 MHz, Dell Inc., Texas, USA) running Windows 2000 operating system, (Microsoft Corporation, Washington, USA). This image is then displayed on the personal computer using Measurement and Automation Explorer (MAX, National Instruments, Texas, USA) and can be manipulated into National Television Systems Committee (NTSC) format. This makes it possible to adjust the contrast and black and white luminance values for each subject to give a clear image for measurement (Figure 2.2).

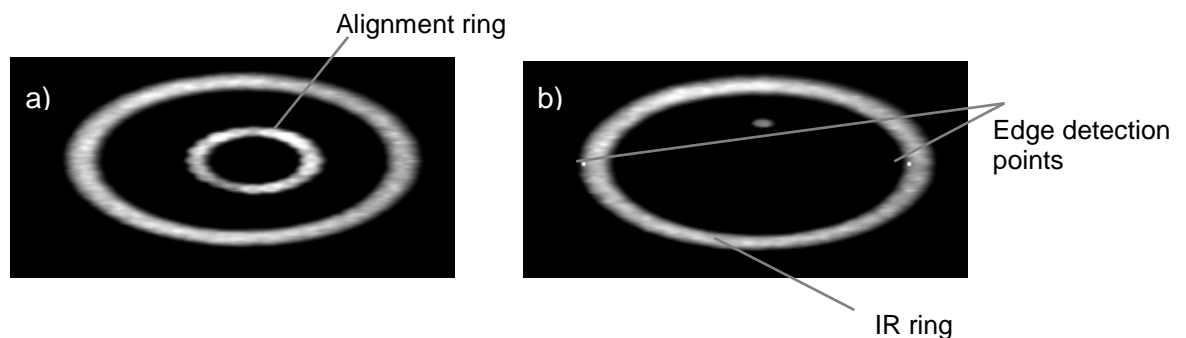


Figure 2.2. High contrast measurement ring image as seen on the personal computer using Measurement and Automation Explorer (a) without mask in place and (b) with mask in place.

The NTSC image is then converted into a binary image using Labview software and Vision programming (Version 6.i, National Instruments, Texas, USA). The edge of the ring is contained within a pixel 'staircase' of changing intensity, and the size of the ring image is measured at a sub-pixel level by thresholding and image analysis at a sampling rate of 20 Hz. The measurement is taken along the horizontal from the

outside edge of the ring at the left hand side to the inner edge at the right hand side (Figure 2.3).

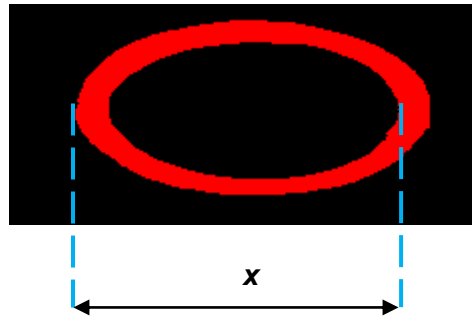


Figure 2.3. Binary ring image used for measuring accommodative change. The distance x is measured by the software in pixels and converted to dioptres.

This minimizes changes in ring diameter when the autorefractor is defocused longitudinally or the eye is looking slightly off axis. The system has been found to be relatively unaffected by focusing errors of ± 5 mm from the cornea and of off axis measurements up to $\pm 10^\circ$ [174]. An increase in ring diameter is produced by myopia or, if the distance refraction is fully corrected, by an increase in accommodative response. The measurement is then converted from pixels into dioptres. The continuous recording software was donated to the myopia laboratory at the University of Bradford by Professor James Wolffsohn, Aston University, Birmingham.

2.2.1.1 Calibration of the Shin-Nippon SRW-5000 autorefractor for continuous recording of accommodation

The calibration of the ring diameter in pixels with refractive error in dioptres was determined by Wolffsohn *et al.* [174] using a model eye. The fact that both static and dynamic measurements can be made simultaneously makes this process relatively easy. The axial length of the model eye was altered and static measurements of refractive error were taken over a 6.50 D range. These were plotted against the diameter (in pixels) of the measurement ring in continuous mode. A linear regression was found ($r^2 = 0.99$) with a relationship where a 3.3 pixel increase in ring diameter is

equivalent to 1 D of myopia or alternatively a 1 D increase in accommodative effort. Subpixel precision of the LabView image is utilised to increase measurement resolution. Once the system has initially been calibrated, as long as the threshold level for discriminating the measurement ring is not altered, there is no need to recalibrate for individual subjects.

2.2.1.2 Accommodation measurement

The Shin-Nippon SRW-5000 is initially aligned with the subject's eye and the NTSC ring image viewed using Measurement and Automation software. The black and white luminance levels are set manually to create as high a contrast image as possible to aid measurement. Once these levels have been set, the control panel of the LabView program (Figure 2.4) is used to run the system, and both the NTSC and binary ring images can be viewed simultaneously (Figure 2.4a). Altering the intensity level makes the binary image as clear as possible (Figure 2.4b) and increasing the number of erosions removes the central alignment markers (Figure 2.4c).

With the subject fully corrected for distance and viewing an object at six metres so that accommodation is relaxed, 50 static readings are taken to give a baseline measurement of the binary ring diameter (Figure 2.4d); this is the raw width (Figure 2.4e). Once this measurement is manually inserted into the software (Figure 2.4f) the accommodation trace should be seen in the blue panel running close to zero dioptres (Figure 2.4g). The trace will fluctuate with changes in accommodative response. Any large fluctuations (Figure 2.4h) tend to be blink artefacts. If further measurements are to be taken on a subject the same white, black, raw width and intensity measurements must be used to make the data comparable between sessions.

Once the system is set up for the subject a file name can be inserted (Figure 2.4i), the system is set running (Figure 2.4j) and the accommodation trace is recorded (Figure 2.4k) with the data being sent automatically to an Excel spreadsheet (Microsoft

Corporation, Washington, USA).

From the raw accommodation data, a graph can be plotted showing the accommodation stimulus and the accommodation response for the task (Figure 2.5). The graph of the raw data contains large spikes in the accommodation response which are due to the participant blinking during the task. A filter [175] was used within an Excel spreadsheet to remove these artefacts and smooth the data. Three stages were used in the blink filter. The first replaced any readings less than -6 D or greater than +6 D with an average of the three previous readings as these large deviations are due to blinks or eye movements. The second replaces any readings that differ from the previous reading by more than 0.45 D with an average of the previous three readings. As it has been suggested that the maximum speed of accommodation is 10 D per second [87] any change in accommodation greater than 0.45 D between two consecutive points was assumed to be due to a blink or other artefact. The third is a smoothing function to temper the very high frequency components. The graph in Figure 2.6 shows the same data after the filter has been applied.

The LabView accommodation program can accept input voltages from peripheral devices allowing changes in target position to be recorded in real time and the target position data to be synchronised to the accommodation measurements.

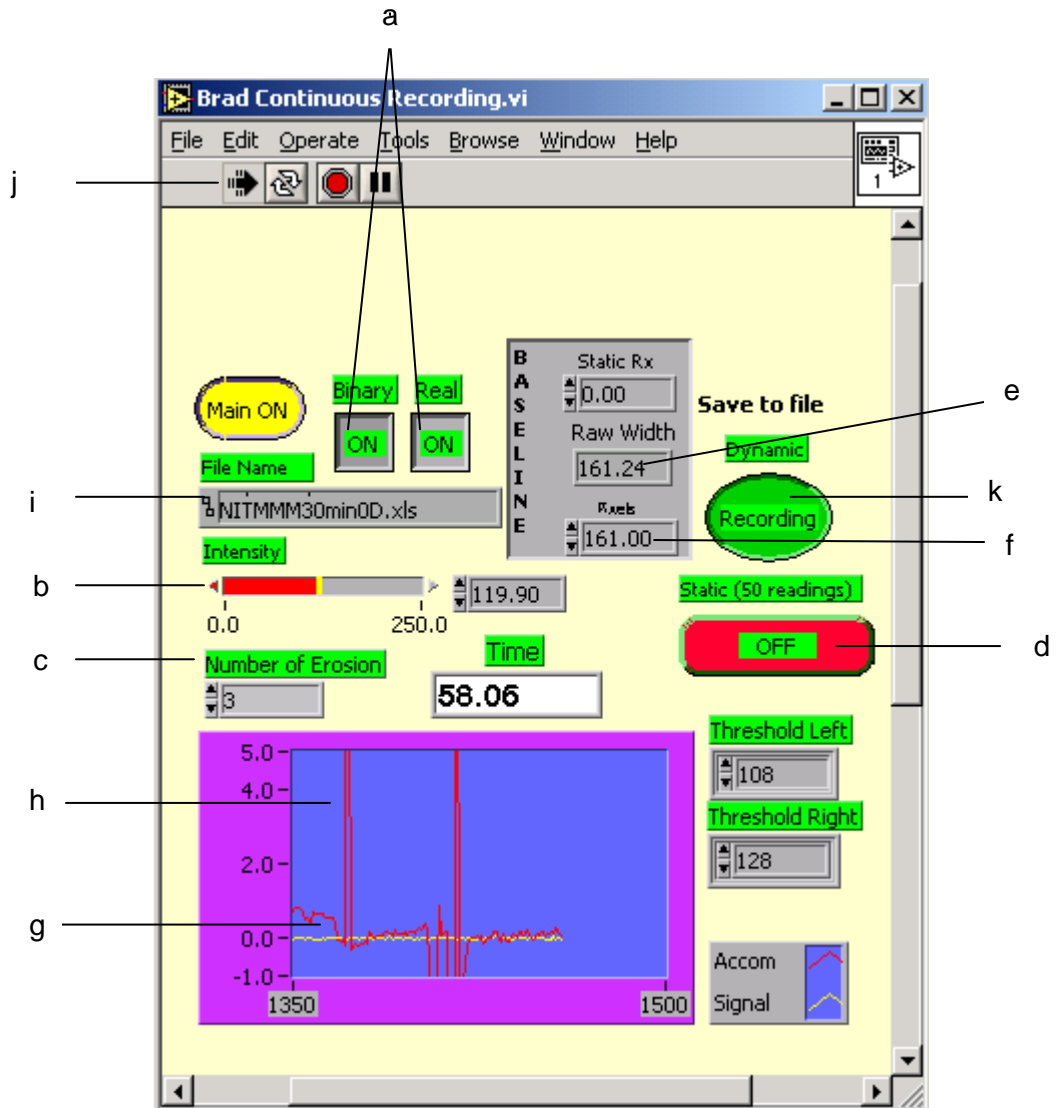


Figure 2.4. Control panel for continuous recording of accommodation [174]. a. displays the NTSC and binary ring images; b. sets the intensity level of the binary ring image; c. sets the number of erosions to remove centration markers; d. control for 50 static readings; e. actual diameter of binary ring image; f. diameter of binary ring image for zero accommodation; g. accommodation trace; h. blink artefact; i. file name for storage of data; j. control to run the system; k. control for recording data.

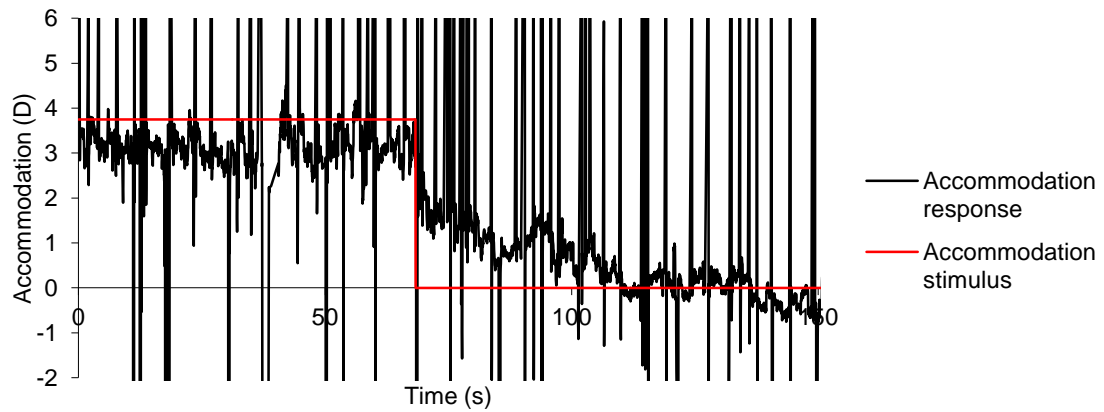


Figure 2.5. Raw accommodation data showing the accommodation stimulus and accommodation response. Large spikes in the data represent blink artefacts and fixation losses.

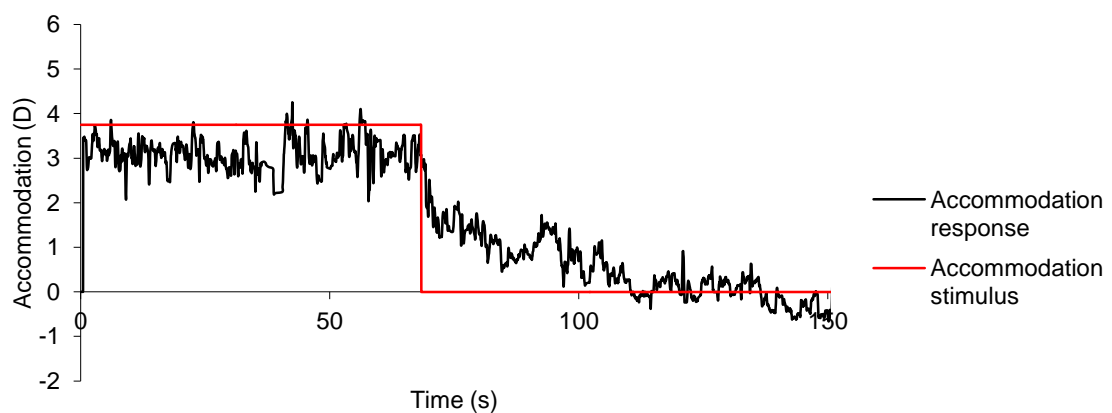


Figure 2.6. Filtered accommodation data showing the accommodation stimulus and accommodation response.

2.2.1.3 Precision of continuous recording

To assess the precision of the continuous recording equipment, an artificial eye (AE) made of an achromatic doublet with a focal length of 20 mm to represent the cornea and lens of the eye, and matt, black card to represent the retina was used. This was mounted on a rail which was attached to the chin rest of the Shin-Nippon SRW-5000 using a clamp. The axial length (AL) of the AE was adjusted until the eye was emmetropic and the static readings from the Shin-Nippon SRW-5000 were ± 0.25 D. The black and white luminance levels were set within the continuous recording measurement and automation software to give as clear a measurement ring as

possible. The raw width and intensity were then set on the continuous recording software so the baseline for the continuous recording was at zero dioptres and the binary image was whole. The AL of the eye was then increased in 0.01 mm steps using a dial guage to measure the change, and 10 static readings and 10 seconds of continuous recording measurements were taken at each level.

For the static readings each measurement produced by the autorefractor was converted to MSE and then for each AL the mean and SD of the ten MSE values was calculated. The mean of the ten seconds worth of continuous recording was calculated for each AL along with the SD.

The accommodation software converts the accommodation trace to positive measurements whereas the static readings were negative. The static readings were, therefore, changed to positive so graphs could be plotted on the same scale; this made no difference to the correlation. There was a slight cylinder in the static readings from the AE which made the static measurements slightly more negative than the continuous recording measurements when the MSE was calculated. The static measurements were, therefore, zeroed by taking the MSE static measurement for the emmetropic eye from all the other measurements. The resultant graphs are shown in Figure 2.7.

The continuous recording data shows a closer correlation and smaller SD than the static data suggesting this may be a more accurate method of measuring refractive error over a period of time.

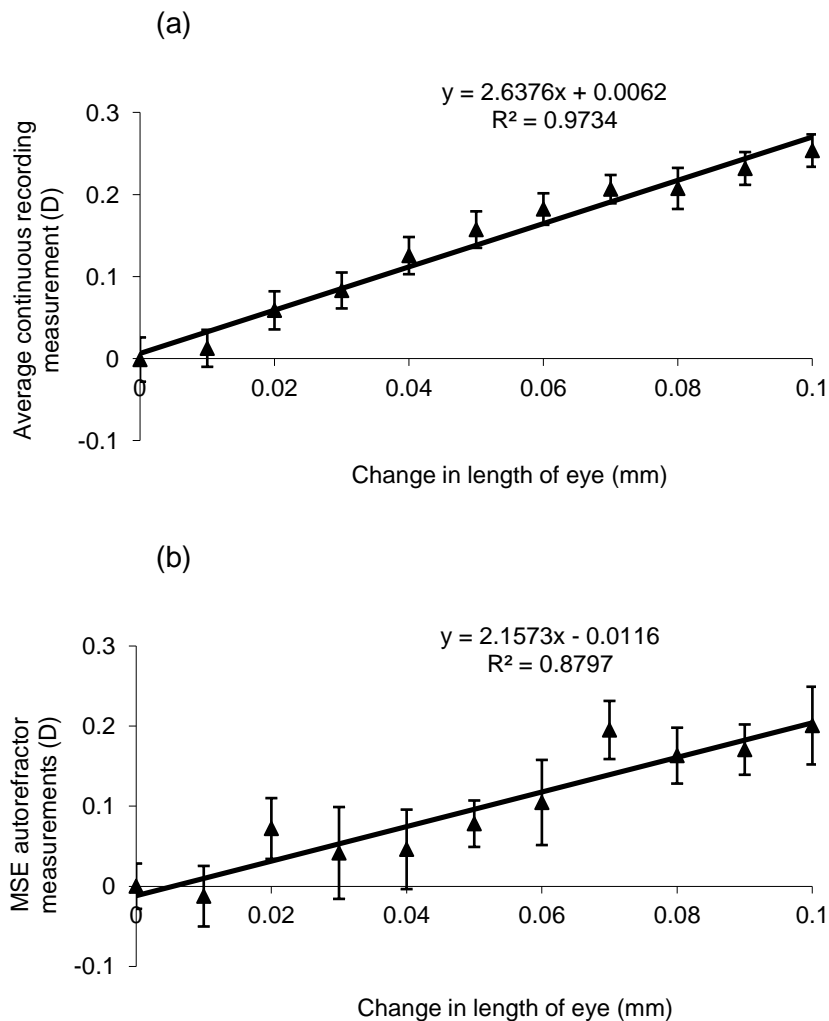


Figure 2.7. (a) mean MSE (D) ± 1 SD calculated from 10 s of continuous recording measurements (D) for each change in AL (mm) and (b) mean MSE (D) \pm SD of 10 autorefractor measurements plotted against change in AL (mm).

2.3 Badal optometer

The Badal optometer was first described in 1876 to determine refractive error [176]. In a Badal system, if the anterior focal plane of the eye is placed at the second focal point of the Badal lens the vergence of the target image is directly proportional to the distance between the target and the first focal point of the Badal lens, and the angular size of the image is independent of target vergence. During the course of the following investigations, a modified Badal lens system will be used to present stimuli during Shin-Nippon SRW-5000 autorefractor measurements and to induce accommodation during

aberration measurements.

2.3.1 Presentation of accommodative stimulus during Shin-Nippon autorefractor measurements

A diagram of the modified Badal system used during presentation of the accommodative stimuli in our investigations is shown in Figure 2.8.

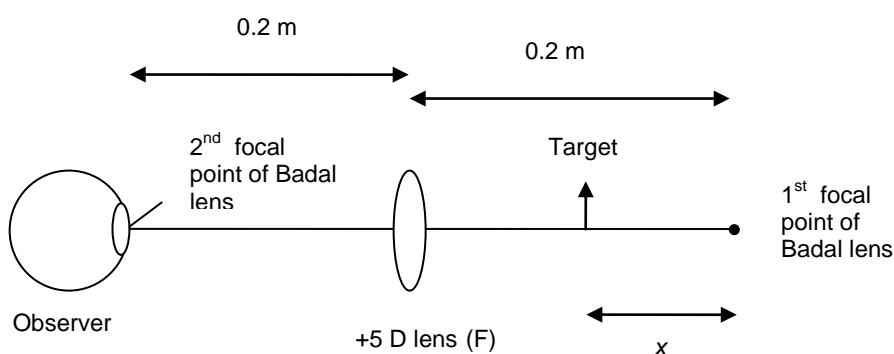


Figure 2.8. Design of Badal system. x = distance of the accommodative target from the 1st focal point of the Badal lens (m). The 2nd focal point of the Badal lens is placed at the corneal apex.

In a Badal system the image vergence at the eye is calculated using the following equation:

$$\text{Target vergence at eye} = -F^2x$$

Altering the target position in the above system therefore produces a linear change in target vergence of 0.25 D for every centimetre moved towards the Badal lens.

2.3.2 Shin-Nippon SRW-5000 autorefractor in the measurement of the accommodative stimulus-response function (ASRF)

The accommodative stimulus-response function (ASRF) can be plotted by using the Shin-Nippon SRW-5000 autorefractor to measure accommodative response whilst a

target is viewed through a Badal lens system under monocular conditions [177]. The use of a Badal system means the size and luminance of the target are kept constant as accommodative demand changes; this limits the accommodative stimulus to blur alone. It is possible, however, as the whole system is close to the eye, proximal accommodation may be active, although, research by Cleary *et al.* [79] has suggested that the use of a Badal system does not induce proximal accommodation for static accommodation measurements.

Ametropia is corrected using a soft contact lens, and the fellow eye is occluded. The actual accommodation response is dependent on the baseline distance prescription, therefore, ten static autorefractor measurements are taken with the participant fixating the 6/6 line of letters on a high contrast black on white Snellen chart at a distance of six metres. Each of these readings is converted into MSE by adding half of the cylinder component to the sphere, and the mean of the ten readings is used as a baseline.

A near target comprising high contrast black on white letters is presented randomly at six accommodative levels: 0, -1, -2, -3, -4 and -4.5 D. As the back vertex power of the Badal lens is +5 DS, the maximum accommodation stimulus possible through the system is -4.5 D. Before each measurement is taken, a few seconds are allowed for adjustment of focus to the new target and each accommodative level is presented five times. Autorefractor readings are converted to MSE values and the mean of the five readings for each accommodative level is taken, giving six accommodation values, one for each of the stimuli. The baseline distance prescription is subtracted from each of the six accommodation response values to give the actual accommodation response. These values can then be plotted against the accommodation stimulus to give the ASRF (Figure 2.9).

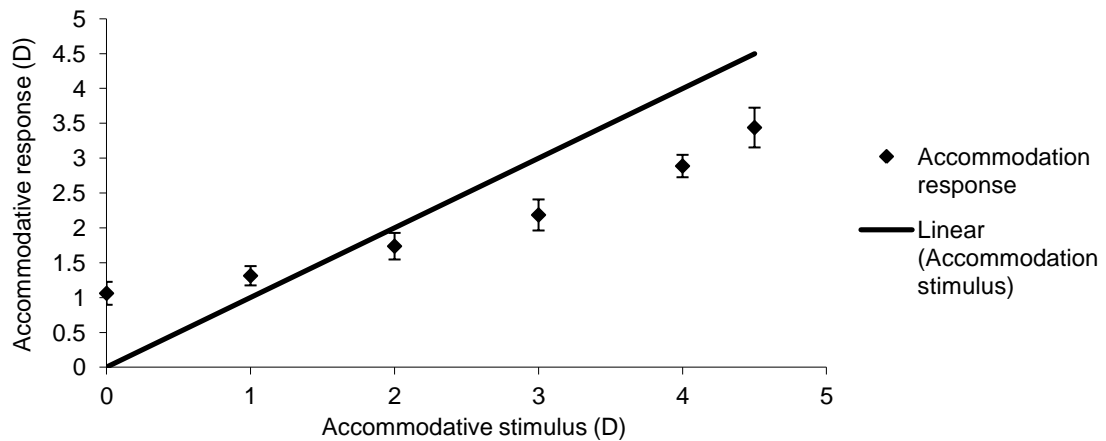


Figure 2.9. An example of an ASRF. If the accommodation response was equal to the accommodation stimulus the function would be linear, with a slope of unity. The graph shows accommodative leads at lower accommodative stimuli and accommodative lag at higher accommodative stimuli.

2.4 Measurement of ocular parameters

2.4.1 IOLMaster (Carl Zeiss Meditec AG)

The IOLMaster is a non-contact device which measures axial length (AL), anterior chamber depth (ACD), corneal radius (CR) and white to white (horizontal visible iris diameter). Its main application is to determine intra-ocular lens implant powers prior to cataract surgery; however, being non-contact it is ideal for refractive error research. Measurements are made by selecting the appropriate mode on the operating panel, aligning and focusing the patient's eye using the video image and then depressing the button on top of the joystick.

2.4.1.1 Measurement of corneal radius

For corneal radius (CR) measurements 'KER' mode is selected. The subject focuses a yellow fixation target while six points of infrared light are reflected from the air/tear film interface. These are positioned in a hexagonal shape, 2.3 mm in diameter. The subject is asked to blink before the measurement is taken to smooth the tear film. The

separation between opposite pairs of points is measured by the instruments software and CR is calculated. Five internal measurements are taken in 0.5 seconds and the average shown on the display. Any of the six points not verified by the software is shown as an X on the printout. The manufacturer recommends taking three readings of CR. If there is a disparity of 0.05 mm or more between corresponding measurements, an error message is automatically generated.

2.4.1.2 Measurement of anterior chamber depth

To measure anterior chamber depth (ACD) the 'ACD' mode is selected. Again, the subject observes a yellow fixation light and the IOLMaster directs a 0.7 mm width slit beam of light through the anterior segment of the eye at 38° to the visual axis. The light beam forms an optical section through the anterior portion of the eye and the software measures the distance between the anterior corneal pole and the anterior surface of the crystalline lens. As a result, the measurement taken includes corneal thickness, and the calculation of the actual ACD by the software requires input of the corneal radii. One shot produces five measurements for ACD, and these are all displayed and averaged automatically.

2.4.1.3 Measurement of axial length

Axial length (AL) is measured by selecting 'ALM' mode. The subject fixates a red light, and a spot and line must be aligned and focused on the video display by the operator before a reading is taken. Measurements are made using partial coherence interferometry [178] based on the Michelson interferometer [179] (Figure 2.10). A laser diode emits infrared light of wavelength $\lambda = 780$ nm, which has a high spatial coherence but short coherence length. This is split into two equal, coaxial beams by a beam splitter (BS). The beams are then reflected into the eye via two mirrors (M_1 and M_2). One is stationary (M_1), whilst the other (M_2) is displaced by a distance (d) and

moves forward and backwards at a regular speed causing a Doppler shift of the light frequency of beam reflected from it [180]. The path difference between the two reflected beams (B_1 and B_2) is then twice the amount of this displacement (d). Both beams enter the eye and reflection takes place at both the cornea (C) and retina (R) giving four reflected beams. The path difference between the beams reflected from the cornea and those reflected from the retina is twice the optical length (OL) of the eye.

On leaving the eye the difference in frequency between the coaxial beams is measured by a photodetector. As the coherence length of the emitted light is low, B_1^C and B_1^R will never interfere. The same is true for B_2^C and B_2^R . If the path differences $2d$ and $2OL$ are equal to each other (within a difference of coherence length) B_2^C and B_1^R will maximally interfere and, by knowing the value of d which produced this interference, OL can be calculated. As the laser light is reflected from the pigment epithelium of the retina, whereas ultrasound is reflected from the internal limiting membrane, a conversion factor is used by the software to calculate AL.

When a reading is taken the signal-to-noise ratio, which is a gauge of the quality of the measurement, is displayed along with the axial length. If it is between 1.6 and 1.9 an exclamation mark will appear on the display along with 'borderline value'. This does not mean the measurement must be rejected but should be evaluated along with the other measurements. The manufacturers suggest taking five separate measurements. If one differs by more than 0.1 mm from the others 'evaluation' appears in the display.

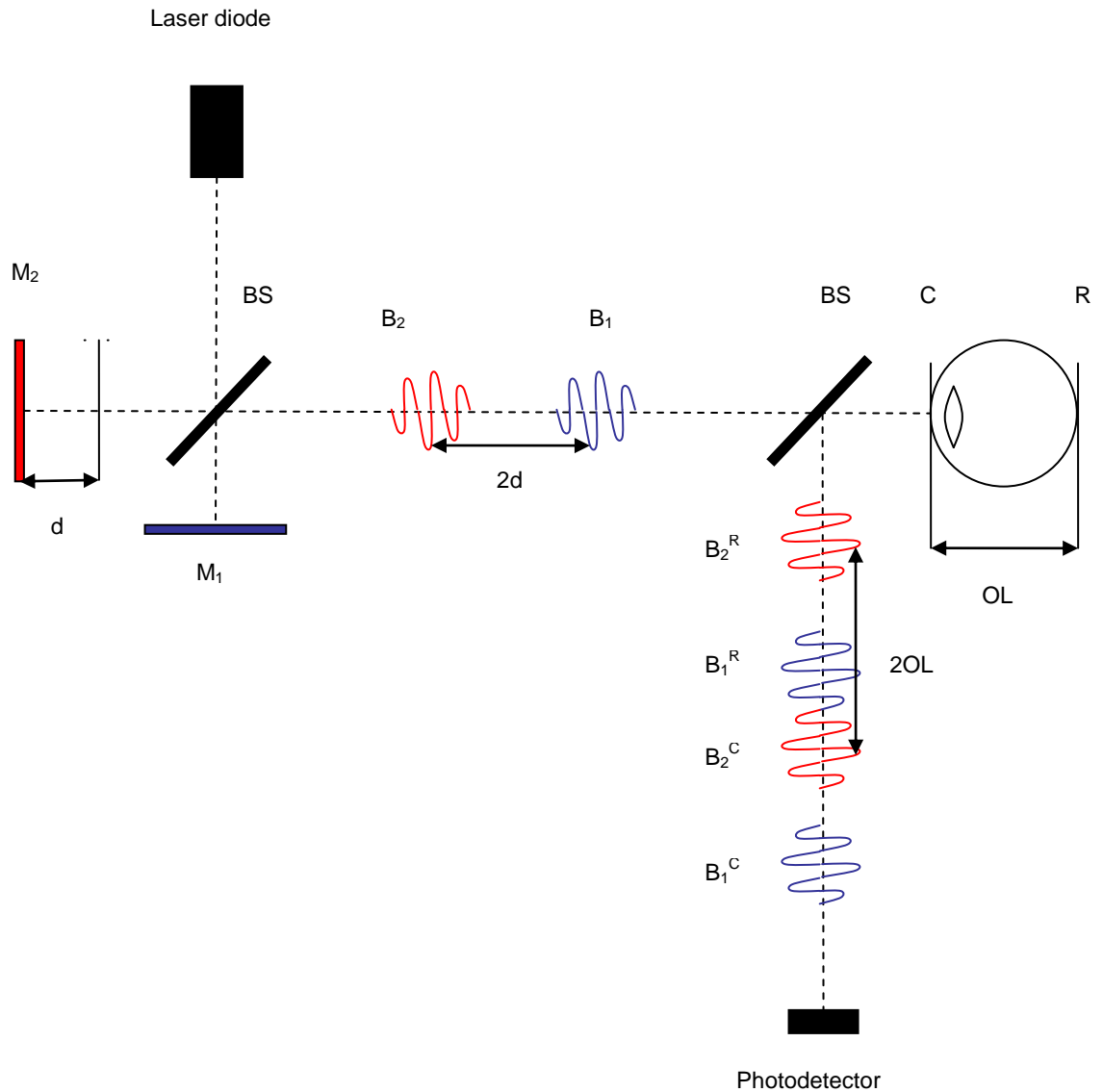


Figure 2.10. Principle of a partial coherence interferometer. BS. beam splitter; M_1 . stationary mirror; M_2 . moveable mirror; d . distance between mirrors; B_1 and B_2 . reflected beams; C. cornea; R. retina; OL. optical length of the eye (redrawn from Haigis *et al.*2000).

2.4.1.4 Validity and repeatability of the IOLMaster

Santodomingo-Rubido *et al.* [181] assessed the validity and repeatability of the IOLMaster as compared to A-scan ultrasonography, keratometry and videokeratoscopy. There was found to be no significant difference between the AL measurements made by the IOLMaster and ultrasonography (mean difference 0.02 mm, $p = 0.47$). The

IOLMaster measured significantly shorter ACD than ultrasonography (mean difference -0.06 mm, $p < 0.02$) however, as this is smaller than the resolution of the ultrasound (± 0.15 mm), and $< 2\%$ of total ACD it was considered clinically insignificant. Mean CR measurements were similar to those of both keratometer (Javal-Schiötz) (mean difference -0.03 mm) and videokeratoscope (EyeSys, EyeSys Vision Inc., Texas) (mean difference -0.06 mm).

Repeatability was excellent for all parameters when a further set of measurements were taken on a second day: AL (mean difference 0.00 mm, $p = 0.75$), ACD (mean difference -0.01 mm, $p = 0.24$) and mean CR (mean difference 0.00 mm). There was found to be no bias for any of the measurements within the range of eyes tested.

2.4.2 LenStar (Haag-Streit Koeniz, Switzerland)

The LenStar is an ocular biometry instrument jointly developed by Haag-Streit (LenStar LS900, Haag-Streit Koeniz, Switzerland) and Wavelight (Allegro Biograph, Wavelight, Erlangen, Germany). AL, crystalline lens thickness (CLT), ACD and corneal thickness (CT) are measured using interferometry as used in the IOLMaster. A superluminescent diode of wavelength $\lambda = 820$ nm with a Gaussian shaped spectrum gives higher axial resolution than the laser diode used in the IOLMaster. The technique has, therefore, been termed optical low coherence reflectometry [182]. A light source of $\lambda = 950$ nm is used to assess by image analysis the central CR, horizontal visible iris width (white-to-white), pupil size and pupil and visual axis alignment. Retinal thickness can be determined by subjective alignment of a cursor. Measurements are taken by asking the participant to fixate a flashing red light and aligning the eye using its image on the monitor. A button on the joystick is depressed to begin the measurement. The instrument takes 16 full eye scans and four keratometric scans per measurement. A proprietary 'intelligent detection system' is used to ensure correct alignment. The subject fixates along the measurement beam to ensure all measurements are taken

along the visual axis. If a blink occurs or there is a loss in fixation, measurement is halted and resumes when fixation is again detected. Due to this, the length of time taken for the measurement depends on the ability of the subject to fixate steadily. Measurements of all parameters are taken at the same time without the need to realign the system.

2.4.2.1 Validity and repeatability of the LenStar

Buckhurst *et al.* [182] have compared measurements taken using the LenStar, to those taken using an IOLMaster and an A-scan applanation ultrasound device (OcuScan, Alcon Surgical, Irvine, California). The white-to-white (mean difference 0.06 mm) and CR (flat meridian: mean difference -0.03 D, steep meridian: mean difference -0.05 D) measurements for the LenStar and IOLMaster were found to be equivalent. ACD was statistically significantly greater with the LenStar than the IOLMaster (mean difference 0.10 mm, $p = 0.014$) and ultrasound (mean difference 0.32 mm, $p = 0.028$). AL measurements made with the LenStar were greater than those made with the IOLMaster (mean difference 0.01 mm, $p < 0.001$) but shorter than ultrasonographic measurements (mean difference -0.14 mm, $p < 0.001$). There was also a bias towards larger disparities with larger axial lengths. Measurements of crystalline lens thickness made by the LenStar were similar to those found by ultrasonography (mean difference 0.16 mm, $p = 0.382$), however a larger intrasession variability and range was found with the ultrasound (± 0.33 mm; range 2.83 to 5.06 mm) compared to the LenStar (± 0.09 mm; range 3.72 to 5.38 mm), leading to the authors to suggest that optical low coherence reflectometry may be the better technique.

Both inter and intra-session repeatability was found to be excellent, and at least comparable to that of the IOLMaster and ultrasound.

2.5 Measurement of monochromatic aberrations

2.5.1 Shack-Hartmann aberrometer

For assessment of ocular aberrations a custom built aberrometer incorporating a Shack-Hartmann (S-H) wavefront sensor was constructed (Figure 2.11). This was necessary as it incorporated a Badal system to stimulate accommodation whilst keeping the image of the pupil in the same plane as the LA. The system was designed by Dr S. S. Chin and Dr K. Hampson at the University of Bradford.

Infra red light of wavelength $\lambda = 830$ nm is emitted from a laser diode (Access Pacific Ltd, Wellingborough, England) and collimated using a +100 DS lens (L_1). The beam passes through a lens relay system comprising two lenses (L_2 and L_3) of focal lengths 50 mm each. A rotating diffuser (D), located at the focal point between L_2 and L_3 averages the interference of the light waves from the retina, reducing speckle and improving the image of the S-H spots [183] (Figure 2.12). A pinhole (PH_1) placed after L_3 , narrows the light beam before it reaches a pellicle beam splitter (BS) which transmits 92% of the laser light out of the system and reflects 8% towards the eye. The 92% of light which leaves the system is reflected by a mirror (M_1) and directed down a light pipe (LP) for safety [183].

The collimated light source travels through a Badal system comprising two concave, protected aluminium coated spherical mirrors (SM_1 and SM_2 ; Edmund Optics, York) of focal length 214 mm each and four plane mirrors (M_2 , M_3 , M_4 and M_5) before entering the eye. The Badal system can be used to stimulate accommodation during the experiments. Initially, lenses were incorporated into the Badal system rather than spherical mirrors; however these produced significant back reflections despite being anti-reflection coated. As the spherical mirrors cannot be placed so the light beam hits them exactly on axis there will be a small amount of induced astigmatism within the system. The magnitude of this will be found during calibration and can be corrected using a cylindrical trial lens during measurements if necessary.

The light entering the eye (beam width 4 mm at the pupil) is imaged from the retina and back through the Badal system. At the BS, 92% of this light is transmitted towards a cold mirror (CM) which transmits infra red light but reflects visible light. The light then passes through another lens relay, the first lens (L_4) having focal length of 100 mm and the second lens (L_5) having a focal length of 50 mm. This lens relay places the image of the pupil on to the lenslet array (LA) which forms the S-H sensor, as it is not possible to place the sensor in the pupil plane. The lenses of this sensor have a focal length of 7 mm and a pitch of 0.2 mm. A pin hole (PH_2) placed at the focal point between these two relay lenses helps to control unwanted reflections. The image on the sensor is captured by a CCD camera (Retiga EXi, Imaging, Canada) placed at the focal length of the lenslet array, and analysed using custom written software in Microsoft Visual C++ installed on a personal computer (PC) courtesy of Dr Karen Hampson, University of Bradford [184].

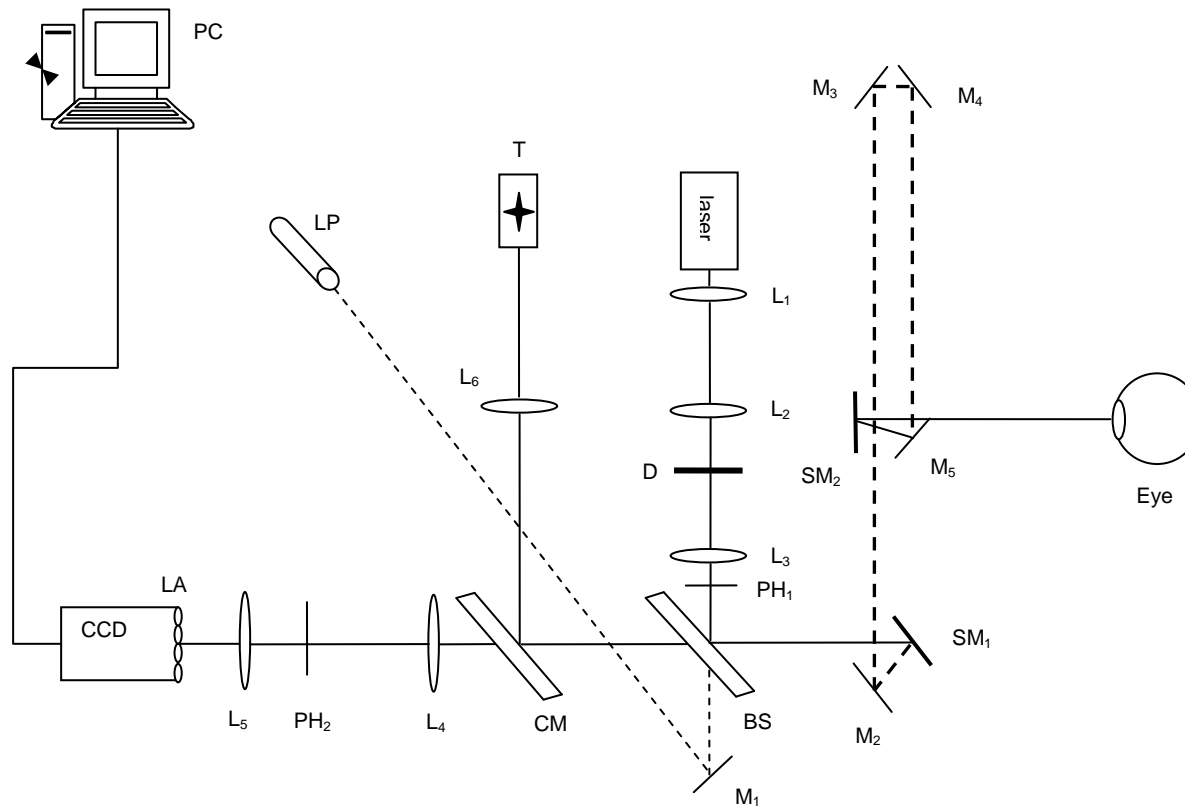


Figure 2.11. Diagram of custom built Shack-Hartmann aberrometer (not to scale). L₁. 10 mm collimating lens; L₂ & L₃. 50 mm lenses to aid collimation; D. diffuser; PH₁. pin hole to narrow light beam; BS. pellicle beam splitter; M₁. mirror; LP. light pipe to absorb unwanted laser light; SM₁ & SM₂. spherical mirrors & M₂, M₃, M₄ & M₅. plane mirrors comprising Badal system; CM. cold mirror; L₄. 100 mm lens & L₅. 50 mm lens to place image of retina on H-S sensor; PH₂. pin hole to control unwanted reflections; LA. lenslet array; T. target; CCD. camera at focal length of LA; L₆. 100 mm lens to focus target.

A target (T) of black, N₅ print on a white background is situated at optical infinity. It is back lit by an LED and the image is reflected by the CM, through the BS and Badal system towards the eye where it is seen by the subject in conjunction with the laser beam. As the wavelength of infra red light is longer than that of white light the target needs to be moved slightly closer L₆ than expected so it is at optical infinity.

The maximum permitted exposure (MPE) of the laser was calculated (Appendix 4) and the laser power at the eye was measured three times before every data collection session using a laser meter (LensCheck, Coherent, Germany), to ensure participant safety.

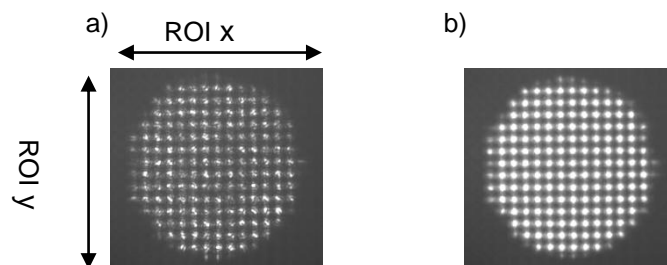


Figure 2.12. Comparison of the homogeneity of the S-H spots without (a) and with (b) a diffuser.

2.5.1.1 Control panel of the Shack-Hartmann aberrometer

The control software used for operating the S-H aberrometer was designed by Dr Karen Hampson from the University of Bradford, and has been used previously in conjunction with an adaptive optics system [185] and a binocular S-H system [186]. The image of the S-H spots is viewed on a personal computer. The control panel is shown in Figure 2.13. Not all the controls on the panel were necessary for the experiments described in this thesis, however the ones used are labelled, and operation of the system is explained below.

A number of settings were adjusted to a baseline before any measurements were taken with the aberrometer. These settings remained constant throughout the data collection. The region of interest (Figure 2.13a) is the area the camera is looking at; the

smaller this area the quicker the system will work (Figure 2.12a). The region of interest was therefore set to the lowest value possible to allow all the S-H spots to be seen by the camera. The size of the pupil over which measurements were taken (Figure 2.13b) was set to 4.8 mm. A number of studies have used larger pupil sizes, however as accommodation causes miosis, we picked a smaller diameter to try to avoid the use of mydriatics e.g. phenylephrine. Hazel *et al* found the average pupil diameter in their study for a 4 D accommodative stimulus was $5.87 \text{ mm} \pm 0.58$ [117]. The number of lenslets that covered this pupil area was 112. The greater the number of lenslets used the higher the order of Zernicke polynomials which can be calculated from the data. The number of frames taken during each measurement (Figure 2.13c) was set at 10, which meant each measurement took about six seconds to complete. The image of the spots on the screen can be made smaller by binning (Figure 2.13d). 2 x 2 binning means each block of four pixels are read as one, causing the image to be condensed and therefore fit better on to the computer screen. This increases the speed of the measurements.

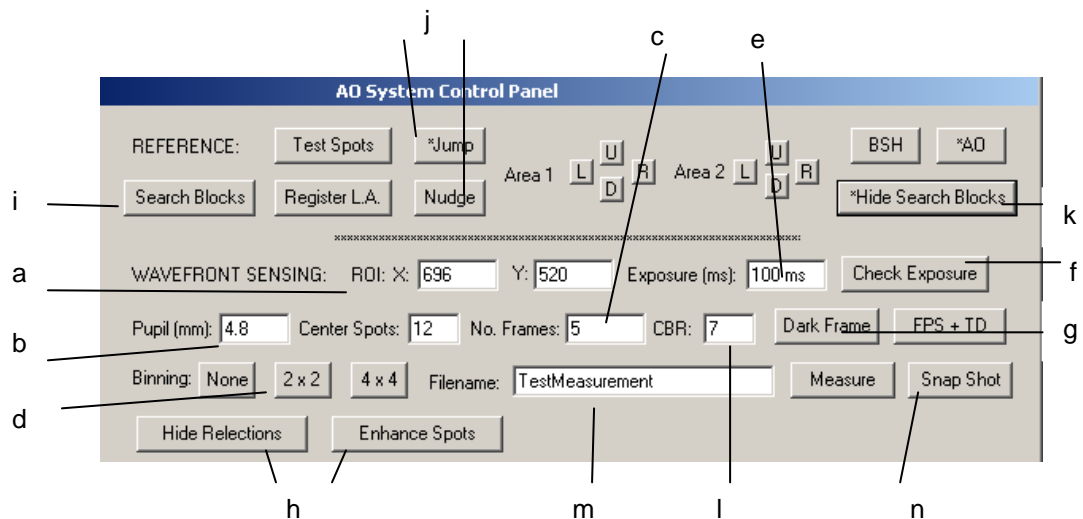


Figure 2.13. Control panel for S-H aberrometer: a. region of interest; b. pupil size setting; c. number of frames/measurement; d. sampling frequency; e. exposure; f. intensity of S-H spots; g. dark frame to remove unwanted reflections; h. ability to enhance spots or reduce reflections; i, j & k. search block controls; l. centroid block radius; m. file name; n. measurement control.

The exposure was adjusted (Figure 2.13e) depending on whether an artificial eye or a real eye was being measured. The S-H spots are much brighter when using an artificial eye as compared to a real eye (Figure 2.14) therefore an exposure of 15 ms was used for the artificial eye and 150 ms for the real eye. Unfortunately as the exposure is increased there is more chance of any reflections in to the system having a detrimental effect on measurements. If the S-H spots are too bright they become saturated leading to errors in measurements. The maximum intensity of the spots can be checked (Figure 2.13f). If this measurement is 255 or above, it is too high and the exposure duration must be reduced.

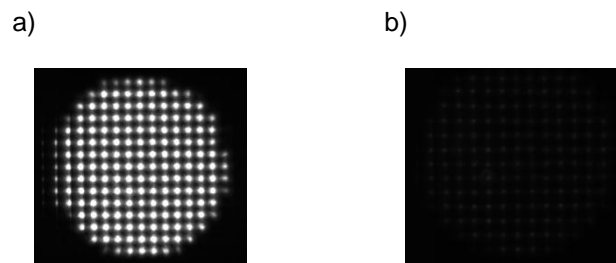


Figure 2.14. Comparison of the visibility of S-H spots measured at the same exposure (15 ms) in an artificial eye (a) and a real eye (b).

Before any measurements were taken a dark frame was performed (Figure 2.13f). This is done in complete darkness with no eye on the system. The background light level for each pixel is measured and averaged over 20 frames. Any unwanted stationary reflections measured during the dark frame are automatically removed from the final measurements. The eye to be measured was then centred on the chin rest using an infra red camera and the image of the S-H spots on the computer screen. The spots could be enhanced or reflections hidden as necessary (Figure 2.13g). Doing either of these only changes the image seen on the computer screen, it has no effect on the actual measurements. Once a clear array of spots was seen on the screen the search blocks were utilised (Figure 2.13h) and centred over the S-H spots (Figure 2.15). The search blocks are the individual regions within which the camera software looks for the

shift of each S-H spot. They can be moved around the screen in large or small steps using 'jump' and 'nudge' buttons (Figure 2.13i). The search blocks could be removed at any time (Figure 2.13j).

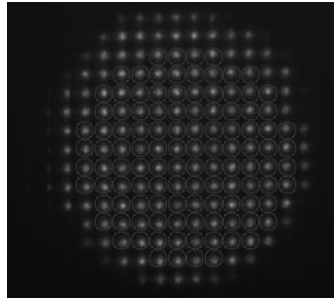


Figure 2.15. Search blocks centred over S-H spots.

The centroid block radius (Figure 2.13k) is measured in pixels and determines the spacing of the search blocks.

Before taking any measurements a file name was created (Figure 2.13l). With the room in complete darkness, a measurement was then taken (Figure 2.13m). The software calculates the first 44 Zernike polynomials (see Appendix 2 for explanation of Zernike polynomials) in each of the ten frames and averages them. The results are saved directly into a text document. The software automatically calculates the refractive power of the eye from these polynomials.

2.5.1.2 Presentation of accommodative stimuli within the Shack-Hartmann aberrometer

The Badal system within the S-H aberrometer is illustrated by a bold dashed line in Figure 2.9. There are two paths of light travelling through the Badal system: one is the laser beam and the other the target. If the path length between SM_1 and SM_2 is twice the focal length of the lenses, i.e. 428 mm, the target will be seen optical infinity and the laser beam will be collimated both when it enters the Badal system and when it emerges on its path into the eye. Similarly it is collimated on its return journey. The image of the pupil is, therefore, in the same plane as the LA.

Shortening the path length between SM₁ and SM₂ serves two purposes: it stimulates accommodation by shortening the path length between the target and the eye, and, providing the eye accommodates fully to the target, allows the image of the pupil to remain in the same plane as the LA. If the target alone was moved to stimulate accommodation the laser would not be in focus on the retina of the accommodated eye, causing the S-H spots to be blurred.

2.5.1.3 Calibration and verification of the Shack- Hartmann aberrometer

The aberrometer was calibrated and verified using both an artificial eye (AE) and real eyes (Appendix 3).

2.5.1.3.i Artificial eye calibration

A good correlation was found between the dioptric power of spherical trial lenses (+1 to -1 D) and the power measured by the aberrometer ($r^2 = 0.996$, $p < 0.001$). The aberrometer measurements were on average 0.05 D more negative than the power of the trial lenses (95 % confidence intervals 0.03 to -0.13 D) which compares favourably to the 0.17 D difference found by Liang and Williams [187]. No statistically significant difference was found between the measurements made during two separate sessions ($p = 0.196$). For spherical aberration (Z12) and total W_{RMS} 3rd to 8th-order the overall intra-session standard deviation was 0.0009 μm in both cases. There was no statistically significant difference between spherical aberration measurements taken on two separate occasions ($p = 0.646$) or total root mean squared wavefront aberrations (W_{RMS}) taken on two separate occasions ($p = 0.196$).

The mean induced cylinder power due to the inclusion of spherical mirrors was -0.92 D \pm 0.06 and the axis was 178.62 ° \pm 1. This was consistent for all spherical lenses used.

It can be represented in power vector format as $MSE = -0.46 \text{ D}$, $J_0 = 0.46 \text{ D}$ and $J_{45} = -0.02 \text{ D}$.

Correcting the AE using trial lenses increased the spherical aberration (Z_{12}) from $0.029 \mu\text{m}$ with no lens in place to $0.056 \mu\text{m}$ with a -6 D lens in place. Total W_{RMS} increased from $0.052 \mu\text{m}$ with no lens in place to $0.130 \mu\text{m}$ with a -6 D lens in place.

2.5.1.3.ii Real eye calibration

For the real eye participants demographics and refractive error range see Appendix 3. When examining a real eye the variation between intra-session measurements increased as compared to those for the AE. For the AE the standard deviation of the spherical aberration and W_{RMS} measurements was, on average, $0.0009 \mu\text{m}$ for each. However, for the real eye this increased to $0.030 \mu\text{m}$ for spherical aberration and $0.048 \mu\text{m}$ for total W_{RMS} . When measurements were repeated on a separate occasion there was found to be no statistically significant inter-session difference for either spherical aberration ($p = 0.286$) or W_{RMS} ($p = 0.953$). For the spherical aberration measurements the mean difference was $0.017 \mu\text{m}$ (95 % confidence intervals -0.107 to $0.073 \mu\text{m}$). For the W_{RMS} measurements there was a mean difference of $0.005 \mu\text{m}$ (95 % confidence intervals -0.114 to $0.104 \mu\text{m}$).

In conclusion, the aberrometer was found to be accurate and repeatable on an AE, however, it was not possible to assess the accuracy of the system when measuring higher-order aberrations as the actual level of aberrations caused by the spherical trial lenses was unknown. For this reason there is presently no gold standard method for calibration of aberrometers. Correction with trial lenses has an effect on the spherical aberration and total W_{RMS} which must be accounted for in any measurements taken. Variability is about 50 times greater when measuring a real eye compared to an artificial eye but is comparable to that found in previous studies [115, 187]. The variability present in the measurements is possibly due to a combination of slight

alignment errors between measurements, patient stability as no bite bar was used during the experiments described in this thesis and short term changes in the ocular aberrations due to tear film instability and accommodative microfluctuations [188, 189].

2.6 Measurement of Visual Acuity (VA)

2.6.1 Bailey Lovie Chart (National Vision Research Institute of Australia 1979)

The Bailey Lovie [190] chart used in the experiments described in this thesis comprises two panels, each with a high contrast chart (100 %) on one side and a low contrast chart (10 %) on the reverse (Figure 2.16). There are 14 rows, each with five letters, ranging in size from 6/60 to 6/3. Letter size progresses geometrically in 0.1 log units and are given in Snellen units as well as logMAR and Visual Acuity Rating (VAR) for a six metre testing distance. The testing distance can be altered, and a scale on the bottom of the chart provides score adjustments for different testing distances. A set of 10, 5 x 4 sanserif optotypes of almost equal legibility are used, as recommended by BS4274 (1968). The between letter and between row spacing is uniform with the between letter spacing equal to one letter width and the between row spacing equal to the height of the smaller letters. A luminance of 160 cd/sqm is recommended, however a tolerable range is between 80 – 230 cd/m².

Chapter 3

Temporal factors and dioptric demand in nearwork-induced transient myopia (NITM)

3.1 Introduction

Myopia development is associated with both genetic and environmental factors. One of the environmental factors identified is nearwork, and the incidence of myopia prevalence appears to be increasing as society moves towards an environment favouring close up tasks [3, 13, 23, 31, 67, 69, 73] and spending less time outdoors [3]. The mechanism behind this is as yet unknown; however, it seems that some people may have a susceptibility to nearwork influences [13, 60] with the possibility that, for them, myopia development and progression is a combination of genetic and environmental factors.

It has been suggested that NITM may be associated with the onset and progression of permanent myopia [106] as myopic individuals have been shown to be more susceptible to nearwork after-effects than emmetropes or hypermetropes [90, 93, 98-100]. In particular, both early onset myopes and progressing myopes appear to demonstrate larger amounts of NITM with longer decay times [90, 98, 99, 101].

In an overview of studies examining NITM, Ong [88] suggests that the longer the duration of a nearwork task, the larger the residual NITM, and the longer it takes to dissipate post task. The same paper suggests there is no relationship between accommodative demand and the magnitude of post-task NITM. The studies reviewed, however, used different experimental paradigms and procedures and therefore comparison is difficult. Table 3.1 below, compares some of the studies investigating NITM, from the earliest one by Lancaster and Williams (1914) [191] which used subjective refraction as a measure of NITM, to more recent studies in which

accommodation is recorded continuously using a specially-adapted autorefractor [100, 101]. Some of the more recent studies may be easier to compare, as the majority of them use a similar laboratory set up [89-93, 95-99], however the task types tend to differ, as all the studies were looking at different aspects of NITM.

Table 3.1. A comparison of recent studies involving NITM.

Study	No./age subjects	Method of measurement	Task type	Dioptric demand/ distance/ duration of task	Average post-task NITM	Duration of NITM post-task	Primary aim of study
Lancaster, Williams 1914 [191]	NK/children - 60 yr #	Subjective far point	Small object	At near point/45 min	1.30 D	< 15 min	Accommodation study
Ostberg 1980 [192]	29/18 - 50 yr #	Laser optometer	Air traffic control (ATC)/office work (TELE)/binocular	Normal working distance/ ATC 2 hours TELE 8 hours	ATC 0.25 D	Resolved within 15 min	Accommodation and visual fatigue with VDU work
Haider <i>et al.</i> 1980 [193]	22/21 - 45 yr #	Subjective VA	VDU/reading/ copying/binocular	Normal working distance/3 hours	VA reduced from 1.08 – 0.82	10 – 15 min	Eye strain related to VDUs with different coloured characters
Jaschinski-Kruza 1984 [194]	7/22 - 41 yr #	Contrast sensitivity (10 c/deg)	VDU/copying text/binocular	Normal working distance/3 hours	≤ 0.50 D	< 7 min	NITM after VDU work
Fisher <i>et al.</i> 1987 [195]	48/21- 35 yr 12 high MYP/low MYP/EMM/HYP	Subjective far point	Reduced snellen/monocular	At nearpoint/10 min	0.20 D	NK	Accommodative hysteresis in refractive groups
Owens, Wolf-Kelly 1987 [196]	28/17- 22 yr #	Polarized vernier optometer	Reading text on VDU or hard copy/binocular	20 cm/1 hour	0.43 D	> 20 min in some subjects	Accommodation differences between VDU and hard copy work
Ehrlich 1987 [197]	15/18 - 30 yr #	Dioptron II autorefractor	Counting numbers/binocular	20 cm/2 hours	0.29 D	> 1 hour	Fusional stress with near work
Tan, O'Leary 1988 [198]	18/19 - 27 yr 8 MYP/5 EMM/5 HYP	Polarized vernier optometer	Snellen letters/monocular	25 cm/15 min	0.26 D	NA	Interaction between dark focus, gain, optimum focus and refractive error
Rosenfield <i>et al.</i> 1992 [199]	10/NK #	Canon R-1 static autorefractor	NK	25 cm/40 min continuous and interrupted	0.20 D both tasks	< 5 min in interrupted task	Effect of task duration on NITM
Rosenfield <i>et al.</i> 1992 [199]	10/NK #	Canon R-1 static autorefractor	NK/monocular	25 cm/distance rx, PH, +2 D, +4 D	0.15 D - distance, PH and +2 D 0 D - +4 D	NK	Effect of accommodative demand on NITM

Study	No./age subjects	Method of measurement	Task type	Dioptric demand/ distance/ duration of task	Average post-task NITM	Duration of NITM post-task	Primary aim of study
Rosenfield <i>et al.</i> (1992) [97]	20/23 - 32 yr 4 EMM/14 MYP/2 HYP	Canon R-1 static autorefractor	Text/binocular	20 cm/20 min	0.14 D (10-20 s post task)	20-50 s	Contribution of disparity vergence to NITM
Rosenfield, Ciuffreda (1994) [96]	16/21 - 33 yr #	Canon R-1 static autorefractor	Adding numbers/ monocular	20 cm/10 min	0.23 D (during 10 s post task)	40 s	Contribution of cognitive demand to NITM
Ong <i>et al.</i> 1994 [94]	16/NK 16 LOM	Canon R-1 static autorefractor	Adding numbers/ monocular and binocular	6 m/40 cm/+ lenses/ prisms/10 min	0.18 – 0.39 D	NK	NITM, blur and disparity vergence
Ciuffreda, Ordonez (1995) [91]	3/2 - 25 yr 2 MYP/1 EMM	Canon R-1 static autorefractor	Adding numbers/ binocular	20 cm/10 min	0.5-1.4 D (during 10 s post task)	20-300+ s	NITM in symptomatic individuals
Ong <i>et al.</i> (1995) [95]	15/22 - 39 yr #	Canon R-1 static autorefractor	Adding numbers/ monocular	20 cm/10 min -5 D/10 min	0.36 D (during 10 s post task)	93 s	Contribution of blur driven & proximal accommodation to NITM
Ciuffreda <i>et al.</i> (1996) [89]	12/21 - 28 yr #	Canon R-1 static autorefractor	Numbers	3 & 5 D 0.25,0.5,1,2,4,8 min	0.3 – 0.6 D	Not specified	Effect of stimulus duration and dioptric demand on NITM
Ciuffreda, Wallis (1998) [93]	44/21 - 30 yr 11 LOM/13 EOM/11 EMM/9 HYP	Canon R-1 static autorefractor	Adding numbers/ binocular	20 cm/10 min	Myopes 0.35 D	EOM 35 s LOM 63 s	Myopia and NITM
Ciuffreda <i>et al.</i> (1999) [92]	9/21- 28 yr Most MYPs	Canon R-1 static autorefractor	Adding numbers through 0,+2,+4 D/ monocular	25 cm/20 min	0 – 0.28 D +2 – 0.17 D +4 – 0.01 D	Not measured	Near-vision lens effects on NITM
Ciuffreda, Lee (2002) [90]	16/17 - 31 yr 4 EMM/HYP/LOM/ EOM	Canon R-1 static autorefractor	Novels/ papers/ binocular	4 hrs/ natural reading distance	EOM 0.13 D LOM 0.12 D EMM 0.09 D	<60 s	Refractive susceptibility to sustained nearwork
Vera-Diaz <i>et al.</i> (2002) [99]	41/18 - 27 yr 13 PM/14 SM/14 EMM	Canon R-1 static autorefractor	Adding numbers/ monocular	25 cm/10 min	EOM 0.28 D LOM 0.21 D SM 0.17 D	SM 42 s PM >120 s	NITM and myopia progression
Wolffsohn <i>et al.</i> (2003) [101]	18/18 - 35 yr 6 EOM/LOM/EMM	Shin-Nippon continuous recording	Numbers +5 D badal/ monocular	0,4,5 D/10 min	EOM 0.75 D LOM 0.66 D EMM 0.14 D	EOM 183.7 s LOM 101.7 s EMM 48.7 s	Refractive error, cognitive demand and NITM
Wolffsohn <i>et al.</i> (2003) [100]	45/6 - 12 yr 35 MYP/ 10 EMM	Shin-Nippon continuous recording	Letters +5 D badal/ monocular	0,2,5,5 D/5 min	MYP 0.47 D EMM 0.19 D (60 s post task, 5 D)	MYP > 180 s	Comparison NITM in myopic & emmetropic Hong Kong children

Study	No./age subjects	Method of measurement	Task type	Dioptric demand/ distance/ duration of task	Average post-task NITM	Duration of NITM post-task	Primary aim of study
Vasudevan, Ciuffreda (2008) [98]	44/21 - 34 yr 15 EMM/15EOM/14 LOM	Canon R-1 static autorefractor	Lecture notes/ binocular	35-40 cm/2 hrs	EOM 0.29 D LOM 0.20 D SM 0.20 D PM 0.27 D	EOM 87 s LOM 60 s SM 36 s PM 69 s	Additivity of NITM

NK = not known, EOM = early onset myope, LOM = late onset myope, PM = progressing myope, SM = stable myope, EMM = emmetrope, HYP = hypermetrope, MYP = myope, # = refractive data not available.

3.1.1 Measurement of NITM

A number of different methods have been used to measure NITM: visual acuity, contrast sensitivity, change in far point (both subjectively and objectively) and more recently continuous recording of accommodation using objective autorefractors. Post-task NITM has generally been found to be small in magnitude (0.14 to 1.30 D) and of a short duration (20 seconds to > 1 hour) [88], therefore, it is essential that any measurement technique must be quick to perform and reliable.

Haider *et al.* [193] used visual acuity measurements when comparing NITM levels between air traffic controllers and office workers. These measurements, however, rely on subjective responses and therefore may not be sensitive to relatively small differences in acuity. Changes in pupil size also affect depth of focus, which means participants with larger pupils may be much more aware of myopic blur than those with smaller pupils [200].

Jaschinski-Kruza [194] suggested that the use of contrast sensitivity may be a more sensitive measure of NITM than a high contrast test chart. He used a spatial frequency of 10 cycles per degree to measure contrast sensitivity before and after a three hour VDU task. This method, however, is again reliant on subjective responses and affected by pupil size.

The most common method of measuring NITM is by using the eye's refractive far point. This has been carried out subjectively by refraction [191], moving a target within a Badal system [195] and taking measurements using an optometer [192, 196, 198]. All these methods are time consuming, with measurements taking up to 15 minutes. They rely on subjective responses and refraction results are dependent on the ability of the practitioner undertaking the measurements.

Ehrlich [197] was the first to measure NITM objectively using a Dioptron II infra-red autorefractor, and since then both the Canon R-1 [19, 20] and Shin-Nippon autorefractors [96, 97, 100, 101] have been used successfully. These instruments take

static measurements, therefore only a finite number of readings can be taken during the post-task period (e.g. the Shin-Nippon SRW-5000 can take up to 45 readings per minute). The temporal resolution of the autorefractor may not, therefore, be adequate to monitor the NITM decay. Development of continuous recording systems used in conjunction with both the Canon R-1 [201] and Shin-Nippon autorefractors allows post-task measurements to be taken constantly [174, 193, 194, 196, 202]. These systems also reduce the variability as more measurements can be taken over a period of time than with a static autorefractor.

3.1.2 Refractive correction

When studying accommodation, any ametropia present must be fully corrected during the task to obtain accurate accommodation responses. In a number of studies this has been done using the participants own spectacles [192-194, 196] which may not always be the optimum prescription. However, when using an autorefractor for post-task measurements this presents a problem, as tilting of spectacle lenses to reduce reflections may induce a cylinder into any measurements taken.

A number of studies have utilised mixed methods of correction with some participants wearing spectacles and others contact lenses [90, 91, 96]. Here, those participants wearing spectacles during the task had to remove their correction before post-task measurements were taken. As a result, more time may have elapsed before any NITM was measured, as compared to the emmetropes and contact lens wearing participants on whom measurements could commence immediately. Another factor which may affect the level of post-task NITM is that once the myopes have removed their spectacles their distance vision will be blurred. It may therefore take longer for their NITM to dissipate than those who can see the distance stimulus clearly, as there is less visual feedback, particularly if they are high myopes [203].

Vera-Diaz *et al.* [99] and Wolffsohn *et al.* [101] used contact lenses to correct all ametropia giving the participants a more natural viewing environment and making NITM measurements more consistent between refractive groups. It has been shown that the presence of contact lenses does not affect the ability to obtain accommodation recordings [204].

3.1.3 Age of participants

Due to the reduction in accommodative ability with increasing years, the age of the participants in a study is important. In the majority of the studies in Table 3.1, the age range was between 20 – 30 years, however there were two studies with participants over the age of 40 years [192, 193]. As these participants may have lower amplitudes of accommodation and different accommodative characteristics compared to younger participants, it is possible that their inclusion may have skewed the results.

3.1.4 Task paradigm

It is possible that the tasks carried out by the participant may affect the resulting level of NITM. In the studies in Table 3.1, tasks have been carried out under a mixture of binocular and monocular conditions. Ong *et al.* [94] however, concluded that it is blur which drives the NITM response not vergence disparity, suggesting that monocular versus binocular viewing should make little difference to the results. Some studies were carried out in a real working environment [192] giving little control over parameters such as distance from task, breaks taken and even consistency of the task. A number of studies were undertaken with the task in real space where both proximal- and blur-driven accommodation come into play [90, 98], whereas others utilised a Badal system to reduce proximal cues to accommodation [100]. It is possible however, that as the Badal system is close to the eye, proximal accommodation may have been stimulated, however, Cleary *et al.* [79] found no significant difference between distance

measurements within a Badal system and those without. Although the type of tasks undertaken differed, e.g. from adding numbers, to reading and VDU work, most were cognitive. Very few studies measured the within-task accommodation response apart from those by Vera-Diaz *et al.* [99] and Wolffsohn *et al.* [101].

It is known that myopes in particular have a lag of accommodation [84]. Without a measure of the within-task response it is difficult to assess how the post-task NITM relates to the actual accommodative response. Mallen *et al.* [205] used a regression quotient in the analysis of their accommodative data to try to overcome this problem. They calculated regression of NITM as a percentage of the within-task accommodation response, with 100 % indicating no regression and 0 % indicating complete regression back to baseline i.e. the response to a 0 D task (Section 3.3.1.5).

3.1.5 Comparison of the results between NITM studies

The task times which have been studied vary from 15 seconds to four hours. The largest amount of NITM (0.50 – 1.40 D) was found by Ciuffreda and Ordonez [91] and was measured about ten seconds after the end of a ten minute, 20 cm task. This was, however, carried out on individuals complaining of NITM symptoms, therefore a high level of NITM may have been expected. Lancaster and Williams [191] also found a large amount of NITM (1.30 D) after a 45 minute near task, however, little information could be found regarding the design of this study, and as the age range included presbyopes (children to 60 years) this is probably not comparable with other studies. Ignoring these two studies, the highest amount of NITM (group mean = 0.75 D) was found in a group of early onset myopes [101]. This was averaged over 180 seconds following a ten minute, 4.50 D task and would probably have been much higher had only the first ten seconds been averaged. Surprisingly, the smallest amount of NITM (group mean = 0.13 D) was found after the four hour reading task [90].

Regression of NITM to baseline also varies considerably between studies. Those using subjective responses to measure NITM tend to give longer regression times with Owens and Wolf-Kelly [196] finding NITM still present 20 minutes after a one hour, 20 cm task. If the studies using autorefractors as a method of measurement are compared, the longest duration of NITM was found by Ehrlich [197], where NITM was still present over an hour after the end of a two hour, 25 cm task. This is a long regression period and may be due to autorefractor measurements being taken without a spectacle prescription in place. As discussed previously, if distance vision was blurred whilst the post-task measurements were taken it may have exacerbated the NITM effect. Some studies have used contact lenses to correct myopia giving a more natural transition from nearwork to distance viewing. Of these studies the longest regression period (183.7 s) was found by Wolffsohn *et al.* [101] in their early onset myopes.

3.1.6 Temporal factors and NITM

A number of studies have tried to address the relationship between task duration and the level and duration of post-task NITM. Haider *et al.* [193] compared the results from two of their studies. In the first they measured VA before and immediately after a VDU task of three-hours duration. Further measurements were taken at 6, 11 and 16 minutes post-task. In the second study, using a different set of participants, the same measurements were taken before and after a one-hour task. After an unspecified break, another one-hour task was performed and VA measurements were taken again. Finally, a four-hour task was performed with unspecified breaks. Measurements of VA were again taken before and after the task. The results showed the one-hour and two-hour tasks caused a comparable slight reduction in VA which recovered rapidly. The four-hour task with breaks gave a larger and longer lasting level of NITM, which was estimated from the VA to be approximately 0.25 D. The three-hour work period produced the largest reduction in VA which took the longest to recover. As VA was

used to estimate the NITM, accuracy was an issue. Also the age of the participants ranged from 21 to 45 years, so there may have been some who did not experience NITM purely because of their age and reduced amplitude of accommodation. As the participants who undertook the three-hour task were different to those for the other tasks, the studies are not directly comparable.

Ciuffreda *et al.* [89] measured NITM in 12 young adults after a 0.25, 0.5, 1, 2, 4 and 8 minute task of unspecified dioptric demand. They found that four minutes of nearwork can cause significant NITM of 0.3 – 0.6 D. There was no comment on whether longer tasks produced larger amounts of NITM or how the length of the task affected regression.

Vasudevan and Ciuffreda [98] have recently shown that NITM displays additivity, by measuring the amount of NITM present one hour into a two hour reading task, and then again at the end of the task. The difficulty with this experiment is that to measure NITM after an hour the participants had to have a 30 second distance break, which may have affected the amount of NITM present after the whole two hours. There were also no measurements taken during the task so the actual amount of accommodation exerted during the task is unknown.

3.1.7 Dioptric value and NITM

Few studies have looked at how altering the dioptric demand of the task affects the post-task NITM magnitude and regression. The study by Ostberg [192] did not assess dioptric demand directly but compared NITM levels after two hours of air traffic control work and eight hours of office work. The premise was that the air traffic control work was more intense. They found a significant amount (0.25 D) of NITM after the air traffic control work, but although NITM was present after the office work it was less, and not statistically significant, suggesting intense work produces larger amounts of NITM. This study was carried out during a normal working day so was not in a controlled

environment and the duration of the tasks undertaken by the two groups was also different, and therefore not comparable. Also, the tasks carried out by the office group will have varied, and presumably they had breaks during the day which may have affected the resultant NITM. The measurements were taken using an optometer and took 15 – 20 minutes to collect. As NITM by its nature is transient, it is possible that some of the effects were missed.

Rosenfield *et al.* [199] carried out a study in which they had three dioptric demands of task. Ten participants viewed a 25 cm task for an unspecified period of time through four conditions. The first was using their distance prescription, the second through a +2 D lens, the third through a +4 D lens, and the fourth through a pinhole. They found a similar amount of NITM (0.15 D) was produced after tasks one, two and four, and no NITM was produced after task three. They therefore concluded that the whole dioptric value of the task needed to be corrected to cancel out NITM. Ciuffreda *et al.* [89] had similar findings. They tested 12 young adults using 3 and 5 D tasks for an unspecified time. They found an equal amount of NITM (0.4 D) was produced with each task, suggesting that the dioptric value of the task has no affect on the level of NITM.

In a study on Hong Kong Chinese children, Wolffsohn *et al.* [100] found slightly different results. They measured NITM after a five minute task at 2.5 and 5 D. NITM was found to be slightly higher after the 5 D task (0.47 D compared to 0.39 D) during the first 60 seconds post task. This difference was not, however, statistically significant.

3.1.8 Symptoms of NITM

The majority of studies reviewed have measured levels of NITM objectively, however only one has asked participants if they were subjectively aware of NITM [91]. Data from three symptomatic individuals was assessed and the authors concluded that these individuals had an abnormal post-task transient myopia profile with three components:

a large initial myopic shift, a slow initial decay and overall increased response variability. It is obviously difficult to quantify subjective symptoms.

Although it appears to be the case that myopes, and in particular progressing myopes, are more susceptible to nearwork after-effects [90, 93, 99, 101], it is unclear whether these individuals are aware of any NITM present or not. It would be thought that symptoms would only be present if the level of NITM was larger than the depth of focus of the individual. As depth of focus differs between individuals [200], a level of NITM which causes symptoms in one person may cause no problems for another. As NITM may cause cumulative distance blur, which may in turn lead to myopia onset and progression, it is possible that this is only a problem in those individuals who are aware of this blur.

3.1.9 Aim of the study

Consequently, the aim of this study was to investigate the effect of task duration and dioptric demand on the size and timecourse of any resultant post-task NITM. In the first experiment, a near vision task of constant dioptric value was undertaken for various periods of time, and measurements of accommodation taken constantly during the task and immediately post-task. The second experiment was carried out in a similar manner, however the dioptric value of the task was altered while task duration remained constant. All participants were asked if they noticed symptoms of NITM, and analysis was carried out on the group as a whole and also the two groups separately, to investigate whether there were any measurable differences in their accommodative responses during the task, or their post-task transient myopia profile.

3.2 Method

3.2.1 Instrumentation

3.2.1.1 Refraction

To assess refraction, a non-cycloplegic, subjective, binocular refraction was carried out on each participant. The astigmatic component was measured using the Jackson crossed cylinder method and the end point of the refraction was taken to be the most positive, least negative sphere to give the best VA.

3.2.1.2 Accommodation

All accommodation responses were measured using a Shin-Nippon SRW-5000 (Shin-Nippon, Japan) open view infrared autorefractor, which had been modified to take continuous recordings [170, 174]. Accommodation readings were taken monocularly to avoid vergence cues, using the right eye only, at a sampling rate of 20 Hz. The Shin-Nippon samples the accommodation response over the central 2.9 mm of the pupil. Any spherical ametropia was corrected using a soft, disposable contact lens (Acuvue Moist, Johnson & Johnson Medical Ltd., United Kingdom) which was allowed to settle for 20 minutes prior to measurements being taken [204].

3.2.1.3 The Task

In experiment one, the task was to play 'minesweeper' on a computer screen at accommodative demands of 0 and 3.75 D for 1, 10, 20 and 30 minute durations. In experiment two, 'minesweeper' was played for one minute at accommodative demands of 0, 1, 2, 3 and 3.75 D (Figure 3.1). This was carried out within a +5.00 D Badal system (Figure 1a) which allowed the target size to be independent of its position, therefore reducing proximity cues (Chapter 2.3). For the 0 D task the monitor screen was placed 20 cm behind the Badal lens. The dioptric demand of the near task was

limited due to the fact that the screen could not be brought any closer to the surface of the Badal lens than 5 cm.

After performing the task, a distance target comprising a Maltese cross (Figure 3.1b) was presented within the Badal system via a mirror (Figure 3.1g and Figure 3.2), and the participant was asked to focus on the target. The Maltese cross was placed 20 cm behind the Badal lens and subtended an angle of 1°.

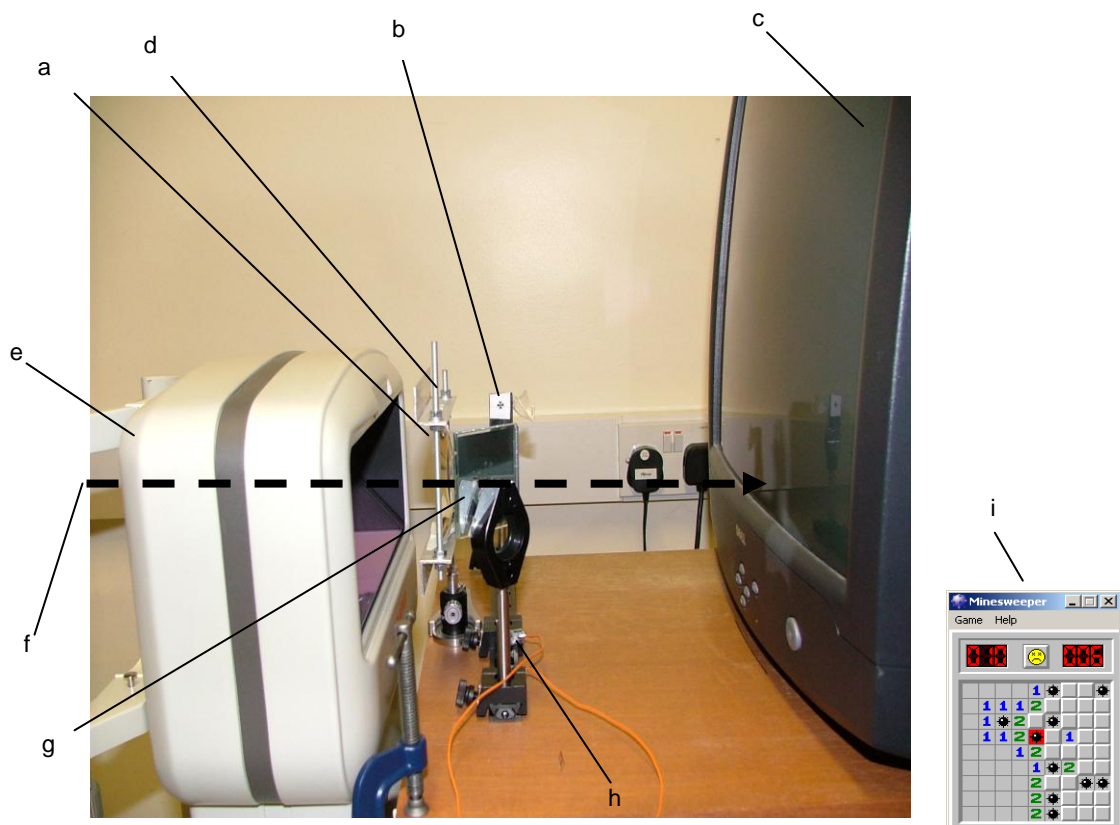


Figure 3.1. Experimental design used to investigate NITM. a. +5 D lens located 20 cm from participants corneal apex; b. Post-task distance target positioned 20 cm from back surface of Badal lens; c. CRT monitor attached to a laptop running 'Minesweeper'; d. clamp to hold Badal lens in place; e. Shin-Nippon SRW autorefractor attached to continuous recording software; f. subjects line of sight; g. mirror to block view of 'Minesweeper' and reflect distance target; h. when the electrical contacts touch the computer software is informed of a change in accommodative stimulus; i 'Minesweeper' game.

This combination of tasks was chosen as it has been shown that a high cognitive near task followed by a passive distance task makes NITM more demonstrable [101].

'Minesweeper' (Figure 3.1i) was chosen as the task as, due to its small overall size (subtending an angle of 7° at the eye), the game fits easily within the Badal lens which has a field of view of 15° . It is also a cognitive task which requires the participant to keep the numbers in focus to be able to play. Each number in the game subtends an angle of 0.7° (42 minutes of arc) at the subject's eye when viewed through the Badal system. Luminance was 55 cd/m^2 as measured with a Minolta LS-100 spot photometer (Konica Minolta, Tokyo, Japan).

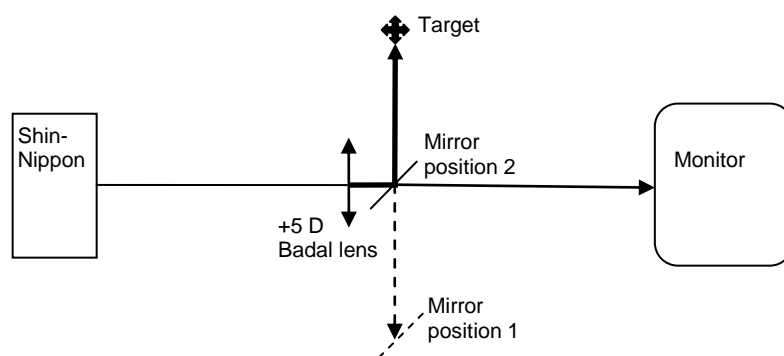


Figure 3.2. Diagram showing the use of the mirror in the experimental design. During within task measurements the mirror is in position 1 and the participant can view Minesweeper. When the mirror is moved to position 2 post-task the Maltese cross is then seen by the participant. As the distance between the target and the Badal lens is 20 cm (illustrated in bold type) the target is viewed at optical infinity.

Accommodation measurements were taken continuously for 60 seconds during the task with the participant focusing straight ahead, to gain information on the actual accommodative response to the task. Accommodation could not be measured throughout the task due to the participants' eye movements. Accommodation measurements were also taken for 90 seconds post-task, to record any NITM effects. A number of studies [100, 101] have found post-task NITM durations in excess of 180 s. However, it was found that particularly after the 30 minute task continuous recording data was difficult to gather due to pupil size and drying of the contact lens. For this reason 90 s of post-task data was collected. All tasks were randomised and there was

a gap of at least 24 hours between each task so no task was influenced by the previous one.

3.2.2 Procedure

3.2.2.1 Pre-task

A questionnaire about the participants' refractive history was completed prior to the experiment to gain information on family history of myopia, age of onset and progression of myopia and any symptoms of NITM (Appendix A5.1). A subjective refraction was carried out and if necessary, an appropriate contact lens was inserted in the right eye and allowed to settle for 20 minutes. The participant then sat in total darkness for five minutes to dissipate any prior nearwork affects [206].

The left eye was occluded and the participant was directed to place their chin on the chin rest of the autorefractor. The refractive status of the right eye was confirmed as Mean spherical equivalent (MSE) plano ± 0.25 D by taking three autorefractor readings with the participant fixating a 6/6 Snellen letter at six metres. With the refractive status at zero dioptres and the participant directed to look at 'minesweeper' at 20 cm (0 D) within the Badal system, the black and white luminance levels were set within the Measurement and Automation software to give as clear a measurement ring as possible. The raw width and intensity were then set on the continuous recording software so the baseline for the continuous recording was at zero dioptres and the binary image was whole. This then meant that any change from zero which occurred with the near task was due to a change in accommodation.

3.2.2.2 Task

The participant played 'minesweeper' whilst remaining on the Shin-Nippon chin rest. Instructions were given to keep the numbers on the screen in focus at all times. Periodically the accommodation response was monitored by static Shin-Nippon

readings. As readings from the Shin-Nippon were at their best when the participant was fixating centrally, 60 seconds before the end of the task, instructions were given to focus on the numbers in the centre of the 'minesweeper' grid and keep them clear. Continuous recording of the accommodation response then began.

3.2.2.3 Post-task

At the end of the task whilst the accommodation was still being monitored, the mirror was moved between the Badal lens and the television screen so the participant could view the distance target. The participant was asked to focus on the Maltese cross. Continuous recording of the accommodation response was then made for the next 90 seconds. Electrical contacts which touched each other when the mirror was moved into place sent a signal to the LabView software to indicate exactly when the target demand had changed.

3.2.3 Participants

Twenty-one participants were recruited with an age range from 18-35 years, and median age of 21 years. The group was composed of six emmetropes (EMMs), eight early onset myopes (EOMs) and seven late onset myopes (LOMs). Myopes were classed as EOMs having onset prior to the age of 15 years and LOMs having onset at 15 years or later [93]. Seven participants were aware of distance vision blur after undertaking periods of near work (33 %). Three of these were LOMs, three EMMs and one an EOM. The mean MSE error of the whole cohort was $-2.47 \text{ D} \pm 2.16$ and median -1.63 D (range -6.50 D to $+0.38 \text{ D}$). A breakdown of the age and mean MSE between those participants who noticed nearwork after-effects (symptomatic group) and those who did not (asymptomatic group) is shown in Table 3.2. Myopia was taken to be $\leq -0.50 \text{ D}$, emmetropia to be $> -0.50 \text{ D} < +0.50 \text{ D}$ and hypermetropia to be $\geq +0.50 \text{ D}$. All subjects had a baseline refractive error with no more than 1.00 D of astigmatism. All

subjects had corrected visual acuity (VA) of at least 6/6 in the right eye with no history of binocular vision anomalies or ocular health problems. Informed consent was obtained from each participant after full explanation of the procedures involved (Appendix A5.2). The study was approved by the University of Bradford Ethics Committee and conformed to the tenets of the Declaration of Helsinki.

Table 3.2. Average MSE and age of the whole cohort, the asymptomatic group and the symptomatic group.

	MSE (D) mean \pm SD	Age (years) median/range
Whole cohort (n = 21)	-2.47 \pm 2.16	21 (19 – 35)
Asymptomatic group (n = 14)	-3.04 \pm 2.25	21.5 (19 – 35)
Symptomatic group (n = 7)	-1.34 \pm 2.10	20 (19 – 29)

3.2.4 Analysis

The raw accommodation data was exported into an Excel spreadsheet (Microsoft Corporation, Washington, USA) and filtered for blinks (Section 2.2.1.2). A running average of 20 cells was applied to the filtered data to further smooth it. The average accommodation levels, pre- and post-task, for the 0 D tasks were used as a baseline.

All statistics were carried out using SPSS version 17 (SPSS Inc., Chicago). Data were checked for normality using a Kolmogorov-Smirnov test. The age of participants and the MSE were found to significantly differ from a normal distribution. In this case a Mann-Whitney test was used to compare the data, as this test ranks the data and carries out the analysis on the ranks rather than the data itself.

Where data was found not to significantly differ from a normal distribution a mixed design ANOVA was used for the analysis. This was necessary as the data contained both repeated-measures and between participants comparisons. When using repeated-measures designs the data was checked for sphericity using Mauchly's test. If sphericity could not be assumed Greenhouse-Gleisser estimates were used.

After the main ANOVA had been examined, further analysis was carried out using standard contrasts within SPSS or post hoc testing using the Bonferroni method. This method was used as sphericity of the data could not be assumed. G*Power 2 was used to aid post hoc power calculations.

3.3 Results

3.3.1 Experiment 1

3.3.1.1 Within-task accommodation

The within-task accommodation level was calculated using the following formula:

$$\text{(average accommodation during last 10 s of 3.75 D task)} - \text{(average accommodation during last 10 s of 0 D task)}$$

This factored out any accommodation due to the proximity of the task. The group mean within-task accommodation levels and standard deviations for each task duration are shown in Table 3.3.

Table 3.3. Group mean within-task accommodation levels (D) \pm 1 SD for each task duration for all participants, the asymptomatic group and the symptomatic group.

Task duration (min)	Within-task accommodation (D)			Difference (asymptomatic – symptomatic)
	All participants	Asymptomatic	Symptomatic	
1	2.25 \pm 0.74	2.30 \pm 0.66	2.15 \pm 0.93	0.15
10	2.45 \pm 0.85	2.62 \pm 0.84	2.12 \pm 0.83	0.50
20	2.34 \pm 0.85	2.66 \pm 0.81	1.70 \pm 0.52	0.96
30	2.66 \pm 1.01	2.82 \pm 0.73	2.36 \pm 1.30	0.46

For all task durations, those participants who suffered NITM symptoms had a lower within-task accommodation level than those who had no symptoms of distance vision blur. This difference was found to be statistically significant ($F_{(1,19)} = 6.075, p = 0.023$).

No statistically significant effect of the duration of the task on the within-task accommodation level was observed ($F_{(3,57)}=0.924$, $p = 0.435$, power = 0.961).

3.3.1.2 Post-task NITM values

For the data to be comparable to previous studies, it was necessary to calculate the level of NITM post-task. For each participant, an average figure was calculated from the 0 D post-task measurements for each of the four task durations. This figure was then subtracted from each individual post task accommodation measurement for the 3.75 D task of equivalent duration, to give an NITM value in dioptres for that moment in time (Table 3.4).

The accommodation was sampled at a rate of 20 Hz, therefore, in order to calculate the NITM value for each second post-task, 20 cells at a time in the Excel spreadsheet were averaged. Ten second averages were also calculated for the first 30 seconds post-task to enable comparison with previous studies. The first second post-task was ignored as it takes the accommodation system approximately one second to respond to a change in stimulus [100, 101].

Table 3.4. 1.3 seconds of data from one participant for two separate tasks: a one minute 0 D task and a one minute 3.75 D. The data shows the period in time when the change in accommodation from distance to near occurs. Column 1: time, column 2: accommodative stimulus for 0 D task, column 3: accommodative response for 0 D task (figures in bold are response post task), column 4: average value of the post task 0 D accommodative response (averaged over 90 sec post task), column 5: accommodative stimulus for 3.75 D task, column 6: accommodative response for 3.75 D task (figures in italics are response post task), column 7: NITM (figures in italics minus value from column 4). It is possible for the accommodative response to drift below zero for the 0 D stimulus.

Time (s)	Accommodative stimulus for 0 D task (D)	Accommodative response (D)	Average post task 0 D accommodation value (D)	Accommodative stimulus for 3.75 D task (D)	Accommodative response (D)	NITM (D)
59.73	0	0.291		3.75	2.710	
59.76	0	0.284		3.75	2.710	
59.81	0	0.273		3.75	2.705	
59.85	0	0.258		3.75	2.693	
59.90	0	0.239		3.75	2.677	
59.94	0	0.216		3.75	2.657	
59.98	0	0.199		3.75	2.631	
60.05	0	0.147		0	2.602	2.919
60.09	0	0.098		0	2.575	2.892
60.13	0	0.049		0	2.551	2.868
60.18	0	0.001		0	2.533	2.850
60.22	0	-0.045		0	2.522	2.839
60.26	0	-0.092		0	2.513	2.830
60.30	0	-0.137		0	2.498	2.815
60.35	0	-0.184		0	2.474	2.791
60.39	0	-0.231		0	2.447	2.764
60.43	0	-0.280		0	2.416	2.733
60.48	0	-0.329		0	2.388	2.706
60.52	0	-0.375		0	2.361	2.678
60.56	0	-0.417		0	2.329	2.646
60.62	0	-0.454		0	2.289	2.606
60.66	0	-0.485		0	2.238	2.555
60.70	0	-0.512		0	2.179	2.496
60.75	0	-0.535		0	2.114	2.431
60.79	0	-0.555		0	2.046	2.363
60.83	0	-0.574		0	1.976	2.293
60.88	0	-0.601		0	1.902	2.219
60.92	0	-0.596		0	1.825	2.142
60.96	0	-0.594		0	1.742	2.059
61.01	0	-0.592	-0.317	0	1.656	1.973

3.3.1.3 Post-task group mean NITM values

The mean level of NITM for each second and over the first 2 -10 s, 11 – 20 s and 21 – 30 s post-task were calculated for each participant for each task. The group mean values for the whole cohort are shown below (Table 3.5 and Figure 3.3 and 3.4). Individual values are shown in Appendix 6, Figures A6.1 and A6.2.

Table 3.5. Group mean level of NITM (D) \pm 1 SD for each task duration during the first 30 seconds post-task.

Task duration (min)	Time post task (s)		
	2 - 10	11 - 20	21 - 30
1	0.79 \pm 0.89	0.66 \pm 0.89	0.77 \pm 0.95
10	0.93 \pm 0.89	0.58 \pm 0.64	0.50 \pm 0.76
20	0.56 \pm 0.65	0.40 \pm 1.03	0.20 \pm 0.93
30	0.69 \pm 0.52	0.67 \pm 0.84	0.50 \pm 0.58

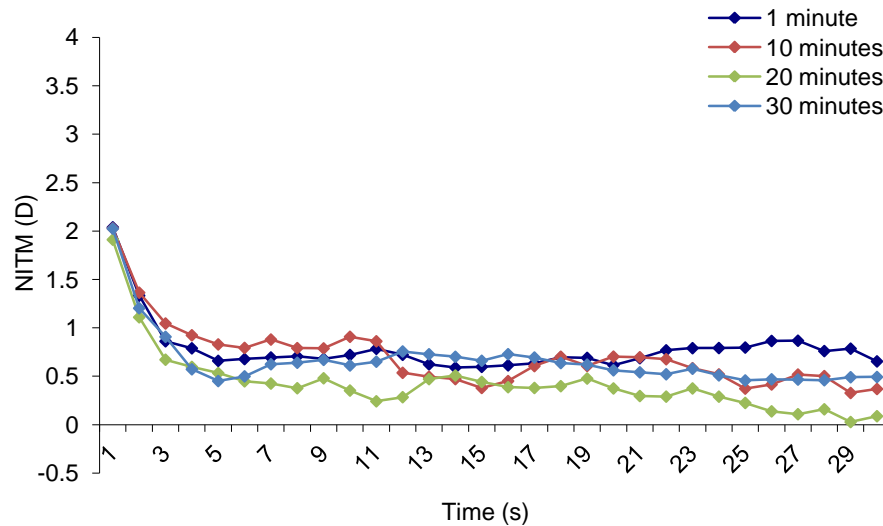


Figure 3.3. Group mean level of NITM per second (n = 21) for each task duration during the first 30 seconds post-task.

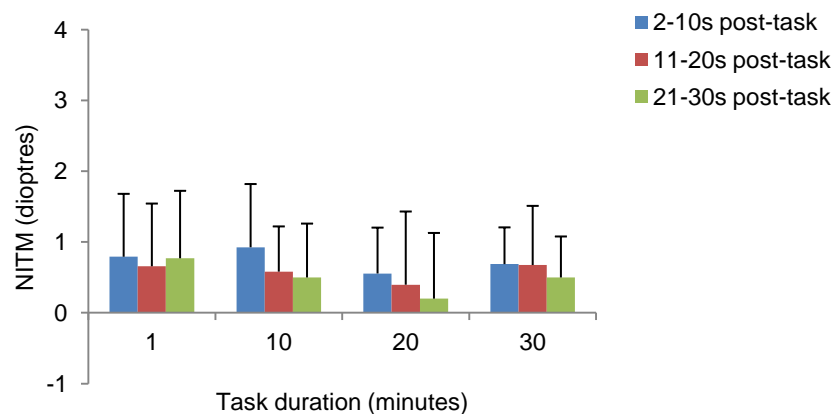


Figure 3.4. Group mean level of NITM (n = 21) for each task duration during the first 30 seconds post-task. The error bars show one standard deviation.

We can see from Table 3.5 that there is a large variation in the level of NITM post task

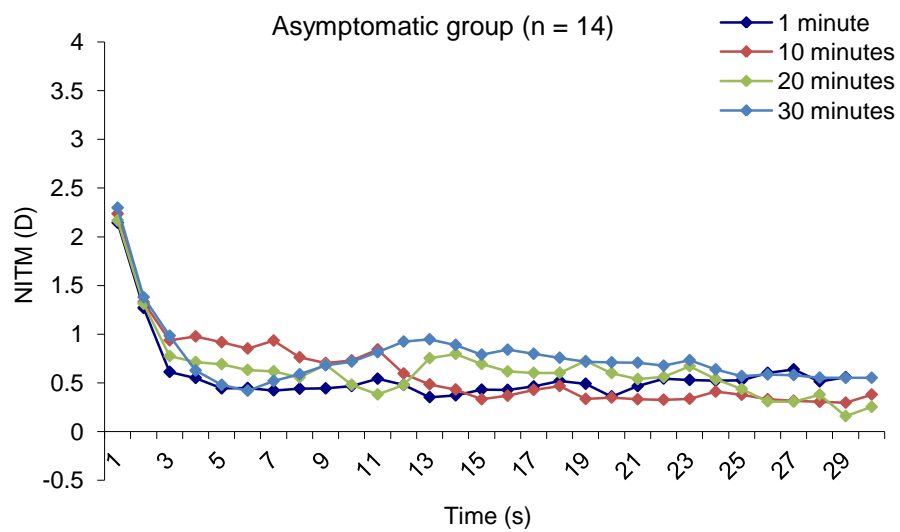
between individuals as shown by the standard deviations (group mean value 0.80 D). There was found to be no overall effect of task duration on the level of NITM post-task ($F_{(3,57)} = 2.306$, $p = 0.086$, power = 0.997). There was a significant effect of time post-task on the level of NITM ($F_{(1,45,27.63)} = 6.521$, $p = 0.009$) with NITM levels reducing with increased post-task time. Using simple contrasts this effect was found to be significant between 10 and 20 seconds post-task ($F_{(1,19)} = 5.928$, $p = 0.025$) and 10 and 30 seconds ($F_{(1,19)} = 8.179$, $p = 0.010$) post-task.

3.3.1.4 Comparison between post-task NITM values of asymptomatic and symptomatic individuals

There was found to be no statistically significant difference in age ($U = 38$, $z = -0.832$, $p = 0.425$) or mean MSE ($U = 28.5$, $z = -1.531$, $p = 0.133$) between the asymptomatic and symptomatic groups.

The mean post-task NITM values for the asymptomatic and symptomatic groups are shown in Figures 3.5 (a) and (b) and 3.6 (a) and (b).

(a)



(b)

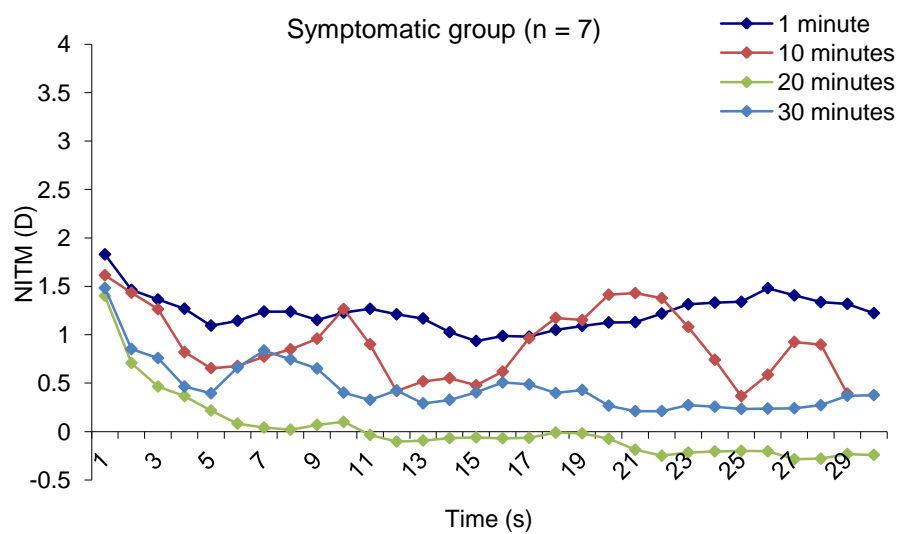


Figure 3.5. Mean level of NITM per second over the initial 30 s post-task for the asymptomatic group (a) and the symptomatic group (b).

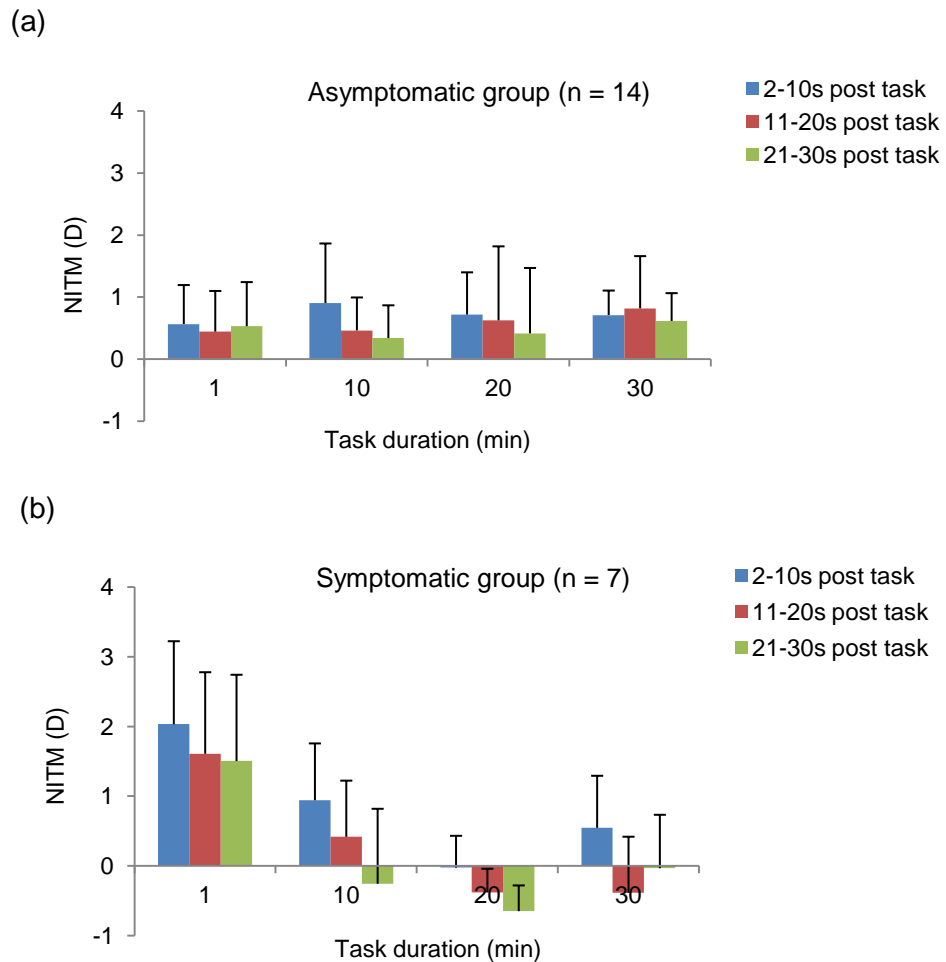


Figure 3.6. Mean level of NITM for the asymptomatic group (a) and the symptomatic group (b). The error bars show one standard deviation.

The mean standard deviation for all tasks was found to be slightly higher for the symptomatic group (0.81 D) than the asymptomatic group (0.72 D). There was no significant overall main effect of whether or not a participant suffered nearwork after-effects on their level of NITM post task ($F_{(1,19)} = 0.013$, $p = 0.912$, power = 0.073).

A significant interaction was found between the duration of the task and suffering of NITM symptoms ($F_{(3,57)} = 3.206$, $p = 0.030$), with the symptomatic group showing lower post-task NITM levels after longer task durations. Simple contrasts showed a significantly lower level of NITM post-task in the symptomatic group, after the 20 minute task as compared to the 1 minute task ($F_{(1,19)} = 5.710$, $p = 0.027$). The

difference between the 1 minute and 30 minute tasks also almost reached significance ($F_{(1,19)} = 4.127, p = 0.056$) with the NITM level after the 30 minute task being lower.

3.3.1.5 Regression

Absolute NITM may not be the best way of analysing the data as this does not take into account the accommodation level during the task. A participant who had higher accommodation during the task may be expected to have a larger amount of NITM during the first ten seconds post-task.

By working out the regression quotient [205] of the post-task NITM we can take into account the level of the accommodative response during the task. The regression quotient was calculated by dividing each of the calculated NITM values (shown in Table 3.4) by the average within-task accommodation value for that participant (Figure 3.7). The resulting values were converted to one second averages for the first 60 seconds post-task and then multiplied by 100 to give a percentage of the within task accommodation value.

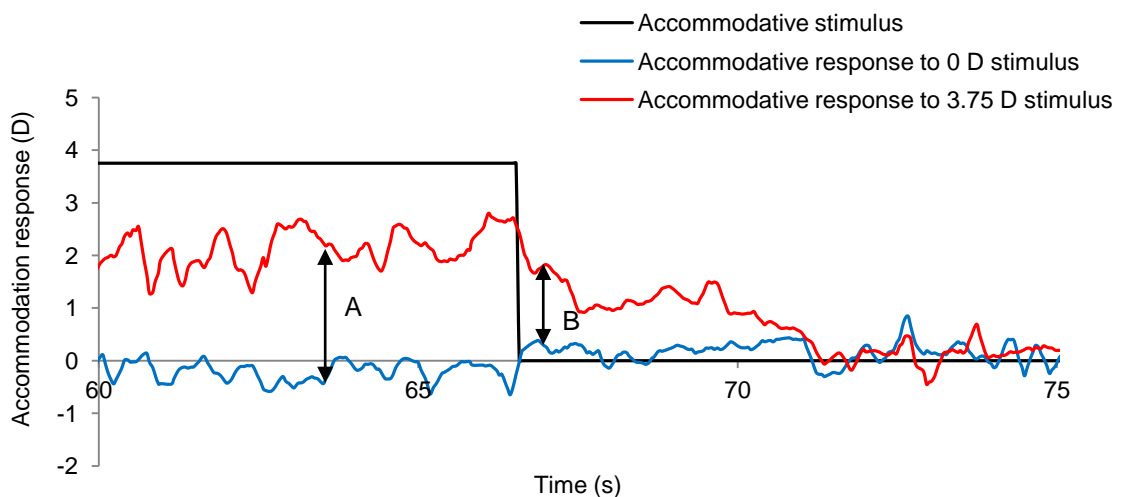


Figure 3.7. Fifteen seconds of accommodation data from one participant for both the 0 D and 3.75 D tasks. The regression quotient is calculated as $(B/A) \times 100$.

3.3.1.6 Post-task regression quotient for the whole cohort

The mean level of regression for each of the ten second, post-task bins, from 2 to 60 seconds was calculated for each participant. For three participants there was no 60 second data as, either due to a small pupil after the near task or dehydration of the contact lens, the post-task accommodation data was difficult to collect and only 30 seconds of post-task measurements were acquired. These participants are therefore excluded from the analysis. Two were in the asymptomatic group and one in the symptomatic group. The group mean values for the whole cohort are illustrated in Figure 3.8. (Individual values are shown in Appendix 6, Figures 6.3 and 6.4). In this graph, to illustrate the variance, standard error of the mean (SEM) is used, as the between participant SD was large and the error bars would have made the graph difficult to read.

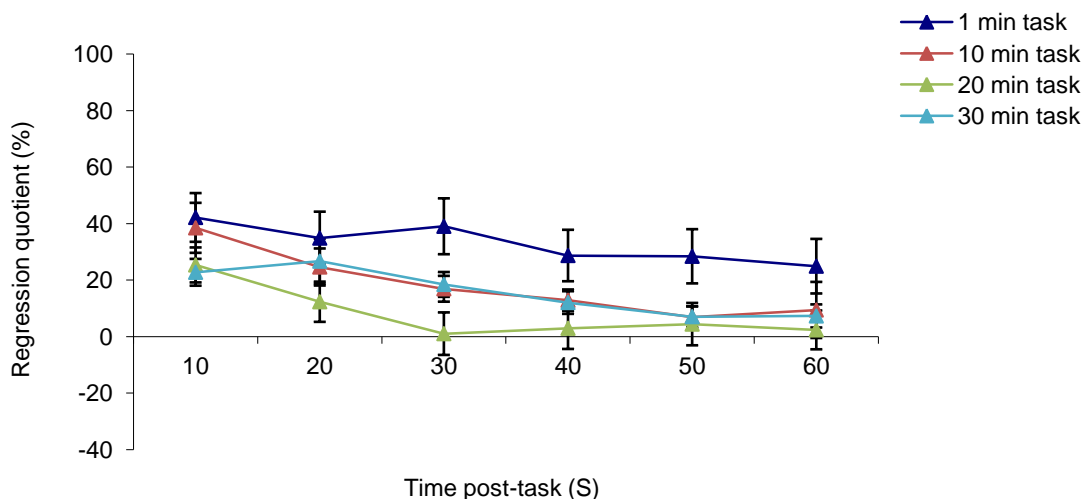


Figure 3.8. Group mean regression quotient (± 1 SEM) ($n = 18$) for each task duration during the first 60 seconds post-task. 100 % = no regression; 0 % = complete regression.

The group mean 2 – 10 s and 51 – 60 s bins were compared for each task duration. There was a main effect of task duration on regression of NITM post-task ($F_{(3,48)} = 3.301, p = 0.028$) with slower regression for the one minute task than the longer task durations. Simple comparisons showed this effect reached statistical significance

between the one minute and twenty minute task durations ($F_{(1,16)} = 7.520, p = 0.014$) and the one minute and thirty minute task durations ($F_{(1,16)} = 5.809, p = 0.028$). There was a significant effect of time post-task on regression of NITM ($F_{(1,16)} = 20.608, p < 0.001$) with NITM regressing more with increased time post-task.

3.3.1.7 Comparison between post-task NITM regression quotient for asymptomatic and symptomatic individuals

The group mean level of the regression quotient post-task for the asymptomatic and symptomatic groups are shown in Figure 3.9 (a) and (b).

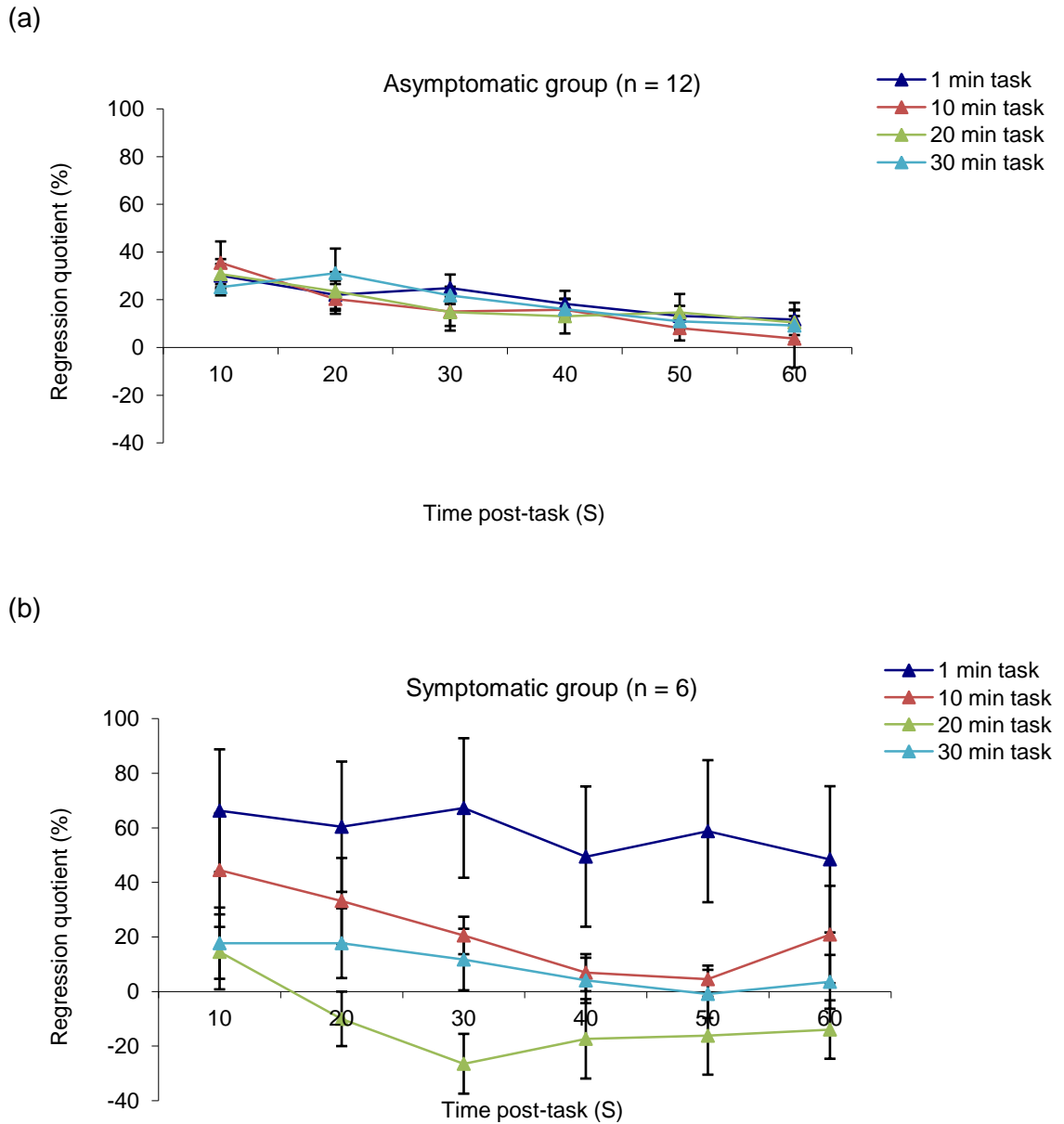


Figure 3.9. Group mean regression quotient of NITM (± 1 SEM) for (a) the asymptomatic group and (b) the symptomatic group.

There was no main effect of suffering nearwork after-effects on regression post-task ($F_{(1,16)} = 1.487, p = 0.240, \text{power} = 0.998$). There was, however, a significant interaction between task duration and suffering NITM symptoms ($F_{(1,48)} = 3.205, p = 0.031$) with those in the symptomatic group having slower regression to the one minute task than those in the asymptomatic group. Simple contrasts showed that this effect reached

statistical significance between the one minute and twenty minute task durations ($F_{(1,16)} = 6.584, p = 0.021$) and the one minute and thirty minute task durations ($F_{(1,16)} = 6.702, p = 0.020$).

3.3.2 Experiment 2

In Experiment 2 the dioptric demand of the task was altered while the task duration remained constant. From the original 21 participants, three were not available for the second part of the study. The 18 remaining participants had an age range again from 18-35 years and median age 20 years. The group was composed of five EMMs, seven EOMs and six LOMs. Seven participants were aware of distance vision blur after undertaking periods of near work (39 %). Three were LOMs, three EMMs and one an EOM. The mean MSE error of the cohort was $-2.35 \text{ DS} \pm 2.28$ and median -1.38 D (range $+0.38 \text{ D}$ to -6.50 D). Within-task accommodation level was calculated for each dioptric demand as for Experiment 1. The results are shown in Table 3.6.

Table 3.6. Group mean within task accommodation response values (\pm SD) for each accommodative stimulus level for all participants, the asymptomatic group and the symptomatic group.

Accommodative stimulus of task (D)	Within-task accommodation (D)			Difference (asymptomatic - symptomatic)
	All participants	Asymptomatic	Symptomatic	
1	0.55 \pm 0.89	0.68 \pm 1.10	0.34 \pm 0.36	0.64
2	1.25 \pm 0.81	1.49 \pm 0.87	0.86 \pm 0.57	0.63
3	2.00 \pm 0.66	1.97 \pm 0.82	2.04 \pm 0.34	-0.07
3.75	2.42 \pm 0.78	2.47 \pm 0.72	2.35 \pm 0.91	0.12

For every level of dioptric demand except 3 D those participants who complained of NITM symptoms had a lower mean within-task accommodation level than those who did not have symptoms. There was no statistically significant difference in the within-task accommodation levels of the two groups ($F_{(1,16)} = 0.676, p = 0.423, \text{power} = 0.905$).

3.3.2.1 Post-task group mean NITM values for the whole cohort

The mean level of NITM over the first 2 -10 s, 11 – 20 s and 21 – 30 s post-task were calculated for each participant for each task as in Experiment 1. The group mean values are shown in Table 3.7 and Figure 3.10. Individual values are shown in Appendix 6, Figures 6.5 and 6.6.

Table 3.7. Group mean level of NITM (D) \pm 1 SD for each accommodative stimulus during the first 30 seconds post-task.

Dioptric demand of task (D)	Time post-task (s)		
	10	20	30
1	0.04 \pm 0.68	-0.21 \pm 0.58	-0.21 \pm 0.59
2	0.03 \pm 0.53	-0.04 \pm 0.62	-0.03 \pm 0.68
3	0.51 \pm 0.78	0.25 \pm 0.84	0.13 \pm 0.92
3.75	0.82 \pm 0.74	0.58 \pm 0.74	0.66 \pm 0.73

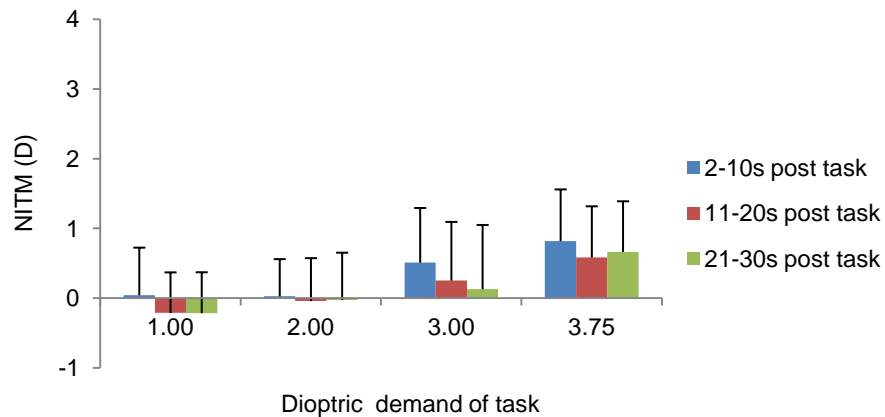


Figure 3.10. Group mean level of NITM (D) for all participants (n = 18) for each accommodative stimulus during the first 30 seconds post-task. The error bars show one standard deviation.

There was found to be a main effect of accommodative stimulus on the level of post-task NITM ($F_{(1.54,24.65)} = 8.902, p = 0.002$); the higher the dioptric value of the task the greater the NITM value post-task. Post hoc tests were carried out using the Bonferroni method and the p values for these are shown in Table 3.8.

Table 3.8. Table showing p -values for the post hoc tests performed to compare the level of NITM post-task for tasks of different dioptric demands. * indicates those p -values significant at the 0.05 level.

Dioptric value of task	1	2	3	3.75
1	-----	1.000	0.178	0.004*
2	1.000	-----	0.03*	0.011*
3	0.178	0.03*	-----	0.618
3.75	0.004*	0.011*	0.618	-----

There was also found to be a significant effect of time post-task on the level of NITM ($F_{(1.30,20.82)} = 12.408, p = 0.001$). NITM was found to reduce over time. Simple contrasts showed this effect to be significant between the 2 – 10 second and 11 – 20 second time periods ($F_{(1,16)} = 18.332, p = 0.001$) and 2 – 10 second and 21 – 30 second time periods ($F_{(1,16)} = 11.703, p = 0.004$).

3.3.2.2 Comparison between post-task NITM values of asymptomatic and symptomatic individuals

The mean NITM values post-task for the asymptomatic and symptomatic groups are shown in Figure 3.11 (a) and (b).

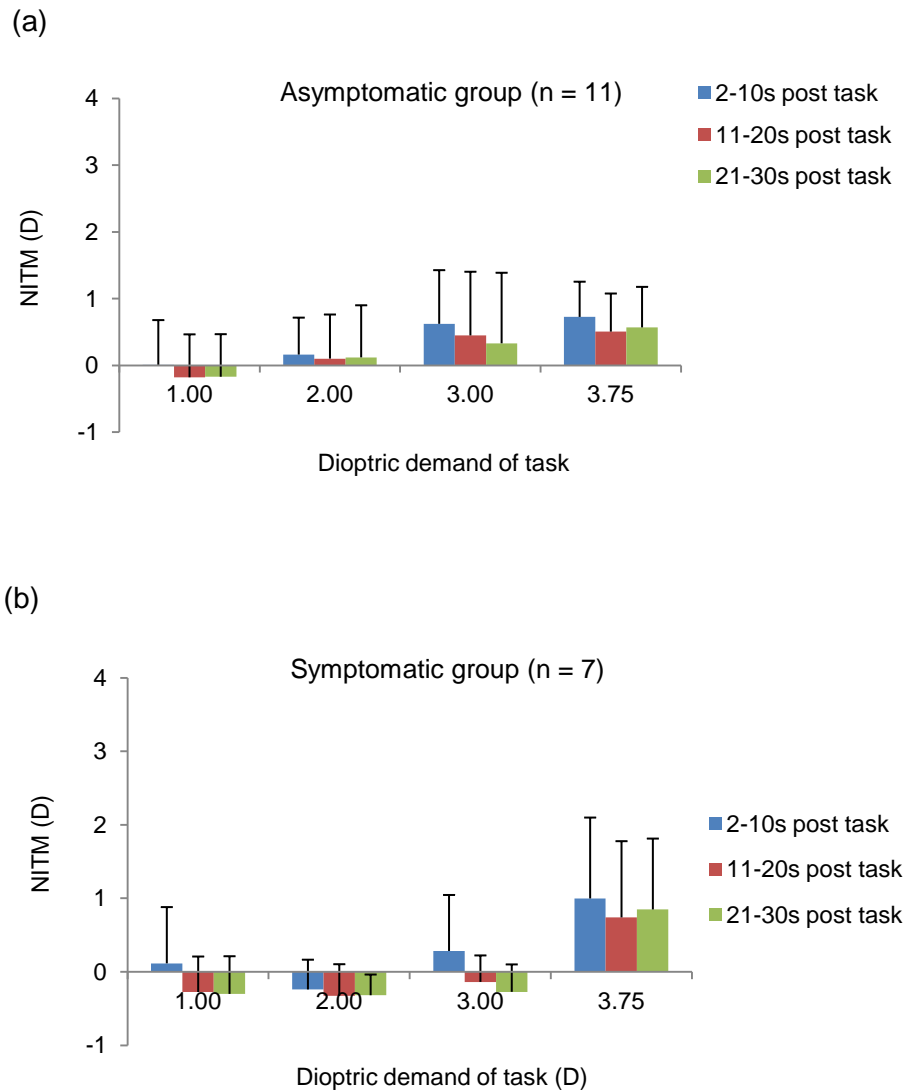


Figure 3.11. Group mean level of NITM (D) for (a) the asymptomatic group and (b) the symptomatic group. Error bars show one standard deviation.

There was no significant main effect of whether or not a participant suffered nearwork symptoms on their level of NITM post-task ($F_{(1,16)} = 0.27, p = 0.611, \text{power} = 0.544$).

3.3.2.3 Post-task regression quotient for the whole cohort

The mean level of regression for each of the 10 second, post-task bins, from 2 to 60 seconds was calculated for each participant. Again, for three participants there was no 60 second data. The group mean values for the whole cohort are illustrated in Figure 3.12. The one dioptre task was excluded from the analysis as for some participants the

NITM was a negative figure which made it impossible to calculate the regression. Individual values are shown in Appendix 6, Figures 6.7 and 6.8.

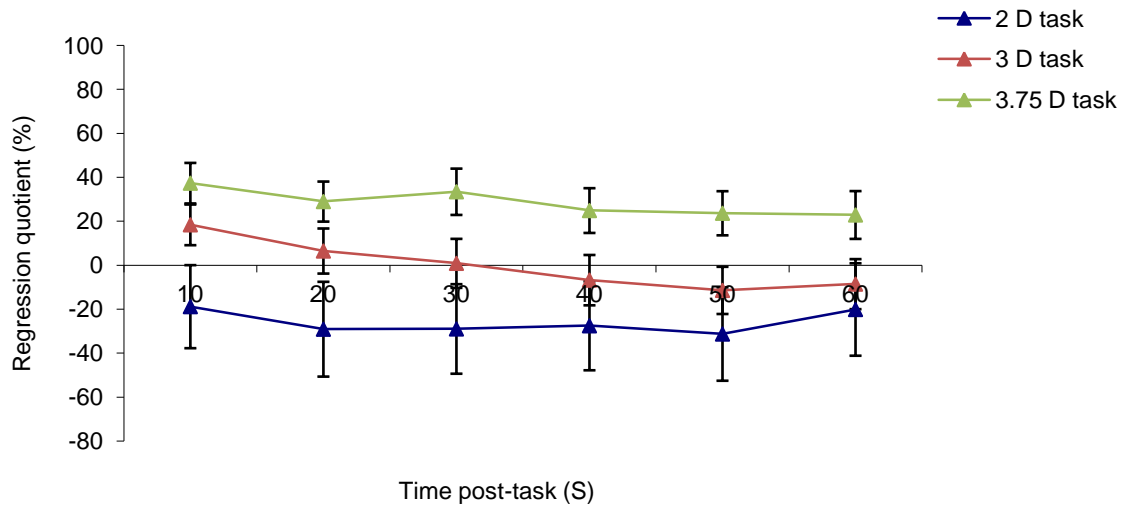


Figure 3.12. Group mean regression quotient for each dioptric demand (± 1 SEM) ($n = 15$) during the first 60 seconds post-task.

The group mean 2 – 10 s and 51 – 60 s bins were compared for each dioptric level. The main effect of dioptric demand of task on percentage regression of NITM post-task was found to be significant ($F_{(2,26)} = 4.505, p = 0.021$) with increased dioptric task giving slower regression post-task. Simple contrasts showed this difference to be significant between the 2 D and 3.75 D task levels ($F_{(1,13)} = 5.773, p = 0.032$).

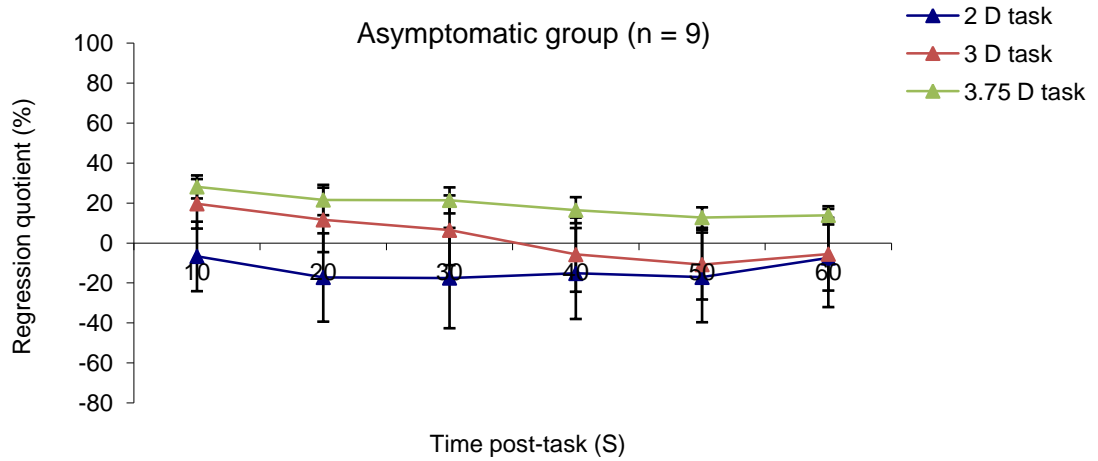
Time post-task had an overall significant effect on regression of NITM ($F_{(1,13)} = 5.096, p = 0.042$) with greater regression after 51 – 60 s post task than 2 – 10 s. There was also a significant interaction between the dioptric value of the task and the time-post task ($F_{(1.24,16.13)} = 4.377, p = 0.046$) with slower regression for greater dioptric task values.

3.3.2.4 Comparison between post-task NITM regression quotient for asymptomatic and symptomatic individuals

The group mean post-task regression quotient for the asymptomatic and symptomatic

groups are shown in Figure 3.13 (a) and (b).

(a)



(b)

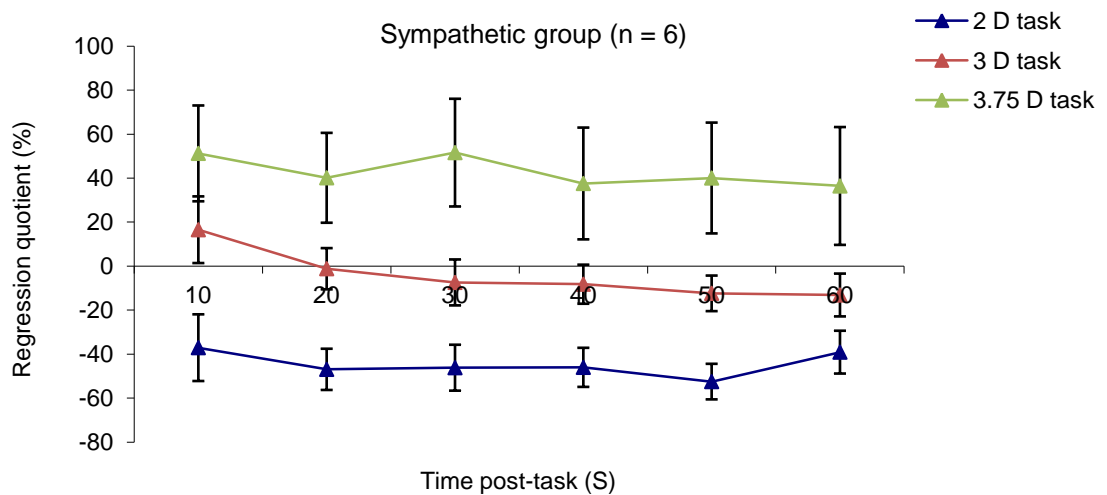


Figure 3.13. Group mean regression of NITM (D) \pm 1 SEM for the asymptomatic group (a) and the symptomatic group (b).

From Figure 3.13 it appears that the regression post-task in the asymptomatic group is similar for all dioptric demands, whereas in the symptomatic group there appears to be a noticeable dose effect with the regression being reduced after the higher dioptric demands. There was no main effect of suffering nearwork after-effects on regression of

accommodation post-task ($F_{(1,13)} = 0.039$, $p = 0.846$, power = 0.110).

3.4 Discussion

The literature regarding the effect of near task duration and dioptric demand of task on the size and time-course of NITM is inconclusive. The aim of this experiment was to investigate the contribution of these factors to the incidence and severity of NITM. The main findings of this study show that increasing task duration does not increase the level, or slow the regression of post-task NITM, however an increase in the dioptric demand of the task does increase the level and slow the regression of post-task NITM. A secondary finding was that those participants who suffer symptoms of NITM appear to have a more variable post-task NITM response than those who are asymptomatic and have higher levels and slower regression of NITM, particularly for the shorter task durations and higher dioptric task values.

3.4.1 Within-task accommodation values

The group mean within-task accommodation values show a lag of accommodation to the task at all levels of accommodation, which increases as the dioptric demand of the task increases from 0.45 D for the 1 D task to 1.33 D for the 3.75 D task. The lag of accommodation is large compared with that found by other investigators for similar task demands in a population with a similar age [83]. No lead in accommodation with lower dioptric tasks was observed. As the within-task measurements were taken during the last 60 seconds of each task duration, there is a possibility the participants may have been tiring when these measurements were taken. No significant difference, however, was found between the within-task accommodation for the 1 minute task and the 30 minute task, so there is no evidence that fatigue is a factor. The participants were reminded throughout the experiment to keep the task in focus, and the fact it was a cognitive task should have improved the accommodative response [207]. As the

numbers in the 'minesweeper' game were relatively large targets (equivalent to about 6/48) it is possible a smaller target may have encouraged more accurate accommodation. However, no variation in accommodative response has been shown between target sizes of 14, 21 and 28 minutes of arc [169]. A specially designed computer program which fitted within the Badal lens and consisted of a cognitive task with letters or numbers of 6/6 equivalent may have been a better task.

Those participants who suffered symptoms after nearwork were found to have an accommodative lag which was consistently higher for all tasks except that of 3 D. This reached statistical significance in Experiment 1 but was only a trend in Experiment 2.

3.4.2 Task duration and NITM

The group mean levels of NITM found during experiment 1 varied from 0.56 D to 0.79 D during the first 10 seconds post-task. Using similar continuous recording equipment Wolffsohn *et al.* [101] found values of 0.75 D for their EOMs and 0.66 D for their LOMs, however this was averaged over 180 seconds post-task and would presumably have been much greater during the initial 10 seconds post-task. Compared to most of the other studies our results show a higher level of NITM [90, 91, 96, 98] which may be due to the continuous nature of the recording. In these previous studies autorefractor readings were static and often the participant had to be moved to the autorefractor at the end of the task causing measurements during the initial 2 -10 seconds post-task to be missed. As this period appears to be when NITM is at its highest [101] these missed data could affect i.e. underestimate the NITM levels considerably.

There was found to be a large between subject variability shown by the group mean standard deviation of the NITM being about 0.80 D; this is slightly higher than found in most other studies which have had standard deviation values < 0.6 D [90, 93, 99-101]. This may just be specific to our participants, although Jaschinski-Kruza [194] did

comment that due to the large between subject variability it may not be appropriate to average NITM responses over a whole group.

Increased task duration was not found to increase the level, or slow the regression of NITM post-task. In fact the opposite was found to be true, with the largest levels of NITM being found after the 10 minute task (0.93 D) and slowest regression being found after the 1 minute task. The lowest levels of NITM and quickest regression were found after the 20 minute task. For the 30 minute task duration the NITM level 2 – 10 seconds post task (0.69 D) was found to be slightly higher than that for the 20 minute task (0.56 D) although this was not statistically significant.

As participants were undertaking the task whilst situated on the chin rest of the autorefractor, it would be difficult to undertake any longer task durations due to participant discomfort. If the task was undertaken whilst not on the autorefractor no within-task accommodation levels would be measured, and no data would be collected in the period immediately post-task as the transition to the autorefractor was taking place. Unfortunately, as this is the case the experiment is limited as to the duration of task which can be carried out. It is possible that as task duration increases past 30 minutes the NITM may increase again and the regression slow which would indicate that a task duration of 20 minutes could be the ideal length for minimizing NITM.

When the data for the asymptomatic and symptomatic groups were analysed separately a different pattern was seen. In the asymptomatic group, little difference in the level of NITM or regression post-task was found between different task durations. The symptomatic group had higher levels of NITM and slower regression post-task for the 1 and 10 minute duration tasks than the longer tasks. This is in agreement with Cuiffreda and Ordonez [91] who noted that after a 10 minute task their symptomatic individuals had a large initial post-task myopic shift and slow or only partial regression. As discussed below, it is possible that these symptomatic individuals are the ones who have access to sympathetic innervation of the ciliary muscle.

3.4.3 Dioptric demand and NITM

Unlike previous studies [89, 199] we have found that increasing the dioptric value of a task does indeed cause increased post-task NITM and slower regression. We found negligible amounts of NITM for the 1 and 2 D stimuli, however this increased for the 3 and 3.75 D stimuli. It is possible that this was not found in previous studies due to a time delay between ending the task and taking the accommodation measurements.

When the asymptomatic and symptomatic groups were analysed separately no significant effect of dioptric demand was found. However, examination of the graphs suggests the asymptomatic group have a systematic increase in NITM with increased dioptric value of task, whereas the symptomatic individuals have a similar level of NITM for the 1, 2, and 3 D tasks but a large rise for the 3.75 D task. There is a similar pattern for the regression data.

The fact that no significant difference was found between the two groups may be due to the large between-subject variance, and the small sample size for the symptomatic group. As we recruited the participants before asking them if they suffered from NITM symptoms it was impossible to know how large the symptomatic group would be until the experiment had begun.

It can also be seen that for the lower dioptric tasks, particularly the one and two dioptre tasks, that for some participants both the NITM and regression quotient appear to be negative values. The baseline settings for each participant within the continuous recording software were set with them focusing a 0 D accommodative target within the Badal system. These settings were then used every time measurements were taken. It is possible with some participants that accommodation was still active when these baseline settings were calculated and therefore with the lower accommodative targets accommodation then dropped below zero.

3.4.4 Sympathetic system and NITM

The main innervation to the ciliary muscle controlling accommodation is via the parasympathetic branch of the autonomic nervous system, however, there is also sympathetic innervation present [103]. The parasympathetic system causes excitation and a rapid (one to two second) accommodation response, while the sympathetic system is inhibitory and produces a smaller (maximum of 2 D), slower response (onset of action 10 to 40 seconds) which is directly related to the level of activity of the parasympathetic system [208]. Recent research [105, 205] has shown that about 30 % of individuals have access to this sympathetic innervation, and when it is blocked an increase in NITM is demonstrated.

It is possible that the symptomatic individuals in our study may be the ones who have access to this sympathetic innervation and this could explain why they have larger levels of NITM and slower regression to the one minute task. When an individual who has no access to sympathetic innervation accommodates, excitation of the parasympathetic system causes the accommodative response and when the stimulus is removed the response disappears. A similar effect will occur whether the stimulus lasts 1 minute or 30 minutes. In an individual who has access to sympathetic innervation, accommodation to a stimulus occurs in the same way via the parasympathetic system, however at the same time a sympathetic, inhibitory response builds up to aid reduction of accommodation once the stimulus has been removed. This response is thought to take 10 – 40 s to build up and depends on the level of parasympathetic innervation [103]. Once the accommodative stimulus is removed the sympathetic system is thought to aid in reducing the level of accommodation back to baseline due to its inhibitory role. It is possible that for longer task durations this works effectively, however for the shorter task durations (particularly the one minute task), the sympathetic system may not be working to its maximum capacity before the task finishes and therefore is not as effective at reducing the level of accommodation post-

task. As these individuals are used to having input from the sympathetic system to aid with relaxation of accommodation, if this system is not working efficiently e.g. for short task durations, it may cause them to struggle. Sympathetic access may also explain why the within-task accommodation values are lower in the symptomatic group as the inhibitory action of the sympathetic system may make accurate accommodation more difficult.

If NITM is persistently present, cumulative distance vision blur could cause axial elongation making these individuals more susceptible to myopia development and progression. As already discussed in the introduction, blur causes myopia in animal models. However, the distance vision blur induced with NITM is myopic and animal studies have shown myopic blur causes axial length growth to slow down to compensate [38, 41, 42]. There is little literature available on the effects of blur in humans, however form deprivation has been shown to cause axial elongation [43-46]. Hung and Ciuffreda [106] suggested that axial length regulation may be controlled by change in retinal blur rather than just the presence of blur alone which gives no directional cue. An increase in the area of retinal defocus may retard axial length growth while a decrease in retinal defocus area may increase growth. As NITM induces the equivalent of a slight plus lens at near this may gradually increase over time as the NITM builds up which would reduce retinal blur at near causing axial length growth and myopia.

The participants for our experiment were chosen randomly from the staff and students of the Bradford School of Optometry and Vision Science and were enrolled for the study before being asked if they noticed symptoms of NITM. Although this is a very subjective question and open to interpretation, we consistently found throughout our studies that the percentage of individuals answering yes to this question was about 30%, a similar percentage to those who are thought to have access to sympathetic innervation.

3.4.5 Experimental limitations

A number of experimental limitations have already been discussed in Section 3 such as the visual demand of the task, limited task duration, small sample size and stimulation of accommodation whilst calculating baseline settings for the continuous recording equipment.

The large variability between the accommodation responses of different participants has also been commented on. One participant can have a large effect on the group mean if they have a particularly unusual accommodative response, and this is more noticeable in such a small sample. We did not test for repeatability of post-task accommodation responses, however, Strang *et al.* [209] found post-task regression to be repeatable using a Canon R1 optometer.

Participants were classified as symptomatic or asymptomatic by asking if distance vision blur was ever noticed after a period of nearwork. It is difficult to quantify these symptoms and there is no indication as to whether this distance blur causes a problem during everyday life. The information may have been more reliable had we asked participants to keep a diary for a period of time recording as and when they noticed distance vision blur. Another alternative would be to ask subjects to send a text message at any time in the day when NITM was apparent.

With some participants there was difficulty taking the continuous recording measurements, especially after the 30 minute task duration, as the pupil became too small to get a meaningful accommodative trace before the target change. For other individuals contact lens wear created problems in obtaining a clear ring image due to dryness induced by the prolonged task duration. This meant three participants were removed from the regression analysis, as only 30 seconds of reliable post-task accommodation measurements could be obtained.

Chapter 4

Myopia progression in optometry students over a two year period, ocular correlates and association with nearwork-induced transient myopia (NITM)

4.1 Introduction

4.1.1 Prevalence of myopia in the general population

The prevalence of myopia varies in different areas around the world. Recent population studies indicate levels of 50% in a cohort of 20 to 39 year olds in the United States [7], just below 30% in European adults aged between 17 and 88 years [11, 12], 54% of young adults in the Middle East aged 17 to 40 years [16], 31% in Australian adults aged between 19 to 83 years [2] and over 70% in young adults in some Far Eastern countries [18, 19].

Although there is a hereditary element to myopia development [210], myopia prevalence appears to be increasing [1, 4] and this is believed to be linked to environmental factors, in particular an increase in nearwork [211] and a reduction in outdoor activity [61, 71, 212]. Different generations of genetically related family members in Alaska show a different prevalence of myopia [67] which appears to be associated with a change in the schooling system from voluntary to compulsory. Those schooled after the change showed a higher myopia prevalence (43.4%) compared to those schooled before (13.8%), with little correlation between parental myopia and that of their children. A difference in myopia prevalence between siblings has been observed in an Orthodox Jewish population, where the boys are educated in a nearwork intense environment and have a much higher myopia prevalence (81.3%) than that of their sisters (36.2%) [31]. Populations living in rural environments as

opposed to city dwellers in the same country have also been seen to have a lower prevalence of myopia (2.7% compared to 11.3%) [23].

Daylan *et al.* [1] have shown that in a population of 16 to 22 year old conscripts over a period of 13 years, myopia prevalence increased from 20.3% to 28.3%: this increasing prevalence was greater for low myopes (< 3D) than for high myopes (> 6D). As high myopia appears to have more of a genetic origin [3], this adds weight to the hypothesis that changes in prevalence may also be driven by environmental factors.

A number of studies have linked higher myopia prevalence with higher educational qualifications and professional occupations [1, 11], however, IQ has been shown to be an independent risk factor for myopia [72]. A genetic link between myopia and intelligence may mean that nearwork has little effect on myopia progression and cerebral and ocular growth are both genetically determined.

4.1.2 Prevalence of refractive errors in student populations

Certain occupational groups have been found to have a higher prevalence of myopia than that found in the general population [73, 74]. A number of studies have investigated the prevalence of refractive errors in student populations (Table 4.1). Myopia prevalence in students in Asia [65], America [5, 213, 214] and Europe [25, 26, 76, 112, 215-217] is higher than that of the general population, varying between 22 % in Serbian students to 93 % in Taiwanese medical students. This is thought to be linked to the intense nearwork these students undertake. During these studies various factors associated with myopia progression and development have also been investigated, such as ethnic origin [76], family history [112, 217], personality traits [217], nearwork [112], binocular dysfunction [215], physical activity [75] and darkness exposure [214].

4.1.3 Difficulty in comparison of refractive error studies

Table 4.1 illustrates the difficulty involved when comparing refractive error prevalence studies. There is no standardisation of the protocol between the studies and this may affect the prevalence rates obtained.

4.1.3.1 Classification of refractive error

The criteria used for the classification of refractive error varies between studies. Typically, the classification of myopia ranges from $\leq -0.25\text{D}$ [5, 26, 65] to $\leq -0.75\text{D}$ [112] while the classification for hypermetropia ranges from $\geq +0.25\text{D}$ [5] to $\geq +2\text{D}$ [215] (Table 4.2). Depending on the criterion used, the prevalence of refractive errors within a population will be different compared to studies using an alternative classification. O’Neil and Connon [5] classified emmetropia as 0 D. Such a narrow classification could cause a number of emmetropes to be classified wrongly purely due to instrument or practitioner inaccuracy.

4.1.3.2 Measurement of refractive error

A variety of methods have been used to assess refractive error. A number of studies relied on student information and questionnaires [213, 214, 216, 217]. Inaccuracies in data may be attributed to non-standardised examinations, out of date information and participants giving incorrect information. Studies involving cycloplegic refraction [5, 25, 26, 65, 75, 112, 215] may show a lower myopia prevalence than those involving non-cycloplegic refraction [76, 218] as the use of cycloplegia has been shown to produce a more positive refractive result [172]. There are also studies which have used objective retinoscopy [215] and subjective refraction [5, 25, 26, 218] which may also give a slightly different result to autorefraction [219].

4.1.3.3 Age range

The age range of the participants in the cohort may affect the prevalence of refractive error. Although most of the student population studies tend to have participants in their twenties, there are a number of investigations which include participants over the age of 40 years [214, 216, 218]. Longitudinal studies have indicated that after the age of 40, myopia prevalence tends to reduce [32] which may reduce the myopia prevalence in those cohorts containing older participants.

4.1.3.4 Analysis of data

Methods of data analysis vary between studies. Using the most ametropic eye [213] will overestimate prevalence in a population whereas using both eyes in analysis [5, 65] may artificially inflate the correlation between refractive error and ocular biometry measurements. A number of studies have removed this factor by analysing the right eye only [25, 26, 75, 76, 112, 216, 218] or taking the average mean spherical equivalent (MSE) of the two eyes [214, 217].

4.1.4 Ocular correlates of myopia and myopia progression

Changes in the amount of myopia have been shown to correlate directly to changes in axial length (AL) and vitreous chamber depth (VCD) in both early and late onset myopia [25-27, 56]. There does not appear to be a correlation between changes in refractive error and anterior chamber depth or corneal curvature [65]. The crystalline lens seems to become slightly thinner during myopia progression, however, this may be a way of the eye trying to compensate for the axial length growth [57]. Axial length to corneal radius ratio (AL/CR) shows a strong correlation to refractive error, with myopes having higher AL/CR ratios than emmetropes or hypermetropes. Moreover, children exhibiting an AL/CR ratio greater than three appear to be more prone to developing myopia [58].

4.1.5 Myopia progression

Progression of myopia again varies between populations. There are few longitudinal refractive error studies involving the general population: however, a study on children in China aged between 5 and 15 years has shown an average increase in myopia of -0.21 D per year [64], whereas young adults in New Zealand have been found to progress by only -0.07 D per year [220]. In Singapore [27] children between the age of seven and nine years were found to have an average increase in axial length of 0.3 mm per year equating to about -0.75 D myopic shift.

More literature is available regarding myopia progression rates in cohorts of myopic children. Annual progression rates of between -0.5 D and -0.93 D [27, 135, 139, 141, 144-146, 150] have been reported in children younger than 15 years in the Far East, with slightly lower rates of between -0.36 and -0.73 D [59, 140, 142, 152] in the USA.

In any myopia progression study the repeatability of the instrumentation used is a critical factor in determining whether the progression is genuine, or due to instrument error. In all the studies mentioned above the annual refractive error changes are very small compared to the standard deviation of the group mean change. Bland and Altman [221] devised a method to assess the agreement between two independent variables as opposed to correlation which will only consider the association between two independent variables. This method can determine the repeatability of the measurements taken by an instrument. Having taken two sets of measurements on the same cohort the difference between the first and second measurement is plotted against the mean of the two measurements for each participant. The 95% limits of agreement are calculated, and, during a myopia progression study, if a shift in either prescription or ocular component is greater than the 95% confidence interval it is most likely to represent a true change in the parameter. Zadnik *et al.* [219] calculated these limits of agreement for various measurement methods and found cycloplegic

autorefraction to have the narrowest 95% limits of agreement. Table 4.1 shows the results found for various methods of refraction.

Table 4.1. Mean difference and 95% limits of agreement for the repeatability of refractive measurements on two separate occasions (from Zadnik *et al.* [219]).

Measurement method	Mean difference (D)	95% limits of agreement (D)
Non-cycloplegic retinoscopy	-0.006	-0.78 to 0.77
Non-cycloplegic subjective	-0.063	-0.69 to 0.56
Non-cycloplegic autorefraction	-0.007	-0.72 to 0.71
Cycloplegic retinoscopy	0.075	-0.87 to 1.02
Cycloplegic subjective	-0.013	-0.95 to 0.93
Cycloplegic autorefraction	0.049	-0.27 to 0.37

Table 4.3 compares a number of studies investigating myopia progression in university student populations. In these studies, myopia progression has been found to be at a rate of between -0.10 D and -0.17 D per year (presuming the refractive error changes by the same rate every year), with a corresponding increase in AL of between 0.04 and 0.11 mm per year.

These progression studies are easier to compare than the refractive error studies as they have all used cycloplegic refraction, although some have used autorefraction methods [26, 65, 75, 112] and some subjective refraction [25]. Onal *et al.* [112] compared the two methods and found -0.19 D greater progression over one year using a subjective technique compared to an autorefractor. O’Neal and Connon [5] used retrospective data in their study, the data being taken by a number of practitioners. The 95% limits of agreement of repeatability for subjective refraction by the same practitioner have been estimated at ± 0.63 D [219]. It would be thought when considering repeatability between two different practitioners, these values may be slightly larger, suggesting a shift in prescription of 0.75 D would be needed before it can be considered a true progression in myopia.

4.1.6 Myopia progression and nearwork-induced transient myopia (NITM)

Early onset, late onset and progressing myopes have been shown to be more susceptible to NITM than stable myopes or emmetropes [90, 93, 98, 99, 101]. It is possible that NITM may be either linked to a susceptibility to myopia development and progression, or may even be a causative factor [106]. Alternatively, symptoms of NITM may be linked to myopia itself and have nothing to do with the cause.

Vera-Diaz *et al.* [99] and Vasudevan and Ciuffreda [98] classified progressing myopes as those who had progressed by -0.50 D or more over a two year period. The participants were divided into groups using retrospective refractive data. In the first study [99] this was available from university eye clinic records, whereas the origin of the refractive data for the second study [98] is unknown. The refractive data is therefore most likely to have been taken subjectively by a variety of practitioners and no axial length data were taken to confirm the biometric basis of progression.

The studies discussed above have all used objective measurements of NITM as discussed in Section 3.1.1. As a smaller pupil gives a larger depth of focus [200] two individuals who have the same level of NITM measured objectively may have different levels of retinal blur. One may be aware of distance vision blur whereas the other may not as their smaller pupil size may cause the image to be within their depth of focus.

Only one study has asked the participants if they are subjectively aware of NITM [91], and this study concluded that those who were aware of NITM had an abnormal post-task transient myopia profile with three components: a large initial myopic shift, a slow initial decay and overall increased response variability. As cumulative distance blur has been suggested as pre-cursor to axial length growth and myopia progression [106] it is possible that if an individual is aware of blur caused by NITM they may be more susceptible to myopia progression than those who are not.

4.1.7 Aim of the study

The principal aim of this investigation is to track the development and progression of myopia in a cohort of optometry undergraduates over a two year period. The research will determine whether any correlation is present between myopia progression, and either post-task NITM levels, post-task NITM regression or subjective awareness of NITM. No previous longitudinal study has investigated these associations prospectively. A secondary aim of this study will be to investigate correlations between myopia progression and heritability, ethnic origin, nearwork and participation in sporting activities, in addition to the ocular biometric correlates of myopia and myopia progression.

Table 4.2. Comparison of refractive error prevalence studies on student populations (M = myope, E = emmetrope H = hypermetrope).

Study	Subjects	Number	Age (years)	Refractive method	Criteria (D)	Prevalence (%)	Mean Rx (D) ± SD
Septon 1984 [213] (retrospective)	Optometry students Oregon	447 (most ametropic eye used)	20-37 (average 25)	Questionnaire	E 0 ± 0.37	M 74 E 17 H 9	-2.22 ± 2.33
O'Neal, Connon 1987 [5] (retrospective)	Cadets at United States Air-Force Academy	497 (994 eyes used in analysis)	17-21 (mean 18.5)	Non cycloplegic subjective / cycloplegic subjective	M ≤ -0.25 H ≥ +0.25	M 44 E 19 H 37	-0.55 ± 1.52
Bullimore 1989 [217]	Optometry students Aston	189 (mean sphere of R&L eyes)	18-36 (mean 20.7 ± 2.6)	Questionnaire	E ± 0.50	M 56 E 38 H 6	Not specified
Lin <i>et al.</i> 1996 [65]	Medical students Taiwan	345 (690 eyes used in analysis)	18-21	Cycloplegic autorefraction/ checked by ret	M ≤ -0.25	M 93	Males -4.36 ± 2.68 Females -3.71 ± 2.50
Osuobeni 1999 [218]	Students and staff of King Saud university	152 (RE only used in analysis)	16-50 (average 22.68)	Non cycloplegic autorefraction / subjective	M < -0.50 E ± 0.50 H > +0.50	M 47 E 47 H 6	-0.95
Kinge <i>et al.</i> 1999 [26]	Norwegian engineering students	149 (RE only used in analysis)	Mean age 20.6 ± 1.2	Cycloplegic autorefraction/ subjective	M ≤ -0.25 H ≥ +0.50	M 49 E 25 H 26	-0.81 ± 1.98
Fledelius 2000 [216]	Medical students Copenhagen	294 (RE only used in analysis)	22-41 (median 26)	Student information	M ≤ -0.50	M 50	-2.50 ± 1.86 (myopes only)
Loman <i>et al.</i> 2002 [214]]	Pennsylvania law students	177 (R&L averaged for analysis)	23-44 (mean 27)	Mainly student information	M ≤ -0.50	M 66	Not specified
Logan <i>et al.</i> 2005 [76]	Bradford /Aston 1 st year university students	373 (RE only used in analysis)	17-30 (mean 19.55 ± 2.99)	Non cycloplegic autorefraction	M ≤ -0.50 H ≥ +0.50	M 53	White -1.01 ± 2.19 Asian -1.40 ± 2.57
Onal <i>et al.</i> 2007 [112]	Medical students Turkey	207 (RE only used in analysis)	18-26 (mean 21.11 ± 1.58)	Cycloplegic autorefraction	M ≤ -0.75 H ≥ +1.00	M 33 E 50 H 17	-0.67 ± 1.42

Study	Subjects	Number	Age (years)	Refractive method	Criteria (D)	Prevalence (%)	Mean Rx (D) ± SD
Jorge <i>et al.</i> 2007 [25]	Portuguese science students	118 (RE only used in analysis)	Mean age 26.6 ± 2.3	Cycloplegic subjective refraction	M ≤ -0.50 H ≥ +0.50	M 22 E 29 H 49	+0.23 ± 1.46
Risovic <i>et al.</i> 2008 [215]	Serbian students	230 (method of analysis not clear)	18-27 (mean 22.01 ± 2.52)	Cycloplegic retinoscopy	M ≤ -0.50 H ≥ +2.00	M 24 E 63 H 10	Not specified
Jacobson <i>et al.</i> 2008 [75]	Danish medical students	156 (RE only used)	Mean age 23.1 ± 3.3	Cycloplegic autorefracton	M ≤ -0.50 H ≥ +0.50	M 37	-0.50 ± 1.81

Table 4.3. Comparison of myopia progression studies in student populations.

Study	Participants	Length of study (years)	AL measurement	Refractive method	Change in rx (D/year)	Increase in axial length (mm/year)
O'Neal, Connon 1987 [5] (retrospective)	Cadets at United States Air-Force Academy	2.5	No	Non cycloplegic subjective / cycloplegic subjective	-0.14	N/A
Lin <i>et al.</i> 1996 [65]	Medical students Taiwan	5	Yes (A scan)	Cycloplegic autorefracton/ checked by ret	Males -0.14 Females -0.11	Males 0.10 Females 0.07
Kinge <i>et al.</i> 1999 [26]	Norwegian engineering students	3	Yes (A scan)	Cycloplegic autorefracton/ subjective	-0.17	0.11
Onal <i>et al.</i> 2007 [112]	Medical students Turkey	1	Yes (A scan)	Cycloplegic autorefracton	+0.02 (cycloplegic autorefracton) -0.17 (non cycloplegic subjective)	0.01
Jorge <i>et al.</i> 2007 [25]	Portuguese science students	3	Yes (A scan)	Cycloplegic subjective refraction	-0.10	0.04
Jacobson <i>et al.</i> 2008 [75]	Danish medical students	2	Yes (IOLMaster)	Cycloplegic autorefracton	-0.13	0.07

4.2 Method

The 2007 Bradford School of Optometry and Vision Science intake of first year optometry students were all invited to take part in this study. This sample is not representative of the normal population, as due to the nature of the course there may be a high proportion of participants with refractive errors [213]. These students, however, may be more aware of their own and their family's refractive status than other students and possibly give more reliable information regarding this. Informed consent was obtained from each subject (Appendix 5.3) and the study was approved by the University of Bradford Ethics Committee and conformed to the tenets of the Declaration of Helsinki.

In January 2008 a number of initial measurements were taken. Non-cycloplegic objective refraction was undertaken using an NVision-K 5001/Grand Seiko WR-5100K (Shin-Nippon, Japan) autorefractor [173]. As this autorefractor has an open field-of-view participants were asked to observe a 6/18 letter at six metres (or a spot light at six metres if they could not see the 6/18 target) and five readings were taken for each eye and averaged. The instrument settings used were: power in increments of 0.12 D, cylinder axis to 1° and back vertex distance 0 mm. Cycloplegic agents were not used during the study as the data was taken during a working day and the use of cycloplegia may have lowered interest in participating in the study. Measurements of axial length (AL), anterior chamber depth (ACD) and corneal radius (CR) were taken using an IOLMaster (Carl Zeiss Meditec AG) [181]. Three measurements of AL and CR were taken and averaged. The IOLMaster takes five measurements of ACD and averages them automatically to give one reading. These measurements were repeated in January 2009 and January 2010. All the measurements were taken by a single investigator.

Each year a questionnaire was issued to each participant. The initial questionnaire asked for details of previous refractive history, family refractive history and symptoms

of NITM (Appendix 5.1): the second asked about the amount of time spent undertaking near visual tasks and sporting activities as well as whether participants wore their correction for near work (Appendix 5.4): the third asked about ethnic origin and again about symptoms of NITM (Appendix 5.5). Participants were asked to leave blank any sections where they were unsure of the answers.

4.3 Results

4.3.1 Participants

Out of 104 students entering the optometry course in October 2007, initial data were collected from 97 participants. Over the course of the study 19 students dropped out. Five more were removed from the study: one because they began wearing rigid gas permeable lenses half way through the study and four because their third year prescription had shifted more than 0.50 D towards hyperopia without a corresponding change in axial length, suggesting their accommodation was poorly controlled during autorefractor measurements. The following results therefore comprise the data from the 73 remaining participants. Only data from the first and third year data points are reported here as there were eight participants who were available for the first and third year data collections but not the second year data point. At the beginning of the study, the age range was 18-38 years with median age being 19 years. Thirty-one of the participants were male and 42 female. Only data from the right eye of each participant were used in analysis [222]. The mean spherical equivalent prescription (MSE) was calculated for each participant by adding the spherical component of the prescription to half the cylindrical component. Myopia (MYP) was taken to be $MSE \leq -0.50D$, emmetropia (EMM) to be $MSE > -0.50D < +0.50D$ and hypermetropia (HYP) to be $MSE \geq +0.50D$. MYPs were classed as early onset myopes (EOMs) having onset prior to the age of 15 years and late onset myopes (LOMs) having onset at 15 years or later [93].

Data were analysed using SPSS (SPSS 17.0 for Windows). In all cases the Kolmogorov-Smirnov test was used to check for normality of the data. Where the data were found not to differ from a normal distribution the mean and standard deviation are used as descriptive statistics and parametric statistics used for analysis. Where the data were found to differ significantly from a normal distribution the median and range are used as descriptive statistics (the mean and standard deviation are often quoted in addition, to allow comparison with previous studies), and non-parametric statistics used for analysis. Levene's test was used to check for homogeneity of variance between two independent samples. G*Power 2 was used to aid post hoc power calculations.

4.3.2 Analysis of initial data collection

4.3.2.1 Refractive error

The prevalence of refractive error in the cohort at the first data point was found to be 66% MYPs, 26% EMMs and 8% HYPs. Of the MYPs 60% were EOMs and 40% were LOMs. The distribution of refractive error was found to be significantly different from a normal distribution, therefore non-parametric statistics were used. The data are represented in the histogram in Figure 4.1, with the median MSE of the cohort being -0.93 D (range -8.56 to $+4.81$) and the mean being -1.69 D \pm 2.28. The median amount of astigmatism was -0.37 DC (range 0 to 1.50). There was no statistically significant difference between the MSE of those participants who dropped out of the study (median = -0.13 D, range -9.38 to $+2.50$, mean = -1.69 D \pm 3.21) and those who remained in the study (median = -0.93 D, range -8.56 to $+4.81$, mean = -1.69 ± 2.28), ($U = 705.000$, $z = -1.430$, $p = 0.154$, power = 0.05).

The median MSE of the EOMs was significantly more myopic (median = -3.12 D, range -8.56 to -0.87 , mean = -3.66 D \pm 1.94) than that of the LOMs (median = -0.88 D, range -4.00 to -0.50 , mean = -1.36 D \pm 1.13) ($U = 66.000$, $z = -4.418$, $p < 0.001$).

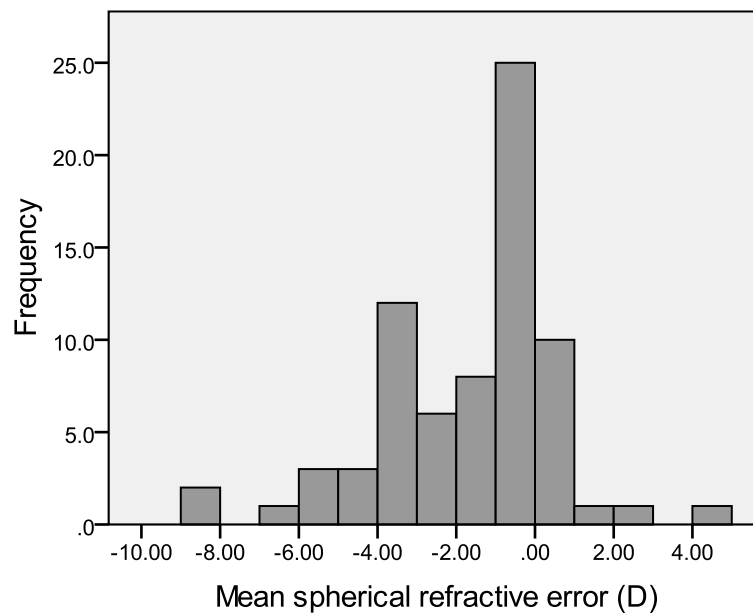


Figure 4.1. First year data showing the spread of mean spherical equivalent refractive errors in optometry students.

4.3.2.2 Comparison of refractive error between males and females

Of the participants 31 were male and 42 female. The mean spherical equivalent refractive error was higher for the male group ($-1.92 \text{ D} \pm 2.45$) than the females ($-1.51 \text{ D} \pm 2.16$). The median however, was higher in the females (-0.94 D range -6.31 to 4.81) than the males (-0.81 range -8.56 to 0.62). Histograms comparing the spread of refractive errors in the male and female groups are shown in Figure 4.2 below.

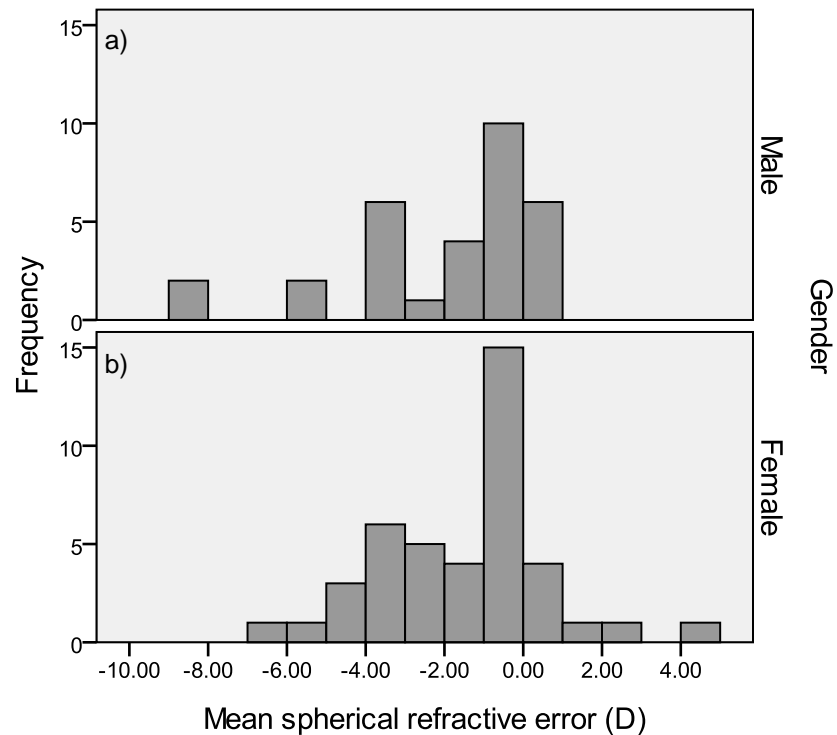


Figure 4.2. Histograms showing the spread of mean spherical equivalent refractive error in (a) female and (b) male optometry students.

Using a Mann-Whitney test the difference in refractive error between the male and female groups was not found to be statistically significantly different ($U = 647.000$, $z = -0.045$, $p = 0.967$, power = 0.112).

4.3.2.3 Ocular components

Mean corneal radius (MCR) of the two principal meridians (CR_1 and CR_2) was calculated for each participant by using the formula: $MCR = (CR_1 + CR_2) / 2$. This was then used to calculate the AL/CR ratio. The data for AL, MCR and ACD were not significantly different from a normal distribution whereas the data for AL/CR ratio were. Non-parametric statistics were therefore used to describe the latter data set and both mean and median values are shown in the table below. The data for the ocular components of the student cohort are shown in Table 4.4.

Table 4.4. Ocular components of first year optometry students.

Ocular component	Mean (\pm SD)
AL (mm)	24.20 \pm 1.18
CR (mm) flattest	7.83 \pm 0.27
steepest	7.70 \pm 0.25
mean	7.77 \pm 0.26
ACD (mm)	3.69 \pm 0.26
	Mean (\pm SD) / median (range)
AL/CR	3.12 \pm 0.15 3.10 (2.79 to 3.66)

4.3.2.4 Correlation of ocular components

As the MSE was not normally distributed, Spearman's correlation coefficient was used to describe the data. A significant negative correlation was found between MSE and AL ($r_s = -0.702$; $p < 0.001$), MSE and AL/CR ratio ($r_s = -0.888$; $p < 0.001$) and MSE and ACD ($r_s = -0.333$; $p = 0.004$). No significant correlation was found between MSE and MCR ($r_s = 0.226$; $p = 0.055$). Figures 4.3 - 4.6 illustrate the scatter plots of these correlations.

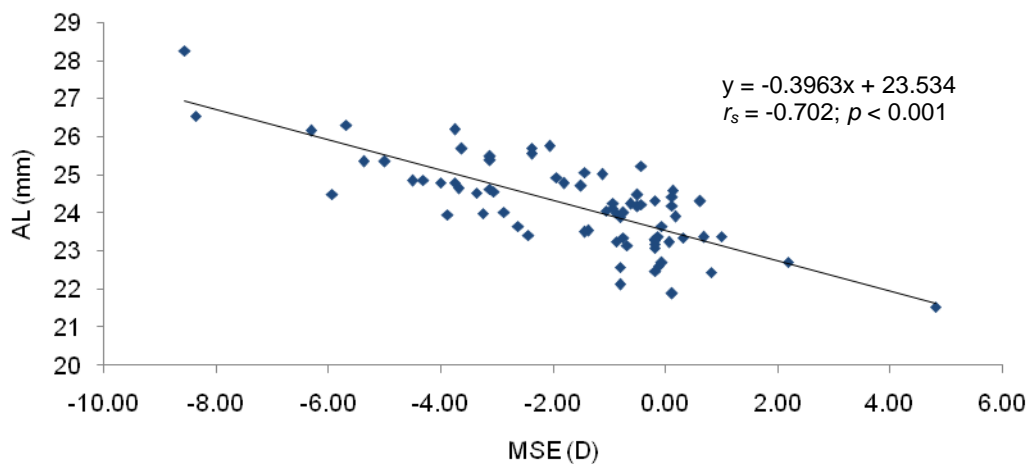


Figure 4.3. Axial length (mm) plotted against mean spherical error (D) at initial data collection.

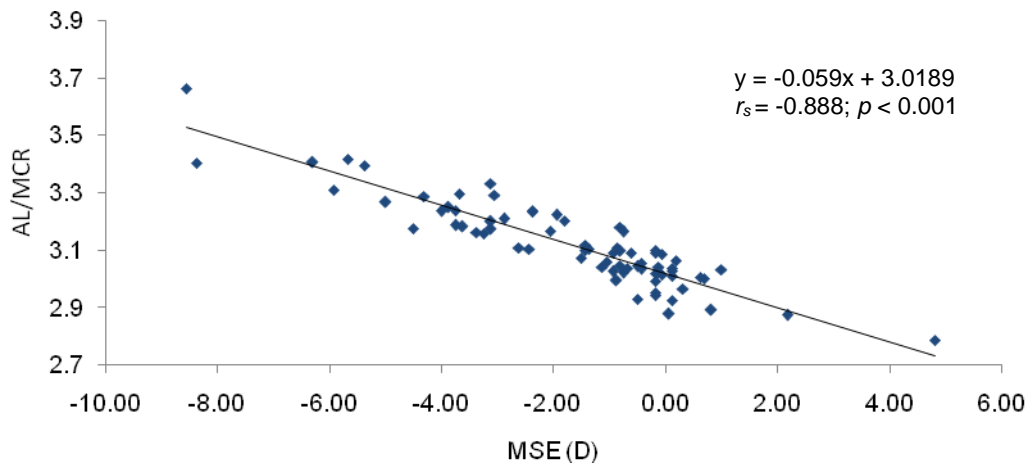


Figure 4.4. AL/CR plotted against mean spherical error (D) at initial data collection.

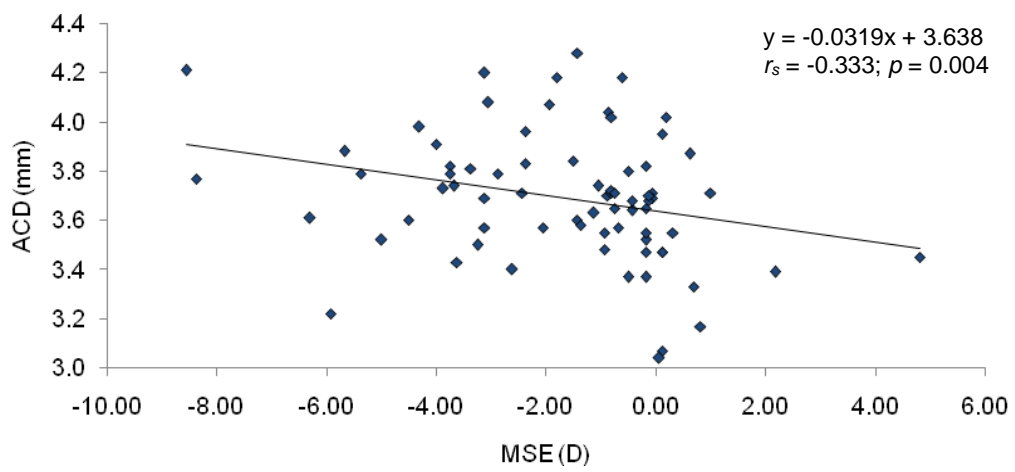


Figure 4.5. Anterior chamber depth (mm) plotted against mean spherical error (D) at initial data collection.

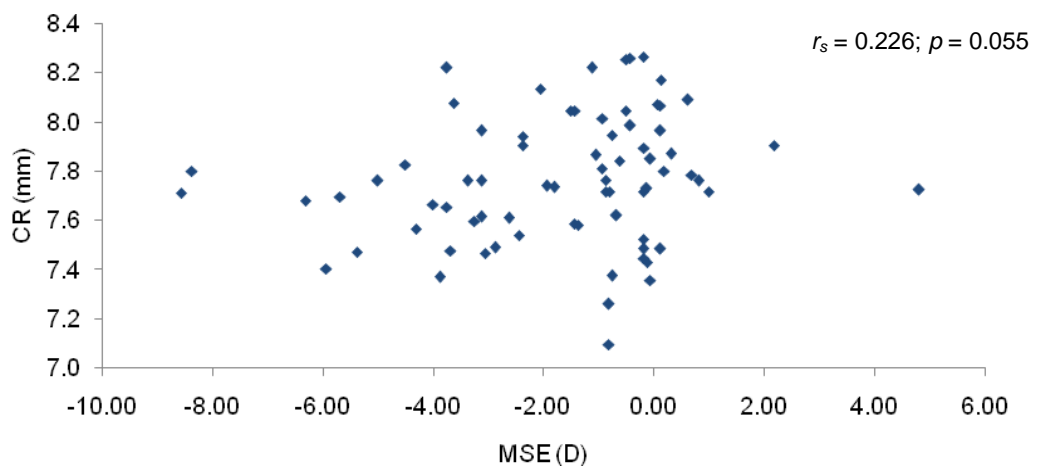


Figure 4.6. Corneal radius (mm) plotted against mean spherical error (D) mean at initial data collection.

4.3.2.5 Familial myopia

Both parental and sibling myopia were analysed in association with refractive error. Seventy-one participants were aware of their familial refractive errors. Forty-four percent of MYPs, 41% of EMMs and 17% of HYPs had at least one parent with myopia. Six participants had no siblings and were, therefore, removed from this part of the analysis. Of the remaining participants, 70% of MYPs, 47% of EMMs and 17% of HYPs had at least one myopic sibling.

The data was analysed further using a method previously described by Bullimore *et al.* [217]. Each participant was given a score of 0, 0.5 or 1 depending on whether they had no, one or two parents with myopia. A similar system was used for sibling myopia where each participant was given a score determined by the proportion of siblings with myopia. The seven participants with no siblings were again excluded. The EMMs and HYPs were classed in a single group of non-myopes (Table 4.5). As the data were significantly different from a normal distribution it would be correct to use the median to represent them. However, in Table 4.5, the mean has been used to enable comparison to the study carried out by Bullimore *et al.* [217].

Table 4.5. Mean index of familial myopia in each refractive group (\pm SD).

Refractive group	Parental myopia	Sibling myopia
Myopes (n = 44)	0.30 \pm 0.39	0.55 \pm 0.44
Non-myopes (n = 21)	0.21 \pm 0.34	0.34 \pm 0.46
Early onset myopes (n = 27)	0.33 \pm 0.39	0.60 \pm 0.43
Late onset myopes (n = 17)	0.24 \pm 0.40	0.47 \pm 0.47

The Mann-Whitney test was used to compare the data above. No statistically significant difference was found between the index of parental myopia in the myopic group compared to the non-myopic group ($U = 487.500$, $z = -0.901$, $p = 0.406$, power = 0.143). The difference between the index for sibling myopia in the myopic group (0.55 \pm 0.44) and the non-myopes (0.34 \pm 0.46) approached statistical significance

($U = 334.500$, $z = -1.917$, $p = 0.055$, power = 0.395). There was no statistically significant difference between the index of parental or sibling myopia for the EOMs compared to the LOMs (parental myopia: $U = 224.500$, $z = -1.202$, $p = 0.244$, power = 0.108 and sibling myopia: $U = 193.000$, $z = -0.941$, $p = 0.350$, power = 0.145).

4.3.2.6 Nearwork and sport

Table 4.6 shows the number of hours per day (median and range) of near and computer work undertaken by the participants and the number of hours per week (median and range) spent undertaking sporting activities.

Table 4.6. Median hours of nearwork, computer work and sporting activities undertaken.

Nearwork (hours/day)	4 (0 – 12)
Computer work (hours/day)	3 (0.5 – 8)
Sports (hours/week)	3 (0 – 15)

The data for nearwork, computer work and sport was found to be significantly different from a normal distribution therefore non-parametric statistics were used. Spearman's correlation coefficient was used to explore the above data. No statistically significant correlation was found between MSE and hours of nearwork ($r_s = -0.035$, $p = 0.767$), computer work ($r_s = 0.009$, $p = 0.937$) or sport ($r_s = 0.168$, $p = 0.155$) undertaken by the participants. When the participants were split into two groups: myopes and non-myopes, there was a trend for the non-myopes to spend slightly more time doing both nearwork (mean = 4.42 hrs \pm 2.22, median = 4 hrs, range 2 to 12) and sports (mean = 4.38 hrs \pm 3.95, median = 3 hrs, range 0 to 15) than the myopes (mean = 3.94 hrs \pm 1.61, median = 4 hrs, range 0 to 7) and (mean = 2.83 hrs \pm 2.34 median = 3 hrs, range 0 to 9.5). However neither of these differences were found to be statistically significant ($U = 556.500$, $z = -0.509$, $p = 0.615$, power = 0.165) for nearwork or ($U = 490.500$, $z = -1.281$, $p = 0.203$, power = 0.485) for sports.

4.3.2.7 Ethnic origin

The participants were mainly from Asian* (58%) or Caucasian (31%) backgrounds with the remainder (11%) being of either mixed race, African, Caribbean or Bangladeshi origins. The number and percentage of myopes and non-myopes in the Asian and White cohorts are shown in Table 4.7.

Table 4.7. Number and percentage of myopes and non-myopes from Asian and Caucasian backgrounds.* = Asian origin included those students from Indian and Pakistani origin.

	Asian*	Caucasian
Myopes	N = 28 (67%)	N = 15 (65%)
Emmetropes	N = 11 (26%)	N = 6 (26%)
Hypermetropes	N = 3 (7%)	N = 2 (9%)

There was a trend for the Asian participants to be more myopic (median = -1.50 D, range -8.56 to +2.19; mean = -2.14 D \pm 2.45) than the Caucasian participants (median = -0.81 D, range -5.00 D to +0.82; mean = -1.26 D \pm 1.52). This difference was not found to be statistically significant ($U = 421.500$, $z = -1.236$, $p = 0.219$, power = 0.375).

4.3.3 Two year follow up data analysis

4.3.3.1 Refractive error

The prevalence of refractive error in the cohort at the two year follow up was found to be 70% MYPs, 23% EMMs and 7% HYPs. Six participants had changed categories: four from emmetropia to myopia, one from hypermetropia to emmetropia and one from myopia to emmetropia. The median MSE of the cohort was -1.00 D (range -8.56 to +5.19) and mean -1.80 D \pm 2.34. The median amount of astigmatism was -0.37 DC (range 0 to 1.50).

4.3.3.2 Myopia progression

4.3.3.2.i Progression in all participants

The values of the ocular parameters measured at the initial and two year data points are shown in Table 4.8. The non-parametric data are shown as both mean and median values. T-tests were carried out on the parametric data and Wilcoxon signed-rank tests on the non-parametric data. The resultant p -values are shown below.

Table 4.8. Ocular parameters measured at the first and third data points with corresponding p -value.

Ocular component	Initial	2 year	Difference (2 year - initial)	P-value
MSE (D)	-1.69 ± 2.28 -0.93 (-8.56 to +4.81)	-1.80 ± 2.34 -1.00 (-8.56 to +5.19)	-0.11	0.006
AL (mm)	24.20 ± 1.18	24.26 ± 1.12	0.06	<0.001
MCR (mm)	7.77 ± 0.26	7.75 ± 0.25	-0.02	0.004
ACD (mm)	3.69 ± 0.26	3.65 ± 0.27	-0.02	0.147
AL/CR	3.12 ± 0.15 3.10 (2.79 to 3.66)	3.13 ± 0.15 3.11 (2.79 to 3.67)	0.01	<0.001

There was a statistically significant reduction in MSE from -0.93 D (range -8.56 – 4.81) to -1.18 D (range -8.56 – 5.19), ($z = -2.727$, $p = 0.006$) and increase in AL from 24.22 mm (± 1.18) to 24.27 mm (± 1.21), ($t_{(72)} = -5.121$, $p < 0.001$) and AL/CR from 3.10 (range 2.79 – 3.66) to 3.11 (range 2.79 – 3.67) ($z = -4.659$, $p < 0.001$) over the duration of the study. There was a statistically significant reduction in MCR from 7.77 mm (± 0.26) to 7.75 mm (± 0.25), ($t_{(72)} = 2.971$, $p = 0.004$) however there was no significant change in ACD. A significant negative correlation was found between the change in AL ($r_s = -0.238$, $p = 0.040$) and change in MSE, and a significant positive correlation between the change in MCR ($r_s = 0.232$, $p = 0.040$) and change in MSE (Figures 4.7 and 4.8).

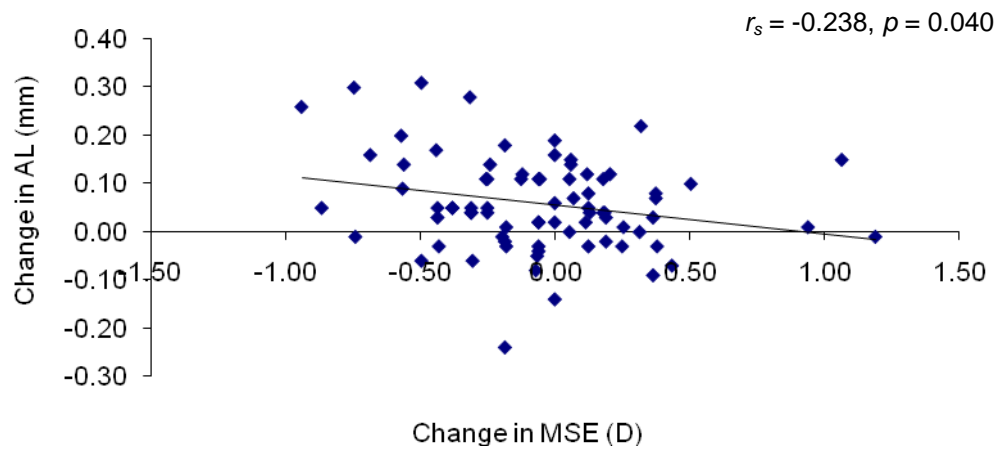


Figure 4.7. Change in axial length (2 year data – initial 1 data) plotted against change in mean spherical equivalent (2 year data – initial data).

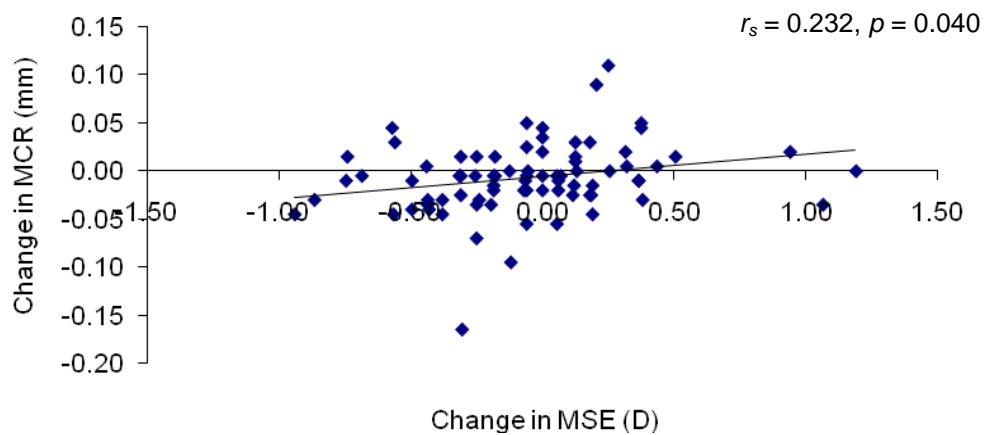


Figure 4.8. Change in mean corneal radius (2 year data – initial data) plotted against change in mean spherical equivalent (2 year data – initial data).

4.3.3.2.ii Myopia progression in refractive groups

The change in ocular parameters was analysed between refractive groups and also according to onset of myopia (i.e. EOMs vs LOMs). The change in the ocular parameters was calculated by subtracting the initial data from the two year data. The results are shown in Tables 4.9 and 4.10. The MSE and AL/CR data was significantly different from a normal distribution therefore the Mann-Whitney and Kruskal-Wallis tests were used for analysis. The rest of the data did not significantly differ from a normal distribution, therefore one-way ANOVA and independent-t test were used.

Table 4.9. Comparison of changes in ocular components over a two year period between refractive groups (2 year data – initial data). The calculated *p*-values are shown.

	MYPs	EMMs	HYPs	P-value
Δ MSE (D)	-0.14 ± 0.31	-0.07 ± 0.34	-0.09 ± 0.36	0.592
Δ AL (mm)	0.07 ± 0.11	0.04 ± 0.09	0.05 ± 0.06	0.517
Δ CR (mm)	-0.01 ± 0.04	-0.01 ± 0.02	-0.03 ± 0.04	0.416
Δ ACD (mm)	-0.01 ± 0.07	-0.01 ± 0.05	-0.01 ± 0.08	0.939
Δ AL/CR	0.01 ± 0.02	0.01 ± 0.01	0.02 ± 0.02	0.405

Table 4.10. Comparison of changes in refractive components over a two year period between EOMs and LOMs (2 year data – initial data). The calculated *p*-values are shown.

	EOM	LOM	P-value	Power
Δ MSE (D)	-0.17 ± 0.31	-0.09 ± 0.31	0.338	0.217
Δ AL (mm)	0.08 ± 0.12	0.05 ± 0.09	0.241	0.260
Δ CR (mm)	0.00 ± 0.04	-0.02 ± 0.05	0.249	0.430
Δ ACD (mm)	-0.01 ± 0.08	-0.01 ± 0.05	0.974	0.050
Δ AL/CR	0.01 ± 0.02	0.01 ± 0.02	0.787	0.050

Although there was a trend for the MYPs to progress slightly more over the two years of the study (-0.14 D ± 0.31) than the EMMs (-0.07 D ± 0.34) and HYPs (-0.09 D ± 0.36) and the EOMs to progress more (-0.17 D ± 0.31) than the LOMs (-0.09 D ± 0.32) there was no statistically significant difference between the type of prescription and any of the changes in ocular parameters.

4.3.3.2.iii Myopia progression and association with AL/CR

Of the 19 participants who were emmetropic at the beginning of the study, six had an AL/CR less than three (mean 2.94 ± 0.04) and the remaining 13 had an AL/CR greater than three (mean 3.05 ± 0.03). The data were not significantly different from a normal distribution therefore an independent t-test was used to compare the progression between these two groups. There was a trend for those with an AL/CR less than three to progress by a greater amount (-0.16 D ± 0.37) than those with an AL/CR greater than three (-0.03 D ± 0.33) however this was not statistically significant ($t_{(17)} = -0.755$, $p = 0.461$).

For the group of EMMs, no correlation was found between change in either MSE ($r = 0.031$, $p = 0.896$) or AL ($r = -0.130$, $p = 0.585$) and AL/CR ratio at the beginning of the study (Figures 4.9 and 4.10).

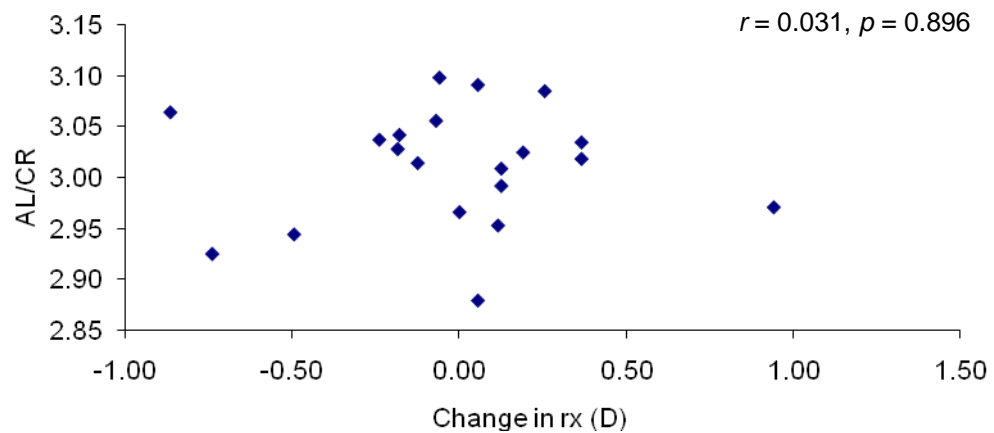


Figure 4.9. AL/CR at the beginning of the study for the emmetropic group plotted against change in mean spherical equivalent (2 year data – initial data).

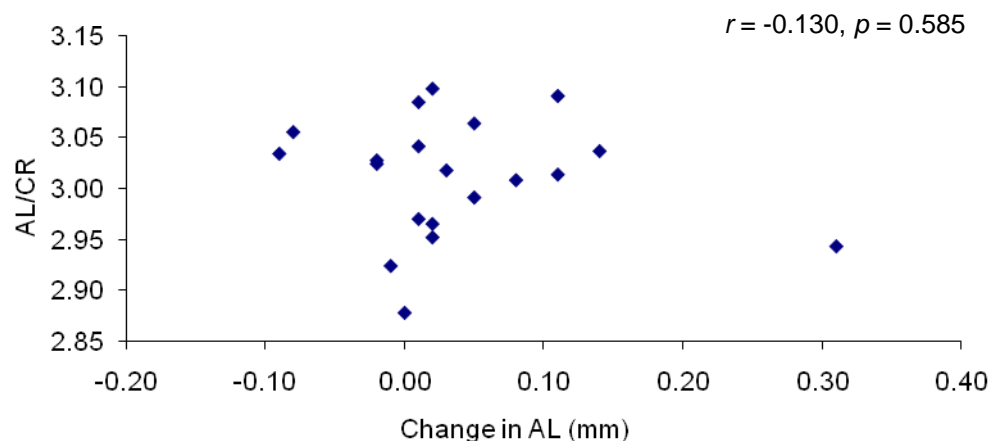


Figure 4.10. AL/CR at the beginning of the study for the emmetropic group plotted against change in axial length (2 year data – initial data).

4.3.3.2.iv Myopia progression with nearwork and sporting activities

Spearman's rho was used to analyse the correlation between myopia progression and hours of nearwork, computer work and sports undertaken by the cohort. There was found to be no correlation between myopia progression and nearwork ($r_s = -0.073$, $p = 0.542$), computer work ($r_s = -0.009$, $p = 0.937$) or sports ($r_s = 0.055$, $p = 0.645$).

4.3.3.2.v Myopia progression and ethnic origin

The progression data was not significantly different from a normal distribution therefore an independent t-test was used to compare the progression in those participants from Asian backgrounds (mean = $-0.12 \text{ D} \pm 0.31$) to those from Caucasian backgrounds (mean = $-0.12 \text{ D} \pm 0.34$) There was no statistically significant difference in progression between the two groups ($t_{(65)} = 0.026, p = 0.979$).

4.3.3.2.vi Myopia progression and spectacle wear for nearwork

During the study the participants were asked if they wore their spectacle correction for nearwork. Of the MYPs, 60% said they wore their correction either all the time or most of the time when doing nearwork. There was a trend for the participants who wore their correction for nearwork to progress by a greater amount ($-0.20 \text{ D} \pm 0.34$) over the two year study than those who did not ($-0.04 \text{ D} \pm 0.25$), however this difference did not reach statistical significance ($t_{(46)} = -1.744, p = 0.088$).

4.3.3.2.vii Subjectively reported NITM and myopia progression

The number of individuals who answered 'yes' when asked at the initial data collection if they ever noticed blurred distance vision after nearwork was 21 (29%). The same question was repeated at the year two data collection at which point 22 participants (30%) answered that they noticed blurred distance vision after nearwork. Sixteen participants (22%) answered yes to this question at both data collection points. This group will be referred to as the 'NITM group' as opposed to those individuals who said they did not notice distance vision blur after nearwork, who will be referred to as the 'non-NITM group'. The group who suffered subjectively from NITM consisted of a higher proportion of LOMs than the group who were not aware of NITM and contained no HYPs. The figures are shown in Table 4.11.

Table 4.11. Number and percentage of participants who were not aware and who were aware of distance vision blur after nearwork in each refractive group at both the initial and 2 year data collections.

Refractive group	Non-NITM (n=57)	NITM (n=16)
Myopes	37 (65%)	10 (71%)
EOM	25 (68%)	3 (30%)
LOM	12 (32%)	7 (70%)
Emmetropes	14 (25%)	6 (37%)
Hypermetropes	6 (10%)	0 (0%)

The median age of the NITM group was 19 years (range 18 to 26 years) and 56% of this group were female. A comparison between the ocular components of the NITM and non-NITM groups is shown in Table 4.12 along with the resultant *p*-values. The non-parametric data are shown as both mean and median values. Unpaired t-tests were carried out on the parametric data and Mann-Whitney tests on the non-parametric data.

Table 4.12. Comparison between ocular parameters of the non-NITM group and the NITM group at the initial data collection.

Ocular component	Non-NITM (n = 57) (mean ± SD; median + range)	NITM (n = 16) (mean ± SD; median + range)	P-value	Power
MSE (D)	-1.84 ± 2.47 -1.37 (-8.56 to +4.81)	-1.16 ± 0.71 -0.75 (-2.38 to +0.32)	0.229	0.370
AL (mm)	24.17 ± 1.24	24.14 ± 0.84	0.945	0.051
MCR (mm)	7.74 ± 0.25	7.88 ± 0.26	0.062	0.469
ACD (mm)	3.69 ± 0.27 3.70 (3.04 to 4.21)	3.70 ± 0.22 3.65 (3.47 to 4.28)	0.851	0.052
AL/CR	3.12 ± 0.16	3.07 ± 0.08	0.169	0.310

No statistically significant differences were found in any of the ocular parameters between the two groups.

Nine percent of those who were not aware of NITM and 13% of those who were aware of NITM progressed by more than 0.50 D (95% confidence interval for repeatability of the NVision-K 5001). Forty nine percent of those who were not aware of NITM and 56% of those who were had an increase in AL greater than 0.04 mm (95% confidence interval for repeatability of IOLMaster). Table 4.13 shows the change in ocular

parameters for the two groups (NITM *versus* non-NITM) with the resultant *p*-values.

Table 4.13. Change in ocular parameters over a two year period for the non-NITM and NITM groups.

Ocular parameter	Non-NITM (n = 57) (mean ± SD; median + range)	NITM (n = 16) (mean ± SD; median + range)	P-value	Power
MSE (D)	-0.10 ± 0.31	-0.12 ± 0.34	0.878	0.107
AL (mm)	0.05 ± 0.09	0.10 ± 0.11	0.062	0.414
MCR (mm)	-0.01 ± 0.04 -0.01 (-0.17 to 0.09)	-0.01 ± 0.03 0.00 (-0.05 to 0.06)	0.793	0.050
ACD (mm)	-0.01 ± 0.07 0.00 (-0.20 to 0.20)	0.02 ± 0.02 0.01 (0.00 to 0.05)	0.674	0.051
AL/CR	0.01 ± 0.02 0.01 (-0.03 to 0.06)	-0.01 ± 0.02 -0.01 (-0.04 to 0.04)	0.453	0.050

There was no statistically significant difference in the changes in MSE, MCR, ACD or AL/CR between the two groups. The participants who suffered NITM symptoms had slightly more AL growth (0.10 mm ± 0.11) than those who did not (0.05 mm ± 0.09). This difference nearly reached statistical significance ($t_{(71)} = -1.90$, $p = 0.062$).

There were five LOMs in the NITM group who reported not wearing their glasses for near vision. For these participants the distance vision blur reported may not have been NITM but purely due to not wearing their glasses. These participants were removed from the analysis and the resultant parameter changes shown in Table 4.14.

Table 4.14. Change in ocular parameters over a two year period for the non-NITM and NITM groups with those myopes who did not wear glasses for nearwork removed from the NITM group and added to the no-NITM group.

Ocular parameter	Non-NITM (n = 62)	NITM (n = 11)	P value	Power
MSE (D)	-0.10 ± 0.30 -0.06 (-0.87 to 0.44)	-0.16 ± 0.39 0.00 (-0.94 to 0.19)	0.502	0.092
AL (mm)	0.05 ± 0.09	0.12 ± 0.13	0.022	0.685
MCR (mm)	-0.01 ± 0.04 -0.01 (-0.17 to 0.09)	0.00 ± 0.03 -0.01 (-0.04 to 0.04)	0.329	0.173
ACD (mm)	-0.01 ± 0.07 0.00 (-0.20 to 0.20)	0.01 ± 0.03 0.04 (-0.05 to 0.06)	0.426	0.286
AL/CR	0.01 ± 0.02 0.01 (-0.03 to 0.06)	0.02 ± 0.02 -0.05 (-0.01 to 0.05)	0.924	0.414

There was no statistically significant difference in the changes in MSE, MCR, ACD or AL/CR between the two groups. The participants who suffered NITM symptoms had more AL growth ($0.12 \text{ mm} \pm 0.13$) than those who did not ($0.05 \text{ mm} \pm 0.09$). This difference reached statistical significance ($t_{(71)} = -2.34, p = 0.022$).

4.3.3.2.viii Myopia progression and objective measurement of NITM

Eleven of the participants who took part in the study on temporal factors and dioptric demand in nearwork-induced transient myopia (Chapter 3) also took part in the longitudinal study. The data were collected during the first year of this longitudinal study and an explanation of the methods used to calculate the levels of NITM and the regression quotient post-task are explained in Section 3.3.1.2 and Section 3.3.1.5 respectively. The data were not found to be significantly different from a normal distribution. Correlations were carried out between the change in both AL and MSE over the duration of the study for these participants and the level of NITM and the regression quotient after a one minute 3.75 D near task. Figures 4.11 – 4.14 illustrate scatter plots of these correlations with the corresponding Pearson correlation coefficient and p-value.

No significant correlation was found between change in AL or MSE and level of NITM post-task, or between change in MSE and regression of NITM post-task. However a negative correlation was found between change in AL and regression of NITM at both the 20 s ($r = -0.63, p = 0.04$) and 30 s time points ($r = -0.75, p = 0.01$) with the regression quotient being higher for those with a larger amount of AL growth.

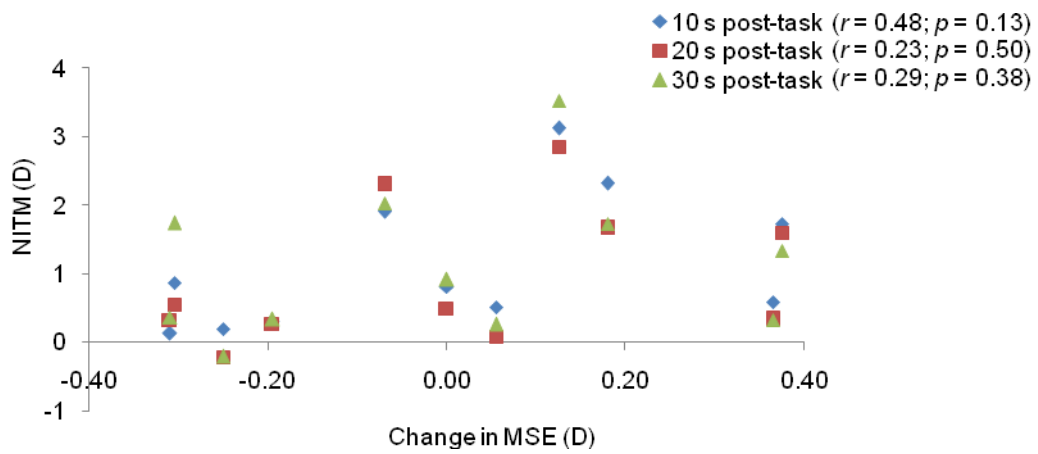


Figure 4.11. Level of NITM 10 s, 20 s and 30 s following a one minute, 3.75 D near task plotted against change in MSE (2 year data – initial data) of 11 participants over a two year period.

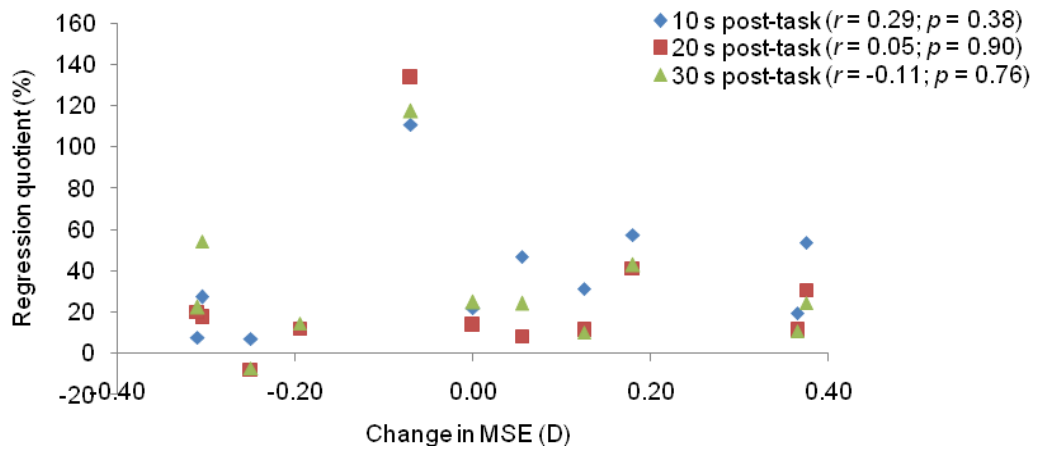


Figure 4.12. Regression of NITM 10 s, 20 s and 30 s following a one minute, 3.75 D near task plotted against change in MSE (2 year data – initial data) of 11 participants over a two year period.

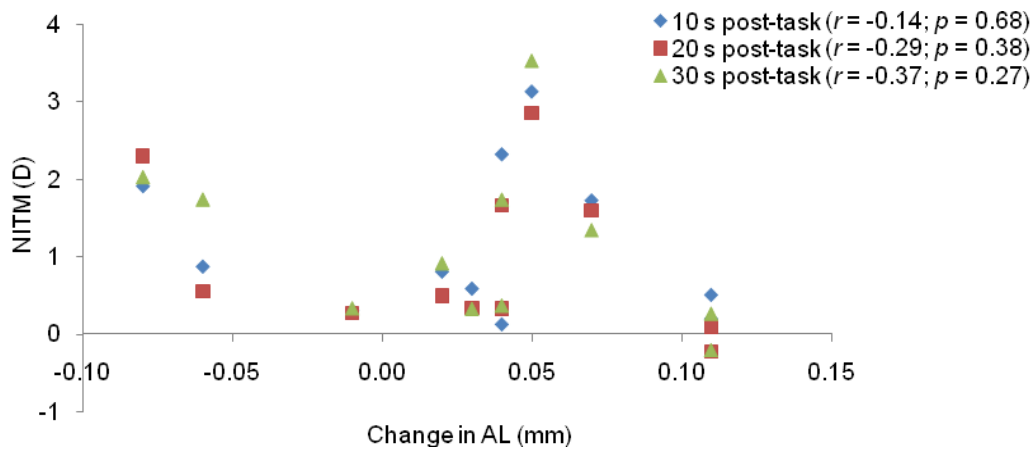


Figure 4.13. Level of NITM 10 s, 20 s and 30 s following a one minute, 3.75 D near task plotted against change in AL (2 year data – initial data) of 11 participants over a two year period.

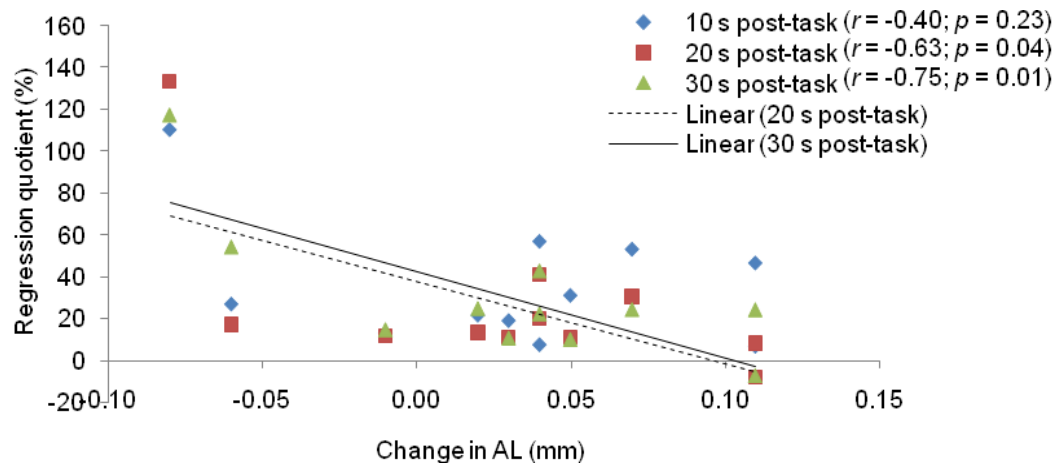


Figure 4.14. Regression of NITM 10 s, 20 s and 30 s following a one minute, 3.75 D near task plotted against change in AL (2 year data – initial data) of 11 participants over a two year period.

4.4 Discussion

Literature suggests that myopes are not only more susceptible to NITM but progressing myopes are more likely to suffer NITM [98, 99]. These findings have come from retrospective data, but not from a prospective, longitudinal study on myopia progression. The main result from our investigation is that no relationship was found between the objective level of NITM post-task and progression of MSE or AL change over a two year period in young adults, however there is a possible correlation between

change in AL and short-term regression of NITM. A relationship was found between those who were aware of symptoms of NITM and AL growth with those who were aware of NITM symptoms having significantly greater AL growth over a two year period compared to those who were not aware of NITM symptoms. Secondary findings were data which added information to a wealth of data regarding the structural correlates of myopia.

4.4.1 Myopia prevalence in a student population

Refractive data studies are difficult to compare directly as they all tend to use different populations, assessment techniques and criteria as we have already seen in Table 4.1. The results of this research show a higher prevalence of myopia (66%) than that found in the general British population (27%) [11], and slightly higher than that found in similar studies on European University populations [25, 26, 76, 112, 215, 216]. As mentioned previously our cohort is not necessarily representative of the student population or the population in general. It is possible that optometry students may be expected to have a higher incidence of refractive error due to a needs driven interest in the course.

There have been two similar investigations involving optometry students [213, 217] however neither are directly comparable as both used a questionnaire to collect refractive data rather than autorefraction. Our first year results show a myopia prevalence greater than that found by Bullimore [217] in UK optometry students. The mean age of the two samples was similar, however the criteria used for classifying myopia were different with emmetropia taken to be ± 0.50 D in the Bullimore study and -0.50 D $<$ $+0.50$ D in our study. The higher prevalence of myopia in our study (66% as opposed to 56%) may therefore be partly due to the different criterion. However, if our data is reclassified using the same criterion as the Bullimore study, the myopia prevalence only reduces slightly to 63%. In the Bullimore study participants

were asked their spectacle prescription by questionnaire and their answer was presumably their most recent subjective spectacle refraction. Our data was taken using non cycloplegic autorefraction which may have resulted in our myopia prevalence being slightly higher, however the results do suggest that there has been some increase in myopia prevalence in the optometry student population in the UK over the last 20 years. A higher myopia prevalence of 74.3% was found by Septon in the USA in 1984 [213]. Septon used the same myopia criterion as in our study, however the eye with the highest amount of ametropia was analysed which may have artificially increased the prevalence. The average age of the participants was five years older than in our cohort, and as we have seen, over a two year period the myopia prevalence in our students has risen from 66% to 70%. By the time the average age of our participants has reached that of Septon's, the myopia prevalence may be very similar.

4.4.2 Ocular biometric correlates of myopia

The results of this study are consistent with previous investigations regarding structural correlates of myopia, finding the main structural correlate to be axial length elongation [25-27, 65, 76, 218]. In this study AL/CR was also found to be correlated with myopia in that myopes tend to have a higher AL/CR. This is in agreement with previous studies [56, 58]. It has been suggested that an AL/CR greater than three in an emmetropic child could be an indicator of future myopia progression [58], however the same relationship has not been found in adults [56]. Our study supports that of McBrien and Adams [56], as no correlation was found between the change in MSE or change in AL of our 19 emmetropes over a two year period and their AL/CR ratio at the initial data collection.

4.4.3 Familial myopia

Our results regarding familial myopia are consistent with those of Bullimore [217]. Although myopes (both EOM and LOM) were found to be more likely than non-myopes to have myopic parents, no statistical significance was found. Myopes were also more likely to have myopic siblings than non-myopes and this relationship almost reached statistical significance. Had we had a greater number of participants this value may have reached significance.

4.4.4 Myopia, nearwork and sporting activities

Unlike a number of previous investigations [61, 71], no correlation was found between the level of myopia and the amount of nearwork, sport or computer work undertaken by the participants. There were probably a number of reasons for not finding this association. The first was that the questionnaires were issued asking average daily and weekly amounts of nearwork and sports. We made no assessment of how accurate the answers were to these questionnaires; this could have been assessed by giving a number of participants a diary to fill in over a period of a few weeks or by random text message contact. The second is that we did not discriminate between outdoor and indoor sports, and it has been found that it is possibly outdoor activity which is protective against myopia as oppose to sports in general [61, 71, 212].

4.4.5 Ethnic origin and myopia

In agreement with Logan *et al.* [76] there was a trend for the Asian students in our population to be more myopic than the Caucasian students, although as in their study, this difference failed to reach statistical significance. Myopia progression was the same between the two groups.

4.4.6 Myopia progression in a student population

In our study we found a significant group mean myopic shift in MSE (0.11 D), increase in AL (0.06 mm) and steepening of corneal curvature (0.02 mm) over a two year period. This equates to an annual change in MSE of 0.06 D and in AL of 0.03 mm which is less than that found in previous cohorts (Table 4.3). As our population is a similar age, if not younger, than in these other studies [5, 25, 26, 65, 75, 112], an equivalent if not higher progression rate may have been expected.

These unexpected results are possibly due to the fact that no cycloplegia was used during the measurements [219] and as a participant may have been accommodating slightly at the first measurement but not the second, the myopic shift may have been underestimated. However, if this was the case, the change in AL should have accounted for the true myopic shift as AL shift during accommodation is small and only evident at higher levels of accommodation [223, 224]. Our increase in AL of 0.03 mm is less than that found in previous studies but equates to a myopic shift of about 0.075 D which is slightly more than was actually found [225]. The slight reduction in mean corneal radius suggests there should have been even more of a myopic shift measured. Our results are closer in value to those found by Grosvenor and Scott [220] who conducted a progression study without using cycloplegia on a similar age group, and found an average of 0.07 D per year progression in MSE and 0.06 mm per year increase in AL.

The changes involved were very small. The 95% limits of agreement of repeatability for the NVision-K 5001 without cycloplegia has been found to be between ± 0.50 D [173] and for the IOLMaster ± 0.04 mm for both AL and MCR measurements [181]. Using this criteria, if we base our results on refraction alone, only the 12% of individuals who had a myopic shift of ≥ 0.50 D can be said to have truly progressed during the two years of the study, however if we use our AL data, 62% of individuals had an increase in AL of ≥ 0.04 mm. As 0.04 mm equates to about a 0.09 D [225] shift in myopia using AL

measurements during myopia studies appears a more accurate assessment technique than using MSE.

Unlike the results found by O'Neal and Connon [5] no statistically significant different change in MSE was found between any of the refractive groups during the two years of the study. This does not necessarily mean there was no difference in progression. It is possible any difference may have been masked by the high standard deviations in the measurements compared to the small amount of refractive change, and also the fact that the present study had a much smaller cohort (73 participants) compared to that of O'Neal and Connon (497 participants).

4.4.7 Myopia progression and subjectively reported NITM

All our participants were asked if they were ever aware of distance vision blur after undertaking near vision. This is obviously a very subjective question and open to interpretation. This question was asked at the first and last visit and if a participant answered yes at both visits they were classed in the NITM group. Although there was a trend for those who were aware of NITM to have a greater increase in AL over the two year period than those who did not notice NITM, this was not statistically significant. Some of the participants in the NITM group who were myopic did not wear their spectacle correction for nearwork. As the distance vision blur in these participants could possibly have been due purely to their myopia and not actual NITM they were then removed from the NITM group. Without these participants the difference in AL increase over two years between the groups reached significance.

We have already established in Chapter 3 that those individuals who are aware of NITM tend to have different post-task accommodative responses to those who do not notice NITM. We discussed the possibility that these participants may be the ones who have access to sympathetic innervation of the ciliary muscle, and the percentage of our population who were aware of NITM (22%) is similar to the percentage of individuals

who are thought to have access to sympathetic innervation (30%) [105, 205]. Although we have found evidence to suggest that suffering symptoms of NITM may be linked AL growth we found no link to progression of MSE. This does not mean there is no link, however, a larger sample and a better way of assessing subjective symptoms of NITM may be needed to provide more accurate data. Diaries could be issued to participants for them to record times when they were aware of NITM and what task they had been undertaking just prior to this.

4.4.8 Myopia progression and objective measurements of NITM

Previous studies [98, 99] have suggested a link between NITM and myopia progression however these studies have used retrospective refractive data to assess myopia progression. The present prospective myopia progression study has shown a possible correlation between NITM and myopia progression. This correlation between NITM and myopia progression appears to be related to AL and regression quotient, possibly because these are more accurate methods of assessing both myopia progression and NITM.

4.4.9 Experimental limitations

This study has limitations in that it is not representative of the student, or the general population as a whole. The number of possible participants was limited to the number of students in the year group, and as 23% of the initial group either dropped out or were removed before data analysis we were left with a relatively small cohort. For a larger, more representative sample of a student population, a further study could be undertaken and opened up to first year university students in general.

In myopia progression studies we are dealing with extremely small changes in parameters. Accuracy may have been improved by using cycloplegia, as non cycloplegic autorefraction has been shown to be considerably more variable than

cycloplegic autorefraction [172]. Cycloplegia was not used in our study however, as it is likely its use would have meant a lower uptake rate among the students. We also removed four participants from the study due to a hyperopic shift in MSE not associated with a change in AL as they were probably accommodating during the first set of measurements. Using cycloplegia would have eliminated this problem.

It would have been more informative to carry the study out over a longer period of time as two year progression changes are very small. As our students were only registered at the University for three years, a two year data collection was the maximum we could obtain. It may have been possible to ask the students to return after a longer period of time; however, the dropout rate would probably have been much higher following completion of the course. The other alternative would be to find a course with a longer duration, such as medicine, although the logistics of moving equipment to another department would have made this more difficult. The other alternative would have been to recruit from the University population as a whole.

No significant effect of nearwork or sporting activities was found on myopia progression in our cohort. It is difficult to find out exactly how much sport or nearwork an individual undertakes, and a diary may have given a more accurate result. Relying on the participants to fill out and return a diary may have been problematic, and it may have been possible to set up a system where the participants text when they are undertaking particular activities.

Chapter 5

A biometric investigation of nearwork-induced transient myopia (NITM)

5.1 Introduction

5.1.1 Accommodation

For the eye to change focus from a distant object to a near object, accommodation must occur. During this process the ciliary muscle contracts and moves forward causing the suspensory ligaments, which connect the lens to the ciliary body, to relax. Due to the elastic properties of the crystalline lens capsule this allows the lens to become more spherical, increasing the refractive power of the eye. When the ciliary muscle is completely relaxed the eye is focused at its far-point and when the ciliary muscle is maximally contracted the eye is focused at its near-point [226].

5.1.2 Biometric assessment of the accommodating eye

A number of techniques are now available to image intraocular structures, providing valuable information regarding the structural changes which occur during accommodation. These techniques include the Scheimpflug technique [227, 228], optical coherence tomography (OCT) [229], ultrasonography [230, 231], partial-coherence interferometry (PCI) [223, 224, 232, 233] and magnetic resonance imaging (MRI) [234, 235]. During accommodation, changes have been found in the axial length (AL) of the eye [224, 231], anterior chamber depth (ACD) [227, 231-233], crystalline lens thickness (LT) [227, 231-234] and crystalline lens position [227]. Below is a brief summary of these techniques along with their advantages and disadvantages with regard to the measurement of accommodation.

5.1.2.1 A-scan ultrasonography

A-scan ultrasonography measures corneal thickness, ACD, LT and AL using high frequency mechanical pulses. Sound is reflected from the ocular structures and the time taken for this to happen is used to build up an image of the internal eye. Traditional ultrasonography is limited to a resolution of ± 0.15 mm [236] however high-frequency ultrasonic biomicroscopy increases resolution to 0.03 – 0.05 mm [237]. It has a high intra-observer repeatability [236, 238] but low inter-observer repeatability [238]. It is an invasive technique, and due to the method of measurement, accommodation must be stimulated in the contralateral eye to the one being measured [230, 231]. It also suffers from image distortion due to media refractive indices and curvatures. However, ultrasonography can measure through opaque corneas and lens opacities and can image through the iris [182].

5.1.2.2 Partial coherence interferometry

Partial coherence interferometry has been described in detail in Section 2.4.1.3. Drexler *et al.* [232] designed a custom instrument to measure structural changes during accommodation, while an ACMaster (Carl Zeiss Meditec AG) [233] and an IOLMaster (Carl Zeiss Meditec AG) [224] have also been used. Resolution and precision for these instruments is much better than for ultrasound, with Drexler's instrument having resolution and precision of 0.009 mm [232] and the IOLMaster having a resolution of 0.01 mm with excellent inter and intra-session repeatability [181]. The PCI instruments are non-invasive, and it is possible to measure the biometry and accommodation simultaneously in the eye which is also focusing on an accommodative target [233, 239]. The IOLMaster does not have the capability of measuring LT, however, the LenStar, a relatively new instrument developed by Haag-Streit Koeniz which is discussed in further detail in Section 2.4.2, does, and it also has the advantage of taking all measurements during a single acquisition [182]. It has been shown that

measurement of AL with the IOLMaster during accommodation may contain errors due to the use of an average refractive error for the internal ocular structures [240]. Errors have been calculated to be in the order of an overestimation of 0.018-0.026 mm for 10.9 D of accommodation.

5.1.2.4 Scheimpflug technique

In the Scheimpflug technique the eye is imaged using a camera perpendicular to a slit beam. This creates an optical section of the cornea and lens. Measurements of central corneal thickness, ACD and LT can be taken as well as measurements of the lens nucleus and cortex. Measurements of the adult human lens using the Scheimpflug technique have been shown to have a good correlation with those produced by MRI [241]. The Scheimpflug technique has the disadvantage that the image of the internal structure of the lens is viewed through the cornea and anterior lens surface, causing distortion of the image [227]. A number of studies do not correct for this distortion, however, Dubbelmann *et al.* report a method for correcting for both the geometry of the Scheimpflug imaging system and for the refraction of the cornea and lens [228].

5.1.2.5 Magnetic resonance imaging

Magnetic resonance imaging can be used to visualize the internal structures of the eye. Unlike X-rays and computerised tomography scans it does not use ionizing radiation. A powerful electro-magnetic field along with radio signals are used to make nuclei within the body detectable by a scanner. An image of the scanned area can then be constructed [237]. MRI has the advantage that it allows for structures behind an opaque iris to be visualized, is non-invasive and does not distort the appearance of the internal structures as they are not viewed through the optics of the eye [234]. However, the scan is carried out with the participant in a supine position which has been shown to cause the crystalline lens to gravitate towards the posterior pole [231]. Imaging small

structures such as the crystalline lens needs higher resolution than for some other tissue scans. Resolution and contrast can be increased by lengthening the scan time, however, this can produce unacceptably low signal-to-noise ratios therefore sometimes resolution has to be a compromise [242].

5.1.2.6 Optical coherence tomography

Modification of retinal OCT by using a light source comprising a longer wavelength of light ($\lambda = 1310 \text{ nm}$), allows imaging of the anterior segment with reduced backscattering from the sclera, thus improving visualization of the ocular structures [243]. OCT is based on low coherence interferometry where the light from a measurement beam is reflected from the ocular structures and interferes with light from a reference beam. Positive interference is measured by an interferometer, allowing an image of the ocular structures to be built up. OCT can give measurements of LT and ACD for accommodation research. Resolution is high, between 0.025 mm and 0.0013 mm [237, 244] and the procedure is non invasive. Iris pigment blocks the typical wavelength of light used, and therefore structures behind the iris cannot be visualized [243] it also suffers from image distortion due to media refractive indices and curvatures.

5.1.3 Change in axial length with accommodation

Both Drexler *et al.* [223] and Mallen *et al.* [224] found an increase in AL with accommodation in young adults ranging from 0.0052 mm to 0.058 mm. Storey and Rabie [231], using ultrasound, also found the AL of the eye changed with accommodation, however, in their study AL was at its greatest when accommodating to a 2 D target and then reduced back to nearer baseline when presented with an 8 D target. As accommodative response was not measured during this study it is

impossible to know by exactly how much the participants were accommodating. The increase in AL was larger in this study than in the previous two (0.1 mm), however; this may be due to the lower resolution of ultrasound compared to PCI. Woodman *et al* [245] found a significant increase in AL immediately following a 30 minute near task, however, 10 minutes post-task task the AL was found to have regressed back to baseline.

5.1.4 Change in anterior chamber depth with accommodation

Anterior chamber depth has been found to reduce during accommodation [231, 232, 236]. A reduction in depth of 0.037 mm/D to 0.057 mm/D [227, 230, 233] has been found. The variation between these values seems to be partly associated with whether the change in ACD per dioptrre was calculated using the accommodative response or accommodative stimulus. Larger values tend to be obtained when accommodative response is used, as this takes into account the lag of accommodation [227, 230, 233]. There is agreement that reduction in ACD changes linearly with both accommodative stimulus [227] and accommodative response [230, 233].

5.1.5 Change in lens thickness with accommodation

Lens thickness increases as the eye accommodates [227, 231, 232, 234, 235]. Increases from 0.043 mm/D to 0.051 mm/D [227, 229, 234] have been found when LT change is calculated using the accommodative stimulus, and from 0.067 mm/D to 0.080 mm/D [230, 233, 235] when calculated using accommodative response. Lens thickness increases linearly with increasing accommodative stimulus [227] and accommodative response [230, 233]. Changes in LT with accommodation have been shown to be entirely due to an increase in the thickness of the lens nucleus, with no change in the cortical thickness [227, 228]. Change in LT with accommodation has been found to be correlated with subjective amplitude of accommodation and

accommodative response [229]. As yet there is no consensus as to whether it is also correlated with age. Koretz *et al.* [227] found no correlation between LT change and age in their study of 100 participants ranging in age from 18 to 70 years, however, Richdale *et al.* [229] did find a correlation. It is possible the differing results may have been due to the smaller sample size and narrower age range in the second study. Crystalline lens equatorial diameter has been found to reduce with accommodation [234, 235, 246] along with surface area [235], however, the volume of the crystalline lens has been shown to increase with accommodation of between 0.17 and 8 D [235].

5.1.6 Change in the position of the lens with accommodation

The anterior pole of the lens has been shown to move forward during accommodation [230-233, 246], however exactly what happens to the posterior pole is inconclusive. A number of studies have found the posterior pole to move away from the cornea [227, 231-233] although, in some individuals the posterior pole appears stationary or even to move forward [230, 246].

There is a possibility that the direction of movement may be age dependant, as in a population under 40 years the majority showed movement of the posterior lens surface away from the cornea, whereas the majority over 40 years showed anterior movement of the posterior lens surface associated with shallowing of the anterior chamber, suggesting anterior translation of the lens during accommodation [227]. Another study of participants under 30 years of age however, found that in 27% of individuals the posterior lens surface either remained stationary, or moved anteriorly [230].

5.1.7 Structural changes of the eye during accommodation and the relation to myopia

It has been suggested that accommodation may be linked to myopia development and progression, therefore it is valuable to be able to quantify any differences in structural

changes during accommodation between myopes, emmetropes and hypermetropes. Drexler *et al.* [223] found a greater increase in AL with accommodation in emmetropes than myopes (0.0127 mm compared to 0.0052 mm) when comparing accommodation between the far-point and near-point. However, the myopic group had a lower amplitude of accommodation than the emmetropic group, and amplitude of accommodation was positively correlated with change in AL. Mallen *et al.* [224] found AL increased significantly more in myopes than emmetropes, to an accommodative stimulus of 6 D (0.058 mm compared to 0.037 mm), but found no correlation between change in AL and refractive error. Woodman *et al.* [245] found a greater increase in AL from baseline after a 30 minute near task for early onset myopes and progressing myopes compared to emmetropes. Again there was no correlation between the increase in AL and the degree of myopia, or the baseline AL. There was however, found to be a weak positive correlation between increase in AL and myopia progression.

A number of studies have compared anterior eye changes with accommodation in myopes and emmetropes, but it is still unclear as to whether there is any difference between the two. Bolz *et al.* [233] simultaneously measured the refraction and biometry in the same eye at six dioptric levels in emmetropes and myopes. They found a difference in the reduction of ACD between the groups (0.047 mm/D for emmetropes and 0.057mm/D for myopes) and also a difference in the increase in LT between the groups (0.063 mm/D for emmetropes and 0.072 mm/D for myopes). This difference reached statistical significance for ACD measurements at 1 and 2 D of accommodative stimulus. Storey and Rabie [231] found a greater increase in LT in their group of myopes of over 5 D. In this group the back surface of the lens was found to move more posteriorly with accommodation than in the lower myopic group. However, Drexler *et al.* [223] found no significant difference between emmetropes and myopes in the change in the anterior segment with accommodation and Ostrin *et al.* [230] found no correlation between changes in biometry (LT and ACD) and spectacle prescription.

5.1.8 Changes in ocular structure associated with nearwork-induced transient myopia

After a period of nearwork some individuals suffer from distance vision blur. This is termed nearwork-induced transient myopia (NITM) and has been discussed at length in previous chapters. It is thought this phenomenon is caused by hysteresis of the crystalline lens, however this has never been proven, as structural changes in the lens during disaccommodation have not been measured with an appropriate degree of precision to demonstrate NITM effects. Woodman *et al.* [245] measured AL before and after a 30 minute near task. They found AL was significantly longer immediately following the near task but this had regressed to baseline 10 minutes post-task. There is a possibility that AL stretch causes NITM rather than hysteresis of the crystalline lens. They found there was no correlation between change in AL and NITM post-task, however, as refraction was measured after biometry measurements, it is possible any NITM present may have dissipated by the time the measurements were taken. Ideally the refraction and biometry measurements would have been taken simultaneously.

5.1.9 Aim of the study

Previous studies have assumed that NITM is lenticular in origin, however lens changes have never been measured in association with NITM measurements. The aim of the study is to show a method which enables tracking of changes in ocular biometry during disaccommodation using an optical high resolution, low coherence reflectometry device (LenStar, Haag-Streit Koeniz, Switzerland). Ultimately we would like to build a system which would record NITM and ocular biometry simultaneously.

5.2 Instrumentation

5.2.1 Measurement of refractive error

This was assessed by non-cycloplegic autorefractometry using the Shin-Nippon NVision-K 5001 (Shin-Nippon, Tokyo, Japan) open view infrared autorefractor [173]. Five readings were taken from the right eye with the participant fixating a 6/60 letter at six metres. The autorefractor produces an average result which was converted to mean spherical equivalent (MSE) i.e. sphere plus half the cylinder.

5.2.2 Ocular biometry

5.2.2.1 LenStar

The AL, LT and ACD were measured using the LenStar (Haag-Streit Koeniz, Switzerland). For baseline readings five measurements were taken and averaged [182].

5.2.2.2 IOLMaster

The AL and ACD were also measured using an IOLMaster (Carl Zeiss, Europe) for comparison. Three readings of the AL were taken and averaged [76]. The IOLMaster takes five readings of the ACD and averages them automatically.

5.2.3 The task

A system consisting of a Badal lens, a pellicle beam splitter and a target was clamped to the LenStar stand allowing the beam splitter and Badal system to be placed in front of the participant's eye (Figures 5.1 and 5.2). The beam splitter (BS) transmitted 92 % of light and reflected 8 % when angled at 45° to the ocular surface, allowing the LenStar target and the accommodative target to be viewed simultaneously, and facilitating accurate alignment. The accommodative target comprised black on white N5 print, subtending 48 minutes of arc at the eye, which was backlit by a 1.2 W tungsten halogen lamp to make it clearly visible. The room illumination was turned off to improve

target visibility. The participant looked towards the LenStar target but tried to keep the print in focus at all times. The print and light were situated on an optical rail (M-MRL-12M, Newport, USA) so they could be moved forwards and backwards simultaneously. The +10 DS Badal lens was located 10 cm from the participants' corneal apex when their head was positioned on the chin rest. Therefore, with the participants full distance correction in place, when the letter target was placed 10 cm from the back surface of the Badal lens it was viewed at optical infinity (Section 2.3). As the print was moved towards the Badal lens the vergence increased and accommodation was stimulated. For every 1 cm moved towards the Badal lens the accommodative demand increases by 1 D. Any spherical ametropia was corrected using a soft, disposable contact lens (Acuvue Moist, Johnson & Johnson Medical Ltd., United Kingdom) which was allowed to settle for 20 minutes prior to measurements being taken [204]. Participants were asked to refrain from performing intense near vision tasks in the hour preceding measurements [102].

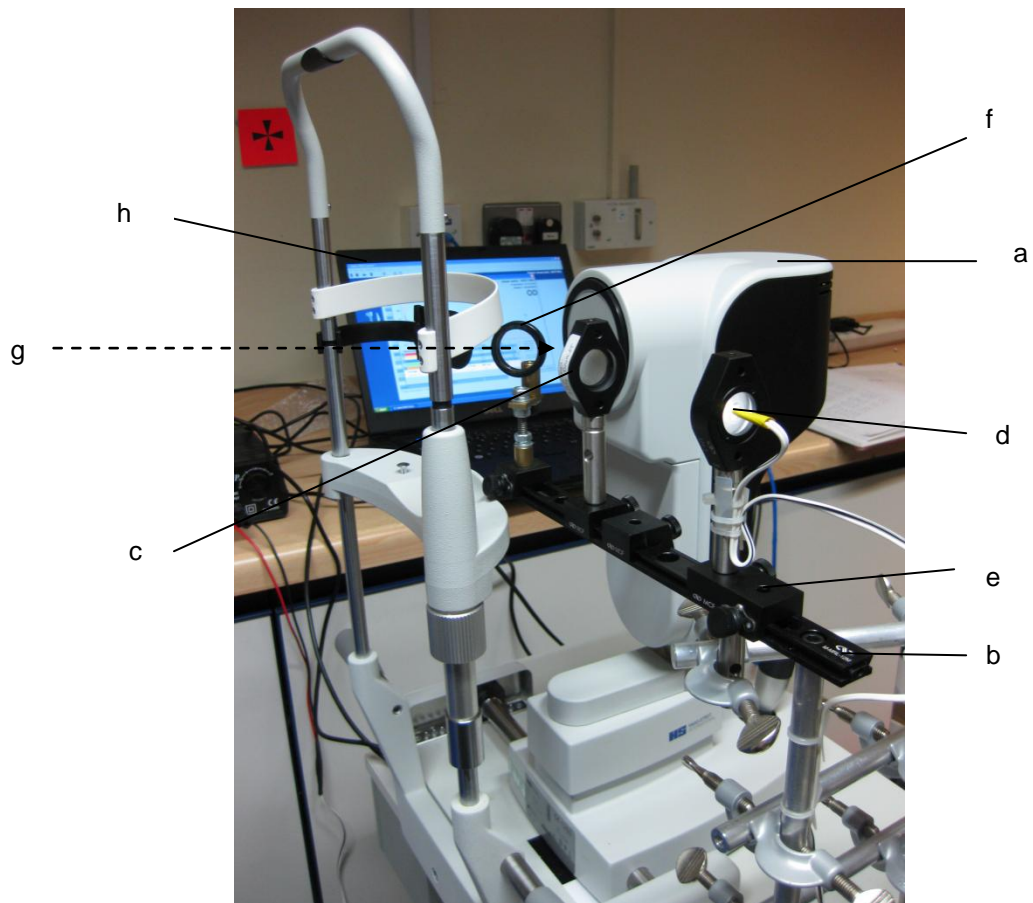


Figure 5.1. Experimental design used to investigate structural changes in the eye during dissaccommodation. a. LenStar (Haag-Streit Koeniz, Switzerland); b. optical rail to enable movement of fixation target; c. +10 D Badal lens located 10 cm from participants corneal apex; d. accommodative target backlit by a tungsten halogen lamp; e. Stopper to enable target to be moved rapidly to optical infinity after the task; f. beam splitter; g. participants line of sight; h. external PC. The LenStar was loaned for this experiment by Aston University.

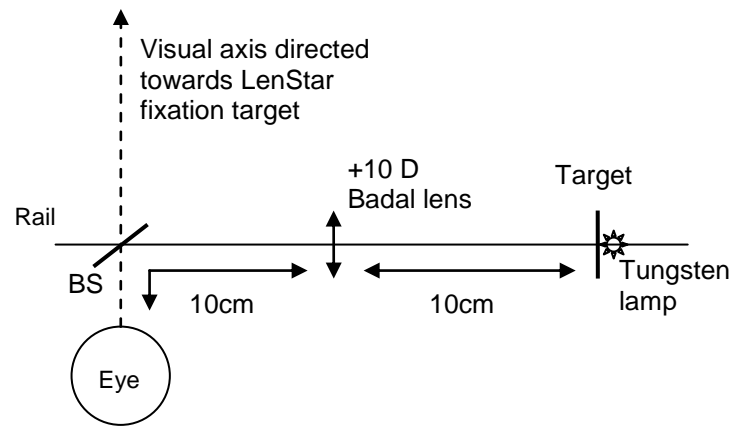


Figure 5.2. Diagram showing the system used to stimulate accommodation whilst taking biometry measurements. The beam splitter (BS) allows the participant to view the LenStar fixation target and the accommodative target simultaneously. The accommodative target is situated at optical infinity when it is 10 cm from the Badal lens. As it is moved towards the Badal lens accommodation is stimulated (1 D per cm movement).

5.2.4 The procedure

Five autorefractor measurements were taken from the right eye only to calculate the MSE, and ocular biometry was performed as per manufacturers' guidelines using the IOLMaster. On ten participants ocular biometry was also performed using the LenStar at this stage. Five biometry measurements were taken as per manufacturer's instructions and measurements of AL, ACD and LT recorded. If the participant had over 0.25 D of myopia they were corrected fully with a daily disposable contact lens in their right eye which was allowed to settle for 20 minutes. The refraction was rechecked using the NVision-K autorefractor to confirm MSE was ± 0.25 D. With the participants chin on the chin rest of the LenStar the accommodation system was placed so the Badal lens was 10 cm from the corneal apex. Adjustments were made to the beam splitter so the participant could view the LenStar fixation target and the accommodation target simultaneously. The participant was asked to keep the N5 letters in focus at all times and with the accommodative target 10 cm from the Badal lens (optical infinity) five biometry measurements were taken using the LenStar. The target was then moved 5 cm towards the Badal lens to give an accommodative stimulus of 5 D and another

five measurements were taken. The Badal system was aligned such that the target did not move horizontally or vertically in the visual field as the stimulus vergence was altered.

The participant viewed a distant target for five minutes to relax the accommodation [206]. With the accommodative target set at 5 D the participant focused on the target for one minute. Again the participant was asked to keep the target in focus at all times. During this time one within task measurement was taken. After one minute the target was manually moved to optical infinity by moving the target 5 cm away from the Badal lens, and timing began. LenStar measurements were commenced immediately the target vergence was changed. Initially the aim was to take measurements every 12 seconds to complete five measurements within 60 seconds. This was carried out on two participants, however, as the length of time taken for the measurement is dependent on the alignment of the system and the participants ability to fixate, it was decided this was not an appropriate method of timing. It was decided, for subsequent participants, to use the 'flash' of light emitted from the LenStar at the end of each measurement as an estimate of the time the measurement was taken. Two researchers were therefore required to collect the data, one to take the measurements and one to move the fixation target and to record the time. All measurements were completed within 80 seconds of the target change, and on average five post task measurements were taken during each data run. This was repeated twice more, giving three sets of data per participant. Between each trial the participant viewed a distant object for five minutes to dissipate any accommodative after-effects [206].

5.2.5 NITM measurements

On one participant (EM) accommodation responses were measured on a separate occasion using a Shin-Nippon SRW-5000 open view infrared autorefractor which had been modified to take continuous recordings [170, 174]. Accommodation readings were

taken monocularly, using the same system which was attached to the LenStar, to stimulate accommodation. Accommodation responses were measured during the one minute 5 D task and then continuously for 60 seconds post-task. The resulting data were then filtered for blinks (Section 2.2.1.2) to produce a smooth graph.

5.2.6 Participants

Eleven participants were recruited with an age range from 22 to 40 years, and a median age of 28 years. All were pre-presbyopic and had astigmatism of no more than 1.00 DC. The mean MSE error of the whole cohort was $-1.81 \text{ DS} \pm 3.04$ and median 0 D (range $+0.69$ to -8.25 D). All subjects had corrected visual acuity of at least 6/6 in each eye, with no history of binocular vision anomalies or ocular health problems. Informed consent was obtained from each participant after full explanation of the procedures involved (Appendix 5.6). The study was approved by the University of Bradford Ethics Committee and conformed to the tenets of the Declaration of Helsinki.

5.3 Results

5.3.1 Comparison between IOLMaster and LenStar

On 10 participants biometric measurements were taken with both the IOLMaster and the LenStar. The results are shown Table 5.1 below.

Table 5.1. Group mean ($\pm 1 \text{ SD}$) AL and ACD measurements for the IOLMaster and the LenStar.

	IOLMaster (n = 10)	LenStar (n = 10)
AL (mm)	24.29 ± 1.64	24.33 ± 1.64
ACD (mm)	3.47 ± 0.37	3.14 ± 0.26

As a Kolmogorov-Smirnov test indicated the data tended towards a normal distribution, a paired samples t-test was used for analysis. Anterior chamber depth was found to be statistically significantly larger when measured with the IOLMaster ($3.47 \text{ mm} \pm 0.37$) as opposed to the LenStar ($3.14 \text{ mm} \pm 0.26$) ($t_{(9)} = 2.382$, $p = 0.041$), and, AL was found

to be statistically significantly larger when measured with the LenStar ($24.33 \text{ mm} \pm 1.64$) as opposed to the IOLMaster ($24.29 \text{ mm} \pm 1.64$) ($t_{(9)} = -3.366, p = 0.008$). As the ACD measurement taken using the IOLMaster includes corneal thickness of approximately 0.544 mm [247], whereas, the measurement taken by the LenStar does not, it would be expected that there would be a significant difference between the two measurements. Ideally we would have measured corneal thickness using the LenStar and added it to the ACD result to compare to the IOLMaster, however as some participants wore contact lenses for data collection, it was not valid to take a measurement of corneal thickness with the LenStar. Bland Altman plots [221] to illustrate the mean difference between the biometry measurements taken by the two instruments and the 95% confidence intervals are shown in Figures 5.3 and 5.4.

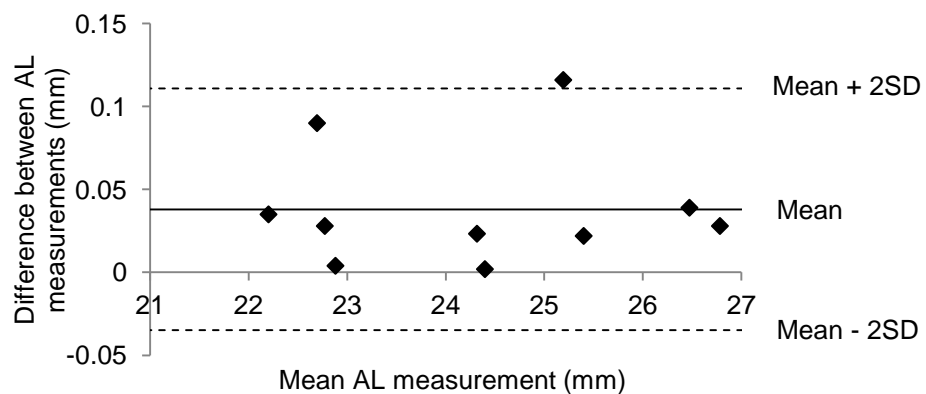


Figure 5.3. A Bland Altman plot to illustrate the difference in AL measurement (LenStar measurement – IOLMaster measurement) plotted against the average AL $[(\text{LenStar measurement} + \text{IOLMaster measurement}) / 2]$.

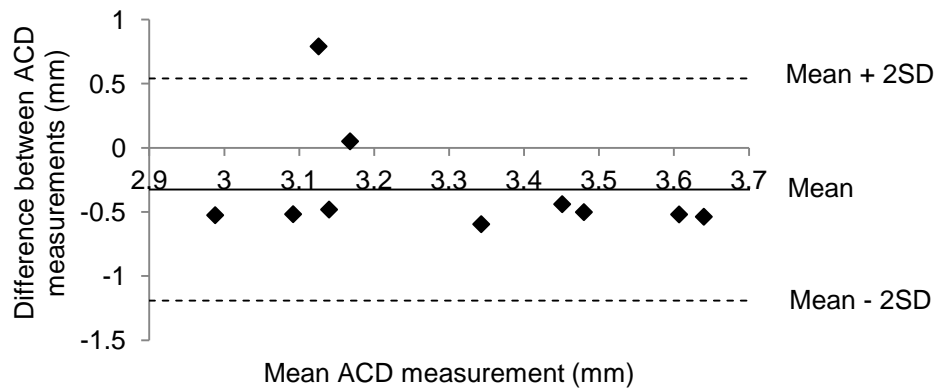


Figure 5.4. A Bland Altman plot to show the difference in ACD measurement (LenStar measurement – IOLMaster measurement) plotted against the average ACD [(LenStar measurement + IOLMaster measurement) / 2].

5.3.2 Comparison of biometry measurements with and without the accommodation stimulation system in place

Ten measurements were taken without and with the beam splitter in place on the LenStar AE to assess the effect the accommodation stimulus system had on the LenStar measurements. Only AL and ACD could be measured using the AE. A Kolmogorov-Smirnov test indicated the data did not tend towards a normal distribution therefore a Wilcoxon signed-rank test was used to compare the means between the two conditions. There was found to be a statistically significant reduction in AL with the beam splitter in place ($23.870 \text{ mm} \pm 0.000$) as compared to no beam splitter in place ($23.878 \text{ mm} \pm 0.004$) ($Z = -2.828, p = 0.008$), however, there was no statistically significant effect of the beam splitter on ACD ($Z = -1.414, p = 0.500$).

On eight participants LenStar measures of AL, ACD and LT were taken both with and without the beam splitter and accommodation measurement system in place to assess the effect of the system on measurements of the human eye. The results are shown in Table 5.2.

Table 5.2. Group mean (± 1 SD) AL, ACD and LT measurements without and with the beam splitter (BS) in place.

	Without BS (n = 8)	With BS (n = 8)
AL (mm)	24.35 \pm 1.59	24.35 \pm 1.59
ACD (mm)	3.14 \pm 0.23	3.15 \pm 0.22
LT (mm)	3.82 \pm 0.19	3.81 \pm 0.18

A Kolmogorov-Smirnov test indicated the data tended towards a normal distribution therefore a paired t-test was carried out to compare the two conditions. There was found to be a statistically significant reduction in AL with the beam splitter in place (24.348 mm \pm 1.590) as compared to no beam splitter in place (24.354 mm \pm 1.590) ($t_{(7)} = 2.888$, $p = 0.023$). No statistically significant difference was found in either ACD ($t_{(7)} = -0.715$, $p = 0.498$, power = 0.051) or LT ($t_{(7)} = 1.379$, $p = 0.210$, power = 0.052) without and with the system.

5.3.3 Comparison of AL, ACD and LT for 0 D accommodation and 5 D accommodation

The mean of five measurements of AL, ACD and LT taken at 0 D and 5 D accommodative stimuli for each of 10 participants was calculated. The individual results are shown in Table 5.3. A group mean value for each parameter was then calculated and the results are shown in Table 5.4.

Table 5.3. A table to show the mean of five LenStar measurements ± 1 SD taken for each participant of AL, ACD and LT for both the 0 D and 5 D stimuli. There is also a column showing the difference between each measurement for the two accommodative levels (5 D minus 0 D).

Participant	AL (mm)			ACD (mm)			LT (mm)		
	0 D	5 D	Difference	0 D	5 D	Difference	0 D	5 D	Difference
CT	24.33 \pm 0.00	24.34 \pm 0.03	0.01	3.23 \pm 0.02	3.04 \pm 0.02	-0.19	3.91 \pm 0.02	4.08 \pm 0.11	0.17
EM	26.50 \pm 0.01	26.56 \pm 0.02	0.06	3.23 \pm 0.01	3.03 \pm 0.02	-0.20	4.07 \pm 0.02	4.34 \pm 0.01	0.27
BC	24.40 \pm 0.02	24.43 \pm 0.02	0.03	3.05 \pm 0.02	2.91 \pm 0.01	-0.14	3.63 \pm 0.08	3.83 \pm 0.14	0.20
JD	22.22 \pm 0.04	22.22 \pm 0.04	0	2.90 \pm 0.02	2.65 \pm 0.03	-0.25	3.84 \pm 0.03	4.06 \pm 0.11	0.22
AB	25.41 \pm 0.01	25.47 \pm 0.03	0.06	3.35 \pm 0.01	3.08 \pm 0.02	-0.27	4.03 \pm 0.02	4.32 \pm 0.04	0.29
OH	26.80 \pm 0.06	26.80 \pm 0.02	0	3.52 \pm 0.01	3.35 \pm 0.03	-0.17	3.52 \pm 0.01	3.75 \pm 0.01	0.23
NF	22.88 \pm 0.01	22.89 \pm 0.01	0.01	2.73 \pm 0.01	2.54 \pm 0.01	-0.19	3.96 \pm 0.18	4.07 \pm 0.05	0.11
AA	22.79 \pm 0.01	22.83 \pm 0.01	0.04	2.83 \pm 0.01	2.54 \pm 0.01	-0.29	3.81 \pm 0.02	4.13 \pm 0.15	0.32
AE	25.25 \pm 0.01	25.28 \pm 0.02	0.03	3.37 \pm 0.01	3.13 \pm 0.01	-0.24	3.62 \pm 0.02	3.88 \pm 0.01	0.26
TD	22.74 \pm 0.02	22.71 \pm 0.03	-0.03	3.19 \pm 0.21	2.78 \pm 0.19	-0.41	3.40 \pm 0.18	3.72 \pm 0.22	0.32

Table 5.4. Group mean LenStar values ± 1 SD for AL, ACD and LT for both the 0 D and 5 D stimuli. The *p*-value produced from a paired t-test is also shown.

	0 D stimulus	5 D stimulus	Difference	<i>P</i> -value
ACD (mm)	3.14 \pm 0.26	2.91 \pm 0.27	-0.23	< 0.001
LT (mm)	3.78 \pm 0.23	4.00 \pm 0.22	0.22	< 0.001
AL (mm)	24.33 \pm 1.64	24.35 \pm 1.66	0.02	0.059

As a Kolmogorov-Smirnov test indicated the data tended towards a normal distribution, a paired samples t-test was used to compare the means. The group mean ACD was found to be significantly less when accommodating to a 5 D stimulus ($2.91 \text{ mm} \pm 0.27$) than to a 0 D stimulus ($3.14 \text{ mm} \pm 0.26$) ($t_{(9)} = 9.474, p < 0.001$), while the group mean LT was found to be significantly greater during accommodation ($4.00 \text{ mm} \pm 0.22$) than when not accommodating (3.78 ± 0.23) ($t_{(9)} = -11.111, p < 0.001$). There was a trend for the mean AL to be longer during accommodation (24.35 ± 1.66) than when not accommodating (24.33 ± 1.64), however, this was not found to be statistically significant ($t_{(9)} = -2.169, p = 0.058$).

Figure 5.5 shows the correlation between the AL of the eye as measured by the LenStar at 0 D of accommodation, and the change in ocular parameters with 5 D of accommodation. There was found to be no significant correlation between AL and change in AL ($r = 0.461, p = 0.180$), change in ACD ($r = 0.469, p = 0.172$) or change in LT ($r = 0.122, p = 0.737$). Figure 5.6 shows the correlation between the MSE and the change in ocular parameters with 5 D of accommodation. There was found to be no significant correlation between MSE and change in AL ($r = -0.355, p = 0.314$), change in ACD ($r = -0.395, p = 0.259$) or change in LT ($r = -0.165, p = 0.648$).

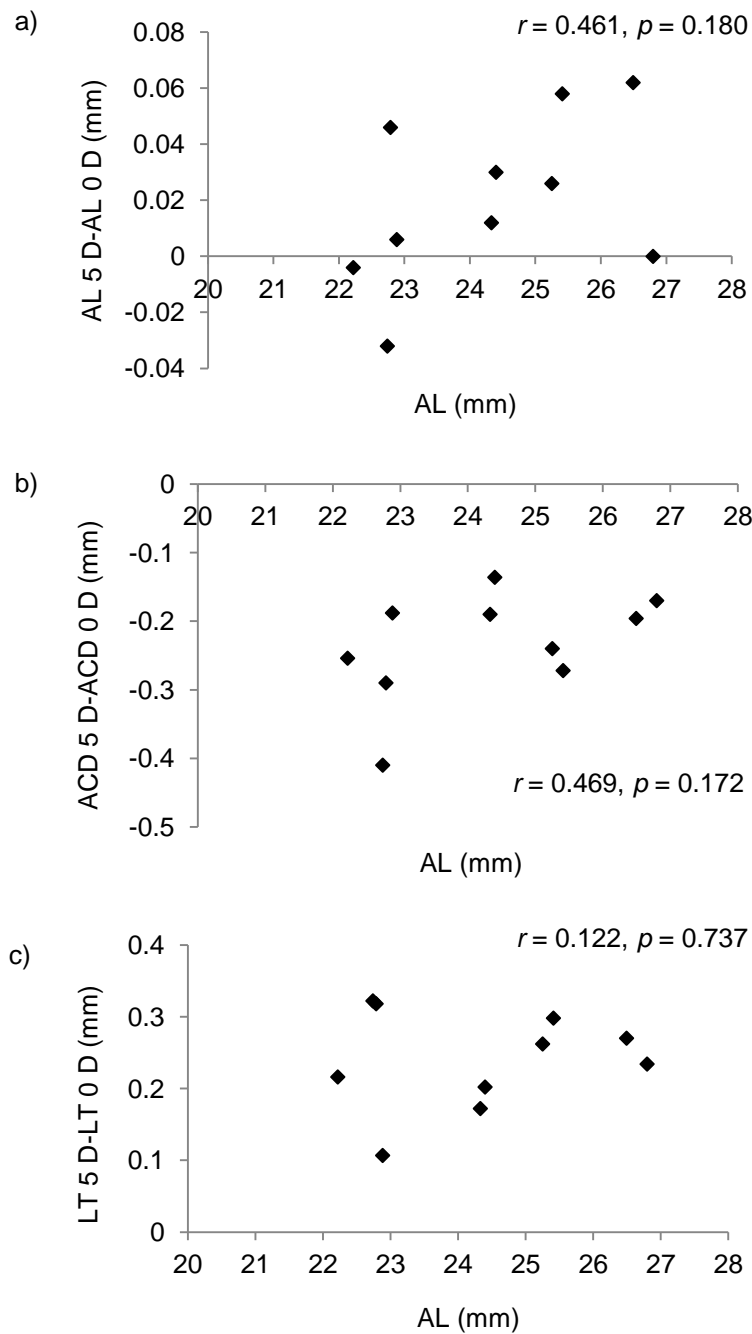


Figure 5.5. Correlation between AL as measured by the LenStar at 0 D and the change in a) AL, b) ACD and c) LT with 5 D of accommodation.

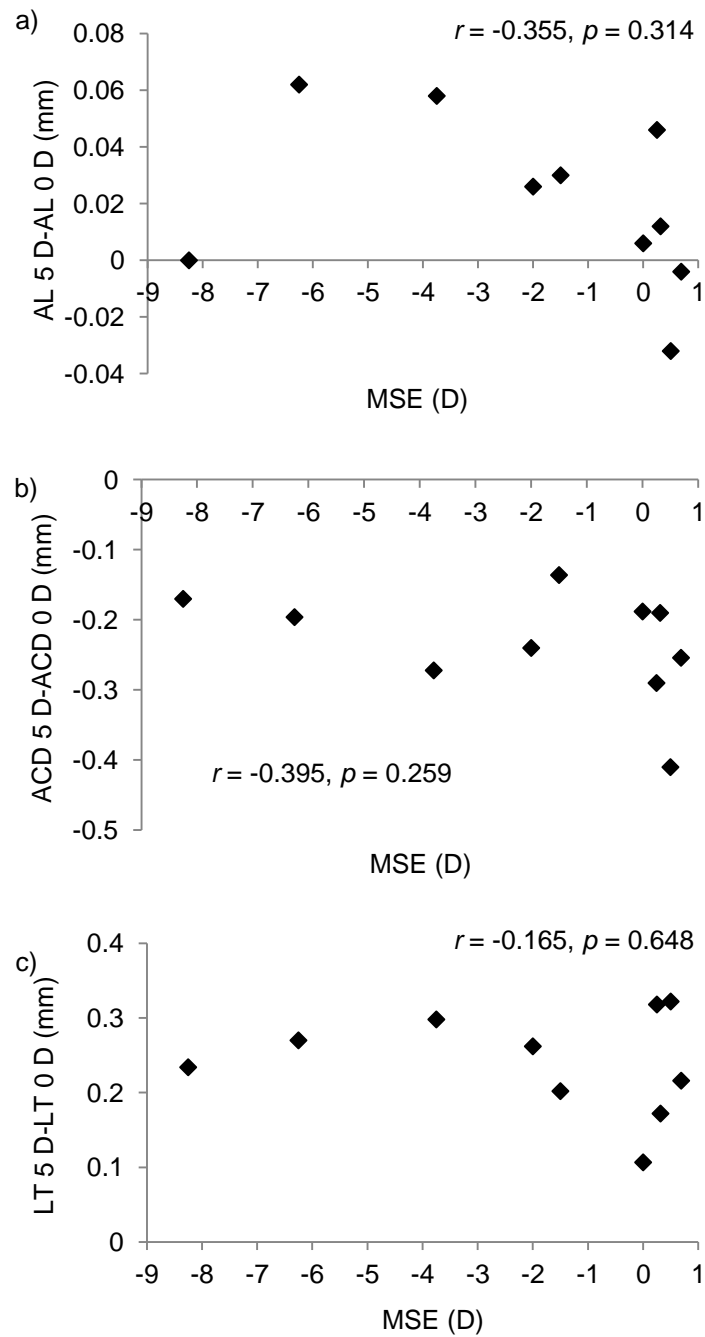


Figure 5.6. Correlation between MSE and the change in a) AL, b) ACD and c) LT with 5 D of accommodation.

5.3.4 Average time to take measurements

When taking biometry measurements using the LenStar the eye is aligned by the participant fixating the red beam and the researcher focusing the image on the monitor.

When the image is focused the measurement is initiated by pressing a button on the

joystick. The instrument takes 16 consecutive scans per measurement [182]. It uses an 'intelligent detection system', where a reflection from the fovea is required for measurements to be taken, to ensure correct alignment. All measurements are therefore taken along the visual axis. If a blink occurs or there is a loss in fixation, measurement is halted and resumes when fixation is again detected. Once the measurement has been acquired, no further measurements can be taken until the calculated result is visible on the screen. For this reason each measurement takes a slightly different length of time, dependant on patient fixation. Measurements of all parameters are taken at the same time without the need to realign the system. We were interested as to how long, on average, it took between taking a measurement and being able to take another. The mean and standard deviation time between each measurement was calculated individually for nine participants. The first post-task time point was excluded as it was easier to have this aligned and therefore it tended to be taken quicker. Two participants had their data taken at time measured intervals as explained in Section 5.2.4 therefore they were excluded from the analysis. The group mean measurement time was then calculated and found to be $14.56 \text{ s} \pm 2.12$. The individual means are shown in Figure 5.7.

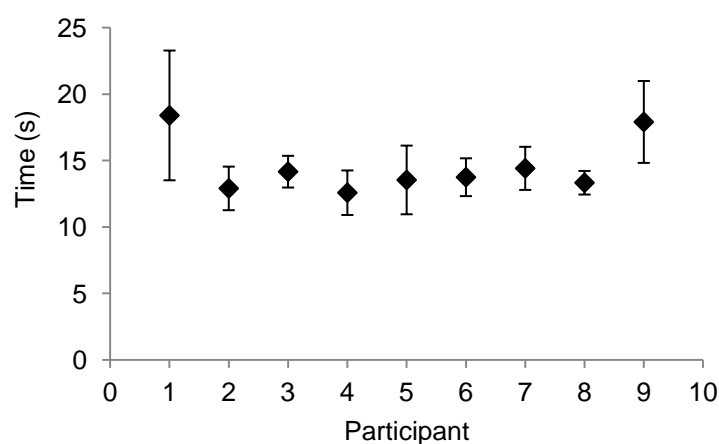


Figure 5.7. Mean length of time from the end of one measurement to the end of the next for each of nine participants. Error bars = ± 1 SD.

5.3.5 Dynamic results

As the measurements were all taken at slightly different time points it was not possible to average the raw data to produce a group mean. For each participant the data points from the three dynamic trials were amalgamated within an Excel spreadsheet (Microsoft Corporation, Washington, USA). This meant a single plot could be produced from each set of three data collections for AL, ACD and LT to illustrate the effect of disaccommodation on ocular biometry. This process is illustrated for the post-task LT changes of participant EM in Figure 5.8.

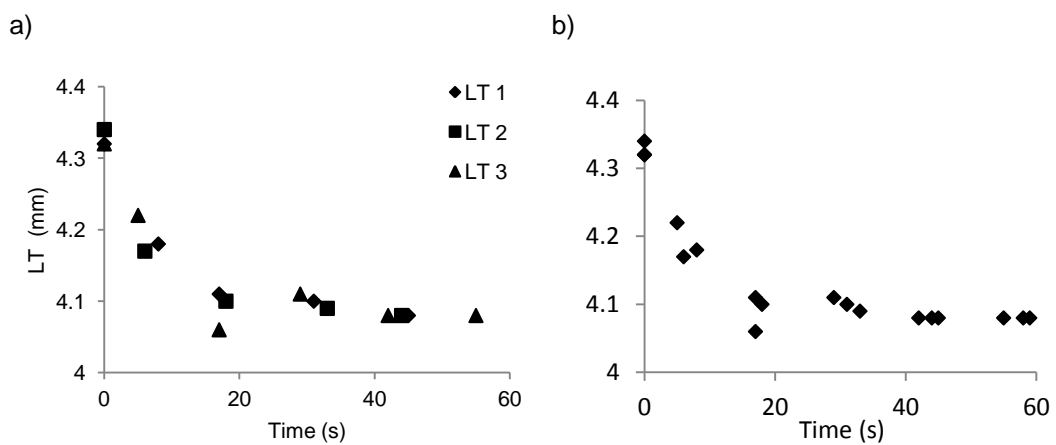
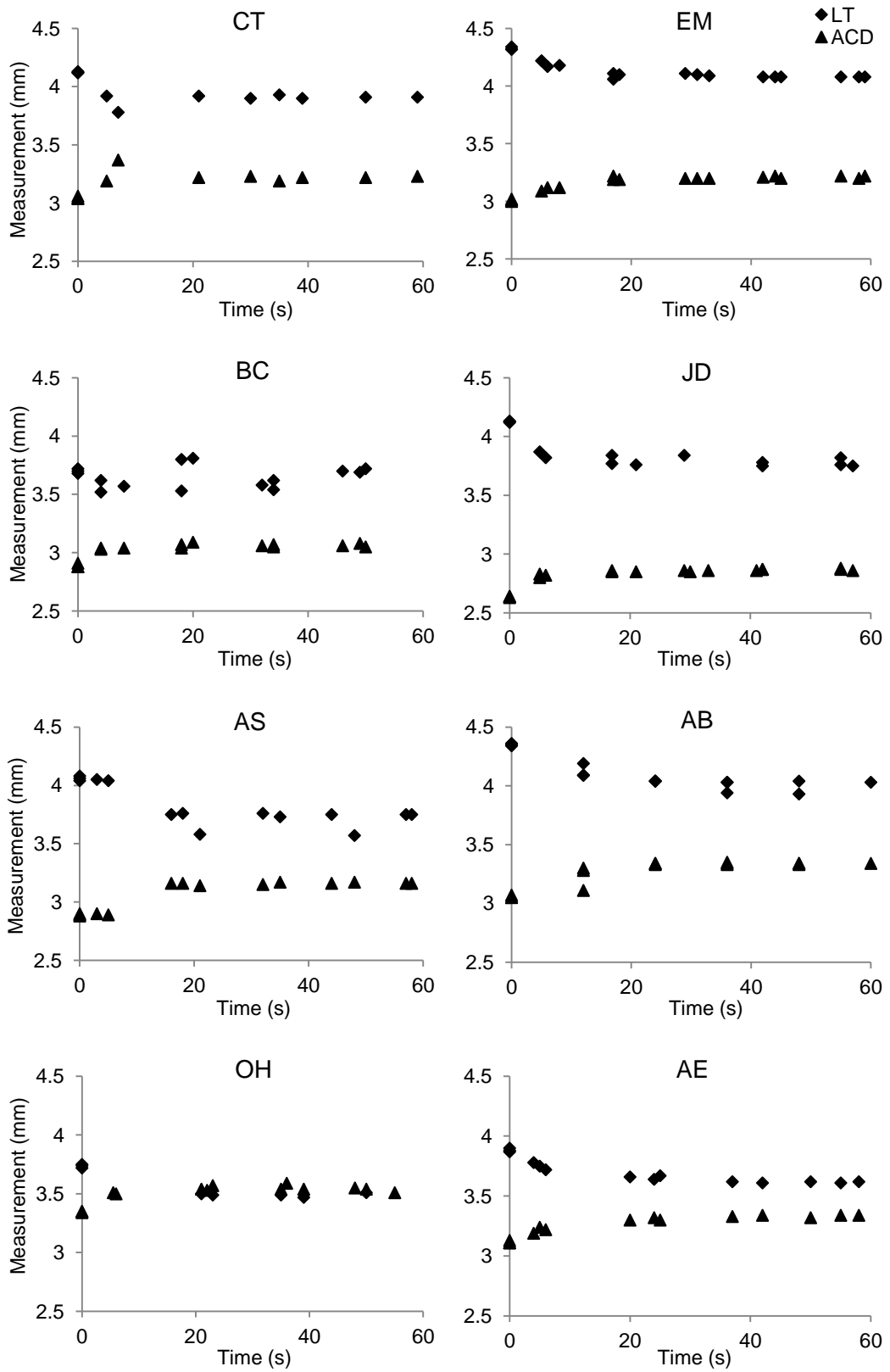


Figure 5.8. LT change plotted against time for participant EM. Graph a) shows the three individual sets of data plotted together. Graph b) shows the points from the three curves amalgamated to produce one curve.

Figure 5.9 shows individual plots of LT changes and ACD changes over time for all 11 participants. As the measurements were taken as quickly as possible post-task there were occasions when the LenStar did not produce readings for all the ocular parameters.



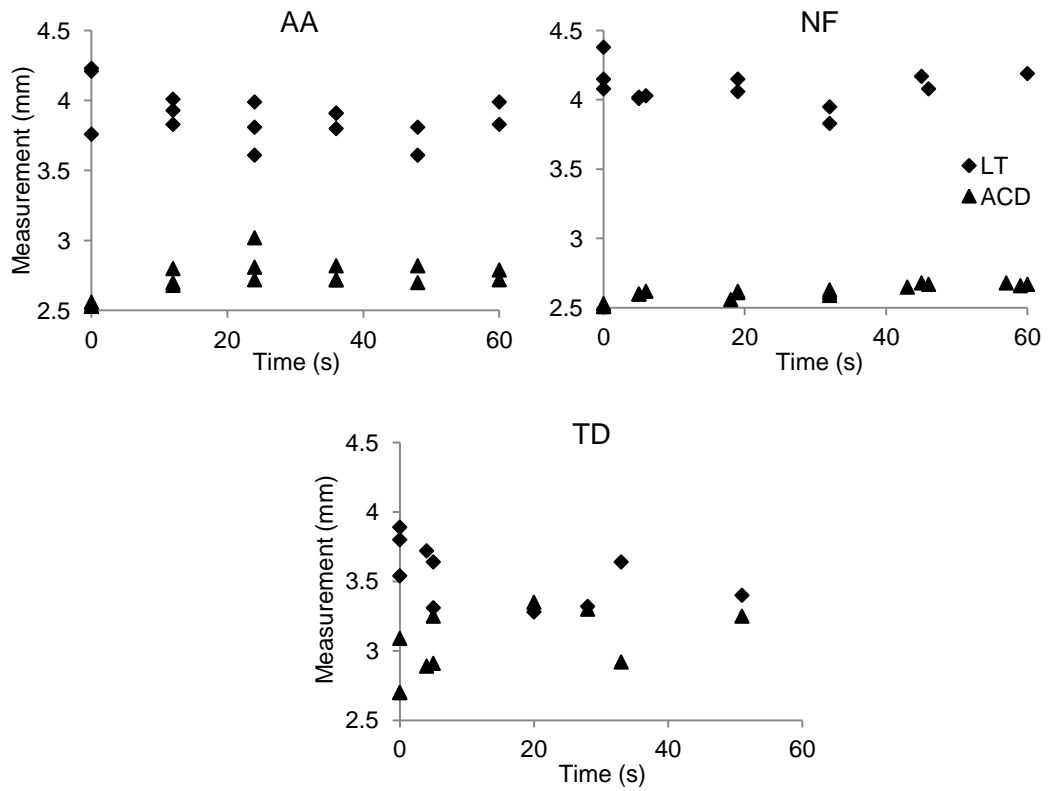


Figure 5.9. Individual plots of change in ACD and LT *versus* time. The plots are made of a combination of the three sets of data taken for each participant.

5.3.6 Lens thickness and associated NITM

For one participant (EM) both biometry and continuous recording of accommodation were carried out on separate occasions for an identical task. Figure 5.10 and 5.11 show graphs illustrating LT and accommodation respectively.

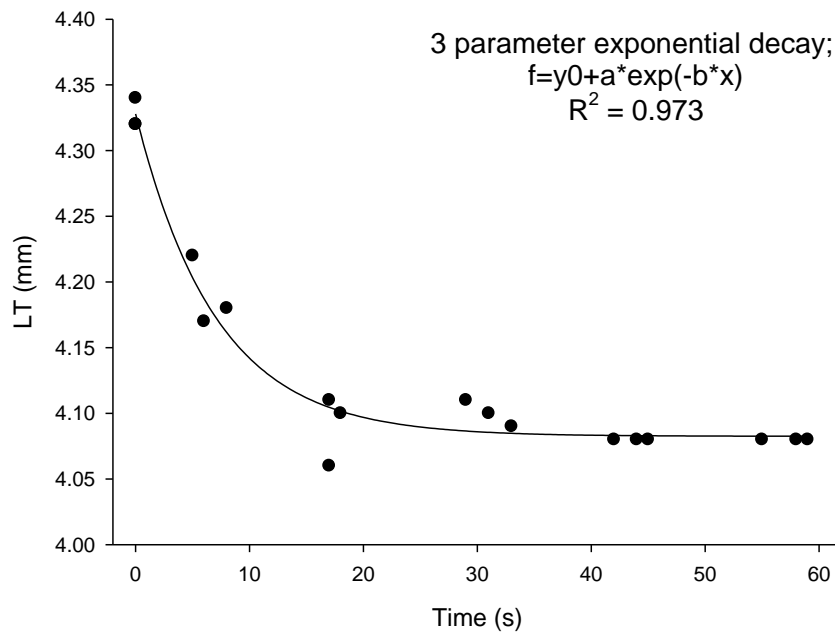


Figure 5.10. LT *versus* time during the period 60s post-task for participant EM. The data are fitted with a three parameter exponential decay curve.

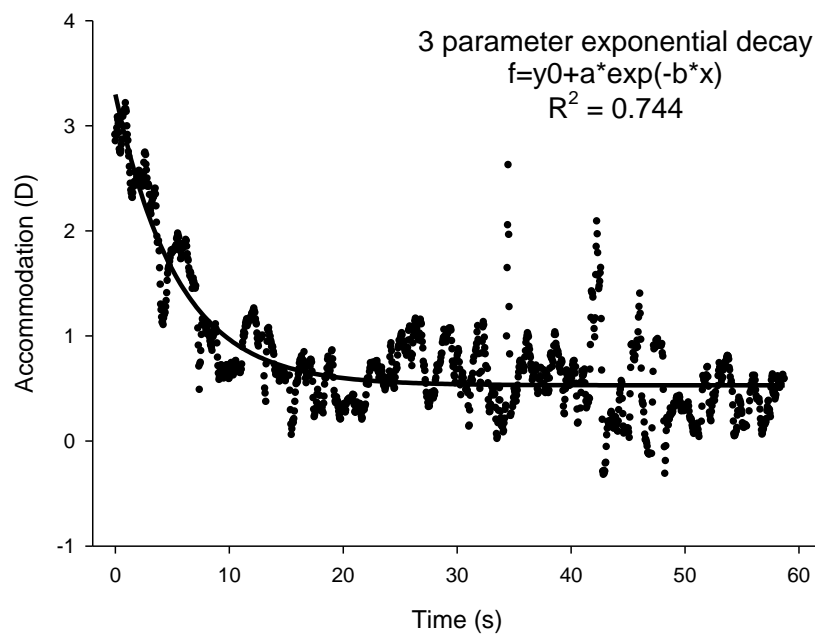


Figure 5.11. Accommodation *versus* time during the period 60s post-task for participant EM. The data are fitted with a three parameter exponential decay curve.

5.4 Discussion

Using an optical high resolution, low coherence reflectometry device (LenStar) this study has shown it is possible to measure ocular biometry during disaccommodation

post-task and to relate this to continuous recording of accommodation. This has not previously been possible due to the resolution of A-scan ultrasound which is on average 0.15 mm [236]. The study has shown that the regression of LT post-task takes a similar form to that of regression of accommodation post-task, therefore, we are a step closer to showing that NITM is lenticular in origin.

Comparison between IOLMaster and LenStar biometry data agree with results by Buckhurst *et al* [182] in that AL measurements were found to be significantly greater with the LenStar than the IOLMaster (0.04 mm in this study and 0.01 mm in the study by Buckhurst *et al*). Measurements of ACD were confounded by the lack of corneal thickness data from the LenStar. If we add average corneal thickness (0.544 mm) [247] onto our mean ACD measured by the LenStar we get a comparison of 3.71 mm for the LenStar against 3.47 mm for the IOLMaster a difference of 0.24 mm as compared to a 0.1 mm difference found by Buckhurst *et al*.

The beam splitter which was used to aid simultaneous viewing of the LenStar target and accommodative stimulus was found to cause a statistically significant reduction in the AL measurement in both an AE and real eyes of 0.008 mm and 0.006 mm respectively. Although this was statistically significant it was felt to be clinically insignificant due to the small value and also the fact that all dynamic measurements were taken with the system in place therefore there would be no comparison of with and without. There was no statistically significant effect of the beam splitter on the ACD or LT.

A comparison of ocular biometry measurements taken for a 0 D accommodative stimulus as compared to a 5 D accommodative stimulus showed changes which compare favourably to previous research. There was a trend for an increase in AL with accommodation in agreement with both Mallen *et al* [248] and Drexler *et al* [223]. This difference of 0.02 mm lies between their measurements. It was close to being statistically significant ($p = 0.059$), and had our cohort been larger, may have reached significance. However, this present study was not specifically looking at AL changes

during accommodation.

The reduction in ACD of 0.046 mm/D equates well with previous studies [227, 230, 233]. It is possible this is an underestimation of the true change, as this is calculated using accommodative stimulus as opposed to accommodative response. As we had four participants over the age of 35 years it is possible this lowered the accommodative response.

Lens thickness change was found to be 0.044 mm/D which corresponds to that found in previous studies (0.043 to 0.051 mm/D) when calculated using accommodative stimulus [227, 229, 230, 234]. Lens thickness changes have been found to be greater when calculated using accommodative response (0.067 to 0.072 mm/D) [230, 233].

At present there is no consensus in the literature as to whether there is a difference in the biometric changes with accommodation between myopes and emmetropes. No correlation was found between the accommodation-induced change in biometry (AL, ACD or LT for 0 D to 5 D shifts) and refractive error.

The goodness of fit of the three parameter exponential decay to both the dynamic LT data and accommodation was high for participant EM. The R^2 is poorer for the accommodation data due to measurement noise and accommodative microfluctuations. The high R^2 of the LT data is encouraging as this indicates these data are relatively noise free.

5.4.1 Experimental limitations

The main limitations for this study were access to the LenStar, and the fact that the continuous recording system was not in the same laboratory as the LenStar, therefore, it was not possible to try to link the two systems. More time spent with the LenStar would have meant a larger cohort could have been used. For some individuals the LenStar measured biometry data easily, however, on others, as we can see from some of the plots (Figure 5.9) there was a problem trying to locate the surfaces of the lens, particularly the posterior surface. Taking the measurements quickly so as not to lose

valuable data post-task sometimes meant difficulty with alignment and missing data points. More time is needed with the instrument to assess why there is this difference between participants. Pupil size is reduced with accommodation and it is possible this may be the source of the measurement difficulties, it would therefore be useful to retake the data after dilation with phenylephrine to see if measurements are easier through a dilated pupil. Phenylephrine, however, has been shown to affect accommodation in some individuals which may affect any NITM present [249].

To date it has not been possible to try to link the LenStar with the Shin-Nippon continuous recording system as has been done previously using the IOLMaster [239]. The LenStar was at Aston University whereas the continuous recording system was at Bradford University which meant biometry and accommodation data could only be taken on one participant and this was done on separate occasions. Until these measurements can be taken simultaneously it will not be possible to conclude that NITM is lenticular in origin, however, a comparison of the regression for the two sets of data suggest a similar pattern.

Chapter 6

The effect of a multichromatic stimulus on the accommodative response of the eye

6.1 Introduction

Under every day circumstances the accommodation system uses defocus, proximity and vergence cues to keep an image in focus on the retina [77]. Under experimental conditions i.e. within a Badal system, where vergence and proximity cues are absent, the accommodation system uses negative feedback in the form of retinal blur to keep an object in focus at different viewing distances [78]. If the difference between the level of accommodation and the distance of the object from the observer is greater than the ocular depth-of-focus then an accommodation response occurs. However, defocus blur is an even-error cue [250] i.e. there is no information as to whether increasing or decreasing accommodative effort would make the image clearer. In theory this should result in the system responding in a trial and error manner to reduce the blur, however, this does not appear to be the case [78]. It has been suggested that the presence of chromatic aberration may change this even-error cue into an odd-error cue giving the accommodation system more directional information on how to reduce blur [203, 251].

6.1.1 Longitudinal chromatic aberration of the eye

Due to the dispersion of the refracting media, the eye displays longitudinal chromatic aberration (Figure 6.1). When a beam of light from point O enters the eye, the path it takes depends on its wavelength, as the refractive indices of the media vary as wavelength varies. Short wavelength light comes to a focus further forward in the eye than long wavelength light [200].

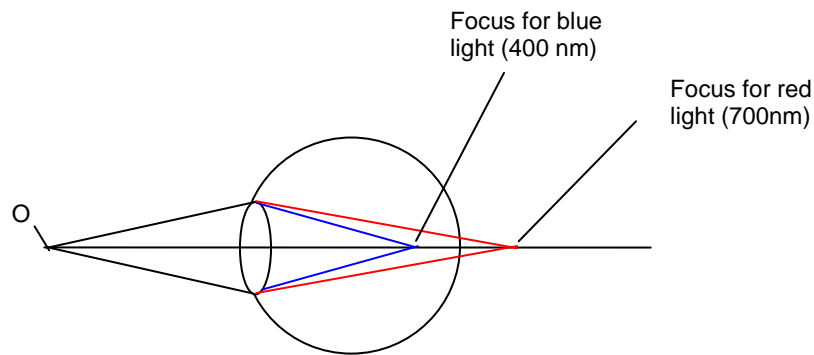


Figure 6.1. Illustration of the chromatic aberration of the eye. Short wavelength light is brought to focus in front of the retina while long wavelength light is brought to focus behind the retina.

For white light under broadband illumination, the difference in focus between the blue (400 nm) and red (700 nm) ends of the spectrum has been shown to be as much as 2 D [252]. In some individuals this chromatic aberration appears to be used as a directional cue to aid focus [203, 251]. For an achromatic target, in an eye which is under-accommodating, the image of the target would have a red fringe and conversely for over accommodation there would be a blue fringe [203]. It is possible these coloured fringes change the even-error blur cue to an odd-error cue giving the visual system more information to work with.

6.1.2 Longitudinal chromatic aberration and emmetropization

There is evidence that longitudinal chromatic aberration may provide a signal to aid emmetropization [253]. In animal studies monochromatic light of different wavelengths has been found to effect the emmetropization process [254, 255] with animals reared in short wavelength light becoming relatively more hypermetropic compared to those reared in longer wavelength light. In humans, Kroger and Binder [168] found that using a short-pass (i.e. blue) filter when viewing a black cross on a white background significantly (0.41 D) reduced accommodative responses. They suggested that the use of paper which absorbs long wavelength light may be effective in reducing the

accommodative stimulus, thereby, reducing myopia progression in children, in a similar way to using cycloplegic agents or near additions.

6.1.3 Accommodation response to monochromatic targets

Intuitively, due to the chromatic aberration of the eye, varying levels of accommodation would be needed to focus targets of different wavelengths. A number of studies have shown that a larger accommodative response is obtained when fixating a red target than a blue target [167-169, 256-259] and that yellow and green targets tend to illicit a similar accommodative response to white targets [259, 260]. If a target is alternated from red to blue whilst being kept at the same accommodative level, a slight shift in accommodation can be measured [167]. It is, however, possible that this is a voluntary reflex and only occurs with trained observers [78]. There does appear to be a large variation in the accommodation response to colour throughout the population with some people able to adopt a strategy to enable them to accurately focus different wavelengths of light whereas others fail to do this [259].

6.1.4 Accommodation response to multichromatic targets

In the real world, however, not all targets are achromatic. What happens when the visual system is faced with a multichromatic target? In a study by Atchison *et al.* [256] in which five participants were required to focus on various coloured stimuli at an accommodative level of 3 D, the accommodative response to a red-on-blue target was significantly lower in three of the five participants than to a black-on-white target, suggesting that those participants were accommodating to the blue background. No significant difference in the variability of the accommodative responses between the two stimuli was found.

Lovasik and Kergoat [169] found no significant difference between the accommodative response at either 40 or 80 cm working distance between three multichromatic stimuli: blue-on-red, blue-on-green and red-on-green. They found the accommodative

response for all three stimuli seemed to be averaged between that for a monochromatic red and a monochromatic blue target, but was closer to that for red than that for blue. The phenomenon could be understandable for the blue-on-red and red-on-green stimuli, but it would be expected that the accommodation response for the blue-on green stimulus would lie closer to that of monochromatic blue. Ciuffreda *et al.* [261] were in agreement as they tested 14 colour combinations and found no significant difference in the accommodative response to a 3 D stimulus between any of them. Charman [258], however, used a target of blue Landolt 'C' on a red background and red on a blue background. From 20 observers he found varying responses to the multichromatic targets. Some participants always focused for the red, some for the blue, some for the background and others for the optotype. There were also a group who appeared equally happy focusing on the background or the Cs. They did not, however, find any participant whose focus seemed to be an average between the two wavelengths. Charman concluded that although there was a lot of variation between participants, they all appeared to be optimizing the illumination contrast in the retinal image by aiming for optimal focus of one of the colours.

6.1.5 Subjective symptoms associated with viewing coloured targets

Although the previous literature has measured the accommodative response to various colours and combinations of colours, only one study has investigated subjective symptoms associated with the use of coloured targets. Matthews *et al.* [262] investigated symptoms after a four hour search and decision making task viewing a computer screen. There was found to be no significant effect of the colour of the print (red on black, green on black, blue on black, white on black, red on blue, red on green and blue on green) on fatigue ratings or reported symptoms.

6.1.6 Accommodative microfluctuations

During steady state accommodation, small temporal fluctuations in accommodative response are exhibited. Campbell *et al.* [263] in 1959 were the first to develop an optometer with high enough spatial sensitivity and temporal resolution to measure these accommodative microfluctuations. Power spectrum analysis is a tool which can be used to investigate microfluctuations during steady state accommodation [264-266]. Accommodation signals can be reduced into sinusoidal waveforms called Fourier components by the mathematical process of Fast Fourier Transform (FFT).

The square of the sinewave component is plotted on the y-axis against its frequency on the x-axis, producing a power spectrum (Figure 6.2). This graph then highlights the dominant frequencies.

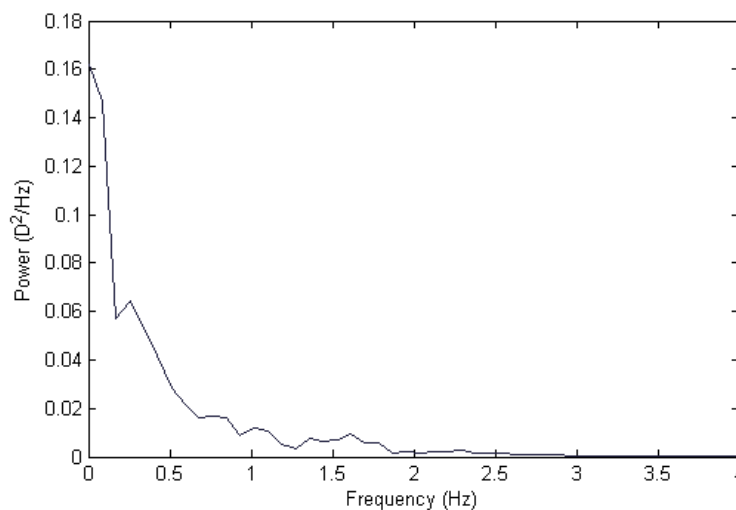


Figure 6.2. Illustration of a power spectrum produced by the process of Fast Fourier Transform.

6.1.6.1 The properties of accommodative microfluctuations

When Campbell *et al.* [264] analysed the power spectra of their accommodation data, two dominant frequencies were evident for a 7 mm pupil. The main one was a low frequency component (LFC) in the region between 0 and 0.5 Hz and the second was a smaller, high frequency component (HFC) at about 2 Hz. These results have been confirmed by a number of subsequent studies [265, 267-272], although the LFC has been found to extend beyond 0.5 Hz and the HFC has been found between

1.2 – 2.5 Hz [273, 274]. Microfluctuations have been recorded as having a frequency ranging from 0 to 6 Hz [265]. They are at their smallest when looking at infinity [264, 273] and have an amplitude of between 0.10 - 0.50 D. The power of the LFC, HFC and root mean square (RMS) (RMS is the standard deviation of the data after it has been filtered for blinks but before the power spectrum density plot has been calculated) have been found to reduce with age in children [275] and a comparison of studies suggests the values are lower in adults than children.

6.1.6.2 Significance of accommodative microfluctuations

It has been suggested these microfluctuations aid the accommodation system in maintaining clear vision by providing an odd-error cue [276] and they may be under both neurological and physiological control [267]. Fluctuation of accommodation in one direction will improve clarity, whilst a fluctuation in the opposite direction will cause increased blur. The fluctuations appear to span the depth-of-focus and can therefore provide information to control accommodation [277]. Charman and Heron [276] suggested the two frequency components had different roles: HFC fluctuations were due to 'plant noise' arising from the crystalline lens, zonules and ciliary body, with the largest contribution to the HFCs being from the periphery of the lens, while the LFC was to help control the steady state accommodation. Winn *et al.* [278] have since shown that HFCs are present throughout the lens and, are possibly, slightly higher in the centre, suggesting the force from the ciliary muscles does not just act on the peripheral lens but is distributed evenly throughout.

In situations where the visual system has very little feedback i.e. with pupil diameters less than 2 mm [264, 269, 270], an empty visual field [264], blur [279] or reduced target luminance [268] the LFC have been found to become more pronounced. Campbell *et al.* [264] found that HFC reduced significantly with a 1 mm as compared to a 7 mm pupil diameter, however this result has not been repeated [269, 270]. The fact that LFC have been found to change consistently with changing visual stimuli adds weight to the fact

that they help with control of accommodation. It is possible that if an image is degraded by blur, or the visual system is faced with an open-loop condition, the amplitude of the LFCs needs to increase to provide consistent feedback to the visual system.

Measurements of accommodation made using autorefractors confirm that microfluctuations exist but not exactly where they originate. Fluctuations in the anterior and posterior lens surfaces during steady state accommodation have been demonstrated using ultrasound techniques [280]. LFCs were found in the anterior chamber, lens and vitreous during steady state accommodation, supporting the idea that these are lenticular and neurological in origin.

The HFC do not appear to be affected by changes in visual stimuli in the same way as the LFC [268-270, 279]. There has been shown to be a significant correlation between the location of the HFC and arterial pulse frequency [267, 281, 282], a correlation which is retained during exercise induced changes in pulse rate [267]. This was not found to be present in aphakic eyes suggesting its source is from the accommodative plant. The mechanism for this could be pulsatile changes in the ciliary ring diameter which leads to changes in lens power. This is supported by the finding that increased ciliary body thickness is associated with a reduction in the HFC with the suggestion that thicker ciliary bodies may dampen the effect of the pulse on accommodation [275]. Alternatively, changes in IOP due to the pulse may cause changes in lens position [280]. The instillation of 0.5% timolol maleate [282] has been found to significantly reduce the RMS value of microfluctuations, again associating their control with factors relating to IOP and ocular vasculature.

Ultrasound investigation during steady state accommodation, however, found no HFCs in the anterior chamber or lens [280]. There were small high frequency fluctuations in the vitreous and axial length but these were not thought to be large enough to account for the values which have been measured using autorefractors.

6.1.6.3 The effect of accommodation on microfluctuations

The overall RMS value of the power spectrum has been found to increase steadily with increased task vergence (0 – 5 D) [265, 283] but reduce again as stimulus vergence reaches the near point of accommodation [283]: this appears to be due to an increase in magnitude of both HFC [270, 273, 283] and LFC [270, 272]. Further, the increase in RMS value has been shown to occur in all refractive groups [272]. It has been attributed to decreased zonular tension with accommodation causing the lens to vibrate more readily giving more noise in the system. Recent research [284] has shown a correlation between increased objective depth-of-focus and microfluctuations with a change in accommodative stimuli from 1 to 4 D. The microfluctuations may therefore increase to provide more information to the visual system due to the larger depth of focus.

6.1.6.4 The effect of colour on microfluctuations

Denieul and Corno-Martin [260] measured accommodative microfluctuations for 28 combinations of print and background colour on two observers. They used a HFC/LFC ratio in their analysis and made a number of observations. Yellow conditions tended to show the highest HFC/LFC ratio, followed by achromatic conditions followed by saturated conditions (red, green and blue). Desaturated red, green and blue were also tested and showed higher HFC/LFC ratio than their saturated counterparts. On a number of occasions the HFC/LFC ratio between two stimuli (e.g. red-on-black and yellow-on-black) was significantly different with no difference in the accommodative response between the stimuli, suggesting the change in microfluctuations was due to the characteristics of the stimuli rather than being caused by an accommodative change. Within the stimuli there were maximum contrast stimuli (colour on black and black on colour) and isoluminant stimuli (colour on white or white on colour). The HFC/LFC ratio was lower in all cases for the isoilluminant stimuli, and analysis of the power spectra suggests this is due to a decrease in the HFC and an increase in the

LFC. This agrees with previous work which suggests the LFC aid the accommodative system [264, 268-270, 279].

6.1.7 Nearwork-induced transient myopia and coloured targets

Although there is a vast literature investigating various aspects of nearwork-induced transient myopia (NITM) only one study appears to have incorporated different target colours. Haider *et al.* [193] investigated reduction in VA after a 3 hour VDU task viewing green or yellow characters on the screen. They found VA was reduced significantly more after viewing green characters than after viewing yellow characters.

6.1.8 Aim of the study

There is a substantial amount of literature investigating the effect of coloured targets on the accommodation system. The majority have studied the static accommodative response, and there is agreement that monochromatic targets of different wavelengths produce different accommodative responses. There is also agreement that the accommodative response to colour varies considerably within the population, with a question as to whether analysing group mean data is the best method [256] and whether individual data may provide more useful information. The effects of multichromatic stimuli on the accommodative response remain equivocal and there is little literature regarding the effect of multichromatic stimuli on dynamic accommodation or NITM. In this age of technology where the use of laptops and ipads is becoming the norm, the demand on the accommodation system is changing. As both accommodation [211] and daylight [61, 71, 212], or lack of, are believed to be associated with myopia development, the accommodation response to multichromatic stimuli is important to investigate. The aim of this study was to investigate the effects of a multichromatic target on various aspects of accommodation: steady state accommodation, dynamic accommodation and NITM, and to investigate both group and individual data.

6.2 Method

6.2.1 Instrumentation

6.2.1.1 Refraction

To assess refraction non-cycloplegic autorefraction was carried out using a Shin-Nippon SRW-5000 autorefractor (Shin-Nippon, Tokyo, Japan) [170].

6.2.1.2 Accommodation

All accommodation responses were measured using a Shin-Nippon SRW-5000 open view infrared autorefractor which had been modified to take continuous recordings [170, 174]. Accommodation readings were taken monocularly to avoid vergence cues, using the right eye only at a sampling rate of 20 Hz. The Shin-Nippon samples the accommodation response over the central 2.9 mm of the pupil. Any spherical ametropia was corrected with a soft, disposable contact lens which was allowed to settle for 20 minutes prior to measurements being taken [204].

6.2.1.3 The target

Two targets were used during the experiment (Figure 6.3). The experimental target was red writing on a blue background, typical of that found in magazine print. This was chosen, as the small luminance contrast between the colours may give poor chromatic cues and cause focus to be less accurate [251]. The participants may also focus between the colours or use an average focus. The control target was high contrast black writing on a white background. This target would be expected to illicit a stable and accurate accommodative response due to its wide spectral bandwidth [285, 286] and high luminance contrast. Both targets subtended an angle of 20 minutes of arc at the eye through the Badal system.

a)

Johnson & Johnson

b)

Johnson & Johnson

Figure 6.3. Targets used during accommodation and colour experiment; a) black-on-white as a control and b) red-on-blue as an experimental target.

Target reflectances were measured using a SpectraScan PR650 spectrophotometer (PhotoResearch inc., USA). Measurements were taken from the red writing and the blue background of the target, and also from a plain white piece of paper as a reference. Three measurements were taken from each and averaged to produce the graphs below (Figure 6.4).

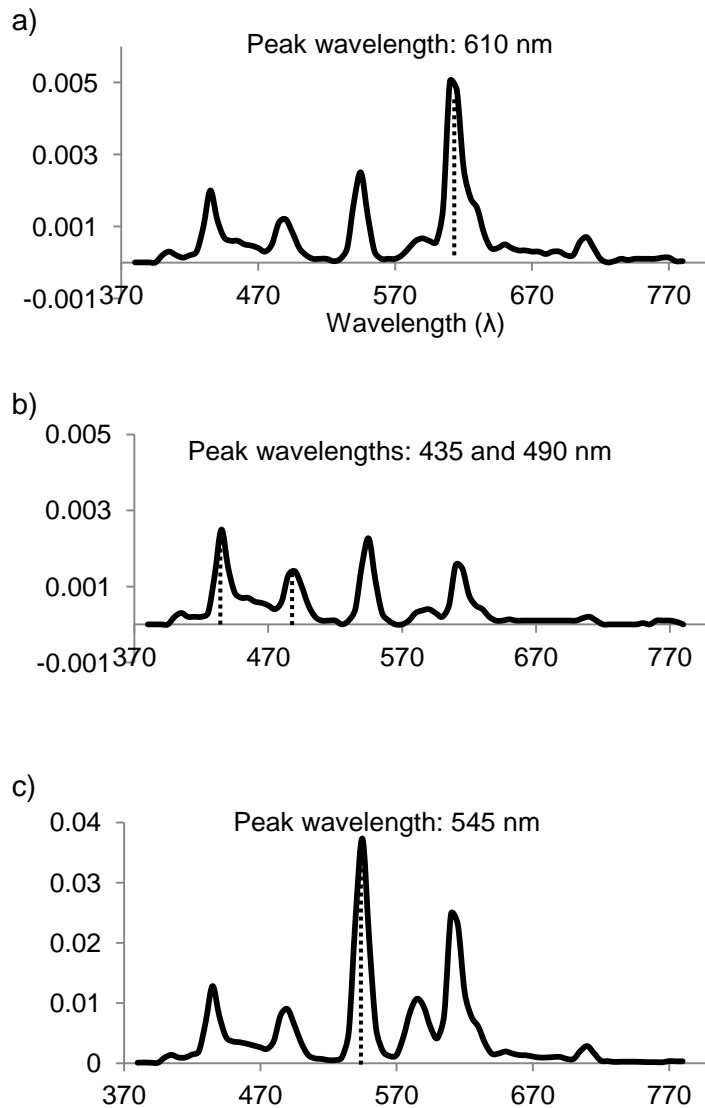


Figure 6.4. The average wavelengths reflected from: a) the red writing, b) the blue background and c) a white piece of paper (note the different scale for this graph). The major wavelength reflected is illustrated on each graph by the dotted black lines.

Figure 6.4a shows a clear peak at 610 nm for the red print; this was used as the ‘red reference’ for the longitudinal chromatic interval. There are two peaks in Figure 6.4b for the blue background; the largest at 435 nm and a smaller one at 490 nm. The 435 nm peak was used as the ‘blue reference’ for the longitudinal chromatic interval as this was the dominant wavelength. There is some ‘crosstalk’ between the measurements for the two colours as the target was very small so the measurement area of the spectrophotometer straddled the red print and blue background. There is also a small

peak at 545 nm in both figures which was not considered as a peak as it was a dominant wavelength in the white 'reference' source. Figure 6.4c shows the spectral distribution of the fluorescent lab lighting reflected by a white surface where there is a strong peak at 545 nm. This was used as a reference for the black on white target.

6.2.1.5 The task

All targets were presented within a +5 D Badal system which allowed the target size to be independent of its position, therefore reducing proximity cues. A modified pen plotter was used to present the target (Figure 6.5). With the participant on the chin rest of the autorefractor (Figure 6.5a) the distance between the Badal lens (figure 6.5b) and the corneal apex was set at 20 cm. The target (Figure 6.5c) could then be presented anywhere between 20 and 2 cm from the back of the Badal lens, allowing the accommodative stimulus to be changed from 0 - 4.5 D. A ruler was attached to the pen plotter for ease of measurement (Figure 6.5d).

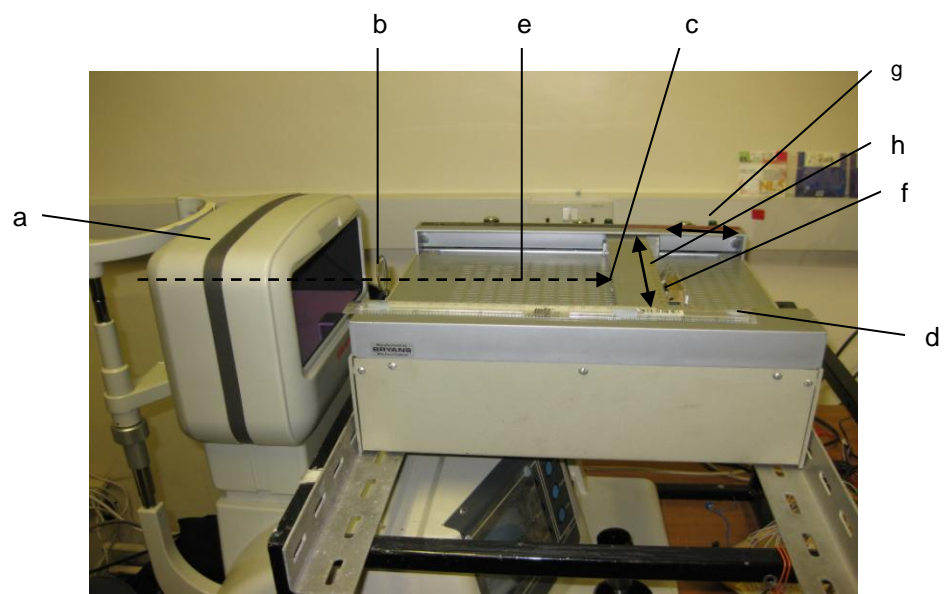


Figure 6.5. Experimental design. a. Shin-Nippon SRW-5000 autorefractor attached to continuous recording software; b. +5 D lens located 20 cm from participants corneal apex; c. position of target; d. ruler to measure distance from back of Badal lens; e. subjects line of sight; f. moveable platform for presenting target in experiment 3; g. X-axis movement of target in experiment 3; h. Y-axis movement of target in experiment 3. NB in experiment 3 the pen plotter was rotated by 180°.

6.2.2 Experiment 1. Steady state accommodation

To measure steady state accommodation, the target was moved manually to the desired distance. The participant was given a couple of seconds to focus on the print and was instructed to keep the print clear at all times. Sixty seconds of continuous recording measurements were taken at five dioptric levels (0, 1, 2, 3 and 4 D) for both targets. Each of these stimuli were presented in a random order.

6.2.3 Experiment 2. Dynamic accommodation

A function generator (Feedback, Sweep function generator, SFG 606) was linked to the pen plotter to produce both sinewaves and squarewaves. The target was moved at a frequency of 0.1 Hz in all cases. Measurements were taken for two different accommodation levels; 0 to 3 D and 2 to 4 D. Both squarewaves and sinewaves were produced for both accommodation levels and for both targets. The participant was asked to keep the target as clear as possible at all times and 90 seconds of accommodation measurements were recorded. The stimulus position was recorded at the same time allowing a graph of accommodation and stimulus to be plotted together. All measurements were taken in a random order.

6.2.4 Experiment 3. NITM measurements

For NITM measurements, the pen plotter was rotated by 180° (Figure 6.5f and Figure 6.6). The participant placed their chin on the chin rest of the autorefractor and the Badal lens (BL) was placed 20 cm from their corneal apex. The targets were placed side by side on a metal platform (Figure 6.5f). Using the mechanics of the pen plotter and an electronic circuit, the platform could be moved forwards and backwards and right and left (Figure 6.5g and h and Figure 6.6), therefore either target could be seen through the Badal lens at either 20 cm (optical infinity) or 8 cm (3 D).

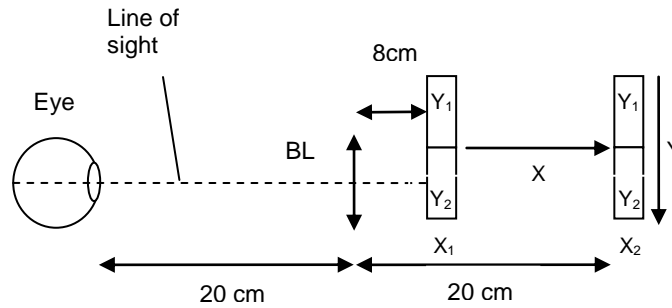


Figure 6.6. Diagram showing the experimental design for the presentation of targets in experiment 3. BL; +5 D Badal lens, Y₁; target 1 (black/white), Y₂; target 2 (red/blue), X₁: target at accommodative demand of 3 D, X₂; target at accommodative demand of 0 D.

Participants were asked to keep the target in focus at an accommodative demand of 3 D for one minute whilst accommodation levels were continuously recorded. The target was then moved electronically to 0 D position, the participant asked to keep it in focus and another 90 seconds of accommodation data were recorded. The distance and near targets were presented randomly in four combinations (Table 6.1).

Table 6.1. Combinations of distance and near targets presented during NITM experiment.

Near (3 D)	Distance (0 D)
Black/white	Black/white
Red/blue	Red/blue
Black/white	Red/blue
Red/blue	Black/white

The presentation of these targets was controlled using an electronic circuit (Figure 6.7) linked to the pen plotter which could move the plate containing the target along both the X and Y-axes.

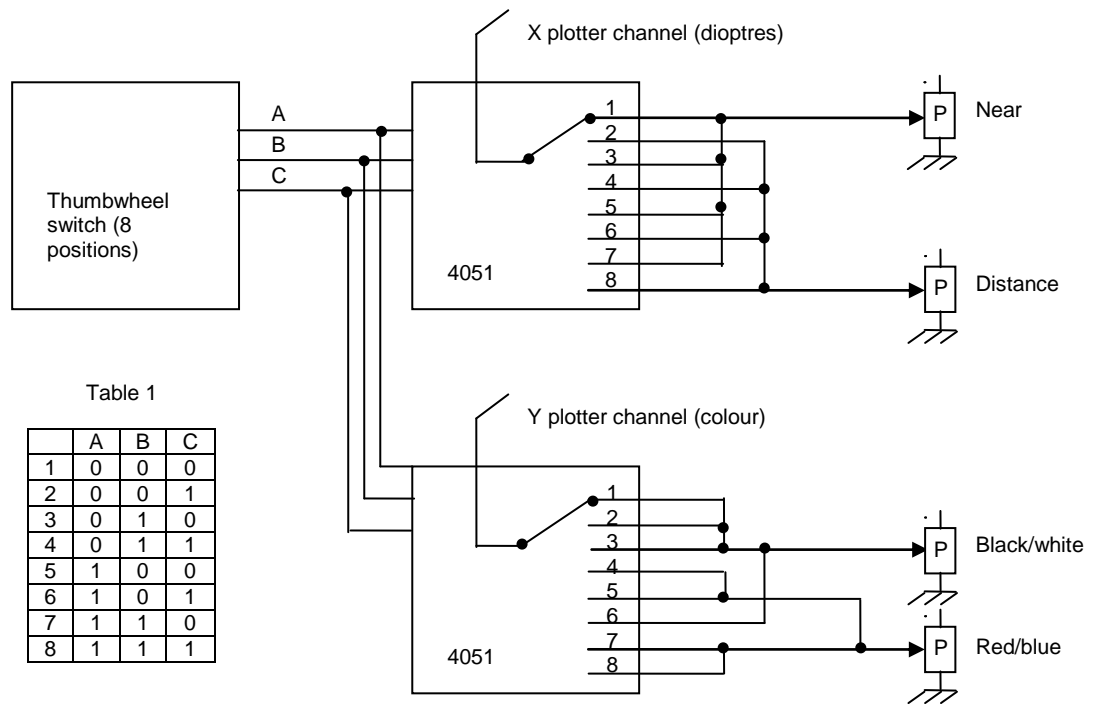


Figure 6.7. Circuit diagram illustrating control mechanism for the movement of the target on the pen plotter in experiment 3. Table 1 shows the eight possible combinations for the thumbwheel switch. 4051 = eight channel analogue switch. P = 100 k Ω , 10 turn potentiometer which send a voltage to the penplotter to position the target.

Sixty seconds of accommodation was recorded with the participant focusing on the B/W target at the 0 D accommodative level. This was used as a baseline when calculating the absolute NITM levels and the regression quotient.

6.2.5 Procedure

On the day of the study participants were asked to refrain from performing intense near vision tasks in the hour preceding the measurements [102]. A questionnaire about the participants' refractive history was completed prior to the experiment to elicit information on family history of myopia, age of onset and progression of myopia and any symptoms of NITM (Appendix 5.1). Five autorefractor measurements were taken from the right eye, with the participant viewing either a 6/18 Snellen letter or a spot light (depending on vision) at six metres binocularly to measure ametropia. The SRW-5000 produces an average refractive error from these 10 measurements and this was

converted to MSE. If necessary, an appropriate soft, disposable contact lens (Acuvue Moist, Johnson & Johnson Medical Ltd., United Kingdom) was inserted in the right eye and allowed to settle for 20 minutes [204].

The left eye was occluded and the participant was directed to place their chin on the rest of the autorefractor. The refractive status of the right eye was confirmed as MSE plano ± 0.25 D by taking three autorefractor readings with the participant fixating a 6/6 Snellen letter at six metres. With the refractive status at zero dioptres, the black and white luminance levels were set within the Measurement and Automation software (MAX, National Instruments, Texas, USA) to provide an optimally clear measurement ring. The raw width and intensity were then set on the continuous recording software so the baseline for the continuous recording was at zero dioptres and the binary image of the measurement ring was complete (Section 2.2). This then meant any change from zero which occurred with the near task was due to a change in accommodation. One of the three experiments was then carried out. At least twenty-four hours elapsed between each experiment.

6.2.6 Participants

Ten participants were recruited with an age range from 19-35 years (median 21.5 years). The group was composed of four emmetropes (EMMs), one hypermetrope (HYP) and five myopes (MYPs). Three of the myopes were late onset (LOM) and two were early onset (EOM). Three participants were aware of distance vision blur after undertaking periods of near work (33%). One was an EOM, one a LOM and one an EMM. The mean MSE error of the whole cohort was $-1.43 \text{ D} \pm 2.39$ and median -0.75 D (range $+1.46$ to -6.50). Myopia was taken to be $\leq -0.50 \text{ D}$, emmetropia to be $> -0.50 \text{ D} < +0.50 \text{ D}$ and hypermetropia to be $\text{MSE} \geq +0.50 \text{ D}$. All subjects had astigmatism of no more than 1.00 D . All subjects had corrected visual acuity (VA) of at least 6/6 in the right eye with no history of binocular vision anomalies or ocular health problems. All participants were screened for colour vision defects using an Ishihara test. No plates

were missed by any subject. Informed consent was obtained from each participant after full explanation of the procedures involved (Appendix 5.7). The study was approved by the University of Bradford Ethics Committee and conformed to the tenets of the Declaration of Helsinki.

6.2.7 Analysis

6.2.7.1 Accommodative response

Sixty five seconds of data for each accommodation level and each colour stimulus were collected. The data were then filtered for blinks (Section 2.2.1.2). Examples of data pre and post filtering for the black/white target collected from participant DG are shown in Figure 6.8.

Sixty seconds of filtered accommodation data for each trial was averaged to give a mean accommodation level for each participant for each experimental condition. Statistical analysis was carried out initially for each participant to assess if the colour of the target had any effect on the level of accommodation. The individual means were then used to produce a group mean for each condition and these were also analysed.

a)

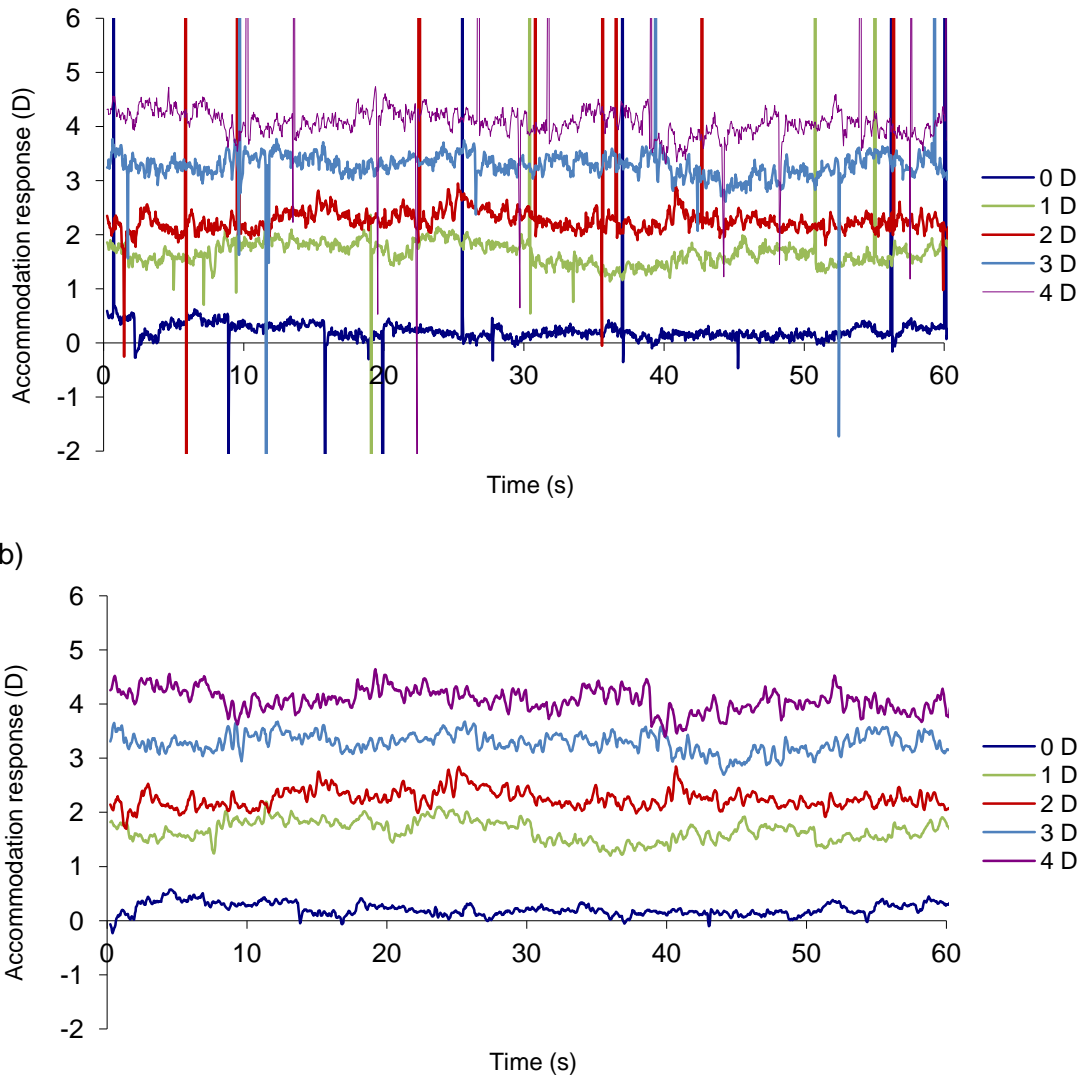


Figure 6.8. Examples of data collected from participant DG for the black/white stimulus for accommodation stimuli of 0, 1, 2, 3 and 4 D. The data is shown before filtering for blinks a) and after being filtered for blinks b). This participant can be seen to over accommodate to all dioptric stimuli.

6.2.7.2 Microfluctuations

The filtered accommodative response data were used to calculate the FFT and produce a power density spectrum plot. In a sample of signal duration (T_{max}) and sampling frequency (f_s) the number of data points (N) is shown by the equation below:

$$\mathbf{N = T_{max} \times f_s}$$

The FFT converts these N points into $N/2$ frequency bins, where the width of each frequency bin is $1/T_{max}$. The maximum frequency is represented by $f_s/2$. The power in

each frequency bin is often normalised by dividing it by the width of the bin producing the spectral density function. The confidence that the power spectrum produced from one FFT will be close to the true power spectrum has been shown to be low. However, if 20 spectra are averaged, the probability density function for each bin approaches a normal distribution [266]. To average a number of spectra the data collected can be split into segments, however making the segments too short can reduce resolution, as the width of each frequency bin then becomes the number of segments divided by T_{\max} . Pugh *et al.* [266] found the longest time a participant could give a useful signal was 50 seconds which means there is a limit to the number of segments one single data run can produce. A number of data runs can be taken but there is the possibility that conditions may change in between trials.

As our system sampled the data at an average of 20 Hz, over a time period of 60 seconds there were 1200 data points per session available for analysis. The number of data points needed to perform a FFT must be 2^n where n is a whole number integer, therefore the first 1024 points from our data were used in the calculation. The data was exported into a Matlab (The Mathworks, Massachusetts, USA) program written by Dr Karen Hampson, University of Bradford. The Welch method of analysis was used where the data set was split into four segments, each containing 256 data points and lasting 12.8 seconds. A power spectrum density analysis was performed on each segment and the results were averaged to produce a power spectrum density plot. A Hamming window was applied to the data before FFT to minimise frequency leakage. The power of the low frequency ($\geq 0.1 \leq 0.6$ Hz), medium frequency ($> 0.6 \leq 1.0$ Hz) and high frequency ($> 1.0 \leq 2.3$ Hz) components were calculated from the power spectrum density plot. The RMS of the sample was also calculated. As each segment was 12.8 seconds long the minimum resolution was 1 divided by 12.8 = 0.08 Hz, and the maximum frequency measured was the sampling frequency (20) divided by 2 = 10 Hz.

6.2.7.3 Squarewaves

When a step input of blur is presented to a subject, there is a latency of about 0.37 seconds before the accommodation system responds, and it takes just over one second from stimulus presentation for the response to become steady [87]. The temporal characteristics of the accommodative response can be analysed by calculating the reaction and response times [287]. Reaction time is the period after a change in stimulus vergence has occurred but before a change in accommodation is observed. Response time is the period measured from the end of the reaction time to the point at which the accommodation response achieves a steady level (Figure 6.9). Reaction time has been found to be independent of step size, direction of accommodative change [271, 288, 289] and also length of prior fixation [289]. Response times appear to be increased for larger step sizes [271] and are affected by the vergence of the fixation target [290]. Reaction and response times do not differ significantly monocularly and binocularly [288].

Previous studies have indicated the difficulties involved in determining the beginning and end of an accommodative response [287, 288]. Both visual inspection and calculated algorithms have been used in studies to calculate these points. In this experiment the point where the accommodation changes occurred were determined using an algorithm in Excel (Microsoft Corporation, Washington, USA) used by Cufflin [175]. All these points were then checked manually to see if they appeared correct. On occasion it was difficult to determine the beginning and end point of the accommodation response and the result given by the algorithm had to be altered manually for a more accurate fit.

Reaction and response times were calculated for both far-to-near and near-to-far responses. Although the response time has been found to differ between far-to-near and near-to-far stimuli [287] the reaction times and response times for both accommodation and disaccommodation were averaged for each condition for each participant to add power to the statistics. Eighteen values altogether were used to

calculate a mean reaction and response time for each participant for each condition.

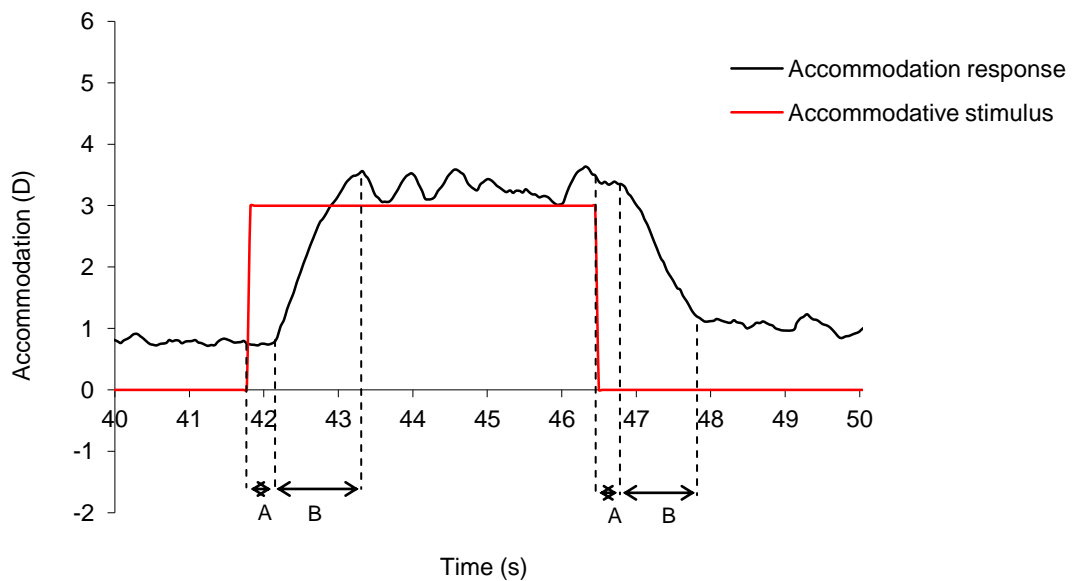


Figure 6.9. A graph of a 10 second trace of accommodation recording showing the accommodative stimulus (red) and accommodative response (black). Reaction (A) and response (B) times are illustrated for both far-to-near and near-to-far responses.

The mean level of accommodation between the end of the response time and the beginning of the subsequent reaction time was calculated to give values for the peak and trough of the accommodation response. A comparison between these values and the values obtained from the black/white was made in an attempt to discover to which wavelength the individual was accommodating to.

6.2.7.4 Sinewaves

When a stimulus is varied sinusoidally the accommodative response is also approximately sinusoidal and fluctuates at about the same temporal frequency as the stimulus. The gain and phase lag of the accommodative response [203] can be calculated. Gain is taken to be the response amplitude divided by stimulus amplitude. Phase lag is the distance in degrees from the peak of the stimulus to the peak of the response (Figure 6.10). The difference between the gain and phase lag of the accommodative response and the accommodative stimulus gives us an idea of the performance of the visual system. Gain has been found to reduce and phase lag to

increase as the temporal frequency of the stimulus is increased [203] and also when chromatic aberration is removed from a stimulus [251].

Determining the peak and trough of the accommodation trace is difficult as the trace is not a smooth sinusoidal curve; it has microfluctuations superimposed. As with the squarewave calculation both visual assessment and algorithms have been used in studies to calculate these points, and an algorithm [175] was again used in this study but each point was also manually verified with some needing to be changed for a better fit. There were nine full sinusoids in the data for each session giving nine values of gain for each participant. The nine peak phase lags and nine trough phase lags were added together to give an average phase lag figure for each participant.

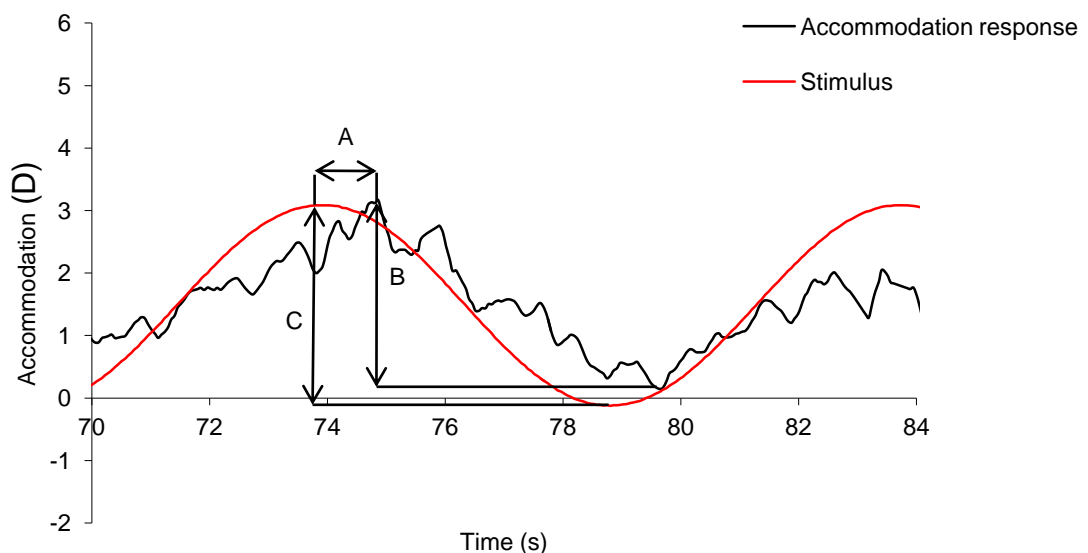


Figure 6.10. A graph of a 14 second trace of accommodation recording showing the accommodative stimulus (red) and accommodative response (black). The phase lag (A) and gain (B/C) are illustrated for the far-to-near response.

As the target oscillated in a regular sinusoid at a frequency of 0.1 Hz it was impossible to rule out any visual prediction of the position of the target.

6.2.7.5 NITM

NITM levels for the first 30 seconds post task and the regression quotient for 60 seconds post task were calculated as in Chapter 3 using 60 seconds of continuous recording measurements with the B/W target at 0 D for baseline.

6.2.7.6 Statistics

All statistics were carried out using SPSS version 17 (SPSS Inc., Chicago). Data were checked for normality using a Kolmogorov-Smirnov test. Where data were found not to significantly differ from a normal distribution a repeated-measures ANOVA was used for the analysis. The data was checked for sphericity using Mauchly's test. If sphericity could not be assumed Greenhouse-Gleisser estimates were used.

Where the data were found to differ significantly from a normal distribution non-parametric statistics were used. Explanations of these tests can be found in the relevant results section. G*Power 2 was used to aid post hoc power calculations.

6.3 Results

6.3.1 Accommodative response

For analysis, the data were normalized to the 0 D B/W response, therefore for each condition for each participant the mean accommodation level for the 0 D B/W response was subtracted from each individual reading. This gave a difference in accommodation for each condition compared to the B/W response. Four different types of response were found, and examples of these can be seen in Figure 6.11. A complete set of individual graphs can be found in Appendix 7.

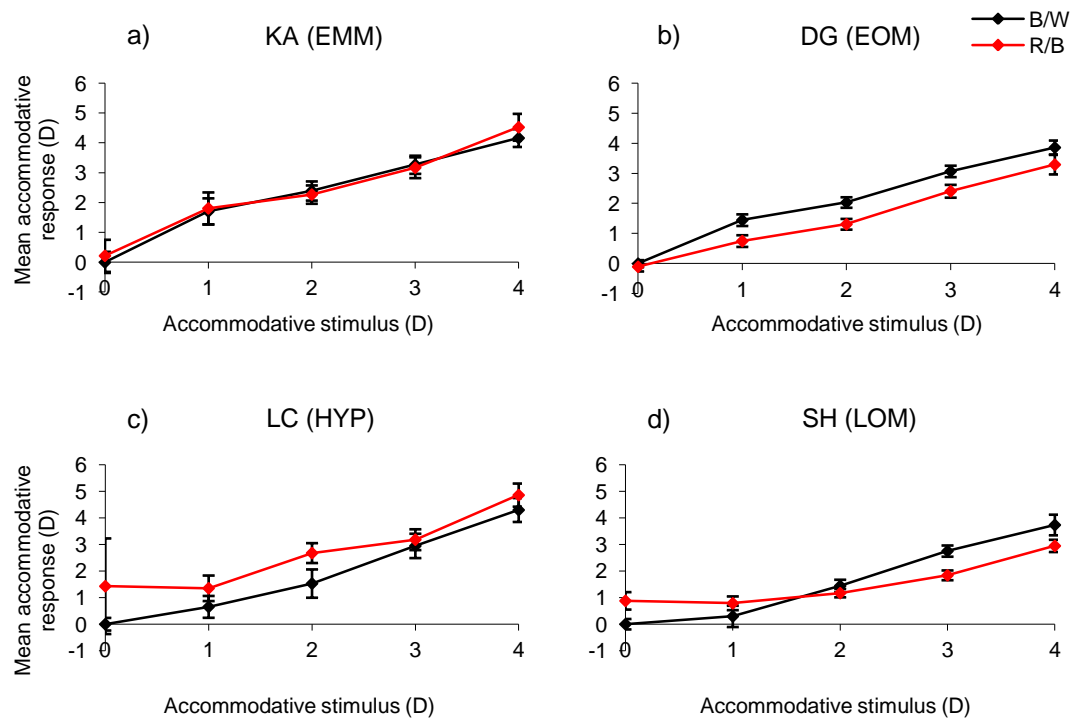


Figure 6.11. Graphs showing the normalised accommodative response for each accommodative stimulus for the B/W condition and the R/B condition. Participants appear to show four different types of responses to the stimuli and an example of each is shown: group 1 (a) show little difference between their accommodative responses to a B/W stimulus and a R/B stimulus; group 2 (b) accommodate less to the R/B target than the B/W target; group 3 (c) accommodate more to the R/B target than the B/W target; group 4 (d) accommodates more to the R/B target below 2 D stimulus and less to the R/B target above a 2 D stimulus.

The individual means were then averaged to produce a group mean result for each condition. These results are illustrated in Table 6.2 and Figure 6.12 below.

Table 6.2. Group mean normalised accommodative responses for the whole cohort \pm 1 SD.

Accommodative stimulus (D)	0	1	2	3	4
B/W	0 \pm 0	0.71 \pm 0.74	1.51 \pm 0.55	2.59 \pm 0.79	3.66 \pm 0.66
R/B	0.20 \pm 0.63	0.94 \pm 0.46	1.65 \pm 0.61	2.62 \pm 0.63	3.60 \pm 0.80

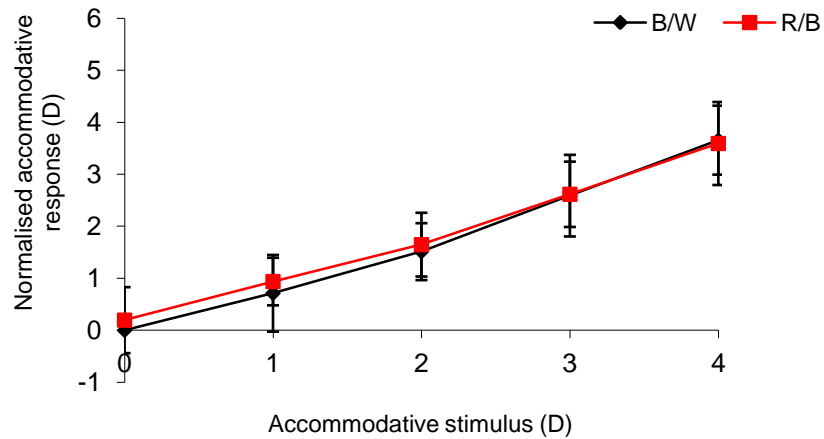


Figure 6.12. Group mean normalised accommodative data for whole cohort. Error bars show 1 SD.

As expected there was found to be a main effect of dioptric stimulus on the level of accommodative response with accommodative response increasing with increased accommodative stimulus ($F_{(1.65,14.86)} = 168.871, p < 0.001$). There was no main effect of the colour of the test type on accommodative response ($F_{(1,9)} = 0.489, p = 0.502, \text{power} = 0.502$) and no interaction between the colour of the stimulus and the dioptric level of the stimulus ($F_{(4,36)} = 0.547, p = 0.702, \text{power} = 0.184$).

6.3.2 Microfluctuations

The LFC, medium frequency component (MFC), HFC and RMS were calculated for each condition for each participant. The individual means were then averaged to give a group mean for each condition which are shown in the Figure 6.13.

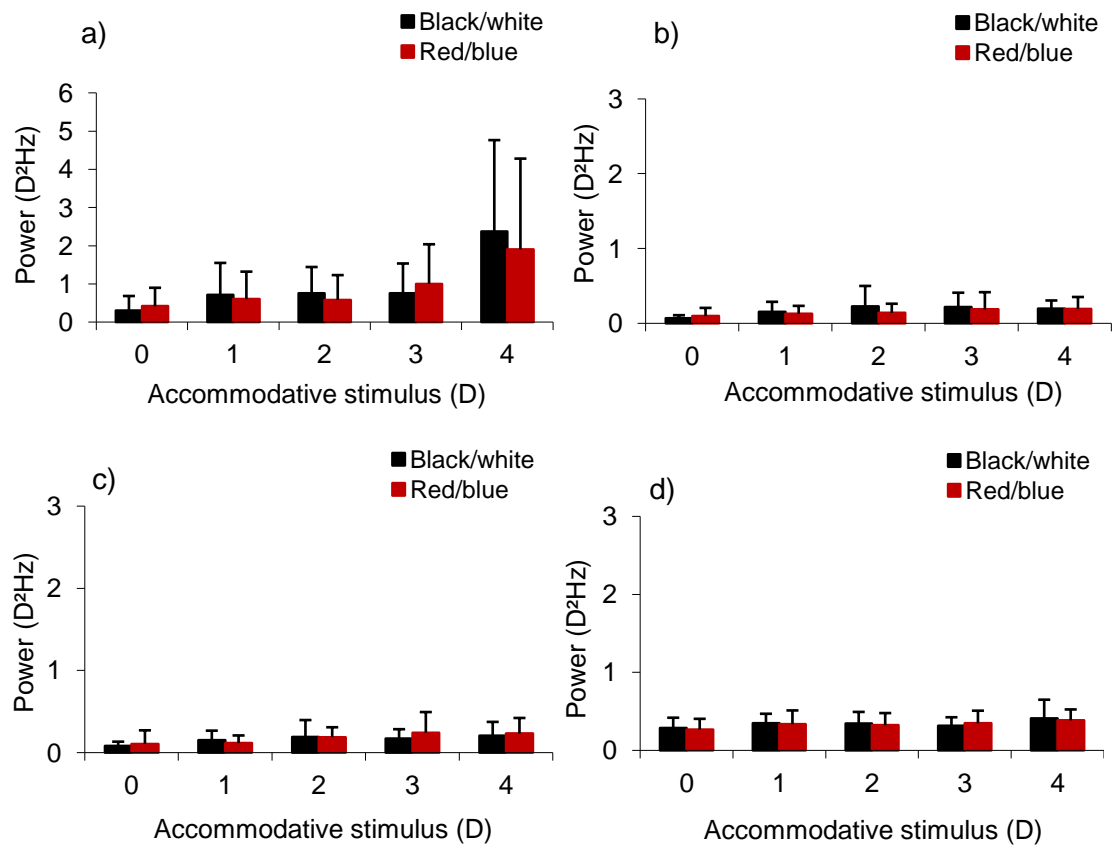


Figure 6.13. Graphs to show the group mean power of the microfluctuations for both black/white and red/blue targets for each accommodative level. a) low frequency, b) medium frequency, c) high frequency and d) RMS. Error bars indicate 1 SD. Note the difference in the x-axis scale for graph a.

As a Kolmogorov-Smirnov test indicated the data for LFC, MFC, HFC and RMS did not tend towards a normal distribution a Friedman's ANOVA was used to compare the values for the different dioptric levels and a Wilcoxon signed-rank test was used to compare the means between the two colour conditions. To reduce type 1 errors the results for the Wilcoxon signed-rank test were only considered significant if $p \leq 0.05/5 = 0.01$.

The resulting statistics can be found in Tables 6.3 and 6.4.

Table 6.3. Results of Friedman's ANOVA analysing changes in power of microfluctuations with changes in the dioptric stimulus to accommodation.

	Black/White	Red/Blue
LFC	$\chi^2(4) = 11.200, p = 0.019$	$\chi^2(4) = 7.739, p = 0.097$
MFC	$\chi^2(4) = 12.400, p = 0.011$	$\chi^2(4) = 6.854, p = 0.142$
HFC	$\chi^2(4) = 11.760, p = 0.015$	$\chi^2(4) = 13.367, p = 0.006$
RMS	$\chi^2(4) = 5.760, p = 0.223$	$\chi^2(4) = 7.216, p = 0.122$

Table 6.4. Results of Wilcoxon signed-rank tests carried out to compare the power of the microfluctuations between the two colour conditions. Only the *p* statistic is shown.

Dioptric value of task	LFC	MRC	HFC	RMS
0	0.625	0.445	0.557	0.625
1	0.375	0.557	0.557	0.432
2	0.432	0.232	0.432	0.375
3	0.160	0.557	0.432	0.375
4	0.432	0.492	0.846	0.846

6.3.3 Squarewaves

The individual reaction and response times were averaged to give a group mean for each stimulus (Table 6.5). One participant (MB) responded so badly to the squarewave stimulus the data were excluded from the analysis (Figure 6.14).

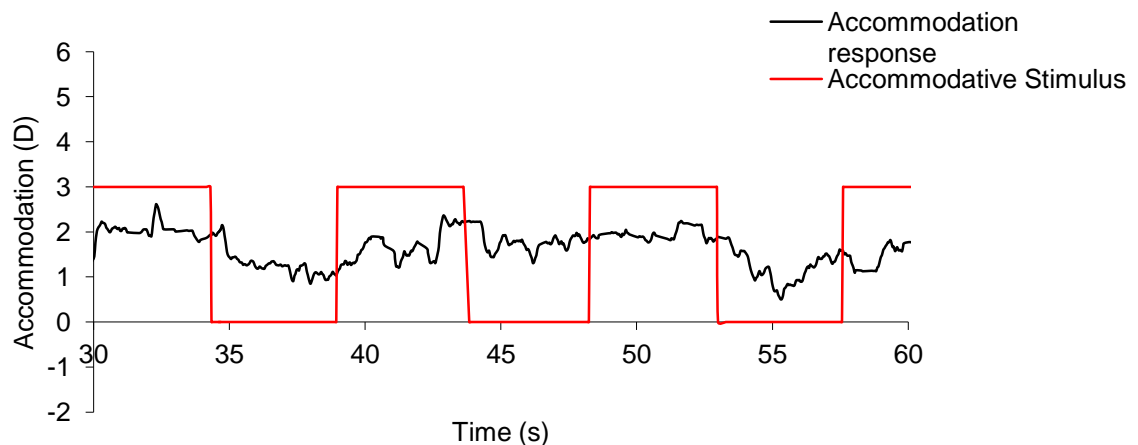


Figure 6.14. 30 s sample of accommodation trace from subject MB for the 0 - 3 D R/B squarewave target. The trace is almost a flat line along the 2 D level. It was not possible to calculate accurate reaction and response times from this trace therefore this subject was excluded from the analysis.

Table 6.5. Group mean reaction and response times \pm 1 SD.

	0-3 D B/W	0-3 D R/B	2-4 D B/W	2-4 D R/B
Reaction time (s)	0.33 \pm 0.08	0.38 \pm 0.12	0.32 \pm 0.11	0.31 \pm 0.06
Response time (s)	1.23 \pm 0.22	1.22 \pm 0.27	1.00 \pm 0.13	0.98 \pm 0.18

The size of the step/diopic level of the target had no significant overall effect on the reaction time ($F_{(1,8)} = 1.308$, $p = 0.286$, power = 0.841), however, it did have a significant effect on the response time ($F_{(1,8)} = 6.689$, $p = 0.032$) with the response times being higher for the 0 - 3 D target than for the 2 - 4 D target. There was no significant effect of colour on either the reaction ($F_{(1,8)} = 2.147$, $p = 0.181$, power = 0.985) or response ($F_{(1,8)} = 0.345$, $p = 0.573$) times and no significant interaction between colour and target step/diopic level for the reaction ($F_{(1,8)} = 0.572$, $p = 0.471$, power = 0.522) or response ($F_{(1,8)} = 0.011$, $p = 0.919$, power = 0.079) times.

Individual dioptric values for the peak and trough of the squarewave response were calculated and are shown in Figure 6.15.

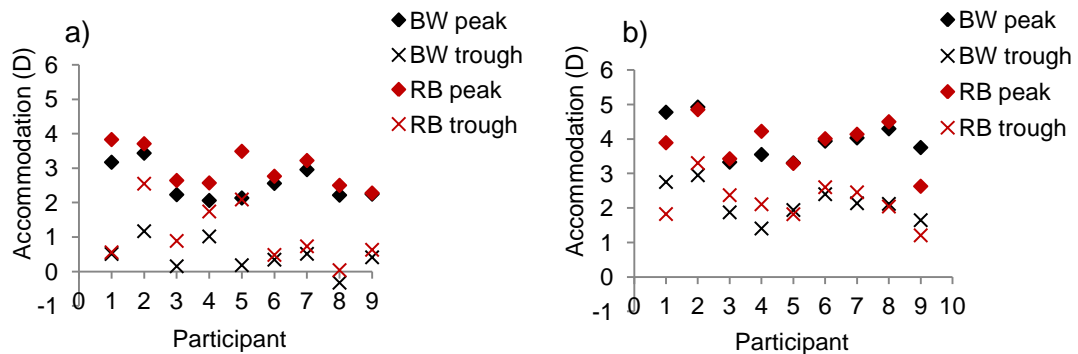


Figure 6.15. Graphs to show the individual accommodative levels in dioptres for the average peaks and troughs of the squarewave stimuli a) 0 – 3 D stimulus and b) 2 – 4 D stimulus.

The average accommodative value for the B/W stimulus was subtracted from that for the R/B stimulus to give a value for the difference in accommodative response between the two targets. The values are shown in Table 6.6.

Table 6.6. The difference between the individual accommodative responses between the two stimuli (R/B – B/W) for the peaks and troughs of the squarewave stimuli for each individual.

	0-3 D		2-4 D	
	Peak	Trough	Peak	Trough
AK	0.66	0.05	-0.89	-0.93
DG	0.27	1.38	-0.08	0.35
EM	0.41	0.74	0.1	0.50
FA	0.51	0.72	0.67	0.70
FR	1.36	1.91	-0.02	-0.12
KA	0.21	0.14	0.07	0.20
LC	0.26	0.22	0.11	0.32
MH	0.28	0.36	0.20	-0.08
SH	0.03	0.22	-1.12	-0.44

For the 0 - 3 D stimulus all participants accommodated more to the R/B target than to the B/W target to a greater or lesser extent (Figure 6.16). For the 2 - 4 D stimulus there were variable responses with some participants accommodating more to the R/B target while some accommodated less to this target (Figure 6.17).

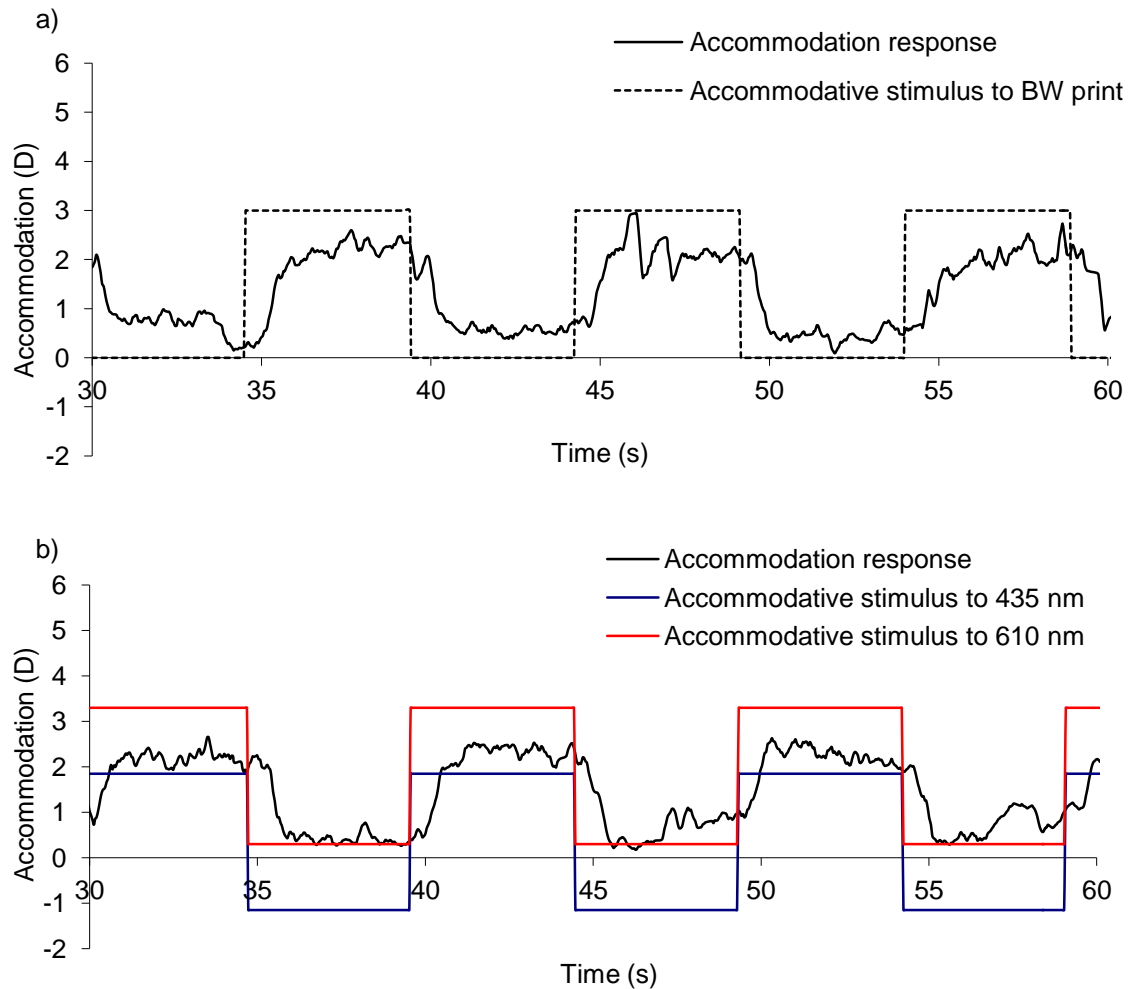


Figure 6.16. Accommodative response traces for participant SH to the 0 - 3 D squarewave stimulus. a) the graph shows the accommodative stimulus for the B/W target and corresponding accommodative response. b) the graph shows the accommodative stimuli for the R/B target. If the individual accommodates to the blue background the stimulus (blue line) will be less than if they accommodate to the red print (red line). In the above graph the accommodation response trace for SH is closer to the red stimulus for distance viewing and closer to the blue stimulus as the target moves closer.

a)

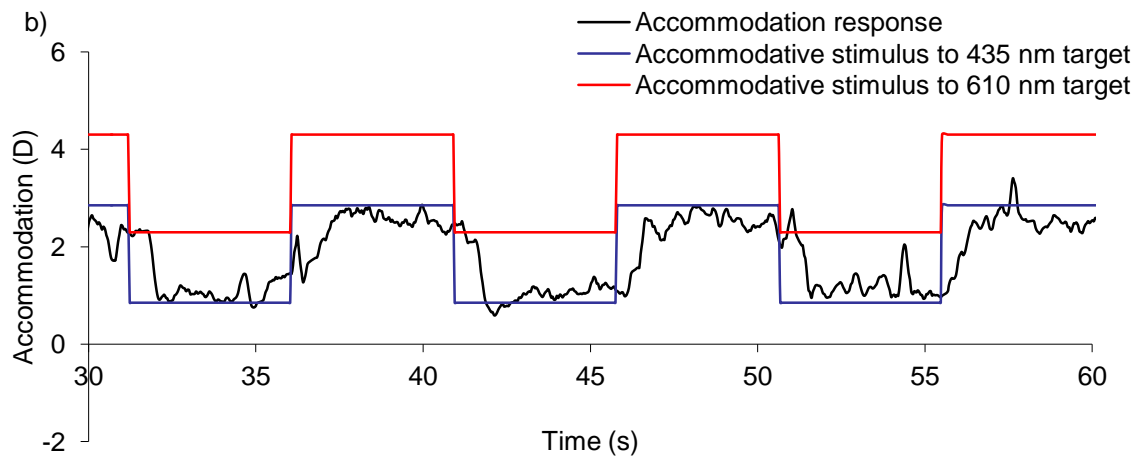
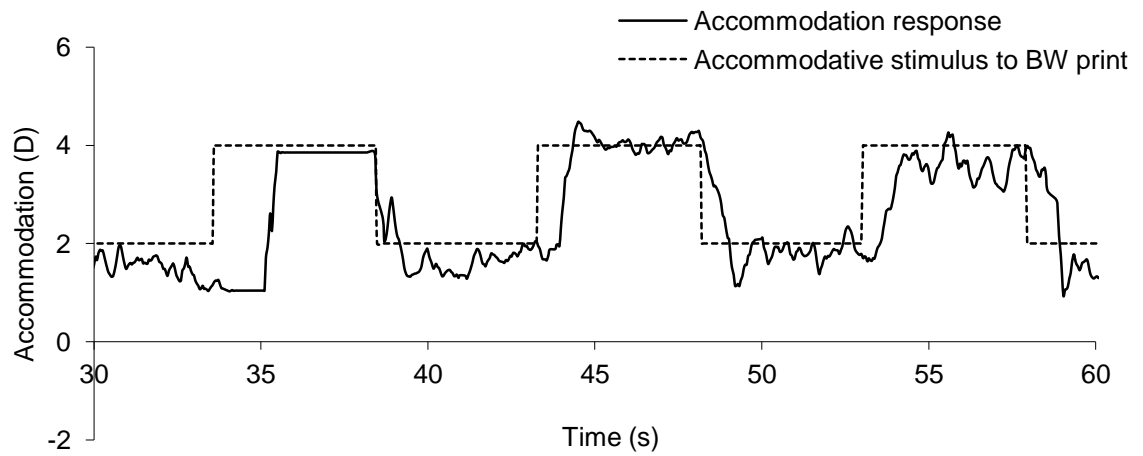


Figure 6.17. Accommodative response traces for participant SH to the 0 – 4 D squarewave stimulus. a) the graph shows the accommodative stimulus for the B/W target and corresponding accommodative response. b) the graph shows the accommodative stimuli for the R/B target. If the individual accommodates to the blue background the stimulus (blue line) will be less than if they accommodate to the red print (red line). In the above graph the accommodation response trace for SH is closer to the blue stimulus for both dioptric levels.

The individual responses were averaged to give a group mean (Table 6.7). Again the data from participant (MB) was excluded.

Table 6.7. Group mean peak and trough responses (± 1 SD) for each of the four squarewave experimental conditions.

	0-3 D B/W	0-3 D R/B	2-4 D B/W	2-4 D R/B
Average peak response (D)	2.56 \pm 0.51	3.00 \pm 0.57	3.99 \pm 0.50	3.89 \pm 0.68
Average trough response (D)	0.44 \pm 0.45	1.08 \pm 0.84	2.14 \pm 0.50	2.19 \pm 0.59

There was a significant main effect of the step size/dioptric level of the target, for both

the peak ($F_{(1,8)} = 57.622, p < 0.001$) and trough ($F_{(1,8)} = 45.217, p < 0.001$) of the accommodative responses. There was no significant overall main effect of colour on either the peak ($F_{(1,8)} = 1.986, p = 0.196, \text{power} = 0.957$) or trough ($F_{(1,8)} = 5.147, p = 0.053, \text{power} = 0.999$) of the responses. There was, however, a significant interaction between the colour of the target and target step size/diopic value for both the peak ($F_{(1,8)} = 6.851, p = 0.031$) and trough ($F_{(1,8)} = 6.406, p = 0.035$) of the responses. The accommodative response to the 0 – 3 D target was greater to R/B than B/W, however, for the 2 – 4 D target there was very little difference in accommodation response between the two colours.

6.3.4 Sinewaves

The mean gain and phase lag for all participants were averaged to give a group mean for each stimulus (Table 6.8). One participant (MB) responded so badly to the sinewave stimulus the data was excluded from the analysis.

Table 6.8. Group mean values for the gain and phase lag (± 1 SD) for each of the four experimental conditions.

	0-3 D B/W	0-3 D R/B	2-4 D B/W	2-4 D R/B
Gain	0.79 \pm 0.15	0.73 \pm 0.29	1.20 \pm 0.26	1.11 \pm 0.25
Phase lag (°)	27.00 \pm 13.23	28.87 \pm 12.80	26.06 \pm 9.56	29.21 \pm 8.58

There was a main significant effect of the dioptric level/step size of the stimuli on the gain ($F_{(1,8)} = 20.218, p = 0.002$) with the group mean gain being higher for the 2 - 4 D stimulus than the 0 - 3 D stimulus. There was however no main effect of target colour on the gain ($F_{(1,8)} = 3.044, p = 0.119, \text{power} = 0.995$) and no significant interaction between colour and dioptric level/step size of stimulus ($F_{(1,8)} = 0.185, p = 0.678$).

There was no main significant effect of the dioptric level/step size of the stimuli ($F_{(1,8)} = 0.020, p = 0.890, \text{power} = 0.212$) or target colour ($F_{(1,8)} = 1.372, p = 0.275, \text{power} = 0.867$) on the phase lag and no significant interaction between colour and dioptric level/step size of stimulus ($F_{(1,8)} = 0.206, p = 0.662, \text{power} = 0.225$).

Individual dioptric values for the peak and trough of the sinewave response are shown

in Figure 6.18.

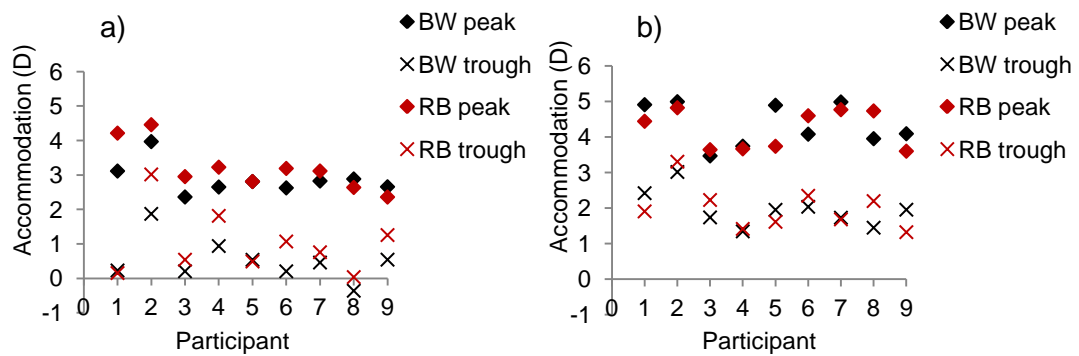


Figure 6.18. Graphs to show the individual accommodative levels for the peaks and troughs of the sinewave stimuli a) 0 – 3 D stimulus and b) 2 – 4 D stimulus.

The average accommodative value for the B/W stimulus was subtracted from that for the R/B stimulus to give a value for the difference in accommodative response between the two targets (Table 6.9).

Table 6.9. The difference between the individual accommodative responses between the two stimuli (R/B – B/W) for the peaks and troughs of the sinewave stimuli for each individual.

	0-3 D		2-4 D	
	Peak	Trough	Peak	Trough
AK	1.10	-0.07	-0.47	-0.51
DG	0.49	1.14	-0.17	0.29
EM	0.59	0.34	0.17	0.49
FA	0.58	0.88	-0.07	0.07
FR	0.00	-0.05	-1.15	-0.34
KA	0.56	0.86	0.52	0.31
LC	0.29	0.30	-0.22	-0.05
MH	-0.25	0.40	0.78	0.75
SH	-0.30	0.71	-0.49	-0.64

The individual responses were averaged to give a group mean (Table 6.10). Again the data from participant (MB) was excluded.

Table 6.10. Group mean peak and trough responses (± 1 SD) for each of the four sinewave experimental conditions.

	0-3 D B/W	0-3 D R/B	2-4 D B/W	2-4 D R/B
Average peak response (D)	2.88 \pm 0.46	3.22 \pm 0.69	4.35 \pm 0.51	4.22 \pm 0.54
Average trough response (D)	0.52 \pm 0.62	1.02 \pm 0.93	1.20 \pm 0.26	1.11 \pm 0.25

There was a significant main effect of the step size/dioptric level of the target, for both the peak ($F_{(1,8)} = 80.013$, $p < 0.001$) and trough ($F_{(1,8)} = 31.245$, $p = 0.001$) of the accommodative responses. There was no significant overall main effect of colour on either the peak ($F_{(1,8)} = 0.794$, $p = 0.399$) or trough ($F_{(1,8)} = 4.984$, $p = 0.056$) of the responses. There was no significant interaction between the colour of the target and target step size/dioptric value for the peak ($F_{(1,8)} = 3.643$, $p = 0.093$) but there was for the trough ($F_{(1,8)} = 7.064$, $p = 0.029$). The accommodative response to the 0 - 3 D target was greater to R/B than B/W, however, for the 2 - 4 D target there was very little difference between the two colours.

6.3.5 NITM

The absolute level of NITM over the first 30 seconds post-task is shown in Figure 6.19.

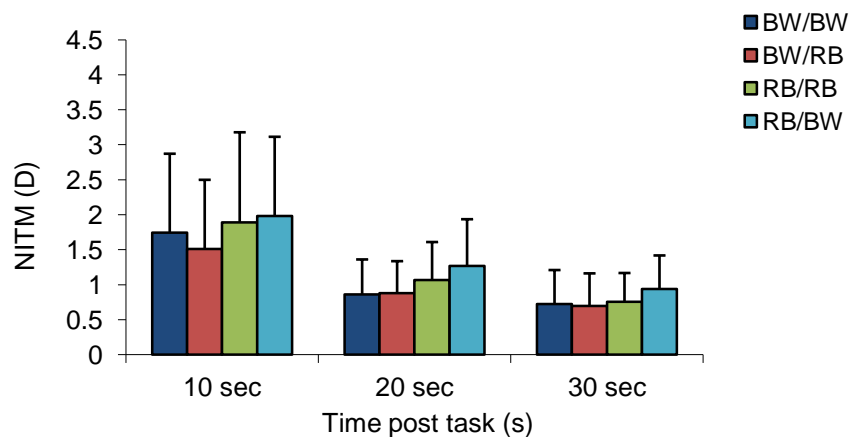


Figure 6.19. Group mean levels of NITM (D) for each of the stimulus combination during the first 30 s post-task. Error bars show 1 SD.

The within-task accommodative response levels were calculated for all four stimulus combinations. The within-task accommodation values for the BW/BW and BW/RB

tasks were amalgamated to give an overall value for the within-task accommodation level to the BW print. The same was carried out for the within-task accommodation levels for the RB/RB and RB/BW tasks. There was a trend for the within-task accommodation to be higher to the R/B ($3.74 D \pm 0.71$) task than the B/W ($3.48 D \pm 0.86$) task however this was not found to be statistically significant ($t_{(19)} = 1.934$; $p = 0.070$, power = 0.153). There was found to be no significant effect of task on the level of NITM ($F_{(3,27)} = 1.028$, $p = 0.398$, power = 0.700) and no significant interaction between task and time ($F_{(2,28,20.55)} = 0.213$, $p = 0.832$, power = 0.178). There was, however, a significant effect of time on the level of NITM post-task ($F_{(1,07,9.60)} = 10.404$, $p = 0.011$) with the level of NITM decreasing with time.

The regression quotient for the first 60 seconds post-task is shown in Figure 6.20. This is important to calculate as it takes into account the within-task accommodative level, as higher accommodation during the task may cause a larger amount of NITM. It has already been shown that participants accommodate differently to different stimuli.

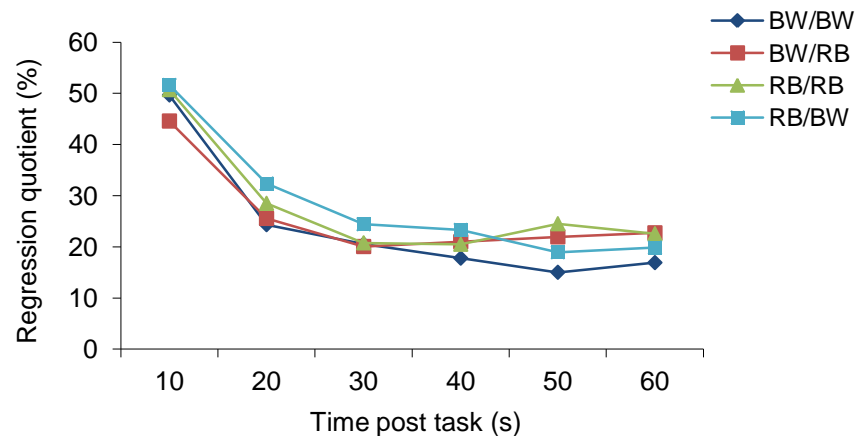


Figure 6.20. Group mean regression quotient for each of the stimuli combinations for the first 30 s post-task.

For analysis the 10 second bin was compared to the 60 second bin. There was found to be no significant effect of task on the regression quotient ($F_{(3,27)} = 0.123$, $p = 0.946$, power = 0.119) and no significant interaction between task and time ($F_{(3,27)} = 0.310$, $p = 0.818$, power = 0.245). There

was however, a significant effect of time on the post-task regression quotient ($F_{(1,9)} = 12.562, p = 0.008$) with the regression quotient being lower after 60 seconds than after 10 seconds.

6.4 Discussion

The literature regarding the effects of multichromatic stimuli on the accommodative system is still unclear. In our world of technology many people now spend a large proportion of their day viewing multichromatic display screens. There is the possibility that due to chromatic aberration this could induce periods of prolonged retinal blur which in turn could be a trigger for myopia development and progression in some individuals.

The main findings of this study were that when comparing the accommodative responses to B/W and R/B static stimuli at various dioptric levels, there appear to be a number of possible accommodative responses within a cohort. In our sample the non-myopes tended to accommodate to the red wavelength or equally to the B/W and R/B. None of our non-myopes accommodated to the blue wavelength.

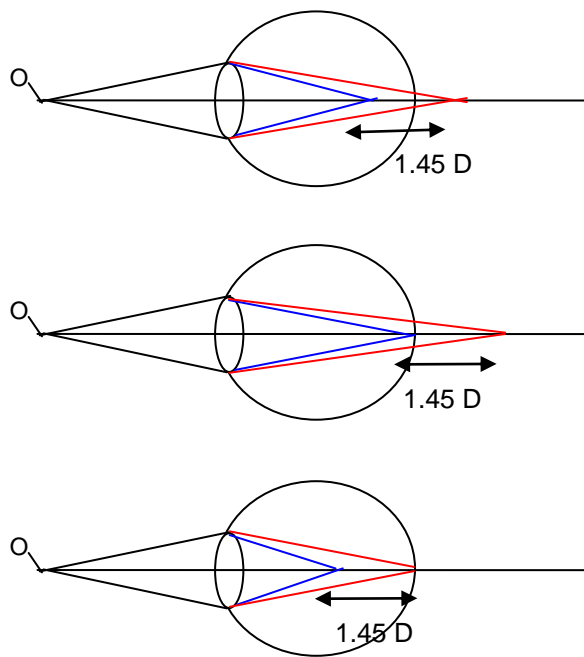
During dynamic accommodation there was a significant interaction between the dioptric value/step size of the target and the colour. For the 0 to 3 D stimulus (sinewave and squarewave) there was a higher group mean accommodative response to the R/B target than the B/W target, however, for the for the 2 to 4 D stimulus there was no difference in the group mean accommodative response between the two targets.

6.4.1 Accommodative response

In agreement with Charman and Tucker [167] we found a number of different responses to our R/B stimulus as compared to our B/W stimulus. However, unlike their study, we found a number of individuals who accommodated equally to the two stimuli. In our sample there appeared to be four different accommodative responses to the static accommodative stimuli. Group 1: individuals who focus equally to R/B and B/W

stimuli at all accommodative levels, group 2: individuals whose accommodative response is less for the R/B stimulus i.e. tending to focus for the blue wavelength, group 3: individuals whose accommodative response is higher for the R/B stimulus i.e. tending to focus for the red wavelength and group 4: individuals whose accommodative response is higher for the R/B stimulus for low accommodative stimuli but lower for the R/B stimulus at higher accommodative levels.

The chromatic difference of refraction between our peak wavelengths of 610 nm and 435 nm is approximately 1.45 D [225] (Figure 6.21). Due to this longitudinal chromatic aberration, those who focused equally to the two targets would be subject to both myopic and hyperopic blur on the retina when observing the R/B target. Those who focused to the blue background would be subject to hypermetropic blur and those focusing for the red print would be subject to myopic blur. Animal studies have shown that hypermetropic blur tends to cause axial elongation and myopia development and progression [38, 41, 42]. They have also indicated that chromatic aberration can affect the emmetropization process [253-255]. If this is the case groups 1, 2 and 4 all have hypermetropic blur present and could be susceptible to myopia. However, groups 1 and 4 also have myopic blur present which may be protective against myopia development [138] suggesting group 2 may be the most at risk.



Group 1: both the red and blue peak wavelengths are out of focus on the retina producing both myopic and hypermetropic blur.

Group 2: The red peak wavelength is out of focus on the retina producing hypermetropic blur which could stimulate axial length growth.

Group 3: The blue peak wavelength is out of focus on the retina producing myopic blur which could slow axial length growth.

Figure 6.21. Illustration of the effects of chromatic aberration when the eye is focused for different wavelengths.

When the group data were analysed no significant difference was found between the responses to the R/B and B/W targets. This is due to the fact that averaging the data disguises the individual variation in the accommodative response suggesting that analysing individual data may be a preferred method.

6.4.2 Microfluctuations

In agreement with previous studies, our data show a significant increase in LFC, MFC and HFC microfluctuations with increasing accommodative stimulus [270, 272, 273, 283] for the B/W target. For the R/B target, however, increased accommodative stimulus only produced a statistically significant increase in the HFC microfluctuations. No increase in RMS was found for either target. There was no significant effect of the colour of the target on microfluctuations at any individual dioptric level.

Denieul and Corno-Martin [260] found an increase in the LFC as their target colours moved towards isoilluminance, suggesting the accommodation system was having

more difficulty in finding focus. We would, therefore, have expected to find the microfluctuations (specifically the LFC) to be greater for the R/B target than the B/W. However, we have also found that participants accommodate by different amounts to the B/W and R/B targets. As the level of accommodative microfluctuations is dependent on the level of accommodation, this could possibly disguise any effect the target colour has on the microfluctuations. Denieul and Corno-Martins results were not the mean of a cohort and were taken from two participants at one accommodative level who were analysed individually.

6.4.3 Dynamic Accommodation

In agreement with previous studies [271, 285, 286] response times to squarewave stimuli were greater for larger dioptric step sizes, however reaction times were unaffected. When considering the sinewave data, phase lag was found to be unaffected by the size of the dioptric step, however gain was significantly higher for the 2 to 4 D step. There was no effect of the colour of the target on either the reaction and response times, or the gain and phase lag.

When considering the peak and trough of the accommodative responses to the dynamic stimuli a significant interaction was found between the dioptric value/step size of the stimulus and the colour of the target. The group mean peak and trough accommodative response to the 0 to 3 D stimuli (both sinewave and squarewave) for the B/W target was significantly lower than to the R/B target by approximately 0.50 D. This may be expected, particularly at the 0 D level, as we already know from studies on the accommodative stimulus response function (ASRF) [82, 83] that there tends to be a lead in accommodation response at low levels of stimuli. It may be expected, however, that as the accommodative stimulus gets higher the accommodative response may start to show some lag. This effect is evident in the fact that the difference in accommodative response between the B/W and R/B targets is slightly greater for the trough of the response than the peak (0.64 D trough and 0.44 D peak for squarewaves

and 0.50 D trough and 0.34 D peak for sinewaves). As the group mean accommodative response to the 3 D dynamic target was higher for the R/B than B/W, it may seem sensible that this would be the case for the trough of the 2 to 4 D stimuli, however, this was not found to be the case as there was no difference between the group mean accommodative response to the B/W and R/B targets at either the peak or the trough. It therefore appears there may be an interaction between the movement of the target and the accommodative response which is more complex than the accommodative response alone.

6.4.4 Experimental limitations

The two main limitations of this study are the difficulty with the analysis of the squarewave and sinewave data and the sample size. We can see from Figures 6.9 and 6.10 that even after filtering there is considerable noise still present in the accommodation traces. Due to this, it is difficult to calculate the exact peaks and troughs of the sinewave data and the beginning and end of the accommodation response for the squarewave data. As there is no single, recognised method for the analysis of dynamic accommodation data, during this study we used a method previously used by Cufflin [175]. All the data were also visually inspected to confirm that the points appeared correct, and occasionally had to be manually altered. Therefore, although we have tried to be as consistent as possible this may mean that comparison of our results with those from other studies may be limited.

Although our study size was large enough to elicit significant effects as far the microfluctuation and dynamic response data were concerned, it was limited when looking at possible accommodative groupings for static accommodation. We found four different accommodative responses within our cohort, however, with larger numbers there could possibly be more. We also found that none of our non-myopes accommodated to the blue wavelength and suggested that accommodating to the blue wavelength may lead to myopia progression, however, a larger sample and a study of

their myopia progression would be needed to confirm this.

Chapter 7

The effect of two different designs of orthokeratology contact lenses on visual function

7.1 Introduction

7.1.1 History of orthokeratology

Orthokeratology (orthok) has been defined as ‘the reduction, modification or elimination of a visual defect by the programmed application of contact lenses’ [291] and has been found to be an effective method for the temporary reduction of moderate amounts of myopia and hypermetropia. In 1962, during a lecture to the Second International Congress for Contact Lenses in Chicago, Dr. George Jesson described an ‘ortho-focus’ procedure he had developed. He used polymethyl methacrylate (PMMA) lenses which were plano in power and fitted flatter than the central cornea by the amount of the refractive error to correct myopia, and steeper than the central cornea to correct hypermetropia. The post-lens tear layer then corrected the refractive error. The lens flattened or steepened the cornea over time, leading to an improvement in unaided vision once the lens was removed. The name orthokeratology was suggested by Newton Wesley at the same meeting [292]. This became the recognised term for the procedure however recently terms such as corneal refractive therapy [293] or corneal reshaping [294] have also been used.

The orthok technique was refined over the next two decades although it was limited to daily wear, the aim being that the patient would have clear vision without correction for a short time during the afternoon or evening. It gave small, clinically significant reductions in the amount of myopia present [295, 296], however studies show that these reductions were not much larger than those induced by conventionally fitted rigid gas permeable (RGP) lenses [297, 298]. Orthok results tended to be variable, with irregular and with-the-rule corneal astigmatism being induced [296]. The refractive

change achieved was temporary and returned to baseline if a retainer lens was not worn [295, 297, 299]. It appears to have produced few adverse effects on either vision or corneal integrity, although it was recommended that the patient needed more frequent follow up visits than a normal contact lens patient [295, 300].

During the 1980s interest in orthok declined due to the unpredictable results, increase in soft lens wear and the advent of refractive surgery. However, in the late 1980s and early 1990s a number of technological advances lead to renewed interest in the procedure. Lathe technology improved, and in 1989 there was a report of the first reverse-geometry lens which improved lens centration, increased the speed of the refractive effects of the lens and made the orthok technique more predictable [301, 302]. Corneal topography equipment became more widely available making it possible to monitor the shape of the entire cornea rather than relying on keratometry readings alone. Higher oxygen permeability rigid lens materials were developed and approved for extended wear by the FDA which meant that orthok lenses could be worn overnight and removed during the day to give clear, lens free vision.

Orthok is now quite widely available in private practice. Academic interest in the procedure has also increased, and research is being undertaken into its effects on corneal structure, visual function and the possibility of it being used as a method of myopia control.

7.1.2 Orthokeratology lens design

In the 1960s and 1970s orthok lenses were similar to normal rigid lenses. There were various designs, but they were generally large diameter lenses to aid stability, fitted at least 0.2 mm flatter than the flattest corneal meridian (K) [295, 303]. Studies indicate that the average reduction in myopia was about 1.00 D with the maximum effect being at six to nine months of wear [295-298]. The maintenance of these changes required at least eight hours lens wear a day [298] and it was impossible to tell when unaided vision would be at its best [295, 297]. Once lens wear was discontinued, all

measurements appeared to return quite rapidly towards pre fit values [295, 297].

The procedure appeared safe in the short term [295, 298, 300]. There are, however, reports of unpredictability, spectacle blur, unwanted corneal distortion and induced with-the-rule corneal astigmatism [295-297]. It also appears that the quality of the uncorrected vision was subjectively poor. Some patients struggled with near vision whilst wearing orthok lenses and had to resort to reading glasses even though they were pre-presbyopic [295]. The Tabb method of lens fitting, which involved inducing changes by reducing the optic zone diameter of the lens rather than fitting the lens flat does appear to have been more predictable and produced little induced astigmatism or spectacle blur [298] which may have been due to improved centration of the lenses.

In 1971 Fontana [304] reported fitting a lens designed to overcome the problem of induced with-the-rule astigmatism which appeared to be due to the superior decentration of a flat fitting lens. Fontana's lens was a one piece bifocal, lathe cut, with a recessed central 6 mm diameter base curve 1.00 D flatter than the paracentral area which was fitted to K. The idea was to make the lens more stable. A program of 3-4 pairs of lenses was used to gradually reduce the prescription, the final pair being retainer lenses which were often of conventional design.

In 1989 there was the report of a new lens design for orthok which reduced the time taken for changes in prescription to take place, increased the amount of myopia which could be corrected and made the process more controllable [301]. Richard Wlodyga an optometrist and Nick Stoyan a contact lens specialist and lens designer collaborated on these new orthok lenses. They felt the procedure would be more controlled if the lens periphery was steeper than the base curve, and so the reverse-geometry lens was born.

Their initial design was the Ortho-K 60, a tri-curve lens design. Three to four sets of lenses were used to produce the corneal change. The initial set was fitted with a back optic zone radius (BOZR) 1.00 D flatter than K, with each subsequent set being 1.00 D flatter each time. The back optic zone diameter (BOZD) was 6mm and the first

peripheral curve was 0.6 mm steeper than the BOZR and 1 mm in width to aid centration. This was termed the tear reservoir. The second peripheral curve provided the edge lift, was 0.7 mm wide and facilitated tear exchange under the lens. The lenses were made of material with a permeability of 80-92 Dk and could be worn overnight, although this was not recommended. The main problems encountered were corneal binding, epithelial staining, debris entrapment, high riding lenses, blurred vision and ghost images.

Over the next few years further research led to the modification of this design and the development of the OK series of lenses which were given FDA approval for daily wear in 1998. The original tri-curve design is now more usually a four or five-curve lens where the second and third peripheral curves closely match the mid peripheral cornea to aid stability. An average of 2.00 D of myopia could be corrected within about 3 months with the result being that this method was termed accelerated orthok. A retainer lens was worn either morning and evening, leaving the patient lens free during the majority of the day, or overnight if the oxygen transmissibility of the lens was suitable [305].

There are a number of disadvantages to using a keratometer alone to fit orthok lenses. A keratometer only measures the axial (sagittal) radius of the cornea at approximately 1.50 mm each side of the corneal apex. The keratometer reading thus gives a single value for corneal radius of curvature. However, at least 90% of the population have corneas with a section which can be described as a prolate ellipse i.e. the apical radius of the cornea flattens from the centre to the periphery [306]. k_c readings therefore give no idea of the shape of the peripheral cornea. It has also been shown that approximately 0.75 D of myopia reduction is evident prior to any changes in k_c readings, as the main structural changes in the cornea occur at the apex and are therefore not measured by the keratometer [307]. The success of fitting using keratometry readings alone is also very dependent on the practitioner being able to assess the fluorescein patterns behind the lens. It needs considerable skill and experience to assess these

patterns and modify the lens fit accordingly, which leads to varying degrees of success with the original reverse geometry lenses.

Two parameters are needed to describe an ellipse such as the cornea. The first is the apical radius (r_0) which indicates the curvature of the section, and the second is the p -value which indicates how rapidly the section flattens or steepens with displacement from the apex. The development of corneal topography systems improved the success of orthok lens fitting. The r_0 and p -value can be obtained from the topography data and Mountford [291] suggested utilising a sag fitting philosophy to either produce a custom made lens or to work out the most appropriate trial lens to choose for the initial lens assessment. This fitting philosophy usually means the initial lens chosen is flatter than a lens based on keratometry readings alone, as the shape of the whole of the cornea is taken in to account and not just the apical radius. It has increased the speed of refractive change and improved the chance of only having to use one lens rather than a series of lenses.

Studies show that modern reverse geometry lenses change the prescription and uncorrected visual acuity (VA) very rapidly indeed with the most change occurring after the first night of wear and little change occurring after 7-14 days [293, 308, 309]. A recent comparison of modern fitting techniques using both empirically fitted lenses and trial sets showed all lens designs to be equally effective at producing a reduction in myopia with no difference between the size of the treatment zone and the subjective ratings and best corrected vision [309].

7.1.3 Myopia reduction

One night of orthok lens wear has been shown to cause a reduction of 0.92-1.18 D in myopia [159, 310, 311], with very little change to the cylinder power [159, 310]. The largest changes in prescription and uncorrected visual acuity (VA) occur during the first week post-lens fitting. After this the changes have been shown not to alter significantly [158, 159, 309]. The average reduction in prescription appears to be between

2.00-3.33 D [293, 308, 309, 312-315] although there have been reports of -5.00 D being corrected [316]. About half the amount of with-the-rule astigmatism present can be corrected although this seems to be quite unpredictable [317].

During the first week post-fitting, the spherical component of the prescription may regress slightly, but not significantly, over the course of the day, becoming more stable towards the end of the week [318]. However, subjectively, patients seem to notice a significant improvement in acuity during the first month which suggests there may be some psychological, or blur adaptation taking place, as in monovision lens fitting [309]. It has been reported that after only a month some subjects can wear their lenses every other night and still achieve good VA during the day [308]. Conversely, a study of Hong Kong practitioners suggests that more than 50% of patients experience some distance vision blur, particularly towards the end of the day [319].

Although orthok is thought to be fully reversible there are actually few studies regarding corneal recovery after cessation of lens wear. Barr *et al.* [320] have shown that in individuals who have worn these lenses for six to nine months, 72 hours after lens removal, their refraction had regressed to 90% of baseline. This regression was assessed only by monitoring acuity and refraction, not corneal changes. A case study by Cheung *et al.* [321] found that in a patient who had worn orthok lenses for one year it took 18 days post lens removal for corneal topography to return to baseline, whereas, Hiraoka *et al* [322] monitored irregular astigmatism, higher-order aberrations and contrast sensitivity in 17 patients and found all parameters returned to baseline within a week.

7.1.4 Corneal response

The normal cornea relies on oxygen from the atmosphere to maintain metabolic activity. Oxygen deprivation causes an increase in thickness and hydration of the corneal stroma, which is termed oedema [323]. During sleep the normal cornea tends to swell slightly due to reduced levels of oxygen behind the closed lids. Studies have shown

this to be in the region of 2-4% [324, 325]. This oedema dissipates once the eye has been open for about an hour [326, 327].

A contact lens on the eye acts as a barrier to the amount of oxygen the cornea receives under both open and closed eye conditions. During open eye conditions, tear exchange occurs underneath the lens due to lens movement during blink. This helps to supply the cornea with oxygen. However, under closed eye conditions the tear pump behind the lens may not function, as the lens is probably immobile. If this is the case, regardless of whether the lens is of soft or RGP design, oxygen can only reach the cornea from the palpebral conjunctiva via the lens itself. Therefore the amount of oxygen the cornea receives is reliant purely on the oxygen transmissibility of the lens.

Closed eye orthok wear seems to suppress the stromal oedema response of the central cornea, however, the peripheral and mid-peripheral swelling response is as predicted from the oxygen transmissibility of the lens [311, 325, 328]. It has been suggested that the reverse geometry lens 'clamps' the central cornea and either prevents the influx of water or forces it laterally. Thus there is a hypoxic response in the central cornea but the consequences of it are suppressed [325]. The cornea seems to adapt to overnight lens wear over a period of time. A reduction in the overnight oedema response of the cornea has been seen after only ten days of lens wear, with a reduction to baseline after 30 days. This has been shown to occur with both orthok and conventional RGP lenses [325].

During orthok treatment the central cornea appears to thin [157-160] and the mid periphery to thicken [157, 160], although a study by Nichols *et al.* [158] found no significant change in peripheral thickness. Research by Alharbi and Swarbrick [157] found central corneal thinning to be significant at day one after the beginning of treatment and stable by day ten, due entirely to thinning of the epithelium. Mid peripheral corneal thickening was significant by day four and stable by day ten and appeared to be stromal in origin. In other studies where mid peripheral corneal thickening was found it appeared to be due to a change in the epithelium

[311, 328, 329]. The differences between these results may have been related to measurement methods; the first study used a pachometer to measure corneal thickness whereas the other three studies used optical coherence tomography. This time scale of change seems to be in agreement with the time scale for refractive and corneal changes mentioned previously. Corneal epithelial changes seem to be due to lens design and are not affected by the lens gas transmission, as opposed to corneal stromal thickness changes which are significantly related to the lens transmissibility [329].

Changes in the sagittal height of the cornea have been shown to account for the refractive changes which occur, suggesting that changes in corneal curvature represent an anterior redistribution of tissue and not an overall corneal bending [160]. Mountford [330] has hypothesised that corneal change under a reverse geometry lens is not purely due to the compression caused by the lens' back surface. He suggested it is due to the difference between this compression force and the negative tension force at the BOZD caused by the tear layer between the lens and the cornea. The mechanism by which the epithelium thins and its implications on corneal integrity are not fully understood as yet, however the variation of epithelial change between subjects suggests the malleability of all corneas is not the same [328].

7.1.5 Contrast sensitivity

High contrast, best corrected VA does not appear to be affected by orthok treatment [309, 313-315, 318, 331] but low contrast best corrected VA has been shown to be reduced [309], and to be worse when the pupil is dilated [314]. The contrast sensitivity function at all spatial frequencies between 3-18 cycles/degree has also been shown to be reduced [313] as has the log mesopic contrast sensitivity [331]. This is challenged by Johnson *et al.* [318] who found after one and seven nights wear of orthok lenses there was no significant reduction in VA at high or low contrast or high or low luminance. Letter contrast sensitivity was also unchanged. This may be due to the

small study size of six subjects or the fact that all their subjects had initial myopia of less than -3.00 D. A high initial spherical prescription seems to be related to worse distance and near vision after treatment [319]. Cheung *et al.* [332] found no significant difference in the best corrected VA at high and low contrasts but uncorrected VA was reduced at low contrast. Thus the degradation appeared to be refractive in origin.

7.1.6 Aberrations

The human eye, like other optical systems, contains aberrations which tend to be reasonably well correlated between the eyes of one subject but largely variable from person to person [114] (see Appendix 2 for explanation of aberrations). The reshaping of the cornea during orthok tends to alter these aberrations. If the procedure has been successful there is a large reduction in the lower order aberration of defocus correlating with the change in the prescription. There has also been shown to be an increase in higher order aberrations following orthok, particularly spherical aberration and to a smaller degree coma [312-315, 328, 331, 333] (Table 7.1). This increase seems to correlate with the amount of myopia corrected [312, 313, 331] and the reduction in contrast sensitivity function [313] and log mesopic contrast sensitivity [331]. As the amount of spherical aberration present in a subject's eye very much depends on corneal curvature and the shape of the crystalline lens, changing the shape of the cornea would be expected to alter this aberration. The increase in coma seems to vary between patients and it has been suggested that this could be due to decentration of the lens [312, 315, 333].

As mentioned above, after six months of treatment VA seems quite stable throughout the day, although aberration measurements have shown defocus (Z4) to increase and spherical aberration (Z12) to decrease [294]. It has been suggested that these changes in aberration may compensate for one another. A study by Berntsen *et al.* [314] found that after a month of orthok lens wear, higher order aberrations were stable during the day through a 3 mm diameter pupil, however once the pupil size was increased to

5 mm the amount of spherical aberration increased significantly. This may have implications for patient selection.

Table 7.1. Comparison of studies investigating the change in aberrations after orthokeratology lens fitting. (W_{RMS} = root mean square wavefront aberration, SA = spherical aberration).

Study	Number of participants	Instrument used	Pupil diameter	Aberrations measured	Baseline (μm) \pm SD	After treatment (μm) \pm SD
Joslin <i>et al.</i> 2003 [315]	9	Shack-Hartmann	6 mm	3 rd order W_{RMS} 4 th order W_{RMS} 5 th order W_{RMS} 6 th order W_{RMS} Total higher-order W_{RMS} (3 rd -6 th order) SA	0.23 \pm 0.11 0.18 \pm 0.10 0.04 \pm 0.03 0.03 \pm 0.02 0.31 \pm 0.13 0.14 \pm 0.10	0.56 \pm 0.37 0.43 \pm 0.15 0.11 \pm 0.07 0.07 \pm 0.05 0.73 \pm 0.38 0.40 \pm 0.15
Berntsen <i>et al.</i> 2005 [314]	20	Shack-Hartmann (COAS G200)	5 mm	3 rd order W_{RMS} 4 th order W_{RMS} 5 th order W_{RMS} 6 th order W_{RMS} Total higher-order W_{RMS} (3 rd -6 th order) SA	0.115 \pm 0.04 0.077 \pm 0.03 0.030 \pm 0.01 0.024 \pm 0.01 0.147 \pm 0.04 0.045 \pm 0.04	0.193 \pm 0.08 0.233 \pm 0.12 0.069 \pm 0.04 0.059 \pm 0.03 0.330 \pm 0.12 0.202 \pm 0.14
Hiraoka <i>et al.</i> 2005 [312]	39	Corneal topography (TMS-2N)	6 mm	3 rd order W_{RMS} 4 th order W_{RMS}	0.323 \pm 0.165 0.297 \pm 0.113	0.633 \pm 0.448 0.849 \pm 0.339
Hiraoka <i>et al.</i> 2007 [313]	23	Shack-Hartmann (KR-9000 PW)	4 mm	3 rd order W_{RMS} 4 th order W_{RMS} Total higher-order W_{RMS} (3 rd & 4 th)	0.074 \pm 0.028 0.038 \pm 0.020 0.085 \pm 0.032	0.258 \pm 0.150 0.134 \pm 0.061 0.297 \pm 0.152

7.1.7 Aim of the study

Although numerous studies have investigated the effect of orthok on visual function, the majority have fitted the same lens design in each eye. During this study a different design of lens will be fitted to each eye and we aim to investigate whether this creates a difference in visual function between the two eyes. One lens will be a C5 design while the other will be an aspheric, back surface polynomial design. Because of the nature of the polynomial lens design, the centre of the back surface of the lens to correct low myopia is basically spherical. The back surface becomes progressively more aspheric in shape as the amount of myopia corrected increases, therefore, in theory, at lower levels of myopia the performance of both lenses should be similar, however with increased myopia one design may possibly perform better than the other. If this is the case would it be possible to modify the cornea to any shape we wish and if so, is there an optimum corneal shape which will produce the best functional results from orthok fitting?

At present little is known about how the orthok fitting procedure affects nearwork functions such as the accommodative stimulus-response function (ASRF) and nearwork-induced transient myopia (NITM). If the fitting of orthok lenses causes increased aberrations and reduced visual function for distance, how does this translate to near vision? Myopes have been shown to have a shallower ASRF to blur-driven stimuli than emmetropes, and this has been linked to myopia progression [82, 83]. Orthok has been shown to cause an increase in positive spherical aberration and an increase in spherical aberration has been shown to produce a shallower ASRF [334]. Once we correct myopia using orthok lenses what happens to the curve? Does accuracy of accommodation increase, decrease or is there no measurable change? Furthermore, myopes tend to be more susceptible to nearwork after-effects than emmetropes [90, 93, 98-100]. Is this susceptibility altered after the correction of myopia with orthok lenses?

The aim of this project is therefore two fold; to assess the effect of two different lens

designs on visual function and to assess the near visual function of myopes, pre and post-orthok fitting, in an attempt to find out the effects the orthok procedure has on nearwork function.

7.2 Method

7.2.1 Recruitment

The participants recruited for this study were also involved in a study concerned with the efficacy of the orthok procedure conducted by Annette Parkinson at the Bradford School of Optometry and Vision Science, University of Bradford. Participants were recruited via an advertisement on the university web site asking for individuals interested in myopia correction by orthok. Individuals who responded to the advertisement were screened initially to check they had a refractive error which was suitable for the orthok fitting procedure (myopia of less than -5 D, refractive with-the-rule astigmatism of less than 1 D and no against-the-rule astigmatism), best corrected VA of at least 6/6 in each eye, no previous experience of orthok lens wear and that there was no evidence of ocular or corneal pathology. If an individual was deemed to be suitable the project was discussed and an information sheet issued (Appendix 5.8), an initial fitting appointment was then arranged. This chapter will only deal with the measurements relevant to this study. For details of the orthok fitting procedure see thesis by Annette Parkinson.

7.2.2 Initial fitting assessment

For all participants measurements were carried out in the order listed below.

7.2.2.1 Measurement of vision

Vision was measured using a high contrast Bailey Lovie chart (Section 2.6), luminance 123 cd/m², initially at a distance of six metres, however the chart was moved closer if no letters could be seen. The results were recorded as visual acuity rating (VAR)

scores where 6/6 is equivalent to VAR 100 and each additional letter read correctly adds one to the score. The participant was encouraged to read as far down the chart as possible. Visions were measured monocularly and two separate charts were used to avoid the participant remembering the letters. The right eye was always measured first.

7.2.2.2 Refraction

A binocularly-balanced subjective refraction was carried out to measure the participants' spectacle prescription, and a +1.00 D blur test performed. The end point of the refraction was the highest positive or lowest negative sphere to give the best VA. The cylindrical component was calculated using the Jackson cross cylinder technique.

7.2.2.3 Measurement of high and low contrast VA

High and low contrast VA were measured monocularly using the Bailey Lovie chart with the participant wearing their fully corrected spectacle prescription. Again, two individual charts were used and the results were recorded using VAR scores. Particularly for the low contrast (10 %) measurements participants were given plenty of time to read the chart and encouraged to read as far as possible [335].

7.2.2.4 Measurement of heterophoria

The distance heterophoria was measured using the Maddox rod and near heterophoria by using a Maddox wing; both were measured with the full distance correction in place [335].

7.2.2.5 Accommodation measurement

Monocular and binocular amplitudes of accommodation were measured with full distance correction using the push-up method with an RAF rule [335].

7.2.2.6 Aberration measurements

Distance aberration measurements were taken for each eye through a natural pupil

using a custom designed Shack-Hartmann (S-H) aberrometer (Section 2.5). Before any measurements were taken, the power of the laser at the eye was measured on three occasions using a laser meter (LensCheck, Coherent, Germany) to ensure this did not exceed the maximum permitted exposure (Appendix 4). Ten frames were taken per measurement with an exposure of 150 ms. Measurements were taken over a pupil diameter of 4.8 mm. Full aperture trial lenses in a trial frame were used to correct any ametropia present. The right eye was always measured first and the eye not being measured was occluded. The participant placed their chin on the chin rest of the aberrometer. The rest was moved both horizontally and vertically until the participant could see the high contrast black on white Snellen letters which were used as a target and subtended 0.35° (21 minutes of arc). The target was initially situated 100 mm behind L_6 (Figure 2.11), however, as already explained, the wavelength of infra red light is longer than that of white light so the target needs to be moved slightly closer to L_6 than expected to be positioned at optical infinity. With the participant looking at the target, it was brought towards L_6 until the letters first became clear. Once the target was clear the chin rest was then moved slightly, if necessary, to get both the target and laser spot visible simultaneously. Once a clear set of S-H spots could be seen on the computer monitor the search blocks (Figure 2.15) were positioned over the spots, the participant was asked to blink and a measurement was taken. For each subsequent measurement the participant was asked to move so the spots were always lined up in the same place with the search blocks. Ten measurements were taken with the participant remaining on the chin rest between each measurement. The participant was asked to close their eye between each measurement to reduce exposure to the laser. Once ten measurements had been taken on the right eye the procedure was repeated for the left eye.

7.2.2.7 Accommodative stimulus response function

Near accommodative function was assessed at baseline by plotting the

accommodative stimulus response function (ASRF) (Section 2.3.2). Spherical ametropia was corrected using a soft disposable contact lens (Acuvue Moist, Johnson & Johnson Medical Ltd., United Kingdom) which was allowed to settle for 20 minutes prior to measurements being taken [204]. Measurements were taken monocularly from the right eye only while the left eye was occluded. The participant was positioned with their chin on the chin rest of the Shin-Nippon SRW-5000 autorefractor (Shin-Nippon, Tokyo, Japan) and directed to fixate a 6/6 high contrast black on white Snellen letter at 6 metres. Ten static autorefractor readings were taken for distance baseline and the average reading was converted to mean spherical equivalent (MSE). The participant was then asked to fixate a high contrast black on white Snellen letter subtending 0.35° (21 minutes of arc) through a + 5 D Badal lens system whilst still situated on the autorefractor chin rest. Accommodation levels of 0, 1, 2, 3, 4 and 4.5 D were presented by altering the distance of the target from the Badal lens. The participant was given a few seconds to clear the target after each change in accommodative stimulus and the accommodative response was measured by taking a static autorefractor reading. Five readings were taken for each accommodative stimulus level and all readings were presented randomly. The participant was encouraged to blink on a regular basis to keep the contact lens from dehydrating as this affected the clarity of the Shin-Nippon measurement ring and increased measurement variability.

7.2.2.8 Nearwork-induced transient myopia

Nearwork-induced transient myopia was measured for the right eye only using the same experimental design as in Section 3.3.2. Spherical ametropia was corrected using the soft disposable contact lens which had previously been inserted to take the ASRF measurements. The left eye was occluded and the participant positioned their chin on the chin rest of the Shin-Nippon autorefractor. During the first task 'minesweeper' was played for a ten minute period at an accommodative stimulus level of 0 D. At the end of this period the participant was asked to fixate a maltese cross at

optical infinity for 90 seconds. Continuous recording of accommodation was undertaken during the 60 second period at the end of the task and for 90 seconds post-task. The second task was exactly the same except 'minesweeper' was played at a 3.75 D accommodative stimulus level. Task one was used as a baseline whilst task two was used as the experimental condition.

7.2.2.9 Post-lens fitting assessment

The orthok lenses were fitted by Annette Parkinson. The lens ordered for the right eye was a reverse geometry C5 design with back surface diameters of 7.0/8.0/9.0/10.0/11.2 mm and the lens ordered for the left eye was an aspheric back surface polynomial, designed so that at diameters of 7.0/9.6/11.2 mm specified sags were produced. The lens in the left eye was specially designed by Tony Hough. The lenses were made from Boston XO material (B&L, Rochester, USA) which has an oxygen permeability of $100 \times 10^{-11} (\text{cm}^3 \text{O}_2)(\text{cm})/[(\text{sec})(\text{cm}^2)(\text{mmHg})]$.

Post-fitting measurements of all the above parameters were taken approximately six months after successful lens fitting. Measurements were taken after the lens had been removed for approximately four hours to allow time for the tear film to stabilise after removal of the lenses. For participant SK ametropia was not completely corrected by the orthok procedure therefore a soft contact lens was again inserted for correction when performing NITM and ASRF measurements.

7.2.2.10 Analysis

All statistics were carried out using SPSS version 17 (SPSS Inc., Chicago). Data were checked for normality using a Kolmogorov-Smirnov test. The data were found not to differ significantly from a normal distribution. Either a paired samples t-test or a repeated-measure ANOVA were used for the analysis. When using repeated-measures designs the data was checked for sphericity using Mauchly's test. If sphericity could not be assumed Greenhouse-Gleisser estimates were used. G*Power 2 was used to aid post hoc power calculations.

7.3 Results

7.3.1 Participants

Over 100 individuals responded to the advert placed on the Bradford University website. Forty three participants were registered on the orthok study conducted by Annette Parkinson, and 13 completed a year of lens wear. Seventeen participants from this study took part in our investigation. There were two reasons why we could not enrol all the participants in our study. Firstly, as we were focusing on visual function at near, it was important all participants were pre-presbyopic. Secondly, it took 16 months to build and validate the aberrometer, by which time a number of participants had already been registered on the original orthok study and commenced lens wear.

The cohort had a median age of 22 years (range 18 to 34). The MSE of the participants was right: $-3.34 \text{ D} \pm 1.39$ and left: $-3.11 \text{ D} \pm 1.34$ with a range of -6.38 D to -0.88 D . The maximum amount of with-the-rule astigmatism was -1 D . Soft contact lens wearers were advised to leave their lenses out the day before the initial measurements were taken, while RGP lens wearers were advised to leave lenses out for a month. Informed consent was obtained from each subject after full explanation of the procedures involved (Appendix 5.9). The study was approved by the NHS National Research Ethics Service and conformed to the tenets of the Declaration of Helsinki.

7.3.2 Baseline data

Of the initial 17 participants 10 discontinued from the study. The reasons for this are shown in Table 7.2.

Table 7.2. A breakdown of the reasons for participant discontinuation from the orthok study (n = 10).

Reason for discontinuation	Number of participants
Poor VA	2
Difficulty handling	1
Unacceptable corneal staining	2
Lost to follow up	4
Poor compliance	1

The baseline parameters for the right eye from the whole cohort, those who withdrew from the study and those for who six month data were collected are shown in Table 7.3.

Table 7.3. Baseline parameters from the right eye for the whole cohort, those participants who discontinued the study and those who completed the study. Values are mean (SD) and are shown for the right eye only.

	Whole cohort (n=17)	Participants who discontinued study (n=10)	Participants who completed study (n=7)
Age	24.18 (5.31)	22.90 (4.77)	26.00 (5.86)
Vision (VAR)	55.12 (13.47)	54.60 (14.14)	55.86 (13.53)
Mean spherical equivalent (D)	-3.34 (1.39)	-3.64 (1.37)	-2.91 (1.40)
Visual acuity (VAR)	104.71 (2.82)	104.80 (2.86)	104.57 (2.99)
Low contrast VA (VAR)	94.18 (5.15)	94.70 (5.23)	93.43 (5.35)
Amplitude of accommodation (D)	9.31 (1.36)	9.73 (1.53)	8.71 (0.86)
Distance phoria (Δ)	0.65 SOP (4.05)	0.85 SOP (4.70)	0.36 SOP (3.21)
Near phoria (Δ)	1.53 XOP (4.80)	1.7 XOP (5.74)	1.29 XOP (3.45)
Spherical aberration (μm)	0.031 (0.045)	0.034 (0.050)	0.027 (0.042)
W_{RMS} (μm)	0.232 (0.049)	0.237 (0.037)	0.226 (0.064)

7.3.3 Six month data

For those seven participants who completed the study the individual baseline and six month parameters are shown in Tables 7.4 to 7.9 with the group mean calculated at the bottom of each table. The mean time the lenses had been removed before the measurements were taken was 3.29 hours \pm 1.15 and the mean number of months the lenses had been continuously worn for before the appointment was 5.29 \pm 1.80.

When analysing the data it was necessary to look at the effect of the orthok procedure on the parameter and also whether there was a difference in the change between the

two eyes as a C5 design lens had been fitted to the right eye and an aspheric back surface lens to the left. A repeated measures ANOVA was therefore carried out for each parameter. When analysing the phoria data, negative was taken to be esophoria and positive exophoria. A paired samples t-test was carried out on this data for distance and near.

Table 7.4. Individual baseline and six month visions as VAR scores for those participants who completed the study. The group mean (± 1 SD) is shown at the bottom of the table.

Participant	Vision (VAR)			
	RE baseline	RE 6 months	LE baseline	LE 6 months
CE	59	104	57	94
AE	39	95	35	84
SK	48	85	64	99
CC	58	105	60	100
KR	62	103	65	104
LV	80	95	74	101
AH	45	105	39	94
Mean (\pm SD)	55.12 \pm 13.47	98.86 \pm 7.54	56.29 \pm 14.23	96.57 \pm 6.63

There was a statistically significant overall effect of the orthok procedure on vision ($F_{(1,6)} = 87.345$, $p < 0.001$) with the VAR score being higher post-orthok (97.71 ± 6.92) than pre-orthok (56.07 ± 13.34). There was no statistically significant difference in the VAR scores between the two eyes ($F_{(1,6)} = 0.093$, $p = 0.771$) and no statistically significant interaction between the orthok procedure and the eye that was fitted ($F_{(1,6)} = 1.077$, $p = 0.339$).

Table 7.5. The individual baseline and six month MSE refractive error in dioptres for those participants who completed the study (n = 7). The group mean (\pm 1 SD) is shown at the bottom of the table.

Participant	Mean spherical equivalent (D)			
	RE baseline	RE 6 months	LE baseline	LE 6 months
CE	-2.75	+0.38	-2.88	+1.88
AE	-5.25	+0.25	-5.50	0.00
SK	-3.50	-1.25	-2.63	+0.25
CC	-3.50	+0.25	-3.00	+0.50
KR	-1.75	-0.25	-1.75	+0.13
LV	-0.88	-0.75	-1.25	-0.13
AH	-2.75	-0.25	-3.65	+0.50
Mean (\pm SD)	-3.34 \pm 1.39	-0.23 \pm 0.60	-2.95 \pm 1.38	+0.45 \pm 0.67

There was a statistically significant overall effect of the orthok procedure on MSE ($F_{(1,6)} = 25.526$, $p = 0.002$) with MSE being lower pre-orthok (-2.93 ± 1.33) than post-orthok ($+0.11 \pm 0.71$). There was no significant overall difference in the MSE between the two eyes ($F_{(1,6)} = 3.061$, $p = 0.131$). There was a significant interaction between the orthok procedure and the eye that it was carried out on ($F_{(1,6)} = 6.486$, $p = 0.044$) with the lens in the left eye having a larger effect on MSE (3.40 D) compared to that in the right (3.11 D).

Table 7.6. The individual baseline and six month high contrast visual acuities as VAR scores for those participants who completed the study. The group mean (\pm 1 SD) is shown at the bottom of the table.

Participant	Visual acuity (VAR)			
	RE baseline	RE 6 months	LE baseline	LE 6 months
CE	103	105	104	94
AE	110	102	110	84
SK	105	105	105	99
CC	105	105	105	105
KR	105	105	105	105
LV	100	105	100	101
AH	104	105	105	99
Mean (\pm SD)	104.71 \pm 2.82	104.57 \pm 1.13	104.86 \pm 2.91	98.14 \pm 7.31

There was no significant overall effect of the orthok procedure on high contrast visual acuity ($F_{(1,6)} = 1.891$, $p = 0.218$, power = 0.999). There was a statistically significant difference in the high contrast visual acuity between the two eyes ($F_{(1,6)} = 6.691$, $p = 0.041$) with the

overall VAR score in the right eye (104.57 ± 2.17) being higher than that in the left (101.50 ± 6.38). There was also a significant interaction between the orthok procedure and the eye that it was carried out on ($F_{(1,6)} = 7.471$, $p = 0.034$) with the lens in the left eye reducing the high contrast VAR score (6.72) by a greater amount than that in the right (0.14).

Table 7.7. The individual baseline and six month low contrast visual acuities as VAR scores for those participants who completed the study. The group mean (± 1 SD) is shown at the bottom of the table.

Participant	Low contrast VA (VAR)			
	RE baseline	RE 6 months	LE baseline	LE 6 months
CE	97	98	93	84
AE	100	79	100	60
SK	94	93	93	78
CC	98	90	98	90
KR	85	91	95	89
LV	90	93	90	88
AH	90	79	95	80
Mean (\pm SD)	94.18 \pm 5.15	89.00 \pm 7.28	94.86 \pm 3.34	81.29 \pm 10.44

The overall effect of the orthok procedure on low contrast visual acuity almost reached statistical significance ($F_{(1,6)} = 5.029$, $p = 0.066$, power = 0.998) with the VAR score being higher before the procedure (94.14 ± 4.35) than after (85.14 ± 9.53). There was no statistically significant difference in the low contrast visual acuity between the two eyes ($F_{(1,6)} = 2.102$, $p = 0.197$, power = 0.889). There was, however, a significant interaction between the orthok procedure and the eye that it was carried out on ($F_{(1,6)} = 13.669$, $p = 0.010$) with the lens in the left eye reducing the low contrast VAR score (13.57) by a greater amount than that in the right (5.18).

Table 7.8. The individual baseline and six month amplitudes of accommodation in dioptres for those participants who completed the study. The group mean (± 1 SD) in shown at the bottom of the table.

Participant	Amplitude of accommodation (D)			
	RE baseline	RE 6 months	LE baseline	LE 6 months
CE	10	11	10	11
AE	8	11	8	11
SK	8.5	11	8.5	12
CC	7.5	7	7.5	7
KR	8.5	9	8.5	9
LV	9	8.5	9	9
AH	9.5	9	9.5	9
Mean (\pm SD)	8.71 \pm 0.86	9.50 \pm 1.55	8.71 \pm 0.86	9.71 \pm 1.70

There was no statistically significant overall effect of the orthok procedure ($F_{(1,6)} = 2.353$, $p = 0.176$, power = 0.919) or the type of lens fitted ($F_{(1,6)} = 2.077$, $p = 0.200$, power = 0.881) on amplitude of accommodation. There was also no statistically significant interaction between the orthok procedure and the eye that it was carried out on ($F_{(1,6)} = 2.077$, $p = 0.200$).

Table 7.9. The individual baseline and six month distance and near phoria measurements for those participants who completed the study. The group mean (± 1 SD) in shown at the bottom of the table. Negative indicates esophoria, Positive indicates exophoria and zero indicates orthophoria.

Participant	Phoria (Δ)			
	Distance baseline	Distance 6 months	Near baseline	Near 6 months
CE	+4.5	-1	0	0
AE	+3.5	-2	+8	+6
SK	-4.5	-4	+1	+3
CC	-2	-1	0	0
KR	-2	-1.5	+3	+4
LV	-1	-1	-3	-5
AH	-1	-1	0	-9
Mean (\pm SD)	-0.65 \pm 4.05	-1.64 \pm 1.11	+1.53 \pm 4.80	-0.14 \pm 5.27

Although in general there was a shift towards esophoria post-orthok for both distance (0.99 Δ SOP) and near (1.67 Δ SOP) this change was not found to be statistically significant for either distance ($t_{(6)} = 1.173$, $p = 0.285$) or near ($t_{(6)} = 1.037$, $p = 0.340$).

Figures 7.1, 7.2 and 7.3 below show the baseline MSE plotted against the six month vision, VA and LCVA.

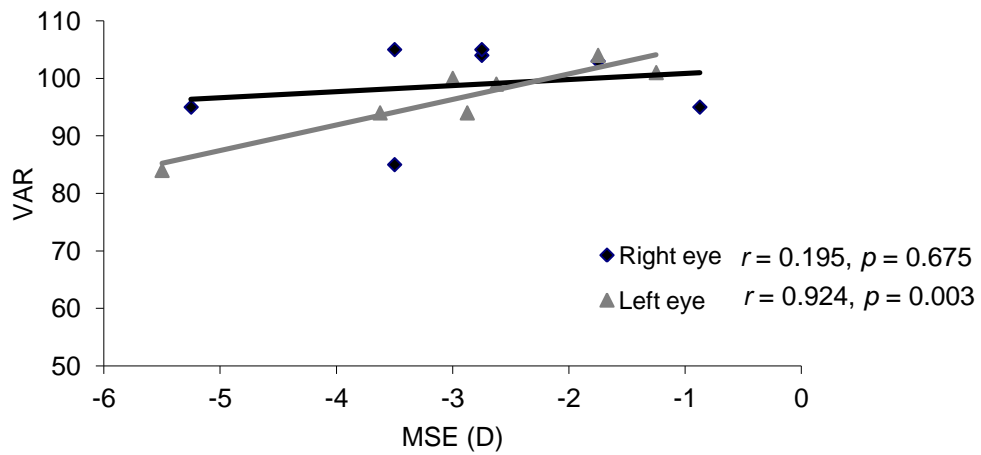


Figure 7.1. Post-orthok high contrast uncorrected VAR score plotted against baseline MSE.

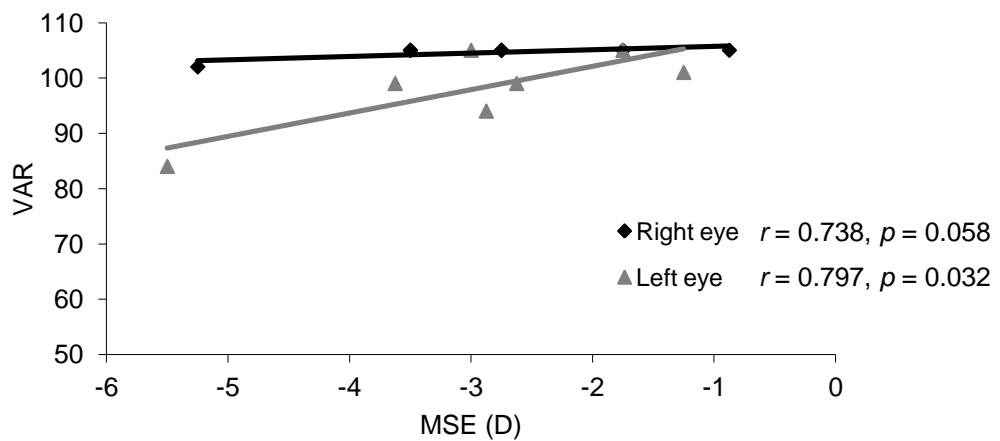


Figure 7.2. Post-orthok high contrast corrected VAR score plotted against baseline MSE.

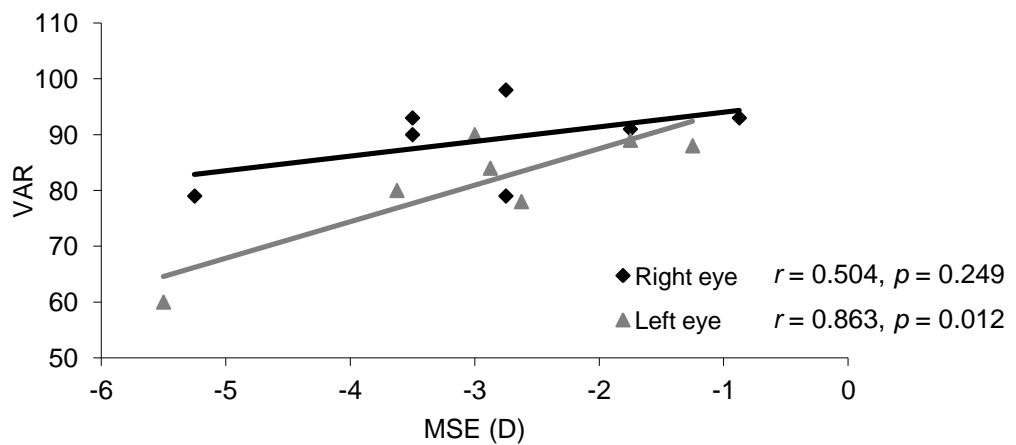


Figure 7.3. Post-orthok low contrast corrected VAR score plotted against baseline MSE.

A statistically significant positive correlation was found for the left eye between the MSE and post-orthok uncorrected high contrast vision ($r = 0.924$, $p = 0.003$), post-orthok corrected high contrast VA ($r = 0.797$, $p = 0.032$) and post-orthok low contrast VA ($r = 0.863$, $p = 0.012$). No significant correlation was found for the right eye.

7.3.4 Aberrations

The mean level of spherical aberration (Z12) was calculated for each participant for each eye from the 10 distance measurements taken pre and post-orthok. The results are shown in Table 7.10.

Table 7.10. Mean level of spherical aberration (Z12) from 10 measurements (\pm SD) for the right and left eyes of each participant pre and post-orthok lens fitting. The group mean (\pm 1 SD) is shown at the bottom of the table.

Participant	Spherical aberration (μm)			
	RE baseline	RE 6 months	LE baseline	LE 6 months
CE	0.005 \pm 0.052	0.150 \pm 0.032	-0.027 \pm 0.023	0.464 \pm 0.055
AE	0.034 \pm 0.022	0.169 \pm 0.100	0.033 \pm 0.039	-0.009 \pm 0.074
SK	0.014 \pm 0.042	0.037 \pm 0.061	0.026 \pm 0.013	0.078 \pm 0.054
CC	0.049 \pm 0.016	0.048 \pm 0.016	-0.031 \pm 0.081	-0.058 \pm 0.086
KR	0.072 \pm 0.024	0.079 \pm 0.030	0.049 \pm 0.038	0.195 \pm 0.041
LV	-0.050 \pm 0.014	-0.069 \pm 0.032	-0.053 \pm 0.025	-0.066 \pm 0.060
AH	0.066 \pm 0.016	0.136 \pm 0.027	0.062 \pm 0.055	0.098 \pm 0.050
Mean (\pm 1 SD)	0.027 \pm 0.042	0.079 \pm 0.082	0.008 \pm 0.045	0.100 \pm 0.185

There was no statistically significant effect of the orthok procedure on spherical aberration (Z12) ($F_{(1,6)} = 2.766$, $p = 0.147$), and no significant difference in spherical aberration between the two eyes ($F_{(1,6)} = 0.002$, $p = 0.966$). There was also no statistically significant interaction between the orthok procedure and the eye it was performed on ($F_{(1,6)} = 0.425$, $p = 0.539$).

The total W_{RMS} from the 3rd to 8th-order were calculated from each measurement. This was carried out within an Excel spreadsheet (Microsoft Corporation, Washington, USA) by squaring each Zernicke term, calculating the sum of these squares and then finally calculating the square root of the sum. The mean W_{RMS} was calculated for each participant for each eye from the 10 distance measurements taken pre and post-task.

The results are shown in Table 7.11.

Table 7.11. Mean higher order W_{RMS} (3rd to 8th order) from 10 measurements (\pm SD) for the right and left eyes of each participant pre and post-orthok lens fitting. The group mean (\pm 1 SD) is shown at the bottom of the table.

Participant	W_{RMS} (μm)			
	RE baseline	RE 6 month	LE baseline	LE 6 months
CE	0.251 \pm 0.080	0.388 \pm 0.077	0.183 \pm 0.069	0.664 \pm 0.085
AE	0.149 \pm 0.039	0.458 \pm 0.100	0.290 \pm 0.135	0.545 \pm 0.263
SK	0.324 \pm 0.042	0.520 \pm 0.106	0.180 \pm 0.033	0.303 \pm 0.040
CC	0.153 \pm 0.034	0.357 \pm 0.075	0.280 \pm 0.076	0.352 \pm 0.119
KR	0.279 \pm 0.068	0.208 \pm 0.048	0.205 \pm 0.055	0.315 \pm 0.052
LV	0.210 \pm 0.019	0.413 \pm 0.088	0.192 \pm 0.061	0.301 \pm 0.064
AH	0.215 \pm 0.039	0.405 \pm 0.076	0.156 \pm 0.047	0.290 \pm 0.099
Group mean	0.226 \pm 0.064	0.393 \pm 0.097	0.212 \pm 0.052	0.396 \pm 0.148

The overall effect of the orthok procedure on W_{RMS} reached statistical significance ($F_{(1,6)} = 23.113$, $p = 0.003$) with the W_{RMS} being lower before the procedure ($0.219 \mu\text{m} \pm 0.058$) than after ($0.395 \mu\text{m} \pm 0.123$). There was no statistically significant effect of the eye fitted on the level of W_{RMS} ($F_{(1,6)} = 0.017$, $p = 0.901$) and no significant interaction between the orthok procedure and the eye fitted ($F_{(1,6)} = 0.060$, $p = 0.814$).

The difference between the pre and post-orthok W_{RMS} and spherical aberration values for each participant were calculated (post-orthok value – pre-orthok value) and plotted against the baseline MSE (Figure 7.4).

a)

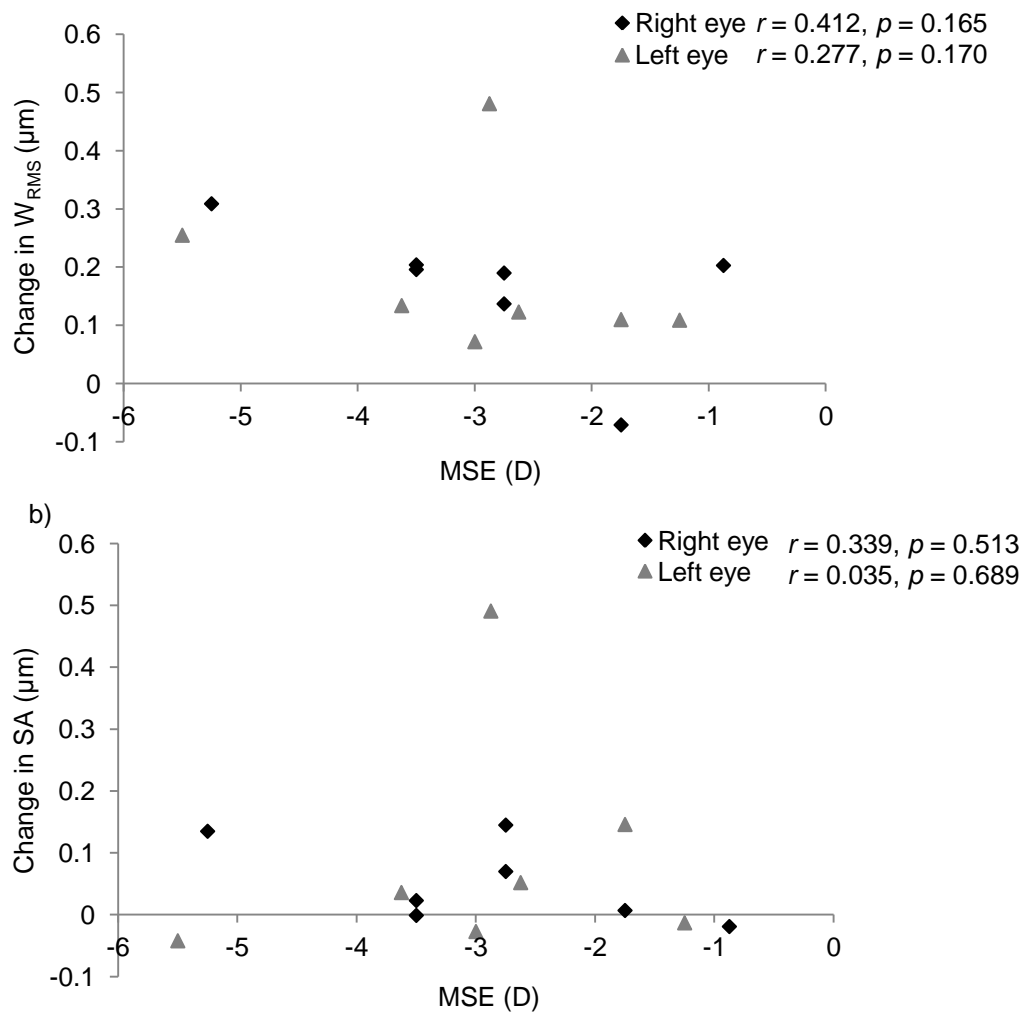


Figure 7.4. Change in a) W_{RMS} and b) spherical aberration (Z12) plotted against baseline MSE for each participant.

There was no correlation between MSE and either change in W_{RMS} or spherical aberration.

7.3.5 Accommodative stimulus response function

ASRF curves were calculated as described in Section 2.3.2 for each participant pre and post-orthok lens fitting. Figure 7.5 illustrates the results for each participant.

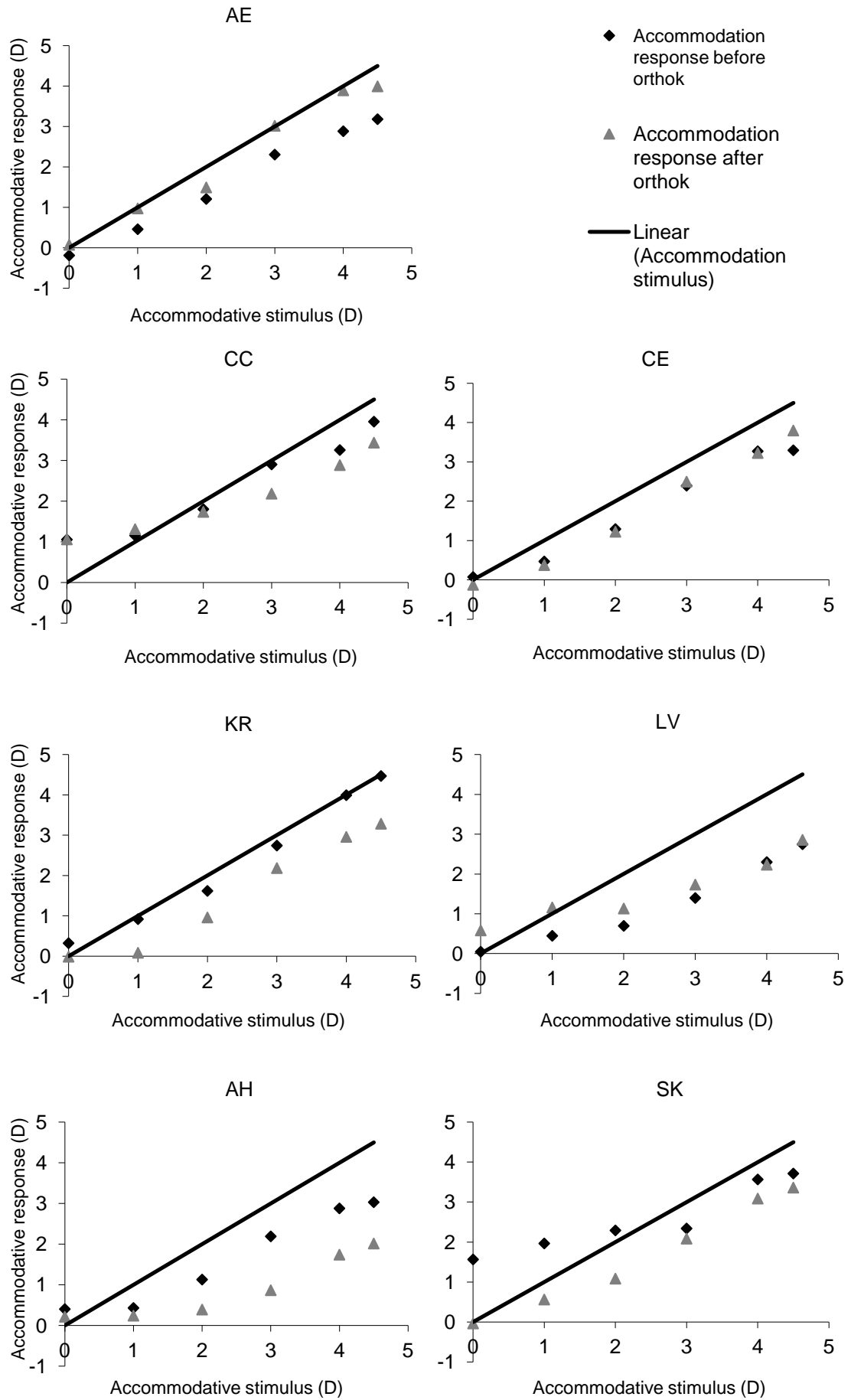


Figure 7.5. ASRF for each participant pre and post-orthok lens fitting.

The accommodative responses for each participant for each stimulus were added together to produce a group mean. The results are shown in Figure 7.6.

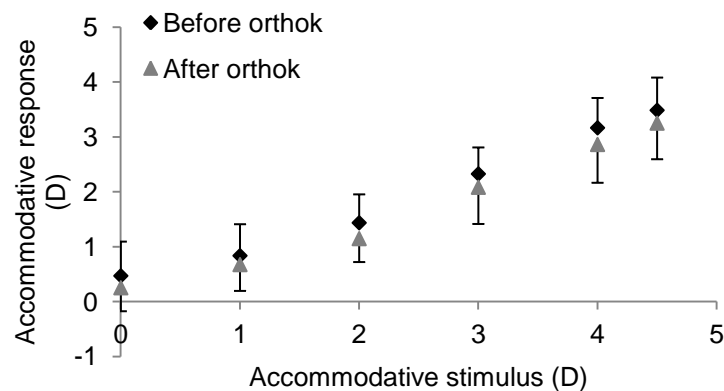


Figure 7.6. Group mean ASRF before and after the orthok procedure. Error bars show 1 SD.

There was a statistically significant effect of the accommodative stimulus on the accommodative response, with a higher stimulus eliciting a higher response, as would be expected ($F_{(1,29,7.75)} = 113.657, p < 0.001$). There was no significant overall effect of the orthok procedure on the accommodative response ($F_{(1,6)} = 1.173, p = 0.320$) and no significant interaction between the dioptric stimulus and the orthok procedure ($F_{(1,42,8.52)} = 0.107, p = 0.834$).

7.3.6 Nearwork-induced transient myopia

Nearwork-induced transient myopia measurements were not possible on participant KR as it was not possible to obtain a clear measurement ring. The data from the remaining six participants are therefore analysed in this section. The within-task accommodation level was calculated per participant for the 3.75 D tasks pre and post-orthok procedure. The group mean was calculated and found to be 2.22 D \pm 0.90 pre-orthok and 2.03 D \pm 1.12 post-orthok. Both the level of NITM and the regression quotient were calculated as in Chapter 3. The 0 D task was used as the baseline. The mean level of NITM and mean regression quotient were calculated for the cohort and the results shown in

Figure 7.7 and 7.8.

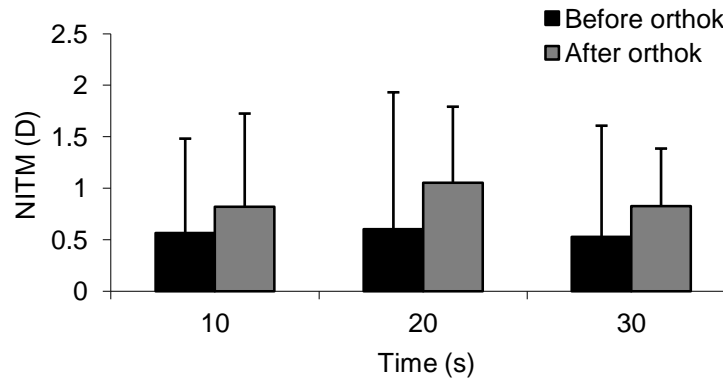


Figure 7.7. Group mean level of NITM pre and post-orthok during the first 30 seconds post-task. The error bars show one standard deviation.

There was no statistically significant overall effect of either time post-task ($F_{(1.01,5.03)} = 0.291, p = 0.614$) or the orthok procedure ($F_{(1.00,5.00)} = 0.507, p = 0.508$) on the level of NITM post-task. There was also no significant interaction between time post-task and the orthok procedure ($F_{(1.11,5.54)} = 0.058, p = 0.842$).

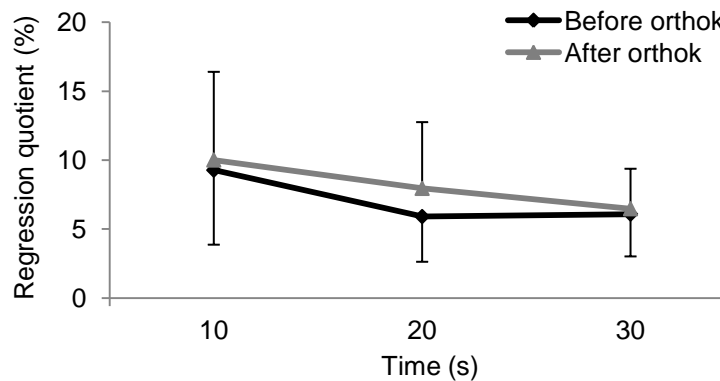


Figure 7.8. Group mean regression quotient pre and post-orthok during the first 30 seconds post-task. The error bars show one standard deviation.

There was no statistically significant overall effect of either time ($F_{(2,10)} = 3.096, p = 0.090$) post-task or the orthok procedure ($F_{(1,5)} = 0.311, p = 0.601$) on the regression quotient post-task. There was also no significant interaction between time post-task and the orthok procedure ($F_{(2,10)} = 0.103, p = 0.903$).

7.4 Discussion

The main finding of this experiment was that the two different designs of orthok lenses do have different effects on visual function. The polynomial lens was found to have a larger effect on the reduction of MSE than the C5 lens. It did, however, also reduce both the high contrast corrected VA and the low contrast corrected VA to a greater extent than the C5 lens. The higher the baseline MSE the greater the detrimental effect of the polynomial lens on both the uncorrected high contrast VA and the corrected high and low contrast VA. Although the orthok procedure was found to significantly increase the W_{RMS} aberrations, no difference was found between the two eyes, and there was no correlation between the MSE at baseline and the change in W_{RMS} .

7.4.1 The effect of orthok on visual function

The effect of orthok lens fitting on distance visual function has been well documented, however there is little evidence of its effect on near visual function. In agreement with previous literature [309, 312-315, 318] this present study found the orthok procedure to have no significant effect on either high contrast uncorrected or best corrected VA. Concerning low contrast best corrected VA, two studies have shown a significant reduction of between two and four letters on the Bailey-Lovie 10% contrast chart [309, 314] after the orthok procedure. A third study [315], found a similar reduction in best corrected low contrast VA, however, this was not found to be significant, probably due to the small sample size of six. This present study has found a greater reduction in low contrast VA of 5 letters in the right eye and 14 in the left. This only just missed statistical significance ($p = 0.066$) but with a larger cohort this may have been reached. Previous studies have found a significant effect of orthok on spherical aberration, 3rd and 4th order W_{RMS} and total W_{RMS} [312-315]. In this experiment a much lower level of spherical aberration was found both before and after the orthok than that found in previous investigations [314, 315] and the mean increase was approximately 0.08 μm which was not a significant change. This is compared to the 0.26 μm increase found by

Joslin *et al.* [315] measured over a 6 mm pupil diameter and the 0.16 μm increase found by Bernstein *et al.* [314] measured over a 5 mm pupil diameter. There are two possible reasons for this difference in magnitude. As the baseline aberration data in the present study were initially taken with spectacle lenses in place and it has been shown that spectacle lenses over -2 D increase the measured spherical aberration (Appendix 3), this may have artificially increased the initial measurements taken from some participants. Due to this the overall change in spherical aberration may be lower than it would have been had it been possible to take the initial measurements without corrective lenses in place. Pupil size is also a factor, as larger pupil sizes give higher levels of aberrations [314, 315]. In our study a 4.8 mm pupil diameter was used and the measurement results were found to be between those found for a 3 mm pupil (0.01 μm increase post-orthok) [314, 315] and those taken using larger pupils. As our sample size is small though it is not possible to rule out the fact that the orthok procedure does indeed increase spherical aberration.

The significant increase in W_{RMS} post-orthok (0.57 μm) in the present study is slightly higher in magnitude than that found in previous literature (0.16 – 0.42 μm) [313-315]. This could possibly be due to the fact that W_{RMS} were calculated up to and including the 8th-order whereas in the other studies it was calculated up to the 4th [313] or 6th-order [314, 315]. Previous literature has linked baseline MSE to increased aberrations following the orthok procedure [312, 313, 331], however, here there was no suggestion of a correlation between baseline MSE and either W_{RMS} or spherical aberration. However, again due to the effect of wearing corrective lenses for the initial measurements, the change in both spherical aberration and W_{RMS} for the more myopic individuals may be artificially reduced in this study.

No significant effect of orthok was found on the magnitude of the distance and near phorias, the amplitude of accommodation or the ASRF, however, an effect cannot be ruled out, again due to the small sample size. An increase in positive spherical aberration has been shown to cause the ASRF to become shallower [334], it may

therefore be expected that the orthok procedure would have the same effect. A larger cohort would need to be investigated to find out if this is the case.

7.4.2 The effect of two different orthok lens designs on visual function

In this study two different designs of lens were fitted to the two eyes of the participants. Both lenses were custom designed. The right lens was a C5 design and the left a polynomial. We were interested in investigating the difference in effect on visual function between these two lenses. The polynomial lens was more effective at reducing myopia, however, it did tend to overcorrect the refraction in some cases. It also caused a significant reduction in best corrected high contrast and low contrast VA. It appears that with the polynomial design of lens there is a correlation between the baseline MSE and the uncorrected VA and best corrected high and low contrast VA, suggesting that this design of lens may not be the one of choice for higher myopes.

Surprisingly there was found to be no significant difference in the change in spherical aberration or W_{RMS} between the two eyes. It may have been expected that if there was a larger reduction in myopia and a reduction in best corrected high and low contrast VA in the left eye it could be due to an increased level of aberrations in this eye as compared to the right [312, 313, 331].

7.4.3 Limitations of the experiment

The main limitation to this study was the difficulty recruiting suitable participants and the high dropout rate, which has led to a small sample size. The participants were being fitted with lenses as part of a second study which had already begun when this project was started. This unfortunately meant that all the participants taking part in the original orthok study could not be recruited. Although the orthok procedure was found to have no significant effect on spherical aberration, ASRF or NITM this may be purely because the sample size was not large enough to show the effect. Greater numbers could also have been recruited if the aberrometer had been built and verified well in

advance of the beginning of the study.

There was a limitation with the aberration measurements in that the baseline measurements were taken with the participants wearing a spectacle correction and the post-orthok measurements were taken with no spectacle lens in place. This may have had an effect the significance of the changes in aberrations with the orthok procedure, however, it should not alter the fact that no significant difference was found between the eyes.

Chapter 8

Conclusions and future work

8.1 Conclusions

This study has come to a number of conclusions:

1. Increased task duration does not increase the level, or slow the regression of post-task nearwork-induced transient myopia (NITM), however, an increase in the dioptric demand of the task does increase the level and slow the regression of NITM. It is also possible that those participants who are aware of blurred distance vision after a period of nearwork may be the ones who have access to sympathetic innervation of the ciliary muscle. This requires further investigation.
2. No relationship was found between the objective level of post-task NITM and the progression of mean spherical equivalent refractive error or axial length change over a two year period in young adults. There is, however, a possible correlation between change in axial length and short-term regression of NITM with those individuals having greater axial length growth taking longer to regress back to baseline post-task. A relationship was found between those who were subjectively aware of symptoms of NITM and axial length growth, with those who were aware of NITM symptoms having significantly greater axial length growth over a two year period compared to those who were not aware of NITM symptoms.
3. The feasibility of measuring the biometric correlates of NITM using a low coherence reflectometry device (LenStar, Haag Streit Koeniz, Switzerland) have been demonstrated. Further investigation is necessary to enable simultaneous continuous measurements of accommodation and biometry.

4. There appear to be at least four different accommodative responses to red/blue accommodative stimuli. There is a possibility that those who have a tendency to accommodate to longer wavelengths of light may suffer hypermetropic retinal blur when viewing multichromatic stimuli, and this may be a trigger for myopia development.

5. Polynomial and C5 designs of orthok lenses have different effects on visual function. The polynomial lens has a larger refractive effect than the C5 lens, whilst also reducing both the high contrast corrected VA and the low contrast corrected VA to a greater extent than the C5 lens. The higher the baseline mean spherical equivalent (MSE) the greater the detrimental effect of the polynomial lens on both the high contrast VA and the corrected high and low contrast VA.

8.2 Future work

There are a number of future projects which could be carried out to gain further incite into the conclusions reached in this thesis:

To investigate whether those individuals who are aware of NITM symptoms do have access to sympathetic innervation of the ciliary muscle, a cohort of young adults would need to be profiled by a previously published method [205]. A cohort of 60 participants would be recruited; 20 emmetropes, 20 early onset myopes and 20 late onset myopes. A questionnaire would be issued asking details of history of refractive error. As discussed in Section 3.4.5 an improved method of assessing NITM symptoms is necessary and participants, once registered on the study, could be asked to report by text message at any time during a certain time period if they noticed blurred distance vision after a period of near work. It would also be useful to record the activity they had been undertaking and whether they were wearing their spectacle correction during the

near task. The cohort could then be split into two groups: an NITM group and a non-NITM group. All would be profiled to assess if they had access to sympathetic innervation of the ciliary muscle. Participants would do a one minute cognitive task within a Badal system at 3.75 D. The task may be an every day task such as playing a game or using 'app' on an iphone. Accommodative response during the task and for 90 seconds post-task would be recorded and analysed as in Mallen *et al.* [205] The aim of the study would be to investigate whether those who suffered NITM symptoms had a longer regression post-task after treatment with timolol maleate (compared to a betaxolol hydrochloride control), which would suggest they were the ones with access to sympathetic innervation of ciliary smooth muscle.

The possible association between static accommodative responses and myopia progression could be investigated by undertaking a myopia progression study in association with static accommodation measurements for various multichromatic stimuli. A longitudinal study, similar to that undertaken in Chapter 4 would be carried out. For a power of 80% to detect a 0.05 mm difference in AL which is greater than the 95% confidence interval of the IOLMaster [181] a cohort of about 120 young adults would need to be recruited. To account for a drop out over the period of the study of about 20% an extra 30 participants would need to be recruited. Autorefraction and biometry would be undertaken at the beginning of the study under cycloplegia, and again after a three year period, to measure myopia progression (lack of cycloplegia and study duration being noted as limitations in Chapter 4). Static accommodation measurements would be taken as in Chapter 6 using a variety of targets (black on white, red on blue, blue on red and more practical targets such as iphone screens). These measurements would initially be repeated on two separate occasions at the beginning of the study to give a baseline and to assess repeatability. There would then be data collection points at the end of year one, two and three. Analysis would be carried out to assess whether there was a link between myopia progression and accommodation characteristics to multichromatic stimuli.

Until recently, due to limitations in the resolution of biometry measuring devices, it has not been possible to take simultaneous measurements of accommodation and ocular biometry, however, the possibility of measuring biometry during disaccommodation has been demonstrated. The next step is to link the LenStar to the Shin-Nippon continuous recording system to enable simultaneous measurements of ocular biometry and accommodation response. Initially, dynamic LenStar data would be collected on a larger cohort, and, as explained in Section 5.4.1, the measurements may be improved by dilating the pupils using phenylephrine hydrochloride. The aim of the study would then be to extend the working distance of the LenStar to make it possible to link it with the Shin-Nippon autorefractor. This would make it possible to simultaneously measure biometry and accommodation from the same eye as has already been demonstrated for the IOLMaster and Shin-Nippon [239]. This would enable us to determine whether NITM is lenticular in origin. If a signal could be superimposed into the accommodation trace at the point where the end of the LenStar measurement occurs it would be possible to know exactly what the accommodation and biometry measurements were at the same point in time. This could be achieved by using a photocell which detects the flash at the the end of the LenStar measurement sequence. This should allow reliable assessment of whether NITM is lenticular in origin.

When collecting the data for Chapter 7 it would have been useful to have measured the effect of orthok lens fitting on near aberrations. A Badal system was built into the aberrometer for this purpose, however, pupil size reduced during accommodation making the near aberration readings extremely variable. Unfortunately as the orthok study had already begun there was not time to investigate how to solve this problem. Dilating pupils with phenylephrine, as has been done in previous studies, may solve the problem. The aim of the study would be to initially validate the aberrometer to take near aberration measurements and once this has been achieved to assess the effect of orthok on these aberrations. The study carried out in Chapter 7 was not conclusive as

to the effect orthok has on nearwork, due to the large drop out rate and therefore small sample size. In Chapter 7 a custom lens design was used to assess the differences between C5 and polynomial designs and it is possible an orthok lens which is presently on the market may have a higher success rate. There was also difficulty recruiting enough suitable participants for the study and it would be useful to collaborate with a study group who already have greater patient throughput, and arrange to have aberration and nearwork measurements taken at the beginning of the study and possibly after a couple of years of lens wear. If it was also associated with a study assessing myopia progression the nearwork effects could be correlated with the axial length changes which occur.

References

1. Bar Dayan, Y., Levin, A., Morad, Y., Grotto, I., Ben-David, R., Goldberg, A., Onn, E., Avni, I., Levi, Y. & Benyamini, O.G. The changing prevalence of myopia in young adults: a 13-year series of population-based prevalence surveys. *Investigative Ophthalmology & Visual Science*, 2005; **46**: 2760-5.
2. Durkin, S.R., Tan, E.W.H., Casson, R.J., Selva, D. & Newland, H.S. Distance refractive error among Aboriginal people attending eye clinics in remote South Australia. *Clinical & Experimental Ophthalmology*, 2007; **35**: 621-626.
3. Morgan, I. & Rose, K. How genetic is school myopia? *Progress in Retinal and Eye Research*, 2005; **24**: 1-38.
4. Vitale, S., Sperduto, R.D. & Ferris, F.L. Increased prevalence of myopia in the United States between 1971-1972 and 1999-2004. *Archives of Ophthalmology*, 2009; **127**: 1632-9.
5. Oneal, M.R. & Connon, T.R. Refractive error change at the United-States Air-Force Academy - class of 1985. *American Journal of Optometry & Physiological Optics*, 1987; **64**: 344-354.
6. Sperduto, R.D., Hiller, R., Podger, M.J., Freidlin, V., Milton, R.C., Wolf, P.A., Myers, R.H., D'Agostino, R.B., Roseman, M.J., Stockman, M.E., Wilson, P.W. Familial aggregation and prevalence of myopia in the Framingham Offspring Eye Study. The Framingham Offspring Eye Study Group. *Archives of Ophthalmology*, 1996; **114**: 326-32.
7. Vitale, S., Ellwein, L., Cotch, M.F., Ferris, F.L. & Sperduto, R. Prevalence of refractive error in the United States, 1999-2004. *Archives of Ophthalmology*, 2008; **126**: 1111-9.
8. Wang, Q., Klein, B.E.K., Klein, R. & Moss, S.E. Refractive status in the Beaver Dam eye study. *Investigative Ophthalmology & Visual Science*, 1994; **35**: 4344-4347.
9. Wu, S.Y., Nemesure, B. & Leske, M.C. Refractive errors in a black adult population: the Barbados Eye Study. *Investigative Ophthalmology & Visual Science*, 1999; **40**: 2179-84.
10. Wensor, M., McCarty, C.A. & Taylor, H.R. Prevalence and risk factors of myopia in Victoria, Australia. *Archives of Ophthalmology*, 1999; **117**: 658-63.

11. Foster, P.J., Broadway, D.C., Hayat, S., Luben, R., Dalzell, N., Bingham, S., Wareham, N.J. & Khaw, K.T. Refractive error, axial length and anterior chamber depth of the eye in British adults: the EPIC-Norfolk Eye Study. *British Journal of Ophthalmology*, 2010; **94**: 827-30.
12. Hendricks, T.J., de Brabander, J., Vankan-Hendricks, M.H., van der Horst, F.G., Hendrikse, F. & Knottnerus, J.A. Prevalence of habitual refractive errors and anisometropia among Dutch schoolchildren and hospital employees. *Acta Ophthalmologica*, 2009; **87**: 538-43.
13. Lyhne, N., Sjolie, A.K., Kyvik, K.O. & Green, A. The importance of genes and environment for ocular refraction and its determiners: a population based study among 20-45 year old twins. *British Journal of Ophthalmology*, 2001; **85**: 1470-1476.
14. Midelfart, A., Kinge, B., Midelfart, S. & Lydersen, S. Prevalence of refractive errors in young and middle-aged adults in Norway. *Acta Ophthalmologica Scandinavica*, 2002; **80**: 501-5.
15. Pfeiffer, N., Wolfram, C., Hoehn, R., Hoffmann, E.M., Lamparter, J., Kottler, U., Adler, M., Blankenberg, S., Wild, P., Mirshahi, A. Prevalence of refractive errors in a large European population: the GHS (Gutenberg Heart Study) eye survey. Association for Research in Vision & Ophthalmology. Fort Lauderdale, Florida. 2011.
16. Mallen, E.A., Gammoh, Y., Al-Bdour, M. & Sayegh, F.N. Refractive error and ocular biometry in Jordanian adults. *Ophthalmic & Physiological Optics*, 2005; **25**: 302-9.
17. Saw, S.M., Chan, Y.H., Wong, W.L., Shankar, A., Sandar, M., Aung, T., Tan, D.T., Mitchell, P. & Wong, T.Y. Prevalence and risk factors for refractive errors in the Singapore Malay Eye Survey. *Ophthalmology*, 2008; **115**: 1713-9.
18. Goh, W.S. & Lam, C.S. Changes in refractive trends and optical components of Hong Kong Chinese aged 19-39 years. *Ophthalmic & Physiological Optics*, 1994; **14**: 378-82.
19. He, M.G., Zeng, J.W., Liu, Y.Z., Xu, J.J., Pokharel, G.P. & Ellwein, L.B. Refractive error and visual impairment in urban children in southern China. *Investigative Ophthalmology & Visual Science*, 2004; **45**: 793-799.
20. Saw, S.M., Yang, A. Chan, Y.H., Tey, F., Nah, G. The increase in myopia prevalence in young male Singapore adults from 1996-1997 to 2009-2010. Association for Research in Vision & Ophthalmology. Fort Lauderdale, Florida. 2011.

21. Wickremasinghe, S., Foster, P.J., Uranchimeg, D., Lee, P.S., Devereux, J.G., Alsbirk, P.H., Machin, D., Johnson, G.J. & Baasanhu, J. Ocular biometry and refraction in Mongolian adults. *Investigative Ophthalmology & Visual Science*, 2004; **45**: 776-83.
22. Shimizu, N., Nomura, H., Ando, F., Niino, N., Miyake, Y. & Shimokata, H. Refractive errors and factors associated with myopia in an adult Japanese population. *Japanese Journal of Ophthalmology*, 2003; **47**: 6-12.
23. Thorn, F., Cruz, A.A.V., Machado, A.J. & Carvalho, R.A.C. Refractive status of indigenous people in the northwestern Amazon region of Brazil. *Optometry & Vision Science*, 2005; **82**: 267-272.
24. Goldschmidt, E. The mystery of myopia. *Acta Ophthalmologica Scandinavica*, 2003; **81**: 431-436.
25. Jorge, J., Almeida, J.B. & Parafita, M.A. Refractive, biometric and topographic changes among Portuguese university science students: a 3-year longitudinal study. *Ophthalmic & Physiological Optics*, 2007; **27**: 287-294.
26. Kinge, B., Midelfart, A., Jacobsen, G. & Rystad, J. Biometric changes in the eyes of Norwegian university students - A three-year longitudinal study. *Acta Ophthalmologica Scandinavica*, 1999; **77**: 648-652.
27. Saw, S.M., Chua, W.H., Gazzard, G., Koh, D., Tan, D.T.H. & Stone, R.A. Eye growth changes in myopic children in Singapore. *British Journal of Ophthalmology*, 2005; **89**: 1489-1494.
28. Saw, S.M., Chua, W.H., Hong, C.Y., Wu, H.M., Chan, W.Y., Chia, K.S., Stone, R.A. & Tan, D. Nearwork in Early-Onset Myopia. *Investigative Ophthalmology & Visual Science*, 2002; **43**: 332-339.
29. Tan, N.W.H., Saw, S.M., Lam, D.S.C., Cheng, H.M., Rajan, W. & Chew, S.J. Temporal variations in myopia progression in Singaporean children within an academic year. *Optometry & Vision Science*, 2000; **77**: 465-472.
30. Lopez-Gil, N., Fernandez-Sanchez, V., Legras, R., Montes-Mico, R., Lara, F. & Nguyen-Khoa, J.L. Accommodation-related changes in monochromatic aberrations of the human eye as a function of age. *Investigative Ophthalmology & Visual Science*, 2008; **49**: 1736-43.
31. Zylbermann, R., Landau, D. & Berson, D. The influence of study habits on myopia in Jewish teenagers. *Journal of Pediatric Ophthalmology & Strabismus*, 1993; **30**: 319-322.

32. Klein, R., Klein, B.E.K., Lee, K.E., Cruickshanks, K.J. & Chappell, R.J. Changes in visual acuity in a population over a 10-year period - The Beaver Dam Eye Study. *Ophthalmology*, 2001; **108**: 1757-1766.
33. Wong, T.Y., Foster, P.J., Ng, T.P., Tielsch, J.M., Johnson, G.J. & Seah, S.K.L. Variations in ocular biometry in an adult Chinese population in Singapore: The Tanjong Pagar survey. *Investigative Ophthalmology & Visual Science*, 2001; **42**: 73-80.
34. Mutti, D.O. & Zadnik, K. Age-related decreases in the prevalence of myopia: Longitudinal change or cohort effect? *Investigative Ophthalmology & Visual Science*, 2000; **41**: 2103-2107.
35. Vitale, S., Cotch, M.F., Sperduto, R. & Ellwein, L. Costs of refractive correction of distance vision impairment in the United States, 1999-2002. *Ophthalmology*, 2006; **113**: 2163-2170.
36. Dandona R., D.L. Refractive error blindness. *Bulletin of the World Health Organization*, 2001; **79**: 237-243
37. Saw, S.M., Gazzard, G., Shih-Yen, E.C. & Chua, W.H. Myopia and associated pathological complications. *Ophthalmic & Physiological Optics*, 2005; **25**: 381-391.
38. Irving, E.L., Sivak, J.G. & Callender, M.G. Refractive plasticity of the developing chick eye. *Ophthalmic & Physiological Optics*, 1992; **12**: 448-456.
39. Wallman, J. & Adams, J.I. Developmental aspects of experimental myopia in chicks - susceptibility, recovery and relation to emmetropization. *Vision Research*, 1987; **27**: 1139-1163.
40. Troilo, D. & Nickla, D.L. The response to visual form deprivation differs with age in marmosets. *Investigative Ophthalmology & Visual Science*, 2005; **46**: 1873-1881.
41. McFadden, S.A., Howlett, M.H.C. & Mertz, J.R. Retinoic acid signals the direction of ocular elongation in the guinea pig eye. *Vision Research*, 2004; **44**: 643-653.
42. Smith, E.L. Spectacle lenses and emmetropization: The role of optical defocus in regulating ocular development. *Optometry & Vision Science*, 1998; **75**: 388-398.
43. Mohny, B.G. Axial myopia associated with dense vitreous hemorrhage of the neonate. *Journal of Aapos*, 2002; **6**: 348-353.

44. Hoyt, C.S., Stone, R.D., Fromer, C. & Billson, F.A. Monocular axial myopia associated with neonatal eyelid closure in human infants. *American Journal of Ophthalmology*, 1981; **91**: 197-200.
45. Johnson, C.A., Post, R.B., Chalupa, L.M. & Lee, T.J. Monocular deprivation in humans - a study of identical-twins. *Investigative Ophthalmology & Visual Science*, 1982; **23**: 135-138.
46. Vonnoorden, G.K. & Lewis, R.A. Ocular axial length in unilateral congenital cataracts and blepharoptosis. *Investigative Ophthalmology & Visual Science*, 1987; **28**: 750-752.
47. Norton, T.T., Essinger, J.A. & McBrien, N.A. Lid-suture myopia in tree shrews with retinal ganglion-cell blockade. *Visual Neuroscience*, 1994; **11**: 143-153.
48. Troilo, D. & Wallman, J. The regulation of eye growth and refractive state - an experimental-study of emmetropization. *Vision Research*, 1991; **31**: 1237-1250.
49. Hodos, W. & Erichsen, J.T. Lower-field myopia in birds - an adaptation that keeps the ground in focus. *Vision Research*, 1990; **30**: 653-657.
50. Smith, E.L., Hung, L.F., Huang, J., Blasdel, T.L., Humbird, T.L. & Bockhorst, K.H. Effects of optical defocus on refractive development in monkeys: evidence for local, regionally selective mechanisms. *Investigative Ophthalmology & Visual Science*, 2010; **51**: 3864-73.
51. Smith, E.L., Ramamirtham, R., Qiao-Grider, Y., Hung, L.F., Huang, J., Kee, C.S., Coats, D. & Paysse, E. Effects of foveal ablation on emmetropization and form-deprivation myopia. *Investigative Ophthalmology & Visual Science*, 2007; **48**: 3914-3922.
52. Wildsoet, C.F. Active emmetropization - Evidence for its existence and ramifications for clinical practice. *Ophthalmic & Physiological Optics*, 1997; **17**: 279-290.
53. Gwiazda, J., Thorn, F., Bauer, J. & Held, R. Emmetropization and the progression of manifest refraction in children followed from infancy to puberty. *Clinical Vision Sciences*, 1993; **8**: 337-344.
54. Sorsby, A. & Leary, G.A. A longitudinal study of refraction and its components during growth. *Special Report Series Medical Research Council (G.B.)*, 1969; **309**: 1-41.
55. Gilmartin, B. Myopia: Precedents for research in the twenty-first century. *Clinical & Experimental Ophthalmology*, 2004; **32**: 305-324.

56. McBrien, N.A. & Adams, D.W. A longitudinal investigation of adult-onset and adult-progression of myopia in an occupational group. Refractive and biometric findings. *Investigative Ophthalmology & Visual Science*, 1997; **38**: 321-33.
57. Saw, S.M., Carkeet, A., Chia, K.S., Stone, R.A. & Tan, D.T.H. Component dependent risk factors for ocular parameters in Singapore Chinese children. *Ophthalmology*, 2002; **109**: 2065-2071.
58. Goss, D.A. & Jackson, T.W. Clinical findings before the onset of myopia in youth .1. Ocular optical components. *Optometry & Vision Science*, 1995; **72**: 870-878.
59. Grosvenor, T., Perrigin, D.M., Perrigin, J. & Maslovitz, B. Houston Myopia Control Study: a randomized clinical trial. Part II. Final report by the patient care team. *American Journal of Optometry & Physiological Optics*, 1987; **64**: 482-98.
60. Hammond, C.J., Snieder, H., Gilbert, C.E. & Spector, T.D. Genes and environment in refractive error: The twin eye study. *Investigative Ophthalmology & Visual Science*, 2001; **42**: 1232-1236.
61. Jones, L.A., Sinnott, L.T., Mutti, D.O., Mitchell, G.L., Moeschberger, M.L. & Zadnik, K. Parental history of myopia, sports and outdoor activities, and future myopia. *Investigative Ophthalmology & Visual Science*, 2007; **48**: 3524-32.
62. Ip, J.M., Kifley, A., Rose, K.A. & Mitchell, P. Refractive findings in children with astigmatic parents: The Sydney myopia study. *American Journal of Ophthalmology*, 2007; **144**: 304-306.
63. Clementi, M., Angi, M., Forabosco, P., Di Gianantonio, E. & Tenconi, R. Inheritance of astigmatism: Evidence for a major autosomal dominant locus. *American Journal of Human Genetics*, 1998; **63**: 825-830.
64. Zhao, J.L., Mao, J., Luo, R., Li, F.R., Munoz, S.R. & Ellwein, L.B. The progression of refractive error in school-age children: Shunyi District, China. *American Journal of Ophthalmology*, 2002; **134**: 735-743.
65. Lin, L.L., Shih, Y.F., Lee, Y.C., Hung, P.T. & Hou, P.K. Changes in ocular refraction and its components among medical students-a 5-year longitudinal study. *Optometry & Vision Science*, 1996; **73**: 495-8.
66. Guggenheim, J.A., Pong-Wong, R., Haley, C.S., Gazzard, G. & Saw, S.M. Correlations in refractive errors between siblings in the Singapore Cohort Study of Risk factors for Myopia. *British Journal of Ophthalmology*, 2007; **91**: 781-784.
67. Sorsby, A. Transmission of refractive errors within Eskimo families. *American Journal of Optometry & Archives of American Academy of Optometry*, 1970; **47**: 244-&.

68. Wu, M.M. & Edwards, M.H. The effect of having myopic parents: an analysis of myopia in three generations. *Optometry & Vision Science*, 1999; **76**: 387-92.
69. Parssinen, O., Hemminki, E. & Klemetti, A. Effect of spectacle use and accommodation on myopic progression: final results of a three-year randomised clinical trial among schoolchildren. *British Journal of Ophthalmology*, 1989; **73**: 547-51.
70. Fulk, G.W., Cyert, L.A. & Parker, D.A. Seasonal variation in myopia progression and ocular elongation. *Optometry & Vision Science*, 2002; **79**: 46-51.
71. Rose, K.A., Morgan, I.G., Ip, J., Kifley, A., Huynh, S., Smith, W. & Mitchell, P. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology*, 2008; **115**: 1279-85.
72. Saw, S.M., Tan, S.B., Fung, D., Chia, K.S., Koh, D., Tan, D.T. & Stone, R.A. IQ and the association with myopia in children. *Investigative Ophthalmology & Visual Science*, 2004; **45**: 2943-8.
73. Simensen, B. & Thorud, L.O. Adult-onset myopia and occupation. *Acta Ophthalmologica*, 1994; **72**: 469-471.
74. Adams, D.W. & McBrien, N.A. Prevalence of myopia and myopic progression in a population of clinical microscopists. *Optometry & Vision Science*, 1992; **69**: 467-73.
75. Jacobsen, N., Jensen, H. & Goldschmidt, E. Does the level of physical activity in university students influence development and progression of myopia? - A 2-year prospective cohort study. *Investigative Ophthalmology & Visual Science*, 2008; **49**: 1322-1327.
76. Logan, N., Davies, L.N., Mallen, E.A.H. & Gilmartin, B. Ametropia and ocular biometry in a UK university student population. *Optometry & Vision Science*, 2005; **82**: 261-266.
77. Ong, E., Ciuffreda, K.J., Overview of accommodation. In *Accommodation, nearwork and myopia*. Santa Ana, Optometric Extension Program, 1997, p.1-18.
78. Fincham, E.F. The accommodation reflex and its stimulus. *British Journal of Ophthalmology*, 1951; **35**: 381-93.
79. Cleary, G., Spalton, D.J., Patel, P.M., Lin, P.F. & Marshall, J. Diagnostic accuracy and variability of autorefractometry by the Tracey Visual Function Analyzer and the Shin-Nippon NVision-K 5001 in relation to subjective refraction. *Ophthalmic & Physiological Optics*, 2009; **29**: 173-81.

80. Morgan, M.W. Accommodation and vergence. *Am J Optom Arch Am Acad Optom*, 1968; **45**: 417-54.
81. Rosenfield, M., Ciuffreda, K.J., Hung, G.K. & Gilmartin, B. Tonic accommodation: a review. I. Basic aspects. *Ophthalmic & Physiological Optics*, 1993; **13**: 266-84.
82. Gwiazda, J., Thorn, F., Bauer, J. & Held, R. Myopic children show insufficient accommodative response to blur. *Investigative Ophthalmology & Visual Science*, 1993; **34**: 690-694.
83. Abbott, M.L., Schmid, K.L. & Strang, N.C. Differences in the accommodation stimulus response curves of adult myopes and emmetropes. *Ophthalmic & Physiological Optics*, 1998; **18**: 13-20.
84. Allen, P.M. & O'Leary, D.J. Accommodation functions: Co-dependency and relationship to refractive error. *Vision Research*, 2006; **46**: 491-505.
85. Mutti, D.O., Mitchell, G.L., Hayes, J.R., Jones, L.A., Moeschberger, M.L., Cotter, S.A., Kleinstein, R.N., Manny, R.E., Twelker, J.D. & Zadnik, K. Accommodative lag before and after the onset of myopia. *Investigative Ophthalmology & Visual Science*, 2006; **47**: 837-846.
86. Gwiazda, J., Thorn, F. & Held, R. Accommodation, accommodative convergence, and response AC/A ratios before and at the onset of myopia in children. *Optometry & Vision Science*, 2005; **82**: 273-278.
87. Campbell, F.W. & Westheimer, G. Dynamics of accommodation responses of the human eye. *Journal of Physiology*, 1960; **151**: 285-95.
88. Ong, E. & Ciuffreda, K.J. Nearwork-induced transient myopia - A critical review. *Documenta Ophthalmologica*, 1995; **91**: 57-85.
89. Ciuffreda, K.J., Colburn, C. & Wallis, D. Effect of stimulus duration and dioptric demand transient myopia. *Investigative Ophthalmology & Visual Science*, 1996; **37**: 778-778.
90. Ciuffreda, K.J. & Lee, M. Differential refractive susceptibility to sustained nearwork. *Ophthalmic & Physiological Optics*, 2002; **22**: 372-379.
91. Ciuffreda, K.J. & Ordonez, X. Abnormal transient myopia in symptomatic individuals after sustained nearwork. *Optometry & Vision Science*, 1995; **72**: 506-10.

92. Ciuffreda, K.J., Rosenfield, M. & Gillard, M.A. Near-vision lens effects on nearwork-induced transient myopia. *Clinical Eye & Vision Care*, 1999; **10**: 205-207.
93. Ciuffreda, K.J. & Wallis, D.M. Myopes show increased susceptibility to nearwork aftereffects. *Investigative Ophthalmology & Visual Science*, 1998; **39**: 1797-1803.
94. Ong, E., Ciuffreda, Kenneth, J., Rosenfield, Mark Accommodation, vergence and transient myopia. *Optometry & Vision Science (suppliment)* 1994; **71**: 129.
95. Ong, E., Ciuffreda, K.J. & Rosenfield, M. Effect of target proximity on transient myopia induced by equidiotric stimuli. *Optometry & Vision Science*, 1995; **72**: 502-5.
96. Rosenfield, M. & Ciuffreda, K.J. Cognitive demand and transient nearwork-induced myopia. *Optometry & Vision Science*, 1994; **71**: 381-385.
97. Rosenfield, M., Ciuffreda, K.J. & Novogrodsky, L. Contribution of accommodation and disparity-vergence to transient nearwork-induced myopic shifts. *Ophthalmic & Physiological Optics*, 1992; **12**: 433-436.
98. Vasudevan, B. & Ciuffreda, K.J. Additivity of near work-induced transient myopia and its decay characteristics in different refractive groups. *Investigative Ophthalmology & Visual Science*, 2008; **49**: 836-41.
99. Vera-Diaz, F.A., Strang, N.C. & Winn, B. Nearwork induced transient myopia during myopia progression. *Current Eye Research*, 2002; **24**: 289-295.
100. Wolffsohn, J.S., Gilmartin, B., Li, R.W., Edwards, M.H., Chat, S.W., Lew, J.K. & Yu, B.S. Nearwork-induced transient myopia in preadolescent Hong Kong Chinese. *Investigative Ophthalmology & Visual Science*, 2003; **44**: 2284-9.
101. Wolffsohn, J.S., Gilmartin, B., Thomas, R. & Mallen, E.A.H. Refractive error, cognitive demand and nearwork-induced transient myopia. *Current Eye Research*, 2003; **27**: 363-370.
102. Arunthavaraja, M., Vasudevan, B. & Ciuffreda, K.J. Nearwork-induced transient myopia (NITM) following marked and sustained, but interrupted, accommodation at near. *Ophthalmic & Physiological Optics*, 2010; **30**: 766-75.
103. Gilmartin, B. A review of the role of sympathetic innervation of the ciliary muscle in ocular accommodation. *Ophthalmic & Physiological Optics*, 1986; **6**: 23-37.

104. Chen, J.C., Schmid, K.L. & Brown, B. The autonomic control of accommodation and implications for human myopia development: a review. *Ophthalmic & Physiological Optics*, 2003; **23**: 401-22.
105. Gilmartin, B., Mallen, E.A.H. & Wolffsohn, J.S. Sympathetic control of accommodation: Evidence for inter-subject variation. *Ophthalmic & Physiological Optics*, 2002; **22**: 366-371.
106. Hung, G.K. & Ciuffreda, K.J. Incremental retinal-defocus theory of myopia development - Schematic analysis and computer simulation. *Computers in Biology and Medicine*, 2007; **37**: 930-946.
107. Mutti, D.O., Jones, L.A., Moeschberger, M.L. & Zadnik, K. AC/A ratio, age, and refractive error in children. *Investigative Ophthalmology & Visual Science*, 2000; **41**: 2469-2478.
108. Jiang, B.C. Parameters of accommodative and vergence systems and the development of late-onset myopia. *Investigative Ophthalmology & Visual Science*, 1995; **36**: 1737-1742.
109. Ting, P.W., Lam, C.S., Edwards, M.H. & Schmid, K.L. Prevalence of myopia in a group of Hong Kong microscopists. *Optometry & Vision Science*, 2004; **81**: 88-93.
110. Goss, D.A. & Jackson, T.W. Clinical findings before the onset of myopia in youth .3. Heterophoria. *Optometry and Vision Science*, 1996; **73**: 269-278.
111. Low, W., Dirani, M., Gazzard, G., Chan, Y.H., Zhou, H.J., Selvaraj, P., Au Eong, K.G., Young, T.L., Mitchell, P., Wong, T.Y. & Saw, S.M. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. *British Journal of Ophthalmology*, 2010; **94**: 1012-6.
112. Onal, S., Toker, E., Akingol, Z., Arslan, G., Ertan, S., Turan, C. & Kaplan, O. Refractive errors of medical students in Turkey: one year follow-up of refraction and biometry. *Optometry & Vision Science*, 2007; **84**: 175-80.
113. Charman, N. Understanding ocular wavefront aberration - Part 2. *The Optician*, 2005; **230**: 18.
114. Porter, J., Guirao, A., Cox, I.G. & Williams, D.R. Monochromatic aberrations of the human eye in a large population. *Journal of the Optometric Society of America A, Optics, Image Science & Vision*, 2001; **18**: 1793-803.
115. Cheng, X., Bradley, A., Hong, X. & Thibos, L.N. Relationship between refractive error and monochromatic aberrations of the eye. *Optometry & Vision Science*, 2003; **80**: 43-49.

116. Carkeet, A., Luo, H.D., Tong, L., Saw, S.M. & Tan, D.T.H. Refractive error and monochromatic aberrations in Singaporean children. *Vision Research*, 2002; **42**: 1809-1824.
117. Hazel, C.A., Cox, M.J. & Strang, N.C. Wavefront aberration and its relationship to the accommodative stimulus-response function in myopic subjects. *Optometry & Vision Science*, 2003; **80**: 151-8.
118. He, J.C., Sun, P., Held, R., Thorn, F., Sun, X. & Gwiazda, J.E. Wavefront aberrations in eyes of emmetropic and moderately myopic school children and young adults. *Vision Research*, 2002; **42**: 1063-70.
119. Paquin, M.P., Hamam, H. & Simonet, P. Objective measurement of optical aberrations in myopic eyes. *Optometry & Vision Science* 2002; **79**: 285-91.
120. Collins, M.J., Wildsoet, C.F. & Atchison, D.A. Monochromatic aberrations and myopia. *Vision Research*, 1995; **35**: 1157-63.
121. Kwan, W.C., Yip, S.P. & Yap, M.K. Monochromatic aberrations of the human eye and myopia. *Clinical & Experimental Optometry*, 2009; **92**: 304-12.
122. Llorente, L., Barbero, S., Cano, D., Dorronsoro, C. & Marcos, S. Myopic versus hyperopic eyes: axial length, corneal shape and optical aberrations. *Journal of Vision*, 2004; **4**: 288-98.
123. Buehren, T., Collins, M.J. & Carney, L.G. Near work induced wavefront aberrations in myopia. *Vision Research*, 2005; **45**: 1297-312.
124. Vasudevan, B., Ciuffreda, K.J. & Wang, B. Nearwork-induced changes in topography, aberrations, and thickness of the human cornea after interrupted reading. *Cornea*, 2007; **26**: 917-23.
125. Atchison, D.A., Pritchard, N., Schmid, K.L., Scott, D.H., Jones, C.E. & Pope, J.M. Shape of the retinal surface in emmetropia and myopia. *Investigative Ophthalmology & Visual Science*, 2005; **46**: 2698-707.
126. Atchison, D.A., Jones, C.E., Schmid, K.L., Pritchard, N., Pope, J.M., Strugnell, W.E. & Riley, R.A. Eye shape in emmetropia and myopia. *Investigative Ophthalmology & Visual Science*, 2004; **45**: 3380-6.
127. Stone, R.A. & Flitcroft, D.I. Ocular shape and myopia. *Annals Academy of Medicine Singapore*, 2004; **33**: 7-15.
128. Atchison, D.A., Pritchard, N. & Schmid, K.L. Peripheral refraction along the horizontal and vertical visual fields in myopia. *Vision Research*, 2006; **46**: 1450-8.

129. Sng, C.C., Lin, X.Y., Gazzard, G., Chang, B., Dirani, M., Chia, A., Selvaraj, P., Ian, K., Drobe, B., Wong, T.Y. & Saw, S.M. Peripheral refraction and refractive error in singapore chinese children. *Investigative Ophthalmology & Visual Science*, 2011; **52**: 1181-90.
130. Smith, E.L., Hung, L.F. & Huang, J. Relative peripheral hyperopic defocus alters central refractive development in infant monkeys. *Vision Research*, 2009; **49**: 2386-92.
131. Liu, Y. & Wildsoet, C. The effect of two-zone concentric bifocal spectacle lenses on refractive error development and eye growth in young chicks. *Investigative Ophthalmology & Visual Science*, 2011; **52**: 1078-86.
132. Hoogerheide, J., Rempt, F. & Hoogenboom, W.P. Acquired myopia in young pilots. *Ophthalmologica*, 1971; **163**: 209-15.
133. Mutti, D.O., Hayes, J.R., Mitchell, G.L., Jones, L.A., Moeschberger, M.L., Cotter, S.A., Kleinstein, R.N., Manny, R.E., Twelker, J.D., Zadnik, K. & Group, C.S. Refractive error, axial length, and relative peripheral refractive error before and after the onset of myopia. *Investigative Ophthalmology & Visual Science*, 2007; **48**: 2510-9.
134. Mutti, D.O., Sinnott, L.T., Mitchell, G.L., Jones-Jordan, L.A., Moeschberger, M.L., Cotter, S.A., Kleinstein, R.N., Manny, R.E., Twelker, J.D., Zadnik, K. & Group, C.S. Relative peripheral refractive error and the risk of onset and progression of myopia in children. *Investigative Ophthalmology & Visual Science*, 2011; **52**: 199-205.
135. Chung, K., Mohidin, N. & O'Leary, D.J. Undercorrection of myopia enhances rather than inhibits myopia progression. *Vision Research*, 2002; **42**: 2555-2559.
136. Adler, D. & Millodot, M. The possible effect of undercorrection on myopic progression in children. *Clinical & Experimental Optometry*, 2006; **89**: 315-21.
137. Ong, E., Grice, K., Held, R., Thorn, F. & Gwiazda, J. Effects of spectacle intervention on the progression of myopia in children. *Optometry & Vision Science*, 1999; **76**: 363-9.
138. Phillips, J.R. Monovision slows juvenile myopia progression unilaterally. *British Journal of Ophthalmology*, 2005; **89**: 1196-200.
139. Edwards, M.H., Li, R.W., Lam, C.S., Lew, J.K. & Yu, B.S. The Hong Kong progressive lens myopia control study: study design and main findings. *Investigative Ophthalmology & Visual Science*, 2002; **43**: 2852-8.

140. Gwiazda, J., Hyman, L., Hussein, M., Everett, D., Norton, T.T., Kurtz, D., Leske, M.C., Manny, R., Marsh-Tootle, W. & Scheiman, M. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Investigative Ophthalmology & Visual Science*, 2003; **44**: 1492-500.
141. Leung, J.T. & Brown, B. Progression of myopia in Hong Kong Chinese schoolchildren is slowed by wearing progressive lenses. *Optometry & Vision Science*, 1999; **76**: 346-54.
142. Fulk, G.W., Cyert, L.A. & Parker, D.E. A randomized trial of the effect of single-vision vs. bifocal lenses on myopia progression in children with esophoria. *Optometry & Vision Science*, 2000; **77**: 395-401.
143. Brown, B., Edwards, M.H. & Leung, J.T. Is esophoria a factor in slowing of myopia by progressive lenses? *Optometry & Vision Science*, 2002; **79**: 638-42.
144. Shih, Y.F., Hsiao, C.K., Chen, C.J., Chang, C.W., Hung, P.T. & Lin, L.L. An intervention trial on efficacy of atropine and multi-focal glasses in controlling myopic progression. *Acta Ophthalmologica Scandinavica*, 2001; **79**: 233-6.
145. Chua, W.H., Balakrishnan, V., Chan, Y.H., Tong, L., Ling, Y., Quah, B.L. & Tan, D. Atropine for the treatment of childhood myopia. *Ophthalmology*, 2006; **113**: 2285-91.
146. Tan, D.T., Lam, D.S., Chua, W.H., Shu-Ping, D.F. & Crockett, R.S. One-year multicenter, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. *Ophthalmology*, 2005; **112**: 84-91.
147. McBrien, N.A., Moghaddam, H.O. & Reeder, A.P. Atropine reduces experimental myopia and eye enlargement via a nonaccommodative mechanism. *Investigative Ophthalmology & Visual Science*, 1993; **34**: 205-15.
148. Stone, J. The possible influence of contact lenses on myopia. *British Journal of Physiological Optics*, 1976; **31**: 89-114.
149. Grosvenor, T., Perrigin, J., Perrigin, D. & Quintero, S. Use of silicone-acrylate contact-lenses for the control of myopia - results after 2 years of lens wear. *Optometry & Vision Science*, 1989; **66**: 41-47.
150. Khoo, C.Y., Chong, J. & Rajan, U. A 3-year study on the effect of RGP contact lenses on myopic children. *Singapore Medical Journal*, 1999; **40**: 230-7.

151. Katz, J., Schein, O.D., Levy, B., Cruiscullo, T., Saw, S.M., Rajan, U., Chan, T.K., Yew Khoo, C. & Chew, S.J. A randomized trial of rigid gas permeable contact lenses to reduce progression of children's myopia. *American Journal of Ophthalmology*, 2003; **136**: 82-90.
152. Walline, J.J., Jones, L.A., Mutti, D.O. & Zadnik, K. A randomized trial of the effects of rigid contact lenses on myopia progression. *Archives of Ophthalmology*, 2004; **122**: 1760-6.
153. Cheung, S.W., Cho, P. & Fan, D. Asymmetrical increase in axial length in the two eyes of a monocular orthokeratology patient. *Optometry & Vision Science*, 2004; **81**: 653-656.
154. Cho, P., Cheung, S.W. & Edwards, M. The longitudinal orthokeratology research in children (LORIC) in Hong Kong: a pilot study on refractive changes and myopic control. *Current Eye Research*, 2005; **30**: 71-80.
155. Kakita, T., Hiraoka, T. & Oshika, T. Influence of overnight orthokeratology on axial elongation in childhood myopia. *Investigative Ophthalmology & Visual Science*, 2010; **52**: 2170-4.
156. Walline, J.J., Jones, L.A. & Sinnott, L.T. Corneal reshaping and myopia progression. *British Journal of Ophthalmology*, 2009; **93**: 1181-5.
157. Alharbi, A. & Swarbrick, H.A. The effects of overnight orthokeratology lens wear on corneal thickness. *Investigative Ophthalmology & Visual Science*, 2003; **44**: 2518-23.
158. Nichols, J.J., Marsich, M.M., Nguyen, M., Barr, J.T. & Bullimore, M.A. Overnight orthokeratology. *Optometry & Vision Science*, 2000; **77**: 252-9.
159. Soni, P.S., Nguyen, T.T. & Bonanno, J.A. Overnight orthokeratology: visual and corneal changes. *Eye Contact Lens*, 2003; **29**: 137-45.
160. Swarbrick, H.A., Wong, G. & O'Leary, D.J. Corneal response to orthokeratology. *Optometry & Vision Science*, 1998; **75**: 791-9.
161. Queiros, A., Gonzalez-Meijome, J.M., Jorge, J., Villa-Collar, C. & Gutierrez, A.R. Peripheral refraction in myopic patients after orthokeratology. *Optometry & Vision Science*, 2010; **87**: 323-9.
162. Kang, P.L., Swarbrick, H. Peripheral refraction in children wearing orthokeratology and gas-permeable lenses. Association for Research in Vision & Ophthalmology. Fort Lauderdale, Florida. 2011.

163. Taberbero, J., Vazquez, D., Seidemann, A., Uttenweiler, D. & Schaeffel, F. Effects of myopic spectacle correction and radial refractive gradient spectacles on peripheral refraction. *Vision Research*, 2009; **49**: 2176-86.
164. Lin, Z., Martinez, A., Chen, X., Li, L., Sankaridurg, P., Holden, B.A. & Ge, J. Peripheral defocus with single-vision spectacle lenses in myopic children. *Optometry & Vision Science*, 2010; **87**: 4-9.
165. Holden, B.A., Sankaridurg, P., Lazon, P., Ho, A., Smith, E.L., Chen, X., Lin, J., Naduvilath, T., Ge, J. Central and peripheral visual performance of a novel contact lens designed to control progression of myopia. Association for Research in Vision & Ophthalmology. Fort Lauderdale, Florida. 2011.
166. Sankaridurg, P., Donovan, L., Varnas, S., Ho, A., Chen, X., Martinez, A., Fisher, S., Lin, Z., Smith, E.L., 3rd, Ge, J. & Holden, B. Spectacle lenses designed to reduce progression of myopia: 12-month results. *Optometry & Vision Science*, 2010; **87**: 631-41.
167. Charman, W.N. & Tucker, J. Accommodation and color. *Journal of the Optical Society of America*, 1978; **68**: 459-71.
168. Kroger, R.H. & Binder, S. Use of paper selectively absorbing long wavelengths to reduce the impact of educational near work on human refractive development. *British Journal of Ophthalmology*, 2000; **84**: 890-3.
169. Lovasik, J.V. & Kergoat, H. Accommodative performance for chromatic displays. *Ophthalmic & Physiological Optics*, 1988; **8**: 443-9.
170. Mallen, E.A.H., Wolffsohn, J.S., Gilmartin, B. & Tsujimura, S. Clinical evaluation of the Shin-Nippon SRW-5000 autorefractor in adults. *Ophthalmic & Physiological Optics*, 2001; **21**: 101-107.
171. Thibos, L.N., Wheeler, W. & Horner, D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optometry & Vision Science*, 1997; **74**: 367-75.
172. Chat, S.W. & Edwards, M.H. Clinical evaluation of the Shin-Nippon SRW-5000 autorefractor in children. *Ophthalmic & Physiological Optics*, 2001; **21**: 87-100.
173. Davies, L.N., Mallen, E.A., Wolffsohn, J.S. & Gilmartin, B. Clinical evaluation of the Shin-Nippon NVision-K 5001/Grand Seiko WR-5100K autorefractor. *Optometry & Vision Science*, 2003; **80**: 320-4.
174. Wolffsohn, J.S., Gilmartin, B., Mallen, E.A.H. & Tsujimura, S. Continuous recording of accommodation and pupil size using the Shin-Nippon SRW-5000 autorefractor. *Ophthalmic & Physiological Optics*, 2001; **21**: 108-113.

175. Cufflin, M.P., *Blur adaptation effects on accommodation in myopes and emmetropes*, in 2007, University of Bradford: Bradford.
176. Atchison, D.A., Bradley, A., Thibos, L.N. & Smith, G. Useful variations of the Badal Optometer. *Optometry & Vision Science*, 1995; **72**: 279-84.
177. Cufflin, M.P., Hazel, C.A. & Mallen, E.A. Static accommodative responses following adaptation to differential levels of blur. *Ophthalmic & Physiological Optics*, 2007; **27**: 353-60.
178. Fercher, A.F., Mengedocht, K. & Werner, W. Eye-length measurement by interferometry with partially coherent light. *Optics Letters*, 1988; **13**: 186-188.
179. Haigis, W., Lege, B., Miller, N. & Schneider, B. Comparison of immersion ultrasound biometry and partial coherence interferometry for intraocular lens calculation according to Haigis. *Graefes Archive for Clinical & Experimental Ophthalmology*, 2000; **238**: 765-73.
180. Hitzenberger, C.K. Optical measurement of the axial eye length by laser Doppler interferometry. *Investigative Ophthalmology & Visual Science*, 1991; **32**: 616-24.
181. Santodomingo-Rubido, J., Mallen, E.A.H., Gilmartin, B. & Wolffsohn, J.S. A new non-contact optical device for ocular biometry. *British Journal of Ophthalmology*, 2002; **86**: 458-462.
182. Buckhurst, P.J., Wolffsohn, J.S., Shah, S., Naroo, S.A., Davies, L.N. & Berrow, E.J. A new optical low coherence reflectometry device for ocular biometry in cataract patients. *British Journal of Ophthalmology*, 2009; **93**: 949-53.
183. Hampson, K.M., Chin, S.S. & Mallen, E.A.H. Binocular Shack-Hartmann sensor for the human eye. *Journal of Modern Optics*, 2008; **55**: 703-716.
184. Hampson, K.M., *The higher-order aberrations of the human eye: relation to the pulse and effect on vision*. 2004, Imperial College of Science, Technology and Medicine: London.
185. Hampson, K.M., Chin, S.S. & Mallen, E.A. Dual wavefront sensing channel monocular adaptive optics system for accommodation studies. *Optics Express*, 2009; **17**: 18229-40.
186. Chin, S.S., Hampson, K.M. & Mallen, E.A. Binocular correlation of ocular aberration dynamics. *Optics Express*, 2008; **16**: 14731-45.

187. Liang, J. & Williams, D.R. Aberrations and retinal image quality of the normal human eye. *Journal of the Optical Society of America A, Optics, Image Science & Vision*, 1997; **14**: 2873-83.
188. Davies, N., Diaz-Santana, L. & Lara-Saucedo, D. Repeatability of ocular wavefront measurement. *Optometry & Vision Science*, 2003; **80**: 142-50.
189. Miranda, M.A., O'Donnell, C. & Radhakrishnan, H. Repeatability of corneal and ocular aberration measurements and changes in aberrations over one week. *Clinical & Experimental Optometry*, 2009; **92**: 253-66.
190. Bailey, I.L. & Lovie, J.E. New design principles for visual acuity letter charts. *American Journal of Optometry & Physiological Optics*, 1976; **53**: 740-5.
191. Lancaster, W.B., Williams, E. R. New light on the theory of accommodation, with practical applications. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, 1914; **19**: 170-195.
192. Ostberg, O., Accommodation and visual fatigue in display work. In E. Grandjean, Vigliani, E. *Ergonomic aspects of visual display terminals*. London, Taylor & Francis Ltd., 1980, p.41-52.
193. Haider, M., Kundi, M., Weibenbock, M., Worker strain related to VDUs with differently coloured characters. In E. Grandjean, Vigliani, E. *Ergonomic aspects of visual display terminals*. London, Taylor & Francis Ltd., 1980, p.53-64.
194. Jaschinski-Kruza, W. Transient myopia after visual work. *Ergonomics*, 1984; **27**: 1181-9.
195. Fisher, S.K., Ciuffreda, K.J. & Levine, S. Tonic accommodation, accommodative hysteresis, and refractive error. *American Journal of Physiological Optics*, 1987; **64**: 799-809.
196. Owens, D.A. & Wolf-Kelly, K. Near work, visual fatigue, and variations of oculomotor tonus. *Investigative Ophthalmology & Visual Science*, 1987; **28**: 743-9.
197. Ehrlich, D.L. Near vision stress: vergence adaptation and accommodative fatigue. *Ophthalmic & Physiological Optics*, 1987; **7**: 353-7.
198. Tan, R.K.T.O.L., D. J. Accommodation characteristics before and after near work. *Clinical & Experimental Optometry*, 1988; **71**: 165 - 169.
199. Rosenfield, M., Ciuffreda, Kenneth, J., Novogrodsky, Lisa, Yu, Anita, Gillard, Margaret Sustained near-vision does indeed induce myopia! *Investigative Ophthalmology & Visual Science (suppliment)*, 1992b; **33**: 710.

200. Rabbetts, R.B., Hull, C., Ocular aberrations. In R.B. Rabbetts *Clinical visual optics*. Oxford, Butterworth-Heinemann, 2007, p.284-312.
201. Pugh, J.R. & Winn, B. Modification of the Canon Auto Ref R1 for use as a continuously recording infrared optometer. *Ophthalmic & Physiological Optics*, 1988; **8**: 460-464.
202. Wolffsohn, J.S., O'Donnell, C., Charman, W.N. & Gilmartin, B. Simultaneous continuous recording of accommodation and pupil size using the modified Shin-Nippon SRW-5000 autorefractor. *Ophthalmic & Physiological Optics*, 2004; **24**: 142-147.
203. Kruger, P.B. & Pola, J. Stimuli for accommodation: blur, chromatic aberration and size. *Vision Research*, 1986; **26**: 957-71.
204. Day, M., Strang, N.C., Seidel, D. & Gray, L.S. Technical Note: Effect of contact lenses on measurement of the accommodation microfluctuations. *Ophthalmic & Physiological Optics*, 2008; **28**: 91-95.
205. Mallen, E.A.H., Gilmartin, B. & Wolffsohn, J.S. Sympathetic innervation of ciliary muscle and oculomotor function in emmetropic and myopic young adults. *Vision Research*, 2005; **45**: 1641-1651.
206. Krumholz, D.M., Fox, R.S. & Ciuffreda, K.J. Short-term changes in tonic accommodation. *Investigative Ophthalmology and Visual Science*, 1986; **27**: 552-7.
207. Kruger, P.B. The effect of cognitive demand on accommodation. *American Journal of Optometry & Physiological Optics*, 1980; **57**: 440-5.
208. Tornqvist, G. The relative importance of the parasympathetic and sympathetic nervous systems for accommodation in monkeys. *Investigative Ophthalmology* 1967; **6**: 612-7.
209. Strang, N.C., Winn, B. & Gilmartin, B. Repeatability of post-task regression of accommodation in emmetropia and late-onset myopia. *Ophthalmic & Physiological Optics*, 1994; **14**: 88-91.
210. Rose, K. High heritability of myopia does not preclude rapid changes in prevalence. *Clinical & Experimental Ophthalmology*, 2002; **30**: 168-172.
211. Hyman, L. Myopic and hyperopic refractive error in adults: An overview. *Ophthalmic Epidemiology*, 2007; **14**: 192-197.

212. Dirani, M., Tong, L., Gazzard, G., Zhang, X., Chia, A., Young, T.L., Rose, K.A., Mitchell, P. & Saw, S.M. Outdoor activity and myopia in Singapore teenage children. *British Journal of Ophthalmology*, 2009; **93**: 997-1000.
213. Septon, R.D. Myopia among optometry students. *American Journal of Optometry & Physiological Optics*, 1984; **61**: 745-51.
214. Loman, J., Quinn, G.E., Kamoun, L., Ying, G.S., Maguire, M.G., Hudesman, D. & Stone, R.A. Darkness and near work: myopia and its progression in third-year law students. *Ophthalmology*, 2002; **109**: 1032-8.
215. Risovic, D.J., Misailovic, K.R., Eric-Marinkovic, J.M., Kosanovic-Jakovic, N.G., Milenkovic, S.M. & Petrovic, L.Z. Refractive errors and binocular dysfunctions in a population of university students. *European Journal of Ophthalmology*, 2008; **18**: 1-6.
216. Fledelius, H.C. Myopia profile in Copenhagen medical students 1996-98. Refractive stability over a century is suggested. *Acta Ophthalmologica Scandinavica*, 2000; **78**: 501-5.
217. Bullimore, M.A., Conway, R. & Nakash, A. Myopia in optometry students: family history, age of onset and personality. *Ophthalmic & Physiological Optics*, 1989; **9**: 284-8.
218. Osuobeni, E.P. Ocular components values and their intercorrelations in Saudi Arabians. *Ophthalmic & Physiological Optics*, 1999; **19**: 489-97.
219. Zadnik, K., Mutti, D.O. & Adams, A.J. The repeatability of measurement of the ocular components. *Investigative Ophthalmology & Visual Science*, 1992; **33**: 2325-33.
220. Grosvenor, T. & Scott, R. Three-year changes in refraction and its components in youth-onset and early adult-onset myopia. *Optometry & Vision Science*, 1993; **70**: 677-83.
221. Bland, J.M. & Altman, D.G. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1986; **1**: 307-10.
222. Ray, W.A. & O'Day, D.M. Statistical analysis of multi-eye data in ophthalmic research. *Investigative Ophthalmology & Visual Science*, 1985; **26**: 1186-8.
223. Drexler, W., Findl, O., Schmetterer, L., Hitzenberger, C.K. & Fercher, A.F. Eye elongation during accommodation in humans: differences between emmetropes and myopes. *Investigative Ophthalmology & Visual Science*, 1998; **39**: 2140-7.

224. Mallen, E.A., Kashyap, P. & Hampson, K.M. Transient Axial Length Change during the Accommodation Response in Young Adults. *Investigative Ophthalmology & Visual Science*, 2006; **47**: 1251-4.
225. Rabbetts, R.B., Spherical ametropia. In R.B. Rabbetts *Clinical Visual Optics* Oxford, Butterworth Heinemann Elsevier, 2007, p.p 67-83.
226. Aitchison, D.A. & Smith, G., Refracting components: cornea & lens. In *Optics of the Human Eye*. Oxford, Butterworth Heinemann, 2000, p.11-18.
227. Koretz, J.F., Cook, C.A. & Kaufman, P.L. Accommodation and presbyopia in the human eye. Changes in the anterior segment and crystalline lens with focus. *Investigative Ophthalmology & Visual Science*, 1997; **38**: 569-78.
228. Dubbelman, M., Van der Heijde, G.L., Weeber, H.A. & Vrensen, G.F. Changes in the internal structure of the human crystalline lens with age and accommodation. *Vision Research*, 2003; **43**: 2363-75.
229. Richdale, K., Bullimore, M.A. & Zadnik, K. Lens thickness with age and accommodation by optical coherence tomography. *Ophthalmic & Physiological Optics*, 2008; **28**: 441-7.
230. Ostrin, L., Kasthurirangan, S., Win-Hall, D. & Glasser, A. Simultaneous measurements of refraction and A-scan biometry during accommodation in humans. *Optometry & Vision Science*, 2006; **83**: 657-65.
231. Storey, J.K. & Rabie, E.P. Ultrasound-a research tool in the study of accommodation. *Ophthalmic & Physiological Optics*, 1983; **3**: 315-20.
232. Drexler, W., Baumgartner, A., Findl, O., Hitzenberger, C.K. & Fercher, A.F. Biometric investigation of changes in the anterior eye segment during accommodation. *Vision Research*, 1997; **37**: 2789-800.
233. Bolz, M., Prinz, A., Drexler, W. & Findl, O. Linear relationship of refractive and biometric lenticular changes during accommodation in emmetropic and myopic eyes. *British Journal of Ophthalmology*, 2007; **91**: 360-5.
234. Jones, C.E., Aitchison, D.A. & Pope, J.M. Changes in lens dimensions and refractive index with age and accommodation. *Optometry & Vision Science*, 2007; **84**: 990-5.
235. Sheppard, A.L., Evans, C.J., Singh, K.D., Wolffsohn, J.S., Dunne, M.C. & Davies, L.N. Three-Dimensional Magnetic Resonance Imaging of the Phakic Crystalline Lens during Accommodation. *Investigative Ophthalmology & Visual Science*, 2011; **52**: 3689-97.

236. Butcher, J.M. & O'Brien, C. The reproducibility of biometry and keratometry measurements. *Eye (Lond)*, 1991; **5 (Pt 6)**: 708-11.
237. Wolffsohn, J.S. & Peterson, R.C. Anterior ophthalmic imaging. *Clinical & Experimental Optometry*, 2006; **89**: 205-14.
238. Urbak, S.F., Pedersen, J.K. & Thorsen, T.T. Ultrasound biomicroscopy. II. Intraobserver and interobserver reproducibility of measurements. *Acta Ophthalmologica Scandinavica*, 1998; **76**: 546-9.
239. Alderson, A., Mankowska, A., Cufflin, M.P. & Mallen, E.A. Simultaneous measurement of objective refraction, accommodation response and axial length of the human eye. *Ophthalmic & Physiological Optics*, 2011; **31**: 100-8.
240. Atchison, D.A. & Smith, G. Possible errors in determining axial length changes during accommodation with the IOLMaster. *Optometry & Vision Science*, 2004; **81**: 283-6.
241. Koretz, J.E., Strenk, S.A., Strenk, L.M. & Semmlow, J.L. Scheimpflug and high-resolution magnetic resonance imaging of the anterior segment: a comparative study. *Journal of the Optical Society of America A Optics, Image Science & Vision*, 2004; **21**: 346-54.
242. Strenk, S.A., Semmlow, J.L., Strenk, L.M., Munoz, P., Gronlund-Jacob, J. & DeMarco, J.K. Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study. *Investigative Ophthalmology & Visual Science*, 1999; **40**: 1162-9.
243. Hoerauf, H., Scholz, C., Koch, P., Engelhardt, R., Laqua, H. & Birngruber, R. Transscleral optical coherence tomography: a new imaging method for the anterior segment of the eye. *Archives of Ophthalmology*, 2002; **120**: 816-9.
244. Konstantopoulos, A., Hossain, P. & Anderson, D.F. Recent advances in ophthalmic anterior segment imaging: a new era for ophthalmic diagnosis? *British Journal of Ophthalmology*, 2007; **91**: 551-7.
245. Woodman, E.C., Read, S.A., Collins, M.J., Hegarty, K.J., Priddle, S.B., Smith, J.M. & Perro, J.V. Axial elongation following prolonged near work in myopes and emmetropes. *British Journal of Ophthalmology*, 2010.
246. Brown, N. The change in shape and internal form of the lens of the eye on accommodation. *Experimental Eye Research*, 1973; **15**: 441-59.
247. AlMahmoud, T., Priest, D., Munger, R. & Jackson, W.B. Correlation between refractive error, corneal power, and thickness in a large population with a wide range of ametropia. *Investigative Ophthalmology & Visual Science*, 2011; **52**: 1235-42.

248. Mallen, E.A.H., Kashyap, P. & Hampson, K.M. Transient axial length change during the accommodation response in young adults. *Investigative Ophthalmology & Visual Science*, 2006; **47**: 1251-1254.
249. Gimpel, G., Doughty, M.J. & Lyle, W.M. Large sample study of the effects of phenylephrine 2.5% eyedrops on the amplitude of accommodation in man. *Ophthalmic & Physiological Optics*, 1994; **14**: 123-8.
250. Stark, L. & Takahashi, Y. Absence of an odd-error signal mechanism in human accommodation. *IEEE Transactions on Biomedical Engineering*, 1965; **12**: 138-46.
251. Kruger, P.B., Mathews, S., Aggarwala, K.R. & Sanchez, N. Chromatic aberration and ocular focus: Fincham revisited. *Vision Research*, 1993; **33**: 1397-411.
252. Gilmartin, B. & Hogan, R.E. The magnitude of longitudinal chromatic aberration of the human eye between 458 and 633 nm. *Vision Research*, 1985; **25**: 1747-53.
253. Rucker, F.J. & Wallman, J. Chick eyes compensate for chromatic simulations of hyperopic and myopic defocus: evidence that the eye uses longitudinal chromatic aberration to guide eye-growth. *Vision Research*, 2009; **49**: 1775-83.
254. Seidemann, A. & Schaeffel, F. Effects of longitudinal chromatic aberration on accommodation and emmetropization. *Vision Research*, 2002; **42**: 2409-17.
255. Qian, Y., Jinhui, D., Liu, R., Chu, R., Zhou, X., *Effects of 430nm and 530nm monochromatic light on refractive development and retinal-cone distribution and density in guinea pigs*, in *Association for Research in Vision & Ophthalmology*. 2011: Fort Lauderdale, Florida.
256. Atchison, D.A., Strang, N.C. & Stark, L.R. Dynamic accommodation responses to stationary colored targets. *Optometry & Vision Science*, 2004; **81**: 699-711.
257. Murch, G.M. Visual accommodation and convergence to multichromatic information displays. *International Symposium Digest Technology Papers*, 1982; **13**: 192 - 193.
258. Charman, W.N. Accommodation performance for chromatic displays. *Ophthalmic & Physiological Optics*, 1989; **9**: 459-63.
259. Kergoat, H. & Lovasik, J.V. Influence of target color and vergence of light on ocular accommodation during binocular fixation. *Current Eye Research*, 1990; **9**: 935-53.

260. Denieul, P. & Corno-Martin, F. Mean response and oscillations of accommodation with colour and contrast. *Ophthalmic & Physiological Optics*, 1994; **14**: 184-92.
261. Ciuffreda, K.J., Rosenfield, M., Rosen, J., Azimi, A. & Ong, E. Accommodative responses to naturalistic stimuli. *Ophthalmic & Physiological Optics*, 1990; **10**: 168-74.
262. Matthews, M.L., Lovasik, J.V. & Mertins, K. Visual performance and subjective discomfort in prolonged viewing of chromatic displays. *Human Factors*, 1989; **31**: 259-71.
263. Campbell, F.W., Westheimer, G. & Robson, J.G. Significance of fluctuations of accommodation. *Journal of the Optical Society of America*, 1958; **48**: 669.
264. Campbell, F.W., Robson, J.G. & Westheimer, G. Fluctuations of accommodation under steady viewing conditions. *Journal of Physiology*, 1959; **145**: 579-94.
265. Denieul, P. Effects of stimulus vergence on mean accommodation response, microfluctuations of accommodation and optical quality of the human eye. *Vision Research*, 1982; **22**: 561-9.
266. Pugh, J.R., Eadie, A.S., Winn, B. & Heron, G. Power spectrum analysis in the study of ocular mechanisms. *Ophthalmic & Physiological Optics*, 1987; **7**: 321-4.
267. Winn, B., Pugh, J.R., Gilmartin, B. & Owens, H. Arterial pulse modulates steady-state ocular accommodation. *Current Eye Research*, 1990; **9**: 971-5.
268. Gray, L.S., Winn, B. & Gilmartin, B. Effect of target luminance on microfluctuations of accommodation. *Ophthalmic & Physiological Optics*, 1993; **13**: 258-65.
269. Gray, L.S., Winn, B. & Gilmartin, B. Accommodative microfluctuations and pupil diameter. *Vision Research*, 1993; **33**: 2083-90.
270. Stark, L.R. & Atchison, D.A. Pupil size, mean accommodation response and the fluctuations of accommodation. *Ophthalmic & Physiological Optics*, 1997; **17**: 316-23.
271. Seidel, D., Gray, L.S. & Heron, G. Retinotopic accommodation responses in myopia. *Investigative Ophthalmology & Visual Science* 2003; **44**: 1035-41.
272. Day, M., Strang, N.C., Seidel, D., Gray, L.S. & Mallen, E.A. Refractive group differences in accommodation microfluctuations with changing accommodation stimulus. *Ophthalmic & Physiological Optics*, 2006; **26**: 88-96.

273. Kotulak, J.C. & Schor, C.M. Temporal variations in accommodation during steady-state conditions. *Journal of the Optical Society of America*, 1986; **3**: 223-7.
274. Winn, B., Pugh, J.R., Gilmartin, B. & Owens, H. The effect of pupil size on static and dynamic measurements of accommodation using an infra-red optometer. *Ophthalmic & Physiological Optics*, 1989; **9**: 277-83.
275. Schultz, K.E., Sinnott, L.T., Mutti, D.O. & Bailey, M.D. Accommodative fluctuations, lens tension, and ciliary body thickness in children. *Optometry & Vision Science*, 2009; **86**: 677-84.
276. Charman, W.N. & Heron, G. Fluctuations in accommodation: a review. *Ophthalmic & Physiological Optics*, 1988; **8**: 153-64.
277. Winn, B., Charman, W.N., Pugh, J.R., Heron, G. & Eadie, A.S. Perceptual detectability of ocular accommodation microfluctuations. *Journal of the Optical Society of America*, 1989; **6**: 459-62.
278. Winn, B., Pugh, J.R., Gilmartin, B. & Owens, H. The frequency characteristics of accommodative microfluctuations for central and peripheral zones of the human crystalline lens. *Vision Research*, 1990; **30**: 1093-9.
279. Niwa, K. & Tokoro, T. Influence of spatial distribution with blur on fluctuations in accommodation. *Optometry & Vision Science*, 1998; **75**: 227-32.
280. Van der Heijde, G.L., Beers, A.P. & Dubbelman, M. Microfluctuations of steady-state accommodation measured with ultrasonography. *Ophthalmic & Physiological Optics*, 1996; **16**: 216-21.
281. Collins, M., Davis, B. & Wood, J. Microfluctuations of steady-state accommodation and the cardiopulmonary system. *Vision Research*, 1995; **35**: 2491-502.
282. Owens, H., Winn, B., Gilmartin, B. & Pugh, J.R. Effect of a topical beta-adrenergic receptor antagonist on the dynamics of steady-state accommodation. *Ophthalmic & Physiological Optics*, 1991; **11**: 99-104.
283. Mieke, C. & Denieul, P. Mean response and oscillations of accommodation for various stimulus vergences in relation to accommodation feedback control. *Ophthalmic & Physiological Optics*, 1988; **8**: 165-71.
284. Yao, P., Lin, H., Huang, J., Chu, R. & Jiang, B.C. Objective depth-of-focus is different from subjective depth-of-focus and correlated with accommodative microfluctuations. *Vision Research*, 2010; **50**: 1266-73.

285. Kotulak, J.C., Morse, S.E. & Billock, V.A. Red-green opponent channel mediation of control of human ocular accommodation. *Journal of Physiology*, 1995; **482 (Pt 3)**: 697-703.
286. Aggarwala, K.R., Kruger, E.S., Mathews, S. & Kruger, P.B. Spectral bandwidth and ocular accommodation. *Journal of the Optical Society of America A Optics, Image Science & Vision*, 1995; **12**: 450-5.
287. Tucker, J. & Charman, W.N. Reaction and response times for accommodation. *American Journal of Optometry & Physiological Optics*, 1979; **56**: 490-503.
288. Heron, G. & Winn, B. Binocular accommodation reaction and response times for normal observers. *Ophthalmic & Physiological Optics*, 1989; **9**: 176-83.
289. Culhane, H.M. & Winn, B. Dynamic accommodation and myopia. *Investigative Ophthalmology & Visual Science*, 1999; **40**: 1968-74.
290. Shirachi, D., Liu, J., Lee, M., Jang, J., Wong, J. & Stark, L. Accommodation dynamics I. Range nonlinearity. *American Journal of Optometry & Physiological Optics*, 1978; **55**: 631-41.
291. Mountford, J.A. *Modern Orthokeratology*. Contact Lenses 4th edition, ed. A. Phillips, J and Speedwell, L: Butterworth Heineman. 1997. 39.
292. Nolan, J. The First Meeting of the International Orthokeratology Society. *Contacto*, 1995; **38**: 9-11.
293. Sorbara, L., Fonn, D., Simpson, T., Lu, F.H. & Kort, R. Reduction of myopia from corneal refractive therapy. *Optometry & Vision Science*, 2005; **82**: 512-518.
294. Stillitano, I., Schor, P., Lipener, C. & Hofling-Lima, A.L. Stability of wavefront aberrations during the daytime after 6 months of overnight orthokeratology corneal reshaping. *Journal of Refractive Surgery*, 2007; **23**: 978-83.
295. Binder, P.S., May, C.H. & Grant, S.C. An evaluation of orthokeratology. *Ophthalmology*, 1980; **87**: 729-44.
296. Kerns, R.L. Research in orthokeratology. Part III: results and observations. *Journal of the American Optometric Association*, 1976; **47**: 1505-15.
297. Polse, K.A., Brand, R.J., Schwalbe, J.S., Vastine, D.W. & Keener, R.J. The Berkeley orthokeratology study part II: efficacy and duration. *American Journal of Optometry & Physiological Optics*, 1983; **60**: 187-198.

298. Coon, L.J. Orthokeratology. Part II: Evaluating the Tabb method. *Journal of the American Optometric Association*, 1984; **55**: 409-18.
299. Swarbrick, H.A. Orthokeratology review and update. *Clinical & Experimental Optometry*, 2006; **89**: 124-143.
300. Polse, K.A., Brand, R.J., Keener, R.J., Schwalbe, J.S. & Vastine, D.W. The Berkeley Orthokeratology Study, part III: safety. *American Journal of Optometry & Physiological Optics*, 1983; **60**: 321-8.
301. Wlodyga RJ, B.C. Corneal moulding: the easy way. *Contact Lens Spectrum*, 1989; **4**: 58-65.
302. Riley, C.M., Horner, D.G., Soni, P.S. Polycon II vs OK-3 lenses in the acute reduction of myopia. *Optometry & Vision Science*, 1992; **69**: 156.
303. Brand, R.J., Polse, K.A. & Schwalbe, J.S. The Berkeley orthokeratology study .1. general conduct of the study. *American Journal of Optometry & Physiological Optics*, 1983; **60**: 175-186.
304. Fontana, A.A. Orthokeratology using the one piece bifocal. *Contacto*, 1972; **16**: 45-47.
305. Harris, D., Stoyan, N. A new approach to orthokeratology. *Contact Lens Spectrum*, 1992; **7**: 37-39.
306. Guillon, M., Lydon, D.P.M. & Wilson, C. Corneal topography - a clinical-model. *Ophthalmic & Physiological Optics*, 1986; **6**: 47-56.
307. Mountford, J. An analysis of the changes in corneal shape and refractive error induced by accelerated orthokeratology. *International Contact Lens Clinic*, 1997; **24**: 128-144.
308. Walline, J.J., Rah, M.J. & Jones, L.A. The children's overnight orthokeratology investigation (COOKI) pilot study. *Optometry & Vision Science*, 2004; **81**: 407-413.
309. Tahhan, N., Du Toit, R., Papas, E., Chung, H., La Hood, D. & Holden, A.B. Comparison of reverse-geometry lens designs for overnight orthokeratology. *Optometry & Vision Science*, 2003; **80**: 796-804.
310. Sridharan, R. & Swarbrick, H. Corneal response to short-term orthokeratology lens wear. *Optometry & Vision Science*, 2003; **80**: 200-6.

311. Wang, J.H., Fonn, D., Simpson, T.L., Sorbara, L., Kort, R. & Jones, L. Topographical thickness of the epithelium and total cornea after overnight wear of reverse-geometry rigid contact lenses for myopia reduction. *Investigative Ophthalmology & Visual Science*, 2003; **44**: 4742-4746.
312. Hiraoka, T., Matsumoto, Y., Okamoto, F., Yamaguchi, T., Hirohara, Y., Mihashi, T. & Oshika, T. Corneal higher-order aberrations induced by overnight orthokeratology. *American Journal of Ophthalmology*, 2005; **139**: 429-36.
313. Hiraoka, T., Okamoto, C., Ishii, Y., Kakita, T. & Oshika, T. Contrast sensitivity function and ocular higher-order aberrations following overnight orthokeratology. *Investigative Ophthalmology & Visual Science*, 2007; **48**: 550-6.
314. Berntsen, D.A., Barr, J.T. & Mitchell, G.L. The effect of overnight contact lens corneal reshaping on higher-order aberrations and best-corrected visual acuity. *Optometry & Vision Science*, 2005; **82**: 490-7.
315. Joslin, C.E., Wu, S.M., McMahon, T.T. & Shahidi, M. Higher-order wavefront aberrations in corneal refractive therapy. *Optometry & Vision Science*, 2003; **80**: 805-11.
316. Cho, P., Cheung, S.W. & Edwards, M.H. Practice of orthokeratology by a group of contact lens practitioners in Hong Kong. Part 2: orthokeratology lenses. *Clinical & Experimental Optometry*, 2003; **86**: 42-6.
317. Mountford, J. & Pesudovs, K. An analysis of the astigmatic changes induced by accelerated orthokeratology. *Clinical & Experimental Optometry*, 2002; **85**: 284-93.
318. Johnson, K.L., Carney, L.G., Mountford, J.A., Collins, M.J., Cluff, S. & Collins, P.K. Visual performance after overnight orthokeratology. *Contact Lens Anterior Eye*, 2007; **30**: 29-36.
319. Cho, P., Cheung, S.W., Edwards, M.H. & Fung, J. An assessment of consecutively presenting orthokeratology patients in a Hong Kong based private practice. *Clinical & Experimental Optometry*, 2003; **86**: 331-8.
320. Barr, J.T., Rah, M.J., Meyers, W. & Legerton, J. Recovery of refractive error after corneal refractive therapy. *Eye Contact Lens*, 2004; **30**: 247-51; discussion 263-4.
321. Cheung, S.W., Cho, P., Bron, A.J., Chui, V. & Chan, B. Case report: the occurrence of fibrillary lines in overnight orthokeratology. *Ophthalmic & Physiological Optics*, 2006; **26**: 525-31.

322. Hiraoka, T., Okamoto, C., Ishii, Y., Okamoto, F. & Oshika, T. Recovery of corneal irregular astigmatism, ocular higher-order aberrations, and contrast sensitivity after discontinuation of overnight orthokeratology. *British Journal of Ophthalmology*, 2009; **93**: 203-8.
323. Wang, J., Fonn, D., Simpson, T.L. & Jones, L. The measurement of corneal epithelial thickness in response to hypoxia using optical coherence tomography. *American Journal of Ophthalmology*, 2002; **133**: 315-9.
324. Holden, B.A. & Mertz, G.W. Critical oxygen levels to avoid corneal edema for daily and extended wear contact-lenses. *Investigative Ophthalmology & Visual Science*, 1984; **25**: 1161-1167.
325. Alharbi, A., La Hood, D. & Swarbrick, H.A. Overnight orthokeratology lens wear can inhibit the central stromal edema response. *Investigative Ophthalmology & Visual Science*, 2005; **46**: 2334-2340.
326. Holden, B.A., Mertz, G.W. & McNally, J.J. Corneal swelling response to contact-lenses worn under extended wear conditions. *Investigative Ophthalmology & Visual Science*, 1983; **24**: 218-226.
327. Mertz, G.W. Overnight swelling of the living human cornea. *Journal of the American Optometric Association*, 1980; **51**: 211-4.
328. Lu, F., Simpson, T., Sorbara, L. & Fonn, D. Malleability of the ocular surface in response to mechanical stress induced by orthokeratology contact lenses. *Cornea*, 2008; **27**: 133-41.
329. Haque, S., Fonn, D., Simpson, T. & Jones, L. Corneal refractive therapy with different lens materials, part 1: corneal, stromal, and epithelial thickness changes. *Optometry & Vision Science*, 2007; **84**: 343-8.
330. Mountford, J.R., D. Dave, T. *Orthokeratology Principles and Practice* Edinburgh: Butterworth-Heinemann. 2004. 269 - 301.
331. Hiraoka, T., Okamoto, C., Ishii, Y., Takahira, T., Kakita, T. & Oshika, T. Mesopic contrast sensitivity and ocular higher-order aberrations after overnight orthokeratology. *American Journal of Ophthalmology*, 2008; **145**: 645-655.
332. Cheung, S.W., Cho, P., Chui, W.S. & Woo, G.C. Refractive error and visual acuity changes in orthokeratology patients. *Optometry & Vision Science*, 2007; **84**: 410-6.
333. Stillitano, I.G., Chalita, M.R., Schor, P., Maidana, E., Lui, M.M., Lipener, C. & Hofling-Lima, A.L. Corneal changes and wavefront analysis after orthokeratology fitting test. *American Journal of Ophthalmology*, 2007; **144**: 378-386.

334. Rae, S.M., Allen, P.M., Radhakrishnan, H., Theagarayan, B., Price, H.C., Sailaganathan, A., Calver, R.I. & O'Leary, D.J. Increasing negative spherical aberration with soft contact lenses improves high and low contrast visual acuity in young adults. *Ophthalmic & Physiological Optics*, 2009; **29**: 593-601.
335. Elliott, D.B. *Clinical Procedures in Primary Eye Care*, Edinburgh: Butterworth-Heinemann. 2007.
336. Charman, W.N. Aberrations and myopia. *Ophthalmic & Physiological Optics*, 2005; **25**: 285-301.
337. Thibos, L.N., Applegate, R.A., Schwiegerling, J.T. & Webb, R. Standards for reporting the optical aberrations of eyes. *Journal of Refractive Surgery*, 2002; **18**: S652-60.
338. Atchison, D.A. Recent advances in representation of monochromatic aberrations of human eyes. *Clinical & Experimental Optometry*, 2004; **87**: 138-48.
339. Castejon-Mochon, J.F., Lopez-Gil, N., Benito, A. & Artal, P. Ocular wave-front aberration statistics in a normal young population. *Vision Research*, 2002; **42**: 1611-7.
340. Brunette, I., Bueno, J.M., Parent, M., Hamam, H. & Simonet, P. Monochromatic aberrations as a function of age, from childhood to advanced age. *Investigative Ophthalmology & Visual Science*, 2003; **44**: 5438-5446.
341. Yoon, G., Wavefront sensing and diagnostic uses. In J. Porter, Queener, H., Lin J., Thorn K., Awwal A. *Adaptive optics for vision science*. New York, Wiley-Interscience, 2006, p.63 - 81.
342. Atchison, D.A. Recent advances in measurement of monochromatic aberrations of human eyes. *Clinical & Experimental Optometry*, 2005; **88**: 5-27.
343. Rozema, J.J., Van Dyck, D.E. & Tassignon, M.J. Clinical comparison of 6 aberrometers. Part 1: Technical specifications. *Journal of Cataract & Refractive Surgery*, 2005; **31**: 1114-27.
344. Webb, R.H., Penney, C.M. & Thompson, K.P. Measurement of ocular local wavefront distortion with a spatially resolved refractometer. *Applied Optics*, 1992; **31**: 3678-3686.
345. He, J.C., Marcos, S., Webb, R.H. & Burns, S.A. Measurement of the wave-front aberration of the eye by a fast psychophysical procedure. *Journal of the Optical Society of America A, Optics, Image Science & Vision*, 1998; **15**: 2449-56.

346. Prieto, P.M., Vargas-Martin, F., Goelz, S. & Artal, P. Analysis of the performance of the Hartmann-Shack sensor in the human eye. *Journal of the Optometric Society of America A, Optics, Image Science & Vision*, 2000; **17**: 1388-98.
347. Navarro, R. & Moreno-Barriuso, E. Laser ray-tracing method for optical testing. *Optics Letters*, 1999; **24**: 951-3.
348. Howland, H.C. & Howland, B. A subjective method for the measurement of monochromatic aberrations of the eye. *Journal of the Optical Society of America*, 1977; **67**: 1508-18.
349. Walsh, G., Charman, W.N. & Howland, H.C. Objective technique for the determination of monochromatic aberrations of the human eye. *Journal of the Optical Society of America A*, 1984; **1**: 987-92.
350. Hong, X., Thibos, L.N., Bradley, A., Woods, R.L. & Applegate, R.A. Comparison of monochromatic ocular aberrations measured with an objective cross-cylinder aberroscope and a Shack-Hartmann aberrometer. *Optometry & Vision Science*, 2003; **80**: 15-25.
351. MacRae, S. & Fujieda, M. Slit skiascopic-guided ablation using the Nidek laser. *Journal of Refractive Surgery*, 2000; **16**: S576-80.
352. Liang, J., Grimm, B., Goelz, S. & Bille, J.F. Objective measurement of wave aberrations of the human eye with the use of a Hartmann-Shack wave-front sensor. *Journal of the Optical Society of America A, Optics, Image Science & Vision*, 1994; **11**: 1949-57.
353. Salmon, T.O., Thibos, L.N. & Bradley, A. Comparison of the eye's wave-front aberration measured psychophysically and with the Shack-Hartmann wave-front sensor. *Journal of the Optical Society of America A, Optics, Image Science & Vision*, 1998; **15**: 2457-65.
354. Moreno-Barriuso, E., Marcos, S., Navarro, R. & Burns, S.A. Comparing laser ray tracing, the spatially resolved refractometer, and the Hartmann-Shack sensor to measure the ocular wave aberration. *Optometry & Vision Science*, 2001; **78**: 152-6.
355. Cheng, H., Barnett, J.K., Vilupuru, A.S., Marsack, J.D., Kasthurirangan, S., Applegate, R.A. & Roorda, A. A population study on changes in wave aberrations with accommodation. *Journal of Vision*, 2004; **4**: 272-80.
356. Radhakrishnan, H. & Charman, W.N. Age-related changes in ocular aberrations with accommodation. *Journal of Vision*, 2007; **7**: 11 1-21.

357. Thibos, L.N., Hong, X., Bradley, A. & Cheng, X. Statistical variation of aberration structure and image quality in a normal population of healthy eyes. *Journal of the Optical Society of America A, Optics, Image Science & Vision*, 2002; **19**: 2329-48.
358. Wang, L. & Koch, D.D. Ocular higher-order aberrations in individuals screened for refractive surgery. *Journal of Cataract & Refractive Surgery*, 2003; **29**: 1896-903.
359. Buehren, T., Collins, M.J. & Carney, L. Corneal aberrations and reading. *Optometry & Vision Science*, 2003; **80**: 159-66.
360. Cervino, A., Hosking, S.L., Ferrer-Blasco, T., Montes-Mico, R. & Gonzalez-Meijome, J.M. A pilot study on the differences in wavefront aberrations between two ethnic groups of young generally myopic subjects. *Ophthalmic & Physiological Optics*, 2008; **28**: 532-7.
361. Henderson, R., Schulmeister, K. & *Laser Safety*, Bristol: Institute of Physics Publishing Ltd. 2004.
362. *Safety of laser products - Part 1 : Equipment, classification and requirements*, in *BS EN 60825-1:2007*. 2007, British Standards Institution: Britain.

Appendix 1

Acronyms and abbreviations

AC/A	Accommodative convergence to accommodation
ACD	Anterior chamber depth
Ach	Acetylcholine
AE	Artificial eye
AEC	Axial edge clearance
AEL	Accessible emission limit
AL	Axial length
AL/CR	Axial length / corneal radius
ASRF	Accommodation stimulus response function
BNC	Bayonet Neill-Concelman
BOZD	Back optic zone diameter
BOZR	Back optic zone radius
BS	Beam splitter
BVD	Back vertex distance
C	Cornea
CCD	Charge-coupled device
cd/m ²	Candela per square metre
CLT	Crystalline lens thickness
cm	Centimetres
CR	Corneal radius
CRT	Cathode ray tube
D	Dioptre
DC	Dioptre cylinder
Dk/t	Critical oxygen transmissibility
DS	Dioptre sphere

e	Eccentricity
EMM	Emmetropia
EMMs	Emmetropes
EOMs	Early onset myopes
FFT	Fast fourier transform
HFC	High frequency component
HYP	Hypermetropia
HYPs	Hypermetropes
Hz	Hertz
K	Flattest corneal meridian
k_c	Central horizontal keratometry reading
k_t	Temporal horizontal keratometry reading
LA	Lenslet array
LED	Light emitting diode
LFC	Low frequency component
LOMs	Late onset myopes
LT	Lens thickness
MAX	Measurement and automation explorer
MCR	Mean corneal radius
MFC	Medium frequency component
Mins arc	Minutes of arc
mm	millimetres
mm/D	millimetres per dioptre
MPE	Maximum permitted exposure
ms	Miliseconds
MSE	Mean spherical equivalent
MRI	Magnetic resonance imaging
MYP	Myopia
MYPs	Myopes

NITM	Nearwork-induced transient myopia
nm	nanometres
NTSC	National television systems committee
OCT	Optical coherence tomography
OL	Optical length
Orthok	Orthokeratology
PC	Personal computer
PCI	Partial coherence interferometry
PMMA	Polymethyl methacrylate
PMs	Progressing myopes
R	Retina
RGP	Rigid gas permeable
RMS	Root mean square
r_o	Apical radius
s	Seconds
SD	Standard deviation
SEM	Standard error of the mean
S-H	Shack-Hartmann
SMs	Stable myopes
TLT	Tear layer thickness
VA	Visual acuity
VAR	Visual acuity rating
VDU	Visual display unit
W	Watts
W_{RMS}	Root mean squared wavefront aberration
μm	micrometres
μW	microwatts
λ	Wavelength

Appendix 2

Aberrations

A2.1 Introduction

In a perfect optical system, working in monochromatic light, rays from a single object point (O) converge to a single image point (O') (Figure A2.1).

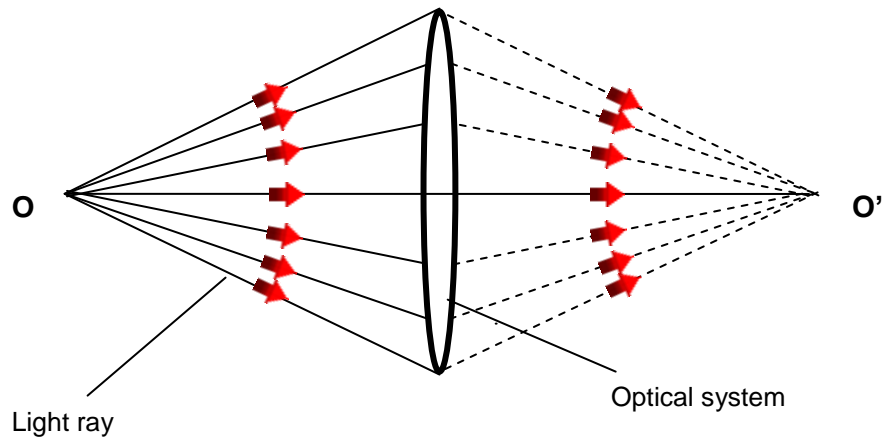


Figure A2.1. A perfect optical system.

If, however, this system suffers from aberrations the light rays will fail to converge on O' (Figure A2.2).

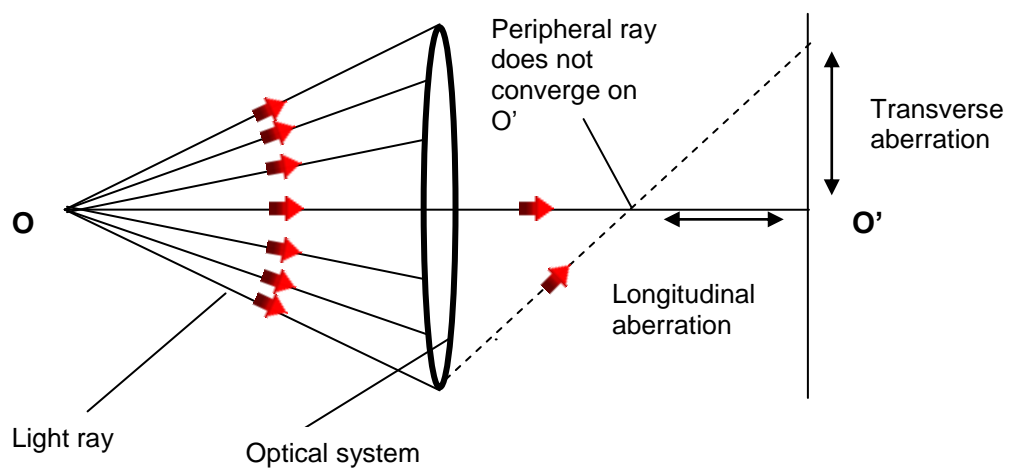


Figure A2.2. An aberrated optical system indicating the path of the central ray and one peripheral ray of light.

The light rays may converge at the wrong longitudinal image point (expressed in mm or D) producing defocus, or the wrong transverse image point (expressed in mm or minutes of arc) producing distortion. They may also fail to converge at any single image point producing aberrations such as spherical aberration, coma and trefoil.

Aberrations of optical systems are usually split into two groups, monochromatic and chromatic. Monochromatic aberrations refer to those aberrations found in an optical system when only one wavelength of light is considered. Chromatic aberrations, which are due to variation in the light ray caused by the change of refractive index of the optical media with wavelength, are also present in an optical system. For the purpose of this literature review all aberrations discussed will be monochromatic only.

Light can also be described in terms of wavefronts, which are perpendicular to the direction of travel of the light rays (Figure A2.3).

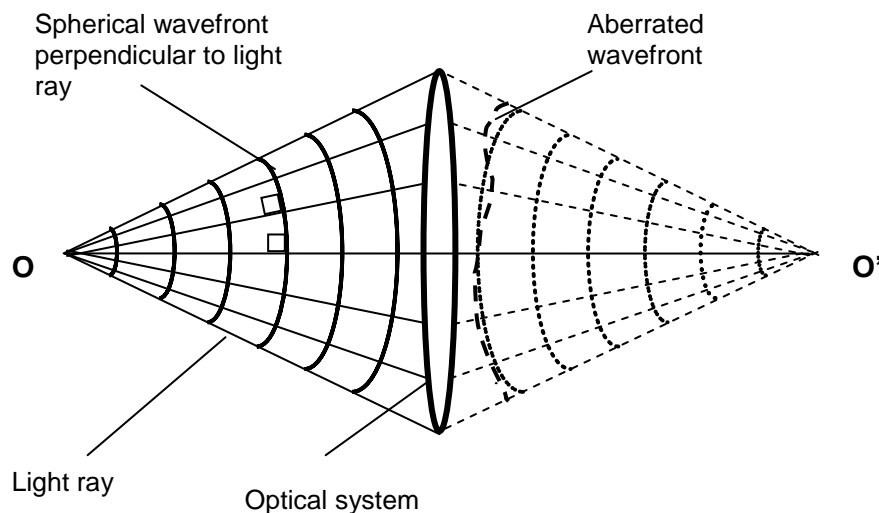


Figure A2.3. Wavefront aberrations are perpendicular to the direction of travel of the light rays.

Spherical wavefronts therefore diverge from the object point and in a perfect optical system converge as spherical wavefronts centred on the image point [336]. The quality of this image point can again be degraded by aberrations which are termed wavefront aberrations.

In the presence of monochromatic aberrations, the image wavefronts are no longer spherical and the departure of the aberrated wavefront from the corresponding ideal wavefront gives the wavefront aberration which can be represented as a polynomial function [336]. If the aberrated wavefront is in advance or ahead of the ideal it is positive, if it is retarded or behind it is negative.

A2.2 The representation of wavefront aberrations

When measuring aberrations in the eye we do not have access to the image side of the optical system. We therefore begin with the object at the image position i.e. on the retina and measure the aberrations on the object side of the eye i.e. across the pupil.

A2.2.1 The Zernike polynomial function series

This series has become a popular way of representing wavefront aberrations mathematically. It has the advantage over other series such as the Taylor series, as all the terms are independent which means adding a higher term does not affect the lower ones. During this study, the conventions used for reporting Zernike wavefront aberrations will be those developed by Thibos *et al.* [337] for the Optical Society of America. These have been adopted by the American National Standards Institute (ANSI 2004). The Zernike series is represented by:

$$W(\rho, \theta) = \sum c_n^m Z_n^m(\rho, \theta)$$

$W(\rho, \theta)$ is a polar representation of the wave aberration in the pupil (Figure A2.4).

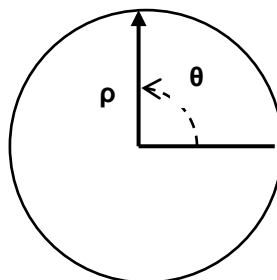


Figure A2.4. Representation of (ρ, θ) in the pupil plane.

The relative distance from the centre of the pupil is represented by ρ . This is the radial coordinate, a polynomial, ranging from zero to one. The meridian is represented by θ , the azimuthal component which is sinusoidal, ranging from zero to 2π . This meridian is measured using the same convention as spectacle cylindrical axes (from three o'clock in an anticlockwise direction) although the angle measurement can go all the way round to 360° .

Each individual Zernike polynomial is described by a double indexing system Z_n^m , where n describes the highest power of the radial polynomial (ρ) and m describes the azimuthal frequency of the sinusoidal component (θ). The coefficient of each Zernike polynomial is represented by c_n^m and is measured in microns (μm). The wavefront forms represented by each individual Zernike polynomial up to and including the fourth order are shown in the Zernike pyramid below (Figure A2.5). The term at the top of the pyramid where $n = 0$ is not shown on the diagram. It is known as piston, which is a constant displacement of a flat wavefront and has no significant affect on image quality. Its coefficient is generally manipulated to make the wavefront aberration at the centre of the pupil zero.

It can be seen that some terms possess the same radial order (n) and the same angular frequency (m) just with the opposite sign. These are rotated versions of the same aberrations. Those aberrations with $m = 0$ are rotationally symmetrical.

Occasionally the Zernike polynomials are described by a single indexing system represented by:

$$W(\rho, \theta) = \sum c_j z_j$$

The relationship between the single index j and n and m is shown in the equation below:

$$j = [n(n+2)+m] / 2$$

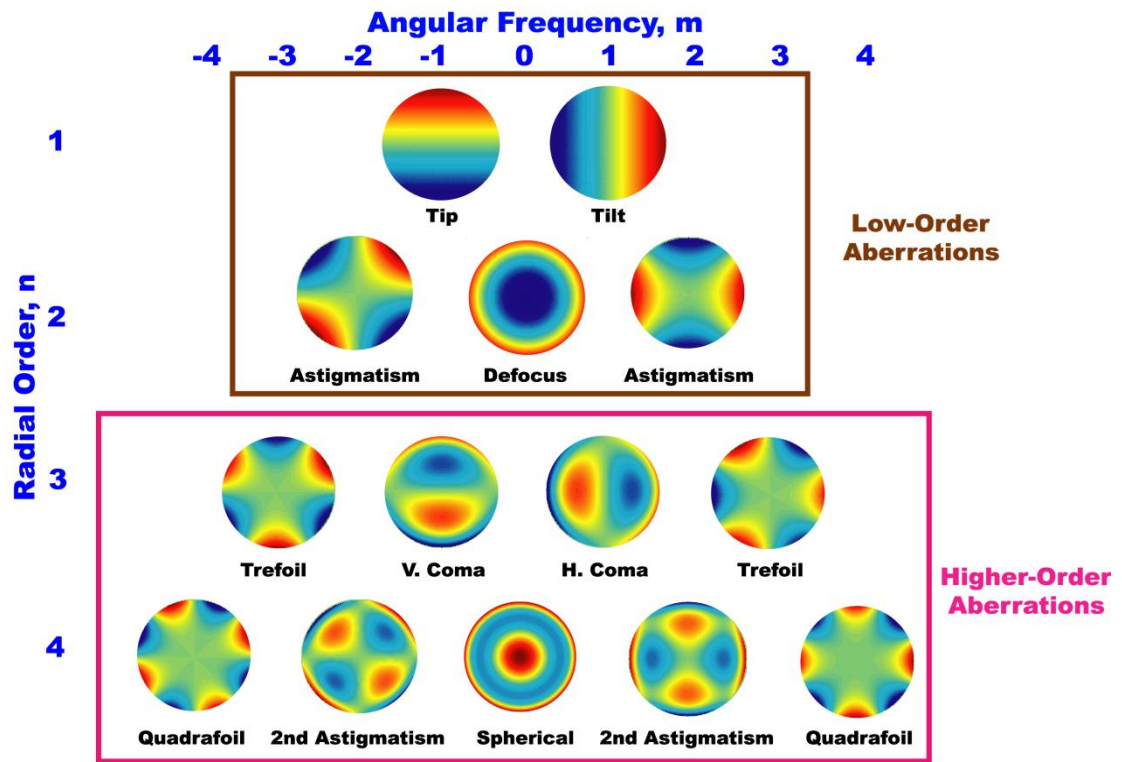


Figure A2.5. Zernike Pyramid illustrating the first four radial orders of wavefront aberrations (courtesy of Karen Hampson, University of Bradford).

Individual Zernike terms correspond to classical optical aberrations. This relationship and the relationship between j , n and m are shown in Table A2.1.

Table A2.1. Zernike polynomials up to the fourth-order as defined by ANSI 2004.

j	n	m	Z_n^m	Description of aberration
0	0	0	1	Piston
1	1	-1	$2\rho\sin\theta$	Vertical tilt
2	1	1	$2\rho\cos\theta$	Horizontal tilt
3	2	-2	$\sqrt{6}\rho^2\sin 2\theta$	Astigmatism (45/135)
4	2	0	$\sqrt{3}\rho^2(2\rho^2 - 1)$	Spherical defocus
5	2	2	$\sqrt{6}\rho^2\cos 2\theta$	Astigmatism (90/180)
6	3	-3	$\sqrt{8}\rho^3\sin 3\theta$	Oblique trefoil
7	3	-1	$\sqrt{8}\rho^3(3\rho^3 - 2\rho)\sin\theta$	Vertical coma
8	3	1	$\sqrt{8}\rho^3(3\rho^3 - 2\rho)\cos\theta$	Horizontal coma
9	3	3	$\sqrt{3}\rho^3\cos 3\theta$	Horizontal trefoil
10	4	-4	$\sqrt{10}\rho^4\sin 4\theta$	Oblique quadrafoil
11	4	-2	$\sqrt{10}\rho^4(4\rho^4 - 3\rho^2)\sin 2\theta$	Secondary astigmatism
12	4	0	$\sqrt{5}\rho^4(6\rho^4 - 6\rho^2 + 1)$	Spherical aberration
13	4	2	$\sqrt{10}\rho^4(4\rho^4 - 3\rho^2)\cos 2\theta$	Secondary astigmatism
14	4	4	$\sqrt{10}\rho^4\cos 4\theta$	Quadrafoil

Wavefront aberrations can be expressed as coefficients of the individual Zernike terms measured in microns (μm). If the square of these coefficients is taken it gives the contribution of that specific Zernike term to the total variance of the wave aberration [338]. The square root of the sum of the squared Zernike coefficients gives the root mean square wavefront error (W_{RMS}) also in μm [225]. The W_{RMS} of the total wavefront aberrations up to a certain order can be specified, giving one value to describe how the actual wavefront deviates from the ideal wavefront.

The effect of aberrations on image quality

First and second-order aberrations are classed as lower-order, while third-order aberrations and above are classed as higher-order (Figure A2.5). The first-order aberrations of tip and tilt represent prism and do not affect image quality. The second-order aberrations of defocus and astigmatism are corrected using spectacle lenses, contact lenses or refractive surgery and therefore W_{RMS} of the higher order wavefront aberrations are often used as a measure of image quality. These aberration measurements vary with pupil size as W_{RMS} values tend to increase as pupil size increases [119, 187, 339, 340]. This means pupil size must always be specified along with any W_{RMS} measurements and care must be taken when comparing measurements from different sources.

How does the size of W_{RMS} for a particular eye and pupil size relate to what the patient actually sees? Charman [113] has shown that for a pupil diameter of 4 mm, 0.14 μm of higher order W_{RMS} corresponds mathematically to about $\pm 0.25\text{DS}$ of blur. He makes the point that the contribution to retinal image quality from higher order aberrations is very small compared to the contribution from defocus. Defocus must therefore be fully corrected before considering the effect higher order aberrations have on visual quality. 0.25D of uncorrected astigmatism may well be more detrimental to retinal image quality than uncorrected higher order aberrations.

The magnitude of higher order aberrations generally reduces as the Zernike order increases [114, 187]. When measuring wavefront aberrations enough terms need to be used to give a good representation of the wavefront, however using too many may cause unnecessary noise. It has been suggested that in a normal eye with a pupil diameter of six mm or less there is no need to go above the sixth to eighth radial order [338, 341].

A2.3 The measurement of wavefront aberrations

There are various methods available for monochromatic wavefront aberration measurement, and detailed explanations can be found in several sources [225, 342, 343]. A summary of these methods is found below.

A2.3.1 Ray tracing

In 1961 Smirnov published a paper describing a subjective ray tracing method for aberration measurement. More recently this has been modified by Webb *et al.* in their technique of spatially resolved refractometry [344]. Two narrow beams of visible light enter the eye: a reference beam and a test beam. The reference beam is fixed and passes through the centre of the pupil while the test beam can be altered to enter through different pupil positions. The subject is required to alter the angular deviation of the test beam to superimpose it on the reference beam. The position of the test beam at the cornea is not altered. This then gives a measure of the transverse aberration of the eye. This technique is slower than other methods although a full set of aberration measurements can be taken in three to four minutes [345]. Measurements are reliant on participant responses rather than being objective, but this can be an advantage in situations where objective methods have failed i.e. when media opacities are present [345]. Wavelengths within the visual spectrum are used during measurements as opposed to infra red light, making this a more natural measuring environment. As only one point is being measured at a time it avoids the problem simultaneous measuring

methods may suffer where measurement points can get confused with each other due to distortion when measuring higher levels of aberrations [342, 346]. Spatially resolved aberrometry is used in the commercially available InterWave Scanner.

The ray tracing method has also been developed into an objective technique by directing a narrow beam of light into the eye through a number of pupil positions [347]. For each position the retinal image is reimaged back through the whole pupil onto a CCD array. The centroids of the retinal images are compared to a reference image to give a measurement of transverse aberration. This technology is used in the Visual Function Analyzer (Tracey Technologies, Houston, Texas).

A2.3.2 Tscherning and cross cylinder aberrometers

This method is similar to the ray tracing method however it measures the retinal image deviation at a number of pupil positions simultaneously. A grid mask placed in front of the eye allows radiation to pass through only certain pupil positions. In order to spread out these retinal image points a defocusing lens is placed in front of the eye. Originally a +5 DS was used by Tscherning however in 1977 Howland and Howland developed a method using a ± 5 DC cross cylinder orientated along $45^\circ/135^\circ$ [348]. This was a subjective method relying on the subject drawing the image of the grid as they saw it.

Walsh *et al.* [349] further developed this technique into an objective method. A beam splitter was inserted between the aberrometer lens and the eye which allowed the distorted image of the grid on the subject's retina to be photographed. The photograph image was then analyzed in the same way as Howland and Howland analyzed their subjective grids.

This objective technique is faster than ray tracing, however in highly aberrated eyes the image produced may not be good enough quality to be analysed. The low sampling density may also limit the accuracy of this method [350]. The Tscherning design is used in the Allegretto Wave Analyzer (Wavelight).

A2.3.3 Sequential retinoscopy

This technique is based on the retinoscopy technique [351]. It is comprised of a projecting and receiving system. A slit beam is created by shining an infra red light source through a screen containing a slit. This beam passes into the eye and reflects from the retina. An aperture stop in the outgoing system, which is conjugate with the retina in emmetropia, in front of the retina in myopia and behind the retina in hypermetropia, acts in the same fashion as the sight hole in a retinoscope. The streak which is reflected from the retina is then imaged in the pupil plane and detected by a group of photodetectors. The slit beam and the photodetectors rotate together around an optical axis, so measurements can be taken every 1° over 360 meridians. The photodetectors are arranged in a pattern with four above the optic axis and four below. They measure light at the corneal plane at diameters of 2 mm, 3.2 mm, 4.4 mm and 5.5 mm. Two reference photodetectors either side of the optic axis aid detector alignment. The difference in direction and speed of the incident beam compared to the reflected beam can be used to estimate the refraction along each meridian. This produces an ametropia map (D) which can be converted to a wavefront map (μm).

This technique has a high dynamic range but measurements are restricted to a maximum six mm pupil diameter due to the positioning of the photodetectors. Although measurements are taken every degree over the full 360° , only four are taken per meridian, again due to the positioning of the photodetectors, which means interpolation of the points in between is necessary. The OPD-Scan (Nidek, Japan) uses this type of technology.

A2.3.4 Shack-Hartmann wavefront sensor

In 1904 Hartmann developed a method of testing the quality of telescope optics by using a grid of holes covering the entrance pupil of the telescope. In the 1960s Shack was looking at improving satellite images and replaced the holes in the Hartmann screen with lens arrays. This technology was then used by Laing *et al.* [352] to develop

the Shack-Hartmann (S-H) sensor for measuring ocular aberrations in the human eye. A narrow beam from a point source is imaged by the eye, reflected on the retina and passed through a series of relay lenses to a Shack-Hartmann wavefront sensor which is conjugate with the pupil plane. It is finally imaged on a CCD camera placed at the focal plane of the lenslet array (f_{LA}). The S-H sensor is made up of an array of micro-lenses and each micro-lens isolates a small amount of the light ray from the eye which hits the sensor. If the eye was a perfect optical system the wavefront at the sensor would be a plane wave, however if an aberrated wavefront hits the sensor, there is a departure of the centroid for each micro-lens from the ideal image position (Figure A2.6). The position of the centroid gives information about the local slope of the wavefront over each micro-lens. The difference between the reference centroid position and the actual centroid position is analysed by computer software and fitted to a set of Zernike polynomials and the wavefront aberrations present in the eye are calculated.

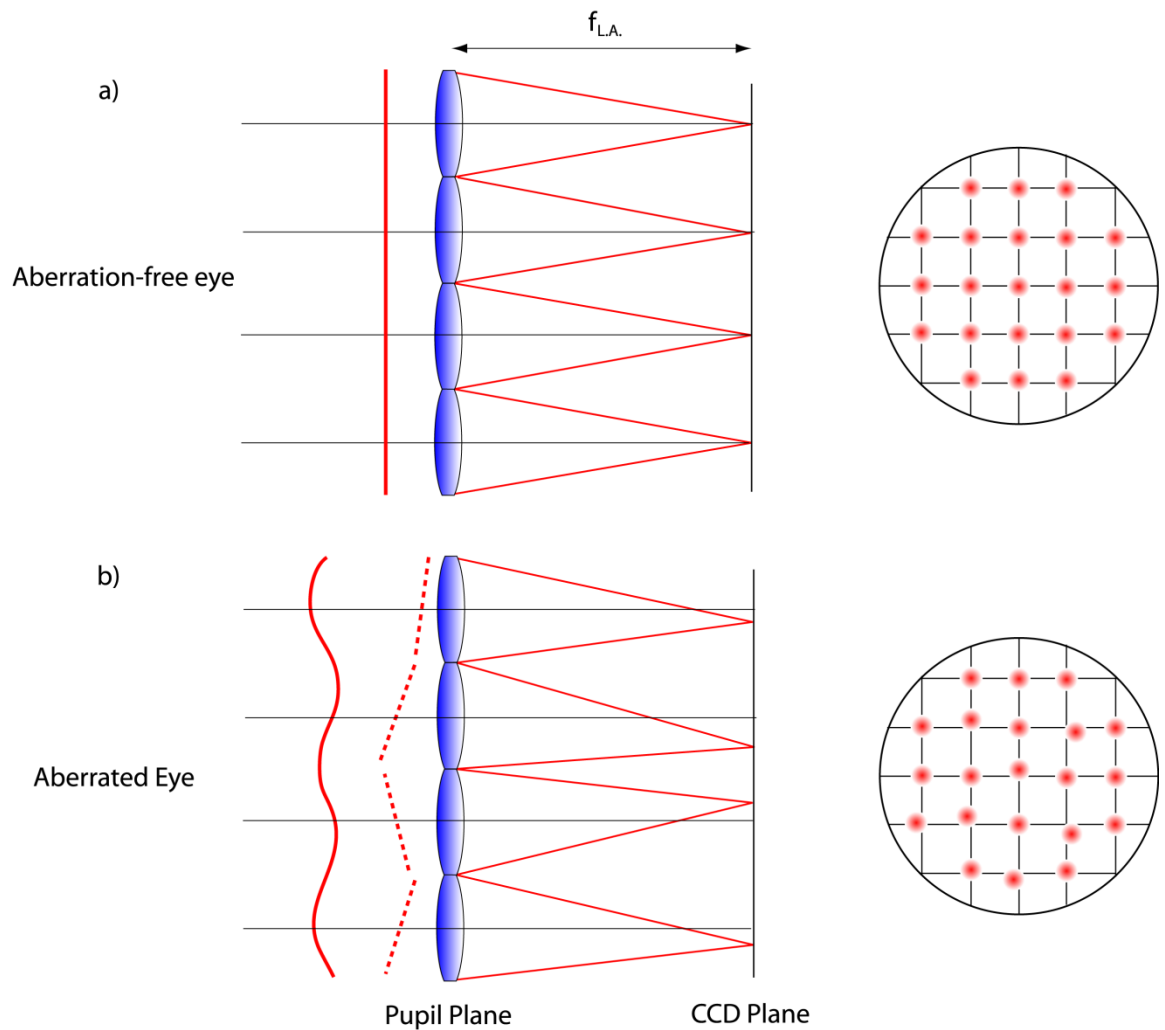


Figure A2.6. A Shack-Hartmann sensor measuring (a) an aberration-free eye and (b) an aberrated eye (courtesy of Karen Hampson, University of Bradford).

The S-H wavefront sensor has been compared to other methods of aberration measurement. It is accurate, repeatable and in agreement with a subjective Smirnov ray tracing technique [353] and has been found to give measurements equivalent to those produced by objective laser ray tracing and spatially resolved refractometry in normal subjects [354]. When compared to an objective cross-cylinder aberroscope there was little correlation between the two instruments although statistical analysis suggested the S-H aberrometer gave better discrimination between the aberrations of different subjects [350].

When high levels of aberration or defocus are present in a system there may be excessive displacement of the S-H spots causing overlap and confusion [342, 346].

Systems which currently use this technology are Zywave (Bausch and Lomb) and WASCA (Carl Zeiss Meditec).

A2.4 Difficulties in comparison of aberration studies

There are a large number of studies investigating the affects of ocular wavefront aberrations on the visual system, however direct comparison of data is difficult for a number of reasons. One of the most obvious confounding factors is the difference in the methods of measurement and representation of aberrations. Over the years technology has changed, and comparison of data from older studies which has been taken using completely different measurement techniques or methods of representation can be confusing [348, 349].

Many of the more recent studies have used the S-H sensor for wavefront measurement, some using custom made instruments [114, 187, 339, 355] whilst others have used manufactured instruments [116, 356]. These are still difficult to compare as there is no standardised methodology. The wavelength (632.8 nm – 830 nm) and intensity (10 - 40 μW) of light used for measurement varies with each study [114, 187, 339, 355]. Some studies use natural pupils [114, 187, 339] however this means accommodation may fluctuate during measurements and data can only be collected from subjects who have a large enough pupil size [339]. It does however give a natural situation which is particularly important when measuring aberrations induced by accommodation. Alternatively, data can be taken at natural pupil sizes, converted into equivalent defocus and then compared [356]. Other studies dilate the pupil using tropicamide [187] or cyclopentolate [115, 116, 357] which means natural pupil size is unimportant and errors due to accommodation fluctuation are mainly removed. Phenylephrine [355] is used in some accommodative studies as pupil size reduces with accommodation making measurements difficult. However phenylephrine does affect accommodation in some subjects [249] and a dilated pupil will give a smaller depth of focus which may

cause the subject to accommodate more than they normally would to achieve the same clarity of vision.

Bite bars are often used to improve subject stability [114, 187, 357] but chin rests [114, 340] are more participant friendly and easier to use on large populations. The pupil size used for aberration measurements tends to vary between studies (3.4 to 7.3 mm diameter) [114, 116, 187, 355, 357], and as W_{RMS} increases with increased pupil size, direct comparison of these studies cannot be made. Population age varies, with very young subjects being studied (7-12 years) [116] as well as young adults (20 to 30 years) and studies encompassing a wider range of ages (21 to 65 years) [114]. Different ranges of refractive error have been investigated and these are corrected in various ways: by using focus correcting mirrors [114], by changing the distance between the subject and the fixation target [187], by spectacle or trial lenses [115, 355, 357] or by using an instrument with a dynamic range large enough for no correction to be required [339].

The effect of these varying parameters on study results is difficult to quantify, therefore when making comparisons between results from different aberration studies consideration must be given to the methodology used.

A2.5 Aberrations in the general population

The zero-order and first-order polynomial terms (piston and tip and tilt) are not significant as far as retinal image quality is concerned. On average, most of the monochromatic aberrations of the eye are second-order (sphero-cylindrical) and have been shown to account for about 92% of the total variance of the wave aberration in the eyes of a normal population measured at a 5.7 mm pupil diameter [114] and 86.2% at a 7 mm pupil diameter [339]. These second-order aberrations can be corrected with spectacle lenses, contact lenses or refractive surgery, leaving third-order aberrations and above present in the optical system. These are known as the higher order aberrations, and their magnitude generally reduces as the Zernike order increases,

although there are wide variations between individuals [114-116, 187, 348, 355-358]. Even after full correction of ametropia it appears residual second-order wave-front variance is still higher than combined third to seventh-order wave-front variance [357]. Higher-order aberrations become more important as pupil size increases.

Studies using a crossed cylinder aberroscope technique [348, 349] found that third-order coma like aberrations play a dominant role in vision degradation at all pupil sizes. More recent population studies have used S-H sensors to measure aberrations. Porter *et al.* [114] found fourth-order spherical aberration to be the only higher order aberration to have a mean value significantly different from zero. This was confirmed by Cheng *et al.* [355], Thibos *et al.* [357] and Radhakrishnan and Charman [356]. Liang and Williams [187] however, found a third of the eyes they tested to have no spherical aberration at all. They used a much smaller sample of only nine subjects and this may account for the discrepancy.

In a population of young children age 7 to 12 years, Carkeet *et al.* [116] found third-order horizontal and vertical coma to significantly differ from zero as well as fourth-order spherical aberration. It is possible that this is due to the younger population [340] or that the majority of the children were of Chinese or Malay descent. Ethnic variation in aberrations has been found with a significant difference between the higher-order aberrations of children of Chinese and Malay descent, particularly vertical coma and to a lesser degree horizontal coma and spherical aberration [116]. There is a possibility this may be corneal in origin due to different anatomical characteristics [359]. Cervino *et al.* [360] found no significant difference in higher order W_{RMS} between a population of British Asian and Caucasian students, although fourth-order spherical aberration was found to be higher in Caucasians. No difference has been found in the level of W_{RMS} with gender in young children [116] or adults [360].

Although aberration values seem to vary widely between individuals, there appears to be some correlation between the eyes of each subject [114, 118, 187, 358] although

Castejon-Mochon *et al.* [339] found that for a 7 mm pupil, only 44% of Zernike values measured were found to be correlated (mainly second and third-order and fourth-order spherical aberration). Wang and Koch [358] found fourth-order spherical aberration to be the most highly correlated Zernike term between the two eyes.

Aberration measurements from third to sixth order for a 20 to 71 year old population show an increase in W_{RMS} with age [358]. He *et al.* [118] however found that emmetropic children had significantly higher third to seventh order W_{RMS} than emmetropic adults. They proposed that this may be because some of the children would go on to become myopic. When a larger age range was studied (5 to 81 years) third to seventh-order W_{RMS} for a 5 mm pupil have been shown to be at their minimum in the fourth decade of life, suggesting that the emmetropization process may include the reduction of higher order aberrations as well as the second order spherocylindrical ones [340]. The over 60 year age group were found to have the highest level of aberrations, with the 0 to 20 years age group, the next highest. It may have been interesting to split these subjects into two groups, those 15 years or younger and those over 15 years. As the emmetropization process is thought to be complete by the age of 15 years and it would have been interesting to see if the children going through this process had greater levels of aberrations than those whose eyes should have stopped growing. Radhakrishnan and Charman [356] found no difference in third to sixth-order W_{RMS} with age although their study was more limited (17 – 56 years) not including the extremes at both ends of the age scale. They also used a natural pupil size, which reduces with age, and expressed their results in terms of equivalent defocus. The results may therefore be due to the compensation of increasing aberrations with age by a reduction in pupil size. They did however, even when using this method, find an increase in fourth-order spherical aberration with age possibly due to changes in shape and refractive index of the crystalline lens.

A2.6 Conclusion

The measurement of ocular aberrations, both lower and higher-order is becoming more widespread in both academic investigations and optometric practice. Much research is being undertaken to investigate how the modification of ocular aberrations due to procedures such as orthok lens fitting, refractive surgery and intra ocular lens implants can affect visual function. Further investigation into this area is necessary.

Appendix 3

Aberrometer calibration and verification

A3.1 Artificial eye

Measurements were carried out using an artificial eye (AE). An achromatic doublet with a focal length of 20 mm was used to represent the cornea and lens of the eye, with matt, black card to represent the retina. The pupil size was 5 mm. The eye was rendered emmetropic using retinoscopy, this retinoscopy result being checked by two practitioners to confirm the result. The eye was then mounted on the chin rest of the aberrometer using a magic arm (Manfrotto, Italy) with the front surface of the achromatic doublet 214 mm from mirror SM₂ (Figure 2.11).

A3.1.1 Accuracy of instrument

All measurements on the AE used an exposure of 15 ms and ten frames were taken per measurement. The AE was centred as accurately as possible using an infrared camera to image the laser beam and by checking the clarity of the image of the Shack-Hartmann (S-H) spots on the computer screen. All measurements were taken in complete darkness. To assess the accuracy of the aberrometer, full aperture trial lenses of known power (+1 to -1 DS in 0.25 DS steps) were used. These were positioned directly in front of the AE so the centre of the trial lens coincided with the AE pupil centre as accurately as possible. A pupil size of 4.8 mm was specified in the aberrometer software and aberration coefficient measurements were taken up to and including the first 44 Zernike polynomials (8th radial order). The dynamic range of the instrument was found to be small, as more than 1 DS of blur caused the S-H spots to become too distorted to measure due to spherical aberration. Verification of cylindrical error was also carried out in this way using trial lenses of ± 0.50 DC at axes of 90, 180, 45 and 135°.

A3.1.2 Intra-session and inter-session repeatability

Ten measurements were taken at each dioptric level without removing the trial lens to assess intra-session repeatability. A second set of measurements were taken, with the AE and any trial lenses used being removed from the system and replaced between each session to assess repeatability between sessions.

A3.1.3 Lens power effect

As the participants in the study wore spectacle lenses for the initial measurements and no spectacle lenses for further measurements it was important to know the effect corrective lenses would have on the aberration measurements. Full aperture trial lenses were used to correct the AE. The trial lenses were placed in front of the AE at 12 mm back vertex distance (BVD) and the axial length of the AE was altered so it was corrected by the trial lenses to simulate as near as possible a real eye situation. Lenses from 0 to -6 D were used, as we chose not to recruit any subjects with a prescription outside this range. Ten readings were taken for each dioptric power and two sessions of measurements were taken with removal and realignment of the AE in between.

A3.2 Real eye evaluation

Before any measurements were taken on a real eye three separate readings of the laser power were measured at the eye. The maximum permitted exposure of the laser had been calculated (Appendix 4) and as long as the laser power measured at the eye is lower than this, it was safe for use. Distance aberration measurements were taken on nine participants. Those who were ametropic were corrected using full aperture trial lenses placed in a trial frame at a BVD of 12 mm. Ten frames were taken per measurement with an exposure of 150 ms. The participant was asked to place their chin on the chin rest and the distance from the mirror SM_2 and the cornea was measured to make sure it was 214 mm (Figure 2.11). The participant was aligned using

the infra-red camera and the spots on the screen to get them as central as possible. The chin rest was moved so the participant could focus on both the red laser spot and the target which was set at optical infinity. After each measurement the participant was asked to stay in position but close their eyes until the next measurement was taken to reduce exposure to the laser. As the participant was not using a bite bar they were asked to keep as still as possible, however small adjustments to their position sometimes had to be made between readings to realign the S-H spots to the measurement grid. Ten measurements were taken without removing the chin from the rest to assess intra-session repeatability. These ten measurements were repeated at another session to assess inter-session repeatability.

A3.3 Measurements used to calibrate the aberrometer

The aberrometer was calibrated and verified using both lower-order and higher-order aberrations. The measurement of the power of the AE/lens combination was calculated by the software for each set of ten frames. This could then be compared against the actual power of the trial lens being measured to test for accuracy.

The total W_{RMS} was calculated for the Zernike polynomials from third to eighth-order to acquire a measure of higher-order aberrations. This was done by squaring each term, taking the sum of the squared terms and finding its square root. Spherical aberration (Z12) was also calculated. For the AE and real eye there was no way of knowing what the W_{RMS} or spherical aberration should be, however, the repeatability of the measurements could be assessed along with the effect of the trial lenses.

The data were checked for normality using the Kolmogorov-Smirnov test. A paired t-test was used to compare the means of parametric data whereas a Wilcoxon signed rank test was used for non-parametric data.

A3.4 Results

A3.4.1 Spherical power

To assess accuracy, the correlation between the spherical trial lens power and the measured spherical power from the first set of data was plotted in Figure A3.1. There was found to be a highly significant correlation between the two ($r^2 = 0.996$, $p < 0.001$). In addition, error bars of ± 1 SD were plotted on the graph however the SD for each group of ten frames was so small the error bars are not visible.

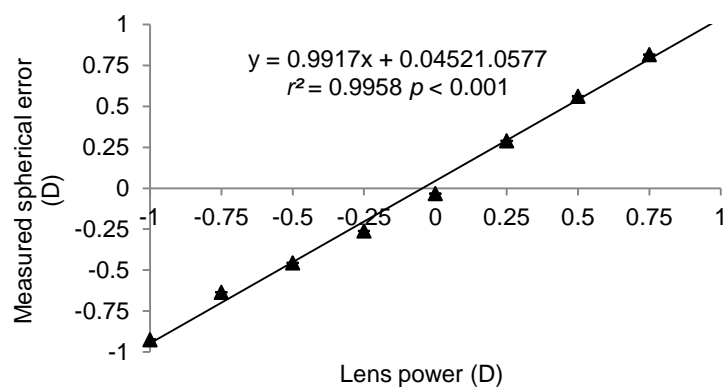


Figure A3.1. Measured spherical error (y-axis) plotted against actual lens power (x-axis) from the first set of measurements. SD error bars are smaller than symbol size.

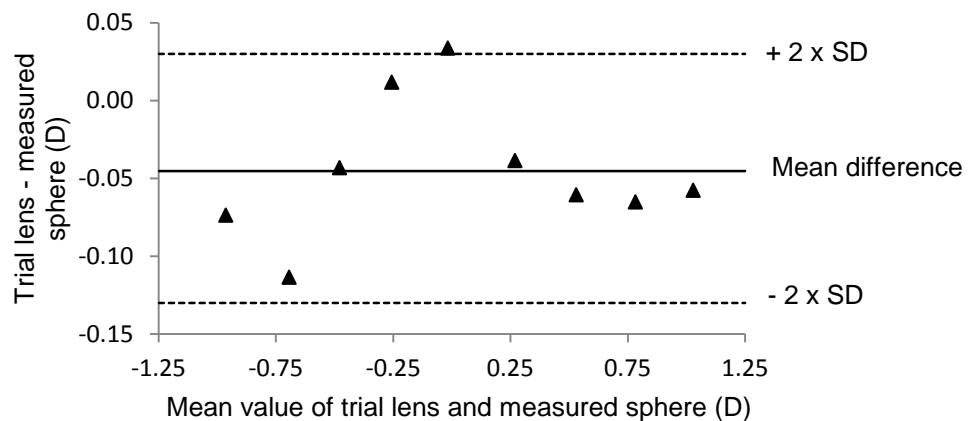


Figure A3.2. Bland Altman plot to compare the power of the actual trial lenses to the spherical measurements taken using the aberrometer. The solid line illustrates the mean difference (0.045 D) while the dashed lines illustrate the 95 % confidence intervals (-0.130 to 0.030 D).

Figure A3.2 shows a Bland Altman plot [221] to compare the spherical measurements taken by the aberrometer to the actual power of the trial lens. The aberrometer

measures on average 0.05 D less than the power of the trial lens with the 95 % confidence intervals lying between 0.03 and -0.13 D. All measurements were within the 95 % confidence intervals.

To assess inter-session repeatability a paired t-test was carried out between the mean of the ten measurements for each dioptric level taken during session one and those measured during session two. There was found to be no statistically significant difference between the measurements ($t_{(8)} = -1.411, p = 0.196$).

For each dioptric level the spherical aberration (Z12) was calculated for each of the first set of ten measurements taken. The mean and standard deviation of these ten measurements was calculated and is shown in Figure A3.3. The overall mean of the standard deviations was 0.0009 μm .

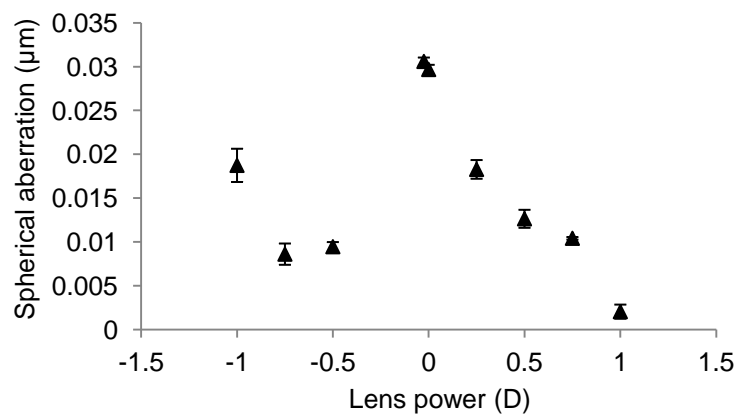


Figure A3.3. Spherical aberration (y-axis) plotted against actual lens power (x-axis) from the first set of measurements. Error bars show ± 1 SD.

To assess inter-session repeatability a paired t-test was carried out between the mean of the ten measurements for each dioptric level taken during session one and those measured during session two. There was found to be no statistically significant difference between the measurements ($t_{(8)} = 0.477, p = 0.646$).

For each dioptric level the W_{RMS} was calculated for each of the first set of ten measurements taken. The mean and standard deviation of these ten measurements was calculated and is shown in Figure A3.4. The overall mean of the standard deviations was 0.0009 μm .

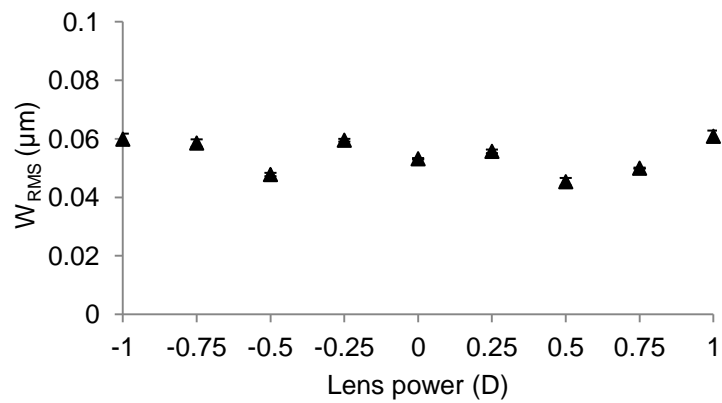


Figure A3.4. W_{RMS} wavefront error (y-axis) plotted against actual lens power (x-axis) from the first set of measurements. Error bars show ± 1 SD.

To assess inter-session repeatability a paired t-test was carried out between the mean of the ten measurements for each dioptric level taken during session one and those measured during session two. There was found to be no statistically significant difference between the measurements ($t_{(8)} = -1.411$, $p = 0.196$).

A3.4.2 Induced cylindrical power

As spherical mirrors were used in the Badal system rather than lenses to reduce unwanted reflections, it was expected that a certain amount of cylindrical power would be induced into the system due to the mirrors being slightly off axis. The induced cylindrical power and axis (mean \pm SD of ten frames) for each dioptric level from the first set of data is shown in Table A3.1.

The mean measured cylinder power of all the dioptric values was $-0.92 \text{ D} \pm 0.06$ and the mean cylindrical axis orientation was $178.62^\circ \pm 1$. To evaluate inter-session repeatability, the mean of the ten induced cylinder powers and axes found for each dioptric value in the first data set was compared to that of the second data set using a paired t-test. There was no statistically significant difference between the readings for either cylindrical power ($t_{(8)} = -0.427$, $p = 0.681$) or axis ($t_{(8)} = 2.078$, $p = 0.071$).

Table A3.1. Mean \pm 1 SD induced cylinder power and axis orientation for each spherical trial lens in data collection one.

Power of trial lens (DS)	Induced cylinder power (DC)	Induced axis ($^{\circ}$)
-1.00	-0.86 \pm 0.01	177.15 \pm 0.46
-0.75	-0.88 \pm 0.00	177.55 \pm 0.06
-0.50	-0.94 \pm 0.00	177.61 \pm 0.05
-0.25	-0.86 \pm 0.00	179.35 \pm 0.11
0	-0.85 \pm 0.00	179.83 \pm 0.02
0.25	-0.98 \pm 0.00	178.72 \pm 0.04
0.50	-0.95 \pm 0.00	179.40 \pm 0.08
0.75	-0.99 \pm 0.00	179.37 \pm 0.01
1.00	-1.01 \pm 0.00	178.55 \pm 0.85

The induced cylinder power in the system was transposed to a power vector format consisting of three components [171]:

Mean spherical equivalent (MSE) = sphere + cylinder/2

Jackson cross-cylinder at axis 0° with power $J_0 = -(\text{cylinder}/2) \cos(2 \times \text{axis})$

Jackson cross-cylinder at axis 45° with power $J_{45} = -(\text{cylinder}/2) \sin(2 \times \text{axis})$

The power vector was calculated from the cylindrical error at each dioptric level, and the mean vector value was found to be: MSE = -0.46 D, $J_0 = 0.46$ D and $J_{45} = -0.02$ D.

These values were used as a compensation factor in the formula below:

Corrected MSE = Measured MSE - (-0.46 D)

Corrected $J_0 = \text{Measured } J_0 - 0.46$ D

Corrected $J_{45} = \text{Measured } J_{45} - (-0.02$ D)

Adjusting subsequent measurements using this compensation factor removed the induced cylindrical error from the measurements.

A3.4.3 Cylindrical power and orientation

All the measurements taken using cylindrical trial lenses were transformed into power

vectors. The compensation factor was then applied. The corrected data from the first set of measurements was then plotted against the actual MSE, J_0 and J_{45} values in Figure A3.5.

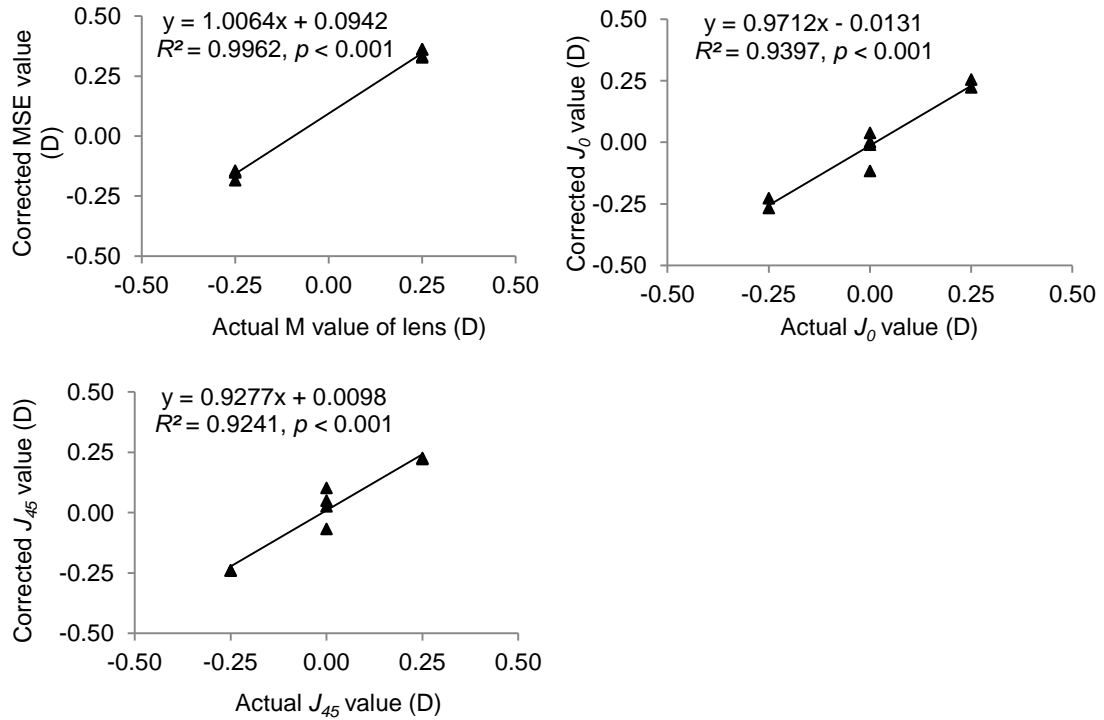


Figure A3.5. Corrected MSE, J_0 and J_{45} (y-axis) plotted against actual MSE, J_0 and J_{45} (x-axis) from the first set of measurements.

To assess inter-session repeatability paired t-tests were carried out to compare the means at each dioptric level from the data measured during session one to those measured during session two, for MSE, J_0 and J_{45} . There was found to be a statistically significant difference between the two sets of readings for the MSE component ($t_{(7)} = -3.459$, $p = 0.011$) but no statistically significant difference between the two sets of readings for the J_0 ($t_{(7)} = 0.313$, $p = 0.764$) or J_{45} ($t_{(7)} = 1.463$, $p = 0.187$) components.

A3.4.4 Lens power effect

Figures A3.6 and A3.7 show the effect that changing the power of corrective lenses has on the spherical aberration and W_{RMS} measurement.

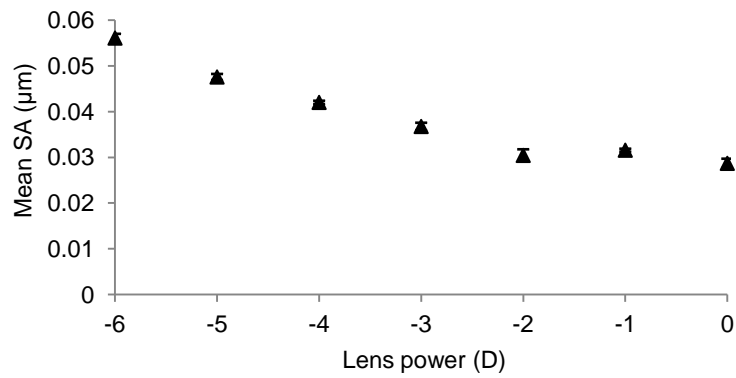


Figure A3.6. The effect of changing the corrective lens power on the measured SA in an artificial eye from the first data set. Error bars indicate ± 1 SD.

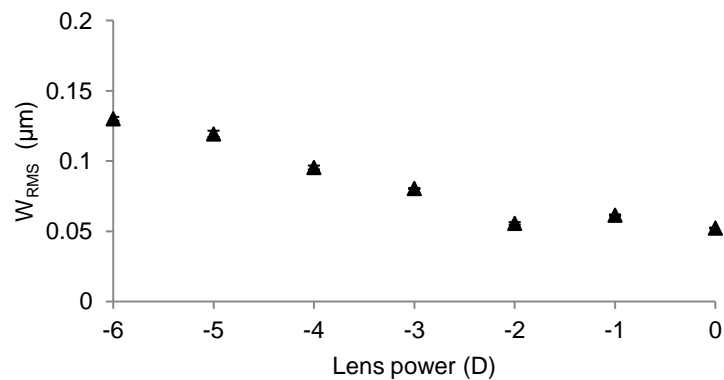


Figure A3.7. The effect of changing the corrective lens power on the measured W_{RMS} in an artificial eye from the first data set. Error bars indicate ± 1 SD.

A3.4.5 Real eye distance calibration

For the real eye calibration data was collected from nine participants with an age range from 25-55 years, and a median age of 29 years. The mean MSE of the cohort was $-1.83 \text{ D} \pm 3.78$ with a median of 0 D (range -7.50 D to +4.50 D). For each individual, the spherical aberration (Z12) was calculated for each of the first set of ten measurements taken. The mean and standard deviation of these ten measurements was calculated and is shown in Figure A3.8. The average standard deviation was $0.030 \text{ } \mu\text{m}$.

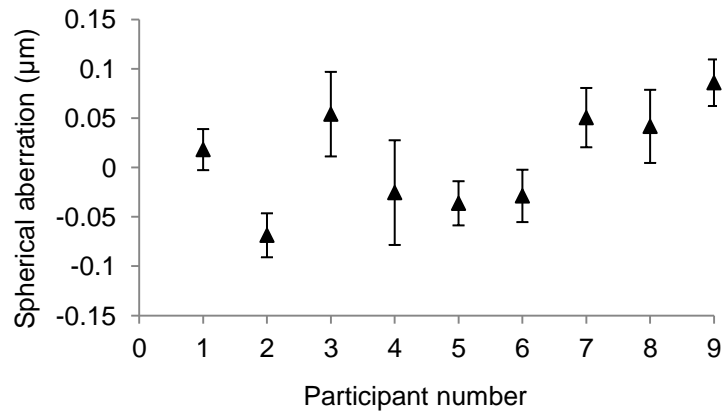


Figure A3.8. Spherical aberration (y-axis) plotted against participant number (x-axis) from the first set of measurements. Error bars show 1 SD.

To assess inter-session repeatability a paired t-test was carried out between the mean of the ten measurements for each participant taken during session one and those measured during session two. There was found to be no statistically significant difference between the measurements ($t_{(8)} = -1.142, p = 0.286$).

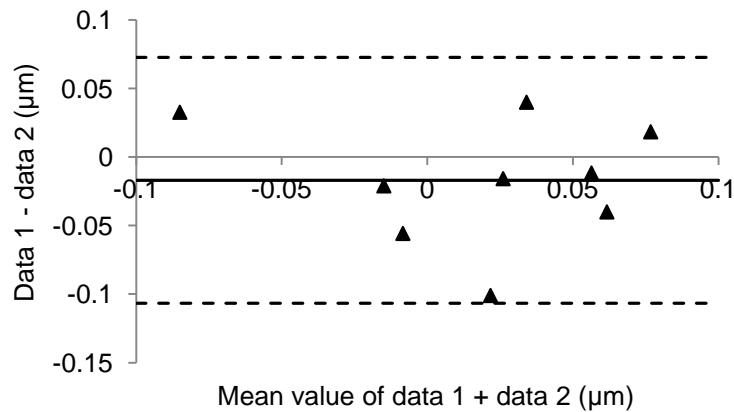


Figure A3.9. Bland Altman plot to compare the spherical aberration for data collection 1 to that for data collection 2. The solid line illustrates the mean difference ($-0.017 \mu\text{m}$) while the dashed lines illustrate the 95 % confidence intervals (-0.107 and $0.073 \mu\text{m}$).

Figure A3.9 shows a Bland Altman plot to compare the spherical aberration for each participant measured in data collection one, to that measured in data collection two. There was a $0.017 \mu\text{m}$ difference between the two measurements with the 95 % confidence intervals lying between 0.073 and $-0.107 \mu\text{m}$. All measurements were within the 95 % confidence intervals.

For each individual the total W_{RMS} (3rd to 8th-order) was calculated for each of the first set of ten measurements taken. The mean and standard deviation of these ten measurements was calculated and is shown in Figure A3.10. The average standard deviation was 0.048 μm .

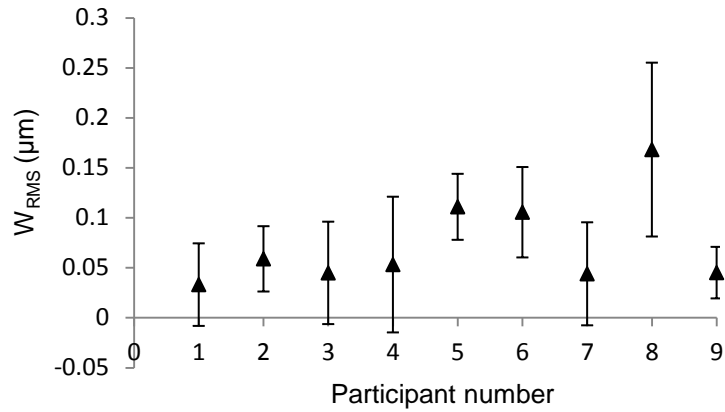


Figure A3.10. W_{RMS} wavefront error (y-axis) plotted against participant number (x-axis) from the first set of measurements. Error bars show 1 SD.

To assess inter-session repeatability a Wilcoxon signed rank test was carried out between the mean of the ten measurements taken for each participant during session one and those taken during session two. There was found to be no statistically significant difference between the measurements ($Z = -0.059$, $p = 0.953$).

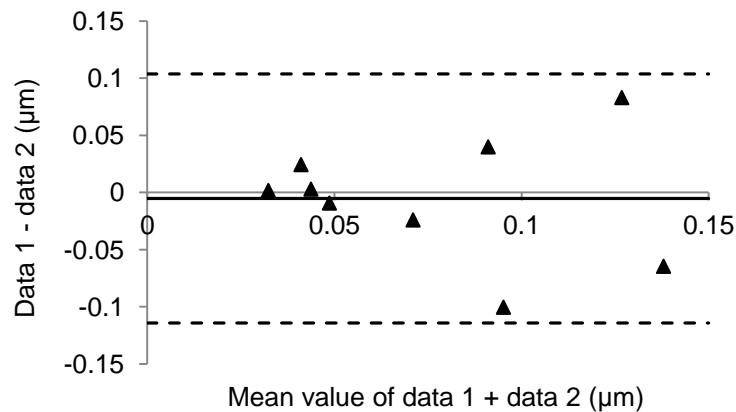


Figure A3.11. Bland Altman plot to compare the W_{RMS} for data collection 1 to that for data collection 2. The solid line illustrates the mean difference (-0.005 μm) while the dashed lines illustrate the 95 % confidence intervals (-0.114 and 0.104 μm).

Figure A3.11 shows a Bland Altman plot to compare the W_{RMS} for each participant

measured in data collection one to that measured in data collection two. There was a 0.005 μm difference between the two measurements with the 95 % confidence intervals lying between 0.104 and -0.114 μm . All measurements were within the 95 % confidence intervals.

A3.5 Conclusion

A3.5.1 Artificial eye

Data collected using an artificial eye showed the aberrometer to measure approximately 0.05 D less than the spherical power of the actual lens measured, with 95 % confidence intervals of between 0.03 and -0.13 D. The intra-session repeatability was excellent with intra-session standard deviations being 0.002 D for spherical measurements, and 0.0009 μm for both spherical aberration and total W_{RMS} . No statistically significant difference was found between the measurements taken during session one and session two for the sphere ($p = 0.196$), spherical aberration ($p = 0.646$) or W_{RMS} ($p = 0.196$). There was found to be an induced cylindrical error of $-0.92 \text{ D} \pm 0.06$ with an axis at orientation $178.62^\circ \pm 1$.

When the artificial eye was corrected using spherical lenses it was found that up to -2 D correction there was no effect of the lenses on the measured spherical aberration or W_{RMS} , however, with larger myopic correction the level of measured spherical aberration increased from 0.031 μm for -2 D to 0.056 μm for -6 D. The level of W_{RMS} also increased from 0.003 μm for -2 D to 0.017 μm for -6 D.

A3.5.2 Real Eye

For the real eyes intra-session standard deviations for spherical aberration and W_{RMS} measurements were found to be higher than those found for the artificial eye (0.030 μm for spherical aberration and 0.048 μm for W_{RMS} as oppose to 0.0009 μm for the AE). There was no statistically significant difference between the measurements taken

during session one and those taken during session two for either spherical aberration ($p = 0.286$) or W_{RMS} ($p = 0.953$). For the spherical aberration measurements there was a mean difference of $0.017 \mu\text{m}$ between the first and second set of data with 95 % confidence intervals lying between -0.107 and $0.073 \mu\text{m}$. For the W_{RMS} measurements there was a mean difference of $0.005 \mu\text{m}$ between the first and second set of data with 95 % confidence intervals lying between -0.114 and $0.104 \mu\text{m}$.

Appendix 4

Laser Safety

The maximum limits of safe exposure to radiation are issued by the International Commission for Non-ionizing Radiation (ICNIRP), and are then incorporated into international laser safety standards [361]. The current standard adopted in Britain is BS EN 60825-1:2007 [362]. The laser used for the Shack-Hartmann aberrometer is a Class 3R laser with a maximum power of 4.6 mW and wavelength of $\lambda = 830$ nm. BS EN 60825-1:2007 defines class 3R lasers as *“lasers that emit in the wavelength range 302.5nm to 10^6 nm where direct intrabeam viewing is potentially hazardous but the risk is lower than for Class 3B lasers, and fewer manufacturing requirements and control measures for the user apply than for Class 3B lasers. The accessible emission limit (AEL) is within five times the AEL of Class 2 in the wavelength from 400nm to 700nm and within five times the AEL for Class 1 for all other wavelengths”* [362].

When using a Class 3R laser, the risk of injury is to the eye rather than the skin. With a wavelength of 830 nm, the radiation is transmitted by the cornea and lens to be focused at a small point on the retina, and absorbed by the retinal pigment epithelium. As the melanin pigment layer is only 5 μm thick, very little power is needed for a large increase in temperature to occur. The retina is therefore at risk from thermal injury.

The maximum permitted exposure (MPE) is the level of exposure, at the cornea, to a source of radiation that can be considered the theoretical border between safe and potentially harmful [361]. The MPE value depends on the wavelength emitted, exposure duration and the size of the irradiated retinal spot. Once the MPE has been determined it is compared to the actual level of exposure. This is done below:-

Our laser is a small source and the angular subtense of the apparent source is less than 1.5 milliradian. The exposure duration (t) will be 10 seconds or greater, so the MPE is given by:

$$\text{MPE} = 10 \times C_4 \times C_7 \text{ Wm}^{-2} \quad (\text{C}_4 \text{ and } C_7 \text{ are correction factors})$$

$$\begin{aligned} C_4 &= 10^{0.002 (\lambda - 700)} \\ &= 10^{0.002 (830 - 700)} \\ &= 10^{0.26} \\ &= 1.82 \end{aligned}$$

And,

$$C_7 = 1$$

Therefore

$$\begin{aligned} \text{MPE} &= 10 \times 1.82 \times 1 \\ &= 18.2 \text{ Wm}^{-2} \text{ for up to 8.3 hours} \end{aligned}$$

The above standard assumes a pupil diameter of 7 mm for the measurement of the corneal irradiance. The MPE for our aberrometer in Watts is therefore given by

$$\begin{aligned} \text{MPE}_{\text{ab}} &= 18.2 \times \pi \times (3.5 \times 10^{-3})^2 \\ &= 0.0007 \text{ W} \\ &= 700 \mu\text{W} \end{aligned}$$

In the aberrometer, a considerable amount of the original laser power is lost as the beam splitter only reflects 8% of the emitted radiation around the system. There are also losses due to reflections at lens and mirror surfaces. The power of the laser at the eye will be measured before each use. As the actual power of our device at the eye measures on average $\leq 6 \mu\text{W}$, and under no circumstances will the participant be viewing this for eight hours, the value falls well below the MPE.

Appendix 5

A5.1 Myopia Questionnaire

Please answer these questions as accurately as possible. You may not know all the information. If there is anything you don't know the answer to just put 'not known'.

1	Name	
2	Contact e-mail address	
3	Do you wear glasses/CLs? (If not go to Q7)	
4	When do you wear your glasses/CLs?	
5	How old were you when you were first prescribed glasses?	
6	When was the last time your prescription was changed?	
7	Do you ever experience blurred distance vision after having done a lot of close work?	

Could you please fill in the table below about the spectacle wearing history of your family. The more information you can give the better.

	Myopia	Emmetropia	Hyperopia	Astigmatism
Mother				
Father				
Sibling 1				
Sibling 2				
Sibling 3				

A5.2 Ergonomic and temporal factors in nearwork-induced transient myopia : Participant information sheet 1

You are being invited to take part in a research study. Before you decide whether to consent to this it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and if anything is unclear please ask for more information. Take time to decide whether you wish to participate. You can withdraw from the study at any time but information already collected may still be used.

Background

Myopia development in children and adults is related to both genetic and environmental factors. As the prevalence of myopia appears to be increasing, identification of the factors involved in its development are important. Myopia development and progression is known to be associated with nearwork, however the exact mechanism of this relationship is still unclear. Nearwork-induced transient myopia (NITM) occurs when distance vision remains blurred after a period of nearwork. It may be that exposure to this myopic blur at distance may contribute to myopia onset and progression.

The aim of this research project is to obtain further information on the role of NITM in the development and progression of myopia in young adults and on interventions that may reduce NITM.

Experimental procedure

The aim of this experiment is to measure how much NITM occurs after varying periods of nearwork. Initially your eyes will be tested to work out your prescription, how well your eyes work together and how good your focusing is at near. Measurements will be taken of length of your eye, the depth of your anterior chamber and the curvature of the front of your eye. This instrument used to do this is called an IOLMaster and it is non contact ie it does not touch the eye.

The experiment comprises eight sessions which involve playing the game 'minesweeper' on a computer whilst looking through an optical system called a Badal optometer. This system allows us to change the amount of focus needed to view an object without changing its size. While you are doing this we will constantly monitor the amount of focus you are using. Each experiment will last for 1min, 10mins, 20mins or 30mins and will be done in a random order. At the end of the task you will be asked to view a distance object and we will record how long it takes for your eye to relax to view distance clearly.

The experiments will be done on the right eye only. If you need glasses we will correct your prescription during the experiments using a soft, daily contact lens. A new lens will be used for every subject and for each visit.

Side-effect/risks

As with all contact lens use there is a slight risk of scratching the front of your eye whilst inserting or removing the lens. We will check for this at the end of the experiment and advise you accordingly. If you experience a red, painful eye within 24 hours of lens removal please contact the lab or seek medical advice immediately. You may also experience slight discomfort due to fixed posture during steady fixation.

Inclusion criteria

To be included in this study you need to be a healthy individual regardless of race or gender. You should not have suffered from any eye diseases or undergone any form of refractive surgery. As this is a nearwork task you need to be 35 years of age or younger to avoid incipient presbyopia effecting the results. If you decide to participate in the study you will be given a copy of the information sheet and asked to sign a

consent form. Once you have done this you may still withdraw from the study at any time, without reason

Confidentiality

All information which is collected about you during the course of this study will be kept strictly confidential and will be coded. Data will be stored at the research site and will be used in the PhD thesis and publications in scientific journals. Nothing that could reveal your identity will be disclosed outside the research site.

Contacts

If you have any further questions or concerns please feel free to contact myself, Alison Alderson (PhD student) or Dr Mallen (PhD supervisor) by email or telephone.

Dr Mallen :- E.A.H.Mallen@bradford.ac.uk

Tel 01274236231

Alison Alderson :- A.Alderson@bradford.ac.uk

Tel 01274236230

I am willing to participate in the NITM study. I am aware this is completely voluntary and is in no way associated with my course work. I am aware that all data will be stored at the University of Bradford and be used for research purposes only.

Name

Signature

Date

Participant copy

A5.3 Ergonomic and temporal factors in nearwork-induced transient myopia: Participant Information sheet 2

You are being invited to take part in a research study. Before you decide whether to consent to this it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and if anything is unclear please ask for more information. Take time to decide whether you wish to participate. You can withdraw from the study at any time but information already collected may still be used.

Background

Myopia development in children and adults is related to both genetic and environmental factors. As the prevalence of myopia appears to be increasing, identification of the factors involved in its development are important. Myopia development and progression is known to be associated with nearwork, however the exact mechanism of this relationship is still unclear. Nearwork-induced transient myopia (NITM) occurs when distance vision remains blurred after a period of nearwork. It may be that exposure to this myopic blur at distance may contribute to myopia onset and progression.

The aim of this research project is to obtain further information on the role of NITM in the development and progression of myopia in young adults and on interventions that may reduce NITM.

Experimental procedure

As part of this project a longitudinal myopia study is being undertaken following the myopia progression of the 2007 cohort of Optometry undergraduates over their three years of study. Measurements of ocular prescription, axial length, corneal curvature and anterior chamber depth will be taken on three occasions between January 2008 and May 2010. Each measurement session will last approximately 10 minutes. A questionnaire will also be issued asking for information about family refractive history and symptoms of NITM. This questionnaire should only take a few minutes to complete. During this period you may also be invited to participate in other smaller studies into NITM. If this is the case further information will be issued at the time.

Please note that this and any related study is not part of your course work, it is purely voluntary and that participation/non participation has no bearing on your final grades.

Side-effects/risks

There are no risks or side-effects from this study.

Inclusion criteria

To be included in this study you need to be a healthy individual regardless of race or gender. You should not have suffered from any eye diseases or undergone any form of refractive surgery. If you decide to participate in the study you will be given a copy of the information sheet and asked to sign a consent form. Once you have done this you may still withdraw from the study at any time, without reason.

Confidentiality

All information which is collected about you during the course of this study will be kept strictly confidential and will be coded. Data will be stored at the research site and will be used in the PhD thesis and publications in scientific journals. Nothing that could reveal your identity will be disclosed outside the research site.

Contacts

If you have any further questions or concerns please feel free to contact myself, Alison Alderson (PhD student) or Dr Mallen (PhD supervisor) by email or telephone.

Dr Mallen :- E.A.H.Mallen@bradford.ac.uk
Tel 01274236231

Alison Alderson :- A.Alderson@bradford.ac.uk
Tel 01274236230

I am willing to participate in the longitudinal myopia study. I am aware this is completely voluntary and is in no way associated with my course work. I am aware that all data will be stored at the University of Bradford and be used for research purposes only.

Name

Signature

Date

Participant copy

A5.4 Myopia Questionnaire 2009

The questions below are all asking for information about possible risk factors for myopia onset and progression. Please answer them as accurately as possible. Thanks.

1. If you wear glasses/contact lenses, do you wear them when you're doing nearwork ie reading/writing?
2. How many hours PER DAY do you spend doing near work?
3. If you wear glasses/contact lenses do you wear them when you're working on the computer?
4. How many hours PER DAY do you spend on the computer?
5. How many hours PER WEEK do you spend playing sports?

A5.5 Myopia Questionnaire 2010

1. What is your ethnic group?

Choose one section from (a) to (e) and tick the appropriate box to indicate your cultural background

<p>(a) WHITE</p> <p><input type="checkbox"/> British</p> <p><input type="checkbox"/> Irish</p> <p><input type="checkbox"/> Any other White background <i>please write in below</i></p> <p>.....</p>	<p>(b) BLACK or BLACK BRITISH</p> <p><input type="checkbox"/> Caribbean</p> <p><input type="checkbox"/> African</p> <p><input type="checkbox"/> Any other Black background <i>please write in below</i></p> <p>.....</p>
<p>(c) ASIAN or ASIAN BRITISH</p> <p><input type="checkbox"/> Indian</p> <p><input type="checkbox"/> Pakistani</p> <p><input type="checkbox"/> Bangladeshi</p> <p><input type="checkbox"/> Any other Asian background <i>please write in below</i></p> <p>.....</p>	<p>(d) MIXED</p> <p><input type="checkbox"/> White and Black Caribbean</p> <p><input type="checkbox"/> White and Black African</p> <p><input type="checkbox"/> White and Asian</p> <p><input type="checkbox"/> Any other Mixed background <i>please write in below</i></p> <p>.....</p>
<p>(e) CHINESE or OTHER ETHNIC GROUP</p> <p><input type="checkbox"/> Chinese</p> <p><input type="checkbox"/> Any other Mixed background <i>please write in opposite</i></p>	

2. Do you ever experience blurred distance vision after having done close up work?

A5.6 A biometric investigation of nearwork-induced transient myopia (NITM)

You are being invited to take part in a research study. Before you decide whether to consent to this it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and if anything is unclear please ask for more information. Take time to decide whether you wish to participate. You can withdraw from the study at any time but information already collected may still be used.

Background

Myopia development in children and adults is related to both genetic and environmental factors. As the prevalence of myopia appears to be increasing, identification of the factors involved in its development are important. Nearwork-induced transient myopia (NITM) occurs when distance vision remains blurred after a period of nearwork. It may be that exposure to this myopic blur at distance may contribute to myopia onset and progression.

When we focus on a near object the muscles in the eye contract and the lens within the eye becomes more spherical allowing us to focus clearly. When we look back in to the distance the muscles relax and the lens returns to its original shape. It is thought NITM occurs when the lens struggles to return to its original shape, however, this has never been proven.

The aim of this experiment is to measure the change in thickness of the lens while it is changing from distance focus to near focus.

Experimental procedure

Initially your eyes will be measured using an autorefractor to work out your prescription. The length of your eye and thickness of the lens inside your eye will be measured by two different instruments; a LenStar and an IOLMaster. At no time will any of these instruments come in to contact with your eye. The experiment will be performed on the right eye only. If you need glasses we will correct your prescription during the experiment using a soft, daily contact lens. A new lens will be used for every subject.

The experiment involves focusing on a printed target for a maximum of three minutes at a time whilst your chin is on the chinrest of the LenStar and measurements are taken. This will be repeated three times The full set of experiments will take no more than an half an hour to perform.

Side-effect/risks

As with all contact lens use there is a slight risk of scratching the front of your eye whilst inserting or removing the lens. We will check for this at the end of the experiment and advise you accordingly. If you experience a red, painful eye within 24 hours of lens removal please contact the lab or seek medical advice immediately. You may also experience slight discomfort due to fixed posture during steady fixation.

Inclusion criteria

To be included in this study you need to be a healthy individual regardless of race or gender. You should not have suffered from any eye diseases or undergone any form of refractive surgery. As this is a nearwork task you need to be 40 years of age or younger to avoid incipient presbyopia effecting the results. If you decide to participate in the study you will be given a copy of the information sheet and asked to sign a consent form. Once you have done this you may still withdraw from the study at any time, without reason.

Confidentiality

All information which is collected about you during the course of this study will be kept strictly confidential and will be coded. Data will be stored at the research site and will be used in the PhD thesis and publications in scientific journals. Nothing that could reveal your identity will be disclosed outside the research site.

Contacts

If you have any further questions or concerns please feel free to contact myself, Alison Alderson (PhD student) or Dr Mallen (PhD supervisor) by email or telephone.

Dr Mallen :- E.A.H.Mallen@bradford.ac.uk
Tel 01274236231

Alison Alderson :- A.Alderson@bradford.ac.uk
Tel 01274236230

I am willing to participate in the NITM study. I am aware this is completely voluntary and is in no way associated with my course work. I am aware that all data will be stored at the University of Bradford and be used for research purposes only.

Name

Signature

Date

Participant copy

A5.7 The effect of a multichromatic stimulus on the accommodative response of the eye

You are being invited to take part in a research study. Before you decide whether to consent to this it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and if anything is unclear please ask for more information. Take time to decide whether you wish to participate. You can withdraw from the study at any time but information already collected may still be used.

Background

Myopia development in children and adults is related to both genetic and environmental factors. As the prevalence of myopia appears to be increasing, identification of the factors involved in its development are important. Myopia development and progression is known to be associated with nearwork, however the exact mechanism of this relationship is still unclear.

During daily life we read print in a variety of fonts, colours and backgrounds in magazines, books and computer screens. Some of these combinations appear subjectively easier to focus on than others and there is a possibility that our focusing mechanism may work differently when viewing different combinations of print styles and colours.

The aim of this experiment is to investigate whether there is a measureable difference in the accommodative response between viewing conventional black print on a white background and red print on a blue background.

Experimental procedure

Initially your eyes will be measured using an autorefractor to work out your prescription. The experiments will be performed on the right eye only. If you need glasses we will correct your prescription during the experiments using a soft, daily contact lens. A new lens will be used for every subject.

The experiment involves focusing on a printed target for up to two minutes at a time. Sometimes the target will be stationary and sometimes it will be moving. The target is observed through an optical system called a Badal optometer. This system allows us to change the amount of focus needed to view an object without changing its size. While you are doing this we will constantly monitor the amount of focus you are using. The full set of experiments will take no more than an hour to perform.

Side-effect/risks

As with all contact lens use there is a slight risk of scratching the front of your eye whilst inserting or removing the lens. We will check for this at the end of the experiment and advise you accordingly. If you experience a red, painful eye within 24 hours of lens removal please contact the lab or seek medical advice immediately. You may also experience slight discomfort due to fixed posture during steady fixation.

Inclusion criteria

To be included in this study you need to be a healthy individual regardless of race or gender. You should not have suffered from any eye diseases or undergone any form of refractive surgery. As this is a nearwork task you need to be 35 years of age or younger to avoid incipient presbyopia affecting the results. If you decide to participate in the study you will be given a copy of the information sheet and asked to sign a consent form. Once you have done this you may still withdraw from the study at any time, without reason.

Confidentiality

All information which is collected about you during the course of this study will be kept strictly confidential and will be coded. Data will be stored at the research site and will

be used in the PhD thesis and publications in scientific journals. Nothing that could reveal your identity will be disclosed outside the research site.

Contacts

If you have any further questions or concerns please feel free to contact myself, Alison Alderson (PhD student) or Dr Mallen (PhD supervisor) by email or telephone.

Dr Mallen :- E.A.H.Mallen@bradford.ac.uk

Tel 01274236231

Alison Alderson :- A.Alderson@bradford.ac.uk

Tel 01274236230

I am willing to participate in the accommodation study. I am aware this is completely voluntary and is in no way associated with my course work. I am aware that all data will be stored at the University of Bradford and be used for research purposes only.

Name

Signature

Date

Participant copy

Appendix 5.8 Patient information sheet for the orthokeratology study carried out by Annette Parkinson

**THE EYE CLINIC
UNIVERSITY OF BRADFORD
BRADFORD
BD7 1DP**

This document outlines the treatment described as Orthokeratology. Orthokeratology requires that you wear specially designed gas permeable contact lenses overnight that will reshape your cornea during sleep in order to provide acceptable unaided distance vision during waking hours. The Orthokeratology effect is temporary and reversible and it may be necessary to wear your retainer lenses during some waking hours to maintain satisfactory distance vision, especially if you fail to wear them as advised. The quality of your unaided vision will be dependant on wearing your lenses as prescribed by your practitioner. The quality of your unaided vision will also depend on how much internal astigmatism is present in your eyes, which is not always predictable. If you do not find the results acceptable then your eyes will return to their normal state over a period of time (one to three weeks) during which we will provide soft lenses to correct your vision until your prescription becomes stable.

BENEFITS

These lenses have been designed to provide excellent visual acuity and oxygen transmission to the eye during wear. The lens design should provide a reduction in the refractive error of a treated eye with a resultant improvement in the unaided vision. This change is believed to be completely reversible and temporary in nature.

RISKS

While no harmful health risks to your eyes are anticipated from using these lenses, as with any contact lens, there are potential risks of irritation to the eye, infections or corneal ulcers. Transient distorted vision that is not corrected with spectacle lenses may occur after removal of the lenses. No harmful effects are expected from any of the examination procedures used in the fitting and performance assessment of these lenses. If you develop any unusual symptoms or prolonged discomfort, removing the lenses, in most cases, will provide immediate relief. However, you should also contact the contact lens practitioner immediately.

In the event that it is believed that these lenses present new risks or the possibility of undesirable side effects, you will be advised of this information so that you may determine whether or not you wish to continue as a volunteer patient in this investigation.

Patients wearing the contact lenses during sleep induce extra risks over daily wear contact lenses but Orthokeratology is not as risky as wearing extended wear soft contact lenses. Extended wear (wearing lenses for one week without removal) contact lenses are marketed and are used in normal optometric high street and hospital practice.

The most common complication for extended wear patients is contact lens induced acute red eye. This is an acute reaction that usually requires no treatment. It is painful for a few hours.

All contact lens patients are exposed to extra risks when wearing contact lenses. The condition that creates most concern is microbial keratitis. This is sight threatening but is very rare. It is best avoided by the wearer ensuring clean and hygienic care and handling of their contact lenses

PARTICIPATION IN THE STUDY

Participants in the study will be required to attend the University on a number of occasions during the 12 month period of the study. Times for these appointments will be arranged at a mutually convenient time. These visits include:

1. An initial visit when the suitability of the participant for Orthokeratology will be assessed and the various measurements required to design the lenses will be made. This visit will normally last between 60 and 90 minutes. Patients who currently wear soft lenses should not wear them on the day of the initial visit. Individuals who currently wear RGP lenses will need a longer period of time without their lenses before the measurements can be made.
2. The next visit will be a collection appointment when the custom designed lenses will be checked for fitting purposes and instructions regarding the insertion and removal of the lenses will be given. At this visit participants will need to wear the lenses for 1 – 2 hours and then have their refraction reassessed to confirm that the corneal reshaping is taking place. The extent of this corneal reshaping will vary from individual to individual at this visit. On successful completion of this visit participants will take the lenses away and commence daily wear (NOT overnight at this stage).
3. The third visit takes place on the morning after the participant has worn the lenses overnight for the first time. The participant will attend the University wearing the lenses so that immediate overnight reactions can be assessed. This visit would normally last 1 hour.
4. Subsequent visits take place at
 - a. 1 week of overnight wear
 - b. 1 month of overnight wear
 - c. 3 months of overnight wear
 - d. 6 months of overnight wear
 - e. 12 months of overnight wear

It would be expected that these visits would also last in the region of 1 hour.

Participants will be given contact information for the University staff involved in the study in case of emergency.

Appendix 5.9 Orthokeratology and near visual function : participant information sheet

You are being invited to take part in a research study. Before you decide whether to consent to this it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and if anything is unclear please ask for more information. Take time to decide whether you wish to participate. You can withdraw from the study at any time but information already collected may still be used.

Background

Apart from focus there are other inherent optical imperfections in the human eye. These are known as wavefront aberrations and they can degrade the image we see. At present we are unsure whether the visual system would be improved if these were corrected or if they are necessary to help the focusing mechanism.

Orthokeratology is a procedure where a specially designed contact lens changes the profile of the cornea (the clear window over the front of the eye) to reduce myopia (short sightedness). Research has shown that this procedure can increase the size of the wavefront aberrations at distance causing a reduction in visual function. Little is known about how the aberrations are changed at near.

The aim of this research project is to measure the change in ocular aberrations for nearwork after orthokeratology lens fitting and to try to assess if this has any affect on near visual function.

Experimental procedure

Aberrations and near visual function will be measured before the orthokeratology fitting and after six months of lens wear. Both visits will last about an hour.

Aberration measurements : A laser beam is used to form a point source on the back of the eye (retina) The light reflected from the eye will be measured by a sensor. During the measurements you will be asked to fixate on the target and try to maintain steady fixation. Each measurement takes a couple of seconds and ten will be taken for distance and near on both the right and left eyes.

Near visual function measurements: There are two separate procedures for measuring near visual function. Both will be performed on the right eye only. The first is to measure what happens to the focusing of the eye after a ten minute task. You will be asked to play 'minesweeper' on the computer for ten minutes at two different focusing levels. Measurements of the eyes focus will then be taken on a machine called an autorefractor. The second is to measure how much effort your eye uses to focus on letters at different distances. 30 measurements will be taken with the eye focusing on letters at different distances, this will take about three minutes to complete. An autorefractor will again be used to take the measurements. During both these experiments a soft contact lens will be worn in the right eye.

Side-effect/risks

You may experience slight discomfort due to fixed posture during steady fixation for all the above experiments and a temporary after-image from the aberration measurements.

Safety remarks

Laser safety of this study has been approved by the University of Bradford ethics committee. The power of the laser entering the eye is several orders of magnitude less than the maximum permissible exposure for up to eight hours of continuous viewing, according to the British laser safety standards.

Inclusion criteria

To be included in this study you need to be a healthy individual regardless of race or gender. You should not have suffered from any eye diseases or undergone any form of refractive surgery. As this is a nearwork task you need to be 35 years of age or younger to avoid incipient presbyopia effecting the results. If you decide to participate in the study you will be given a copy of the information sheet and asked to sign a consent form. Once you have done this you may still withdraw from the study at any time, without reason.

Confidentiality

All information which is collected about you during the course of this study will be kept strictly confidential and will be coded. Data will be stored at the research site and will be used only in the PhD thesis and publications in scientific journals. Nothing that could reveal your identity will be disclosed outside the research site.

Contacts

If you have any further questions or concerns please feel free to contact myself, Alison Alderson (PhD student) or Dr Mallen (PhD supervisor) by email or telephone.

Dr Mallen :- E.A.H.Mallen@bradford.ac.uk

Tel 01274236231

Alison Alderson :- A.Alderson@bradford.ac.uk

Tel 01274236230

I am willing to participate in the study in to orthokeratology and near visual function. I confirm that the nature of the research has been explained to me. I understand that my consent is entirely voluntary and that I may withdraw from the research project at any time. I am aware that all data will be stored at the University of Bradford and be used for research purposes only.

Name

Signature

Date

Participant copy

Appendix 6

Individual NITM and regression quotient plots

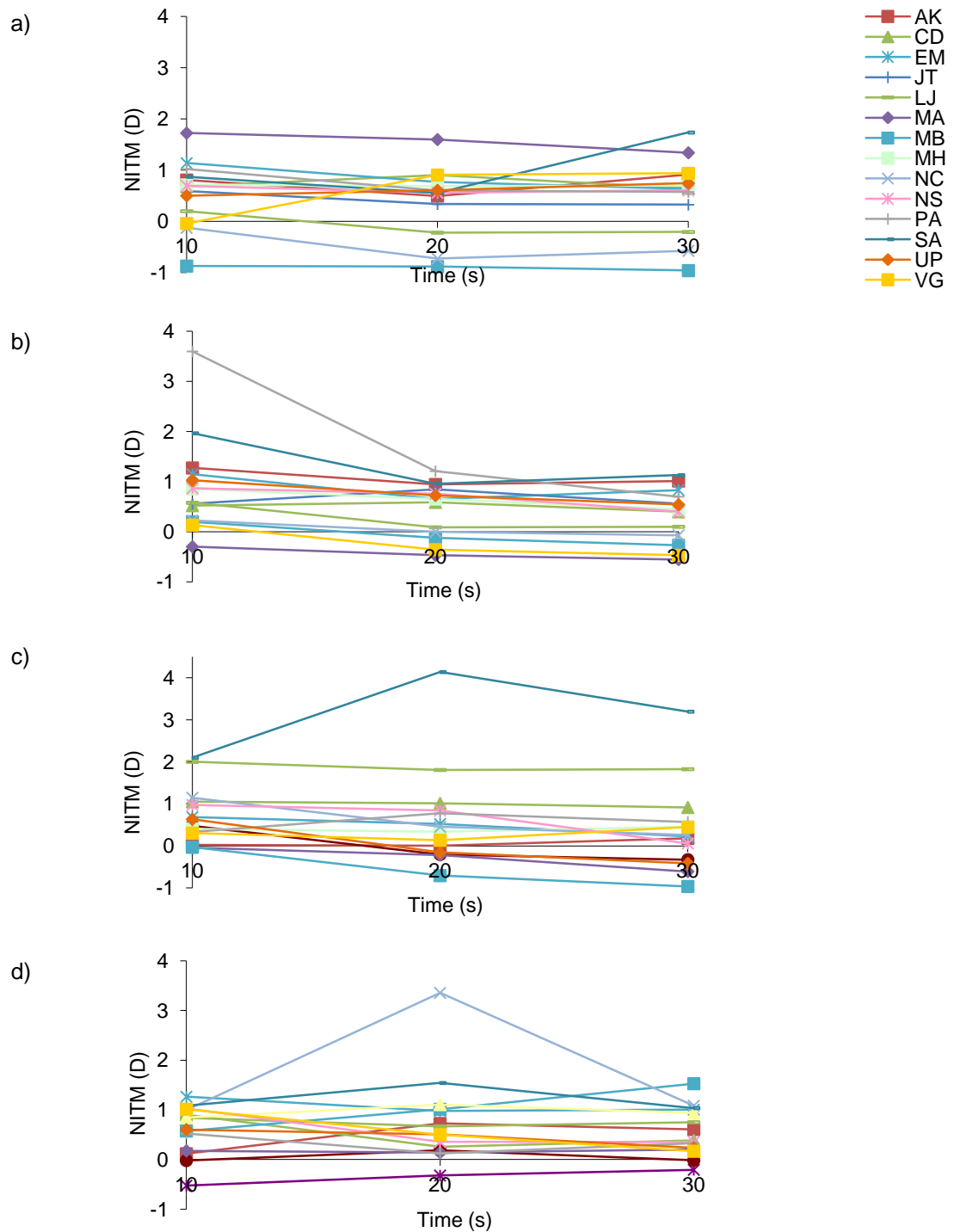


Figure A6.1. Individual post-task NITM values in dioptres during the first 30 seconds post-task for the asymptomatic group: a) 1 minute task, b) 10 minute task, c) 20 minute task and d) 30 minute task.

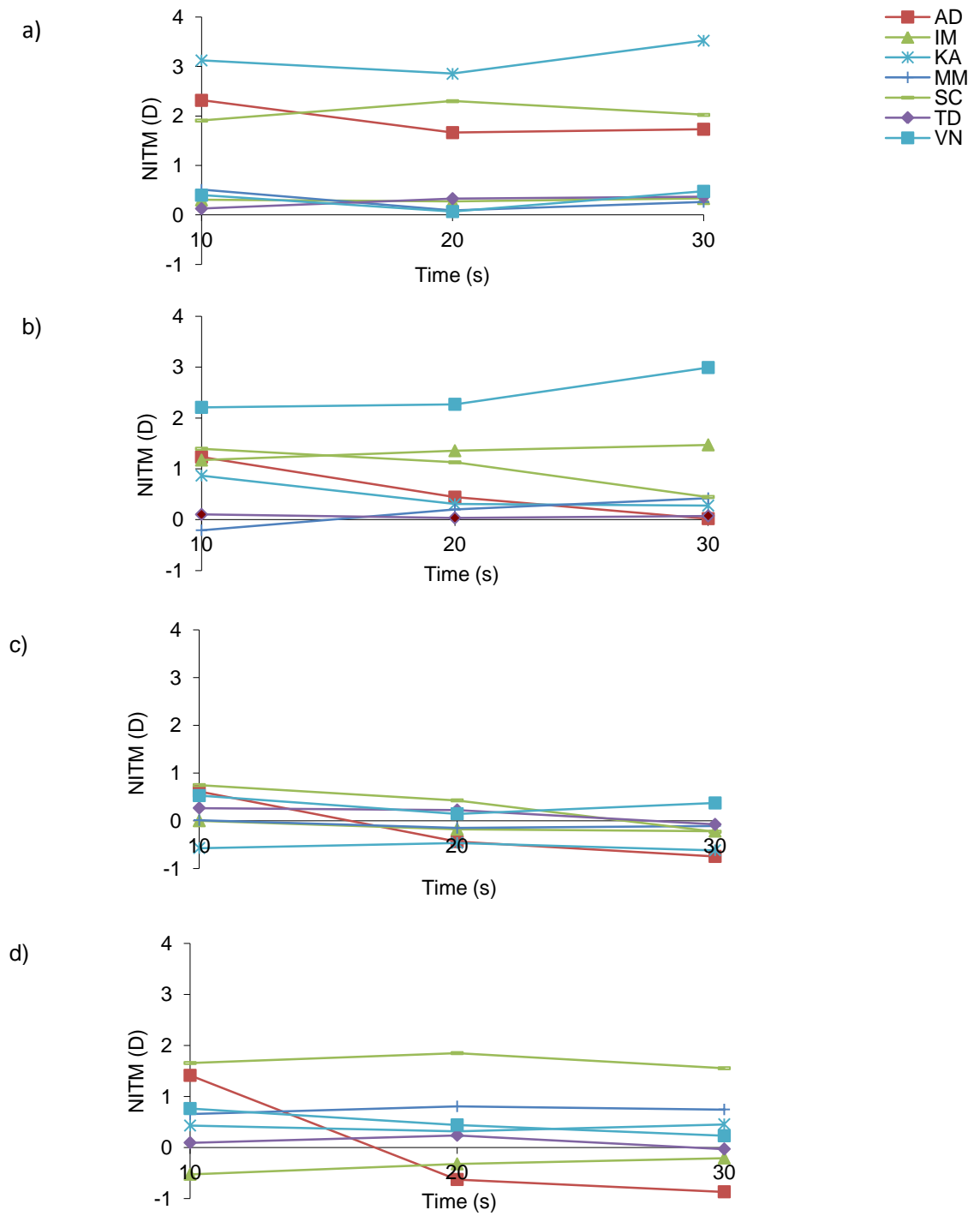


Figure A6.2. Individual post-task NITM values in dioptres during the first 30 seconds post-task for the symptomatic group: a) 1 minute task, b) 10 minute task, c) 20 minute task and d) 30 minute task.

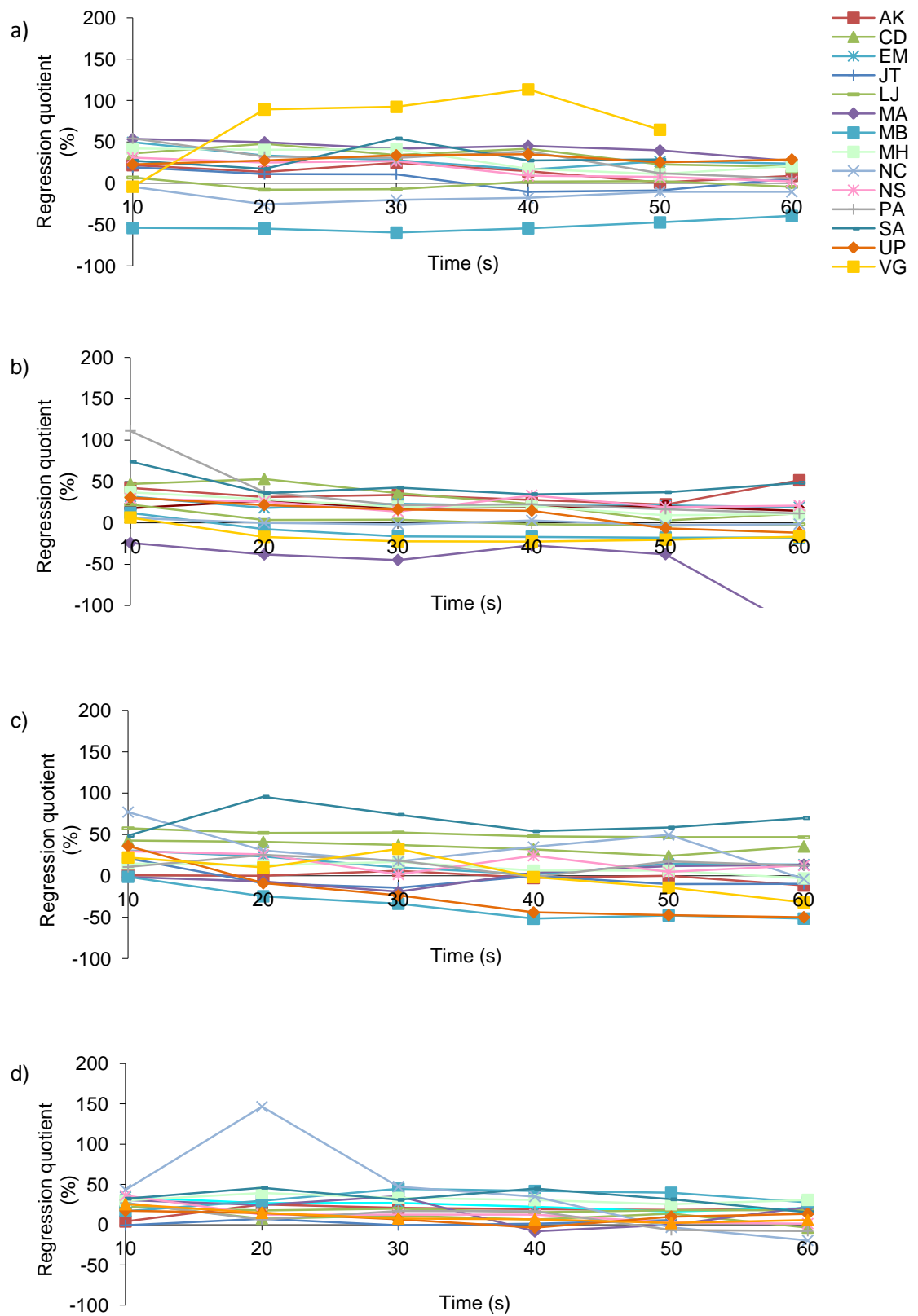


Figure A6.3. Individual post-task regression quotient values during the first 60 seconds post-task for the asymptomatic group: a) 1 minute task, b) 10 minute task, c) 20 minute task and d) 30 minute task.

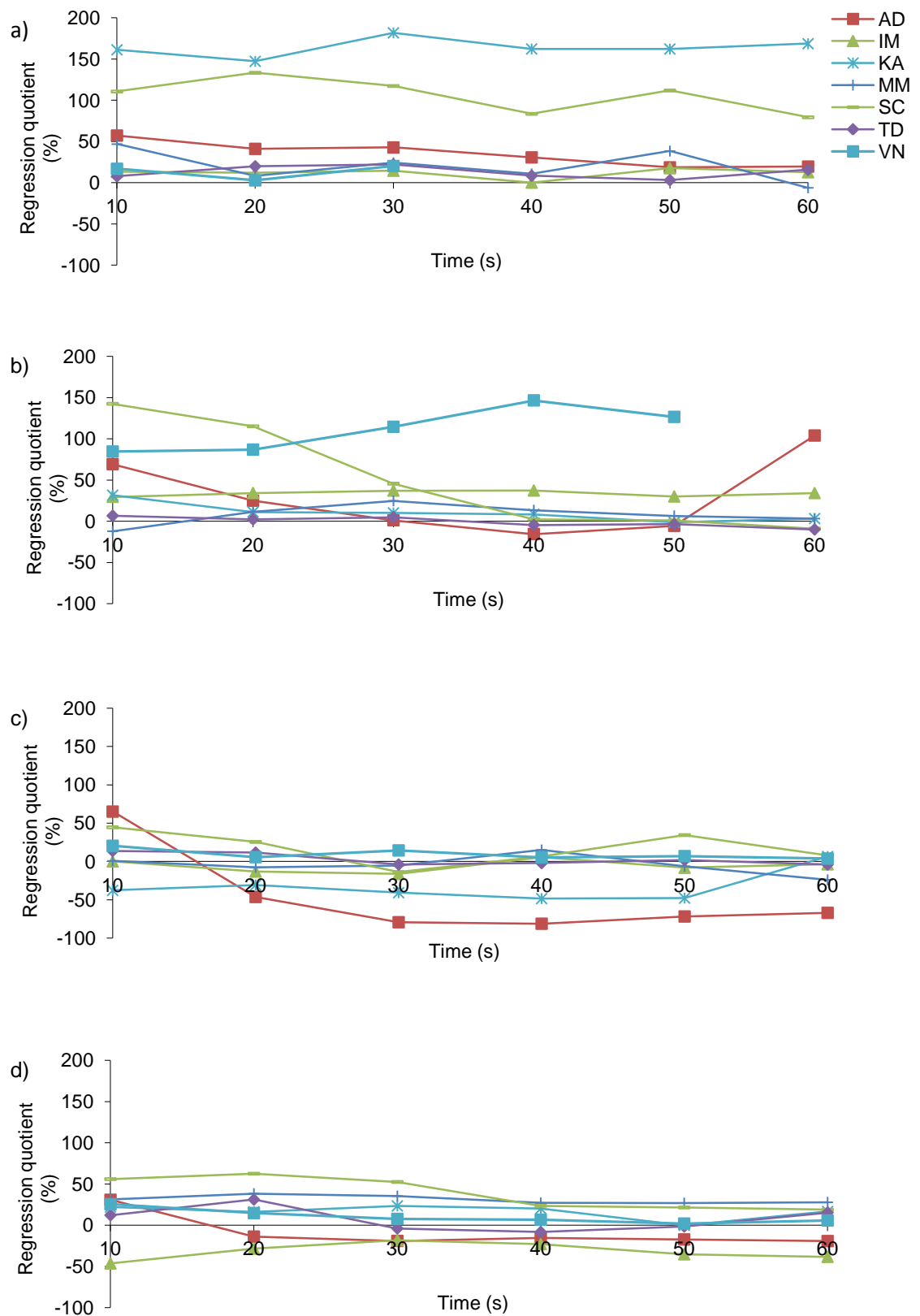


Figure A6.4. Individual post-task regression quotient values during the first 60 seconds post-task for the symptomatic group: a) 1 minute task, b) 10 minute task, c) 20 minute task and d) 30 minute task.

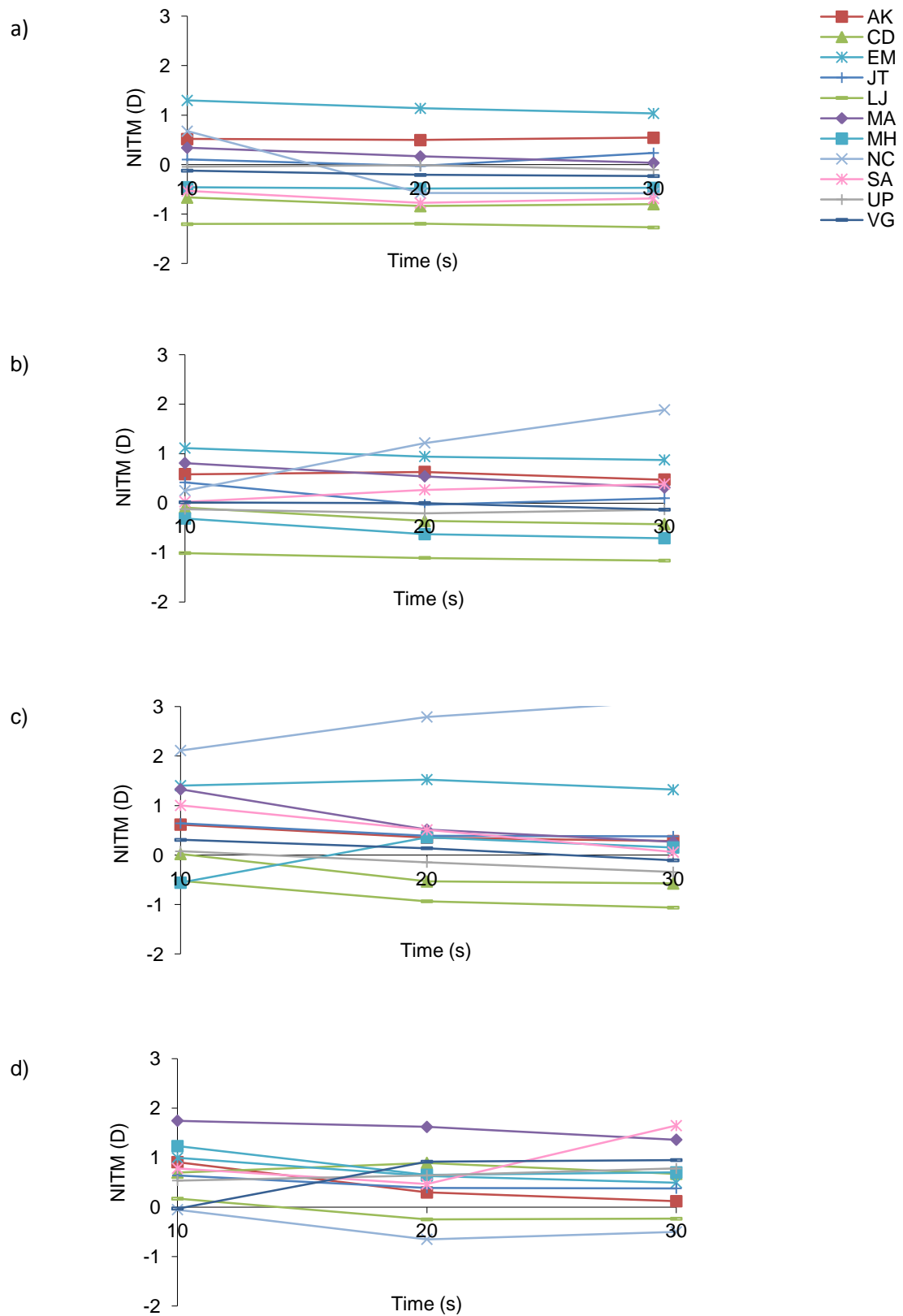


Figure A6.5. Individual post-task NITM values in dioptres during the first 30 seconds post-task for the asymptomatic group: a) 1 D task, b) 2 D task, c) 3 D task and d) 3.75 D task.

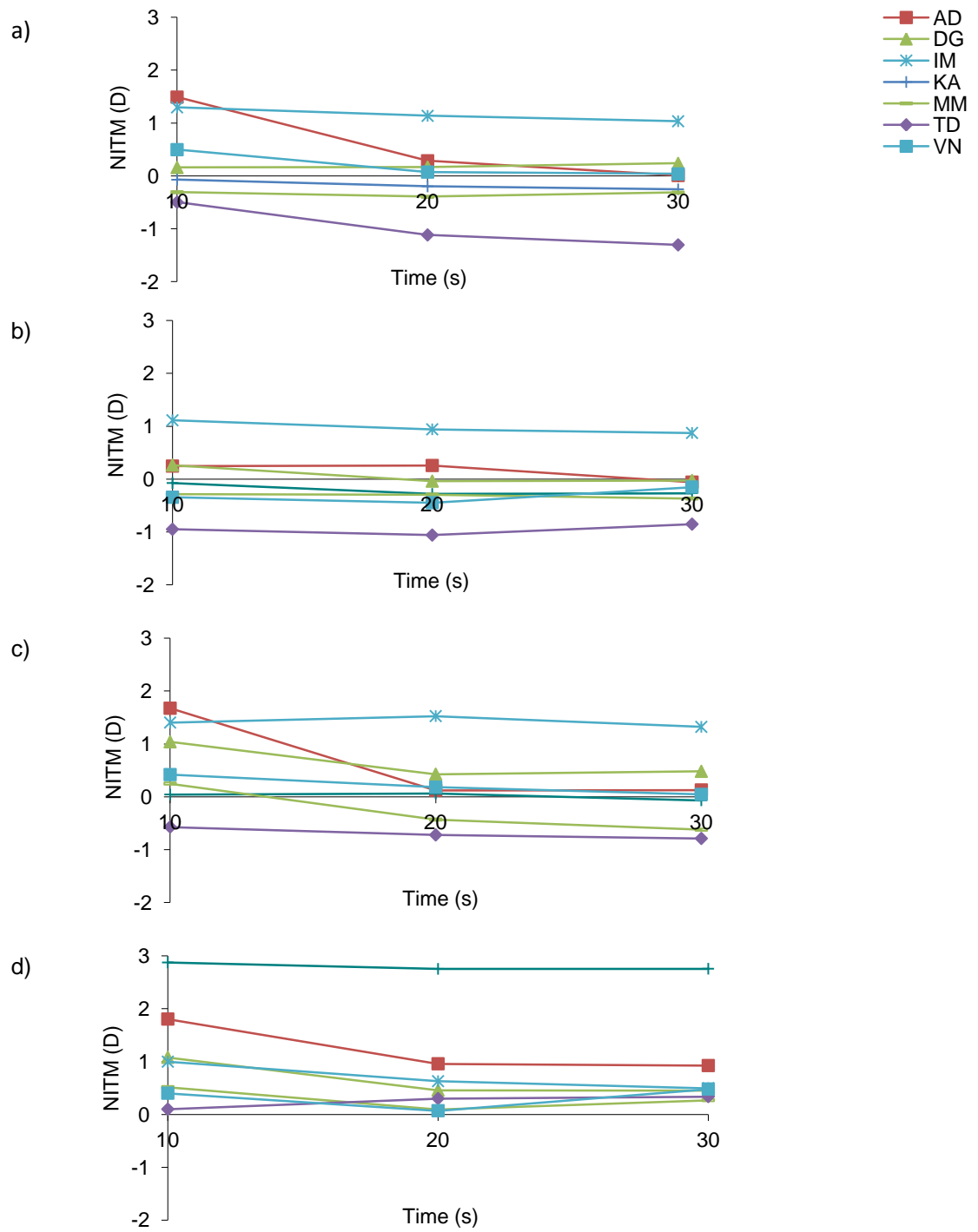


Figure A6.6. Individual post-task NITM values in dioptres during the first 30 seconds post-task for the symptomatic group: a) 1 D task, b) 2 D task, c) 3 D task and d) 3.75 D task.

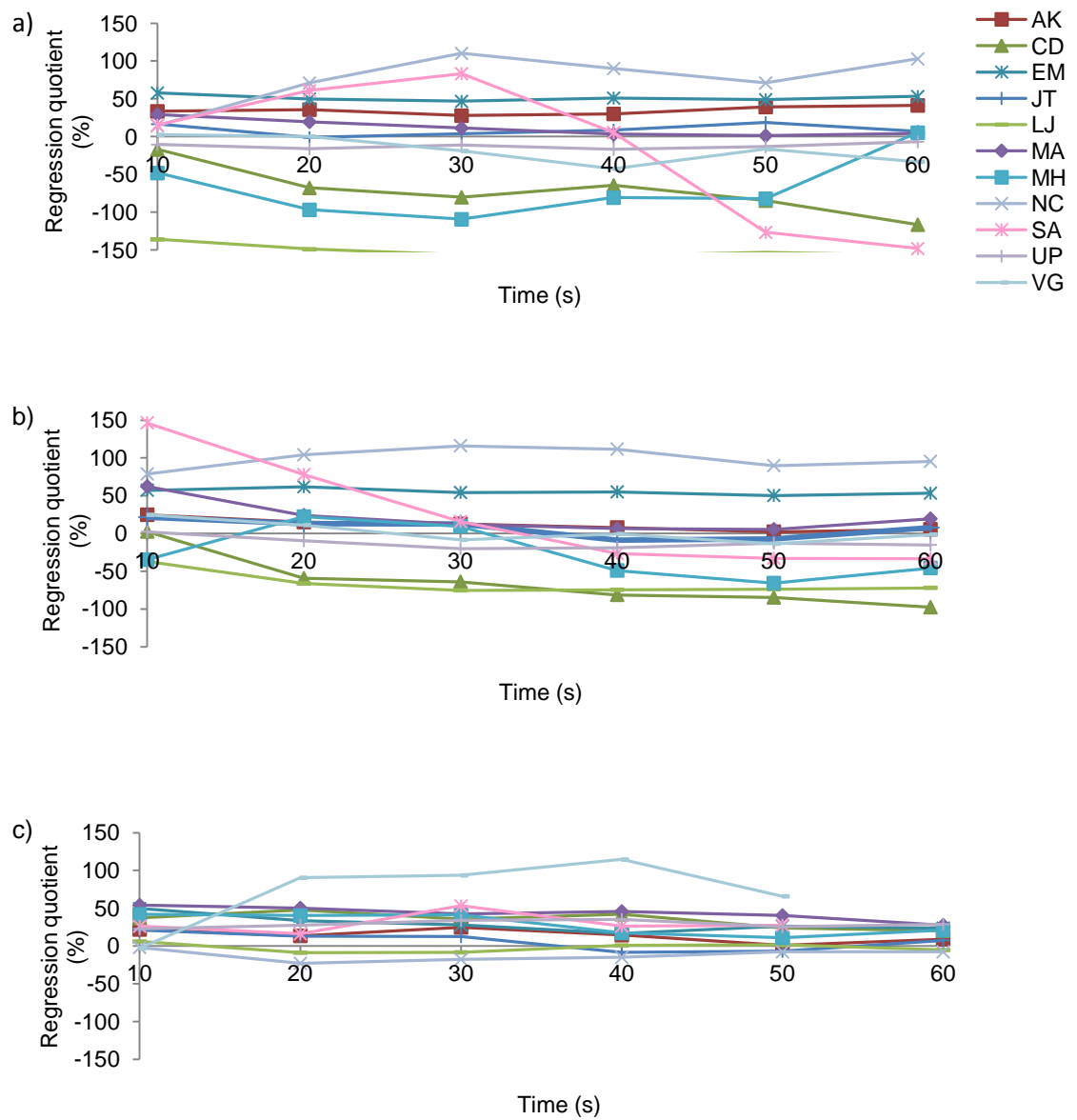


Figure A6.7. Individual post-task regression quotient values during the first 60 seconds post-task for the asymptomatic group: a) 2 D task, b) 3 D task and c) 3.75 D task.

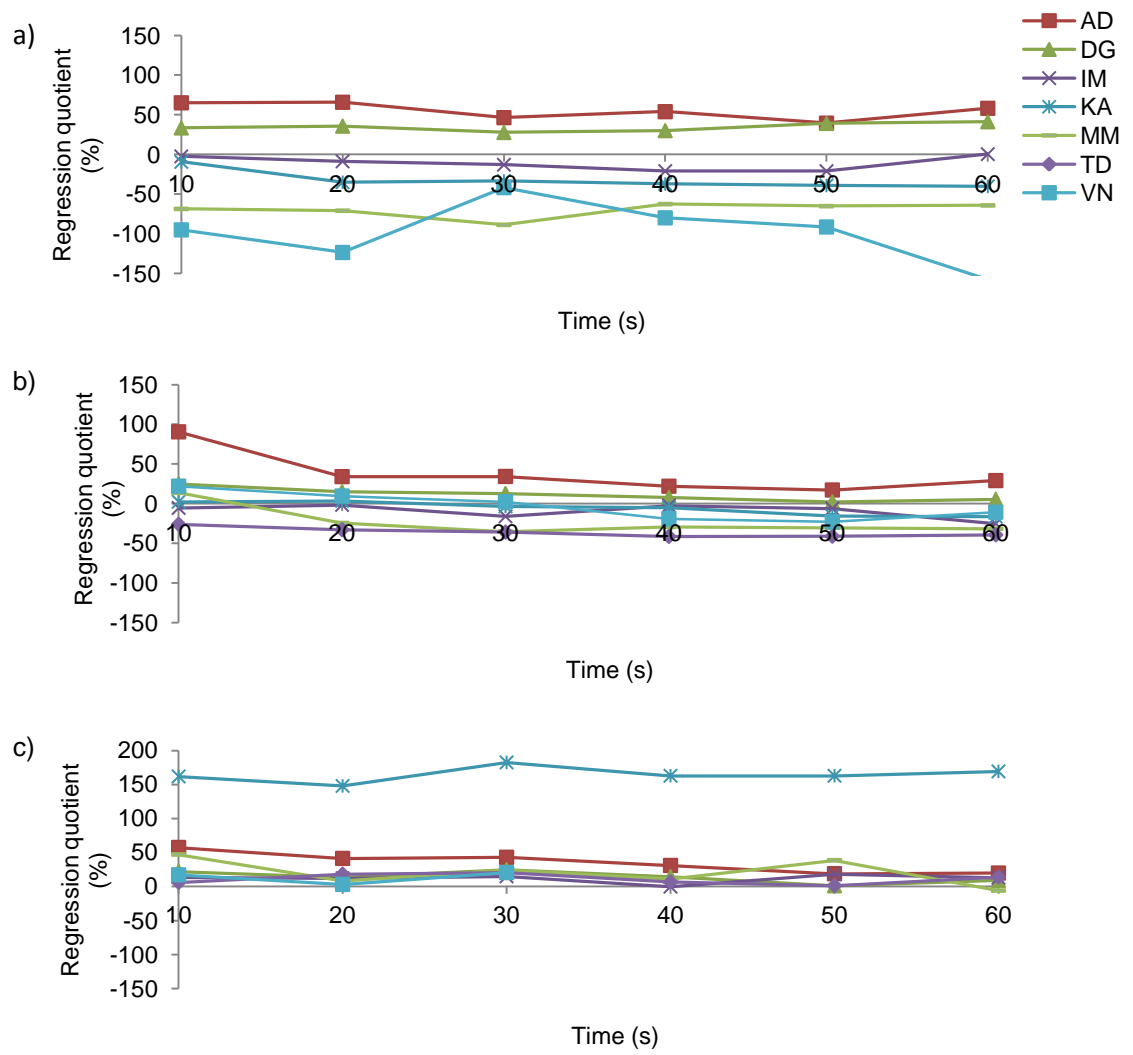
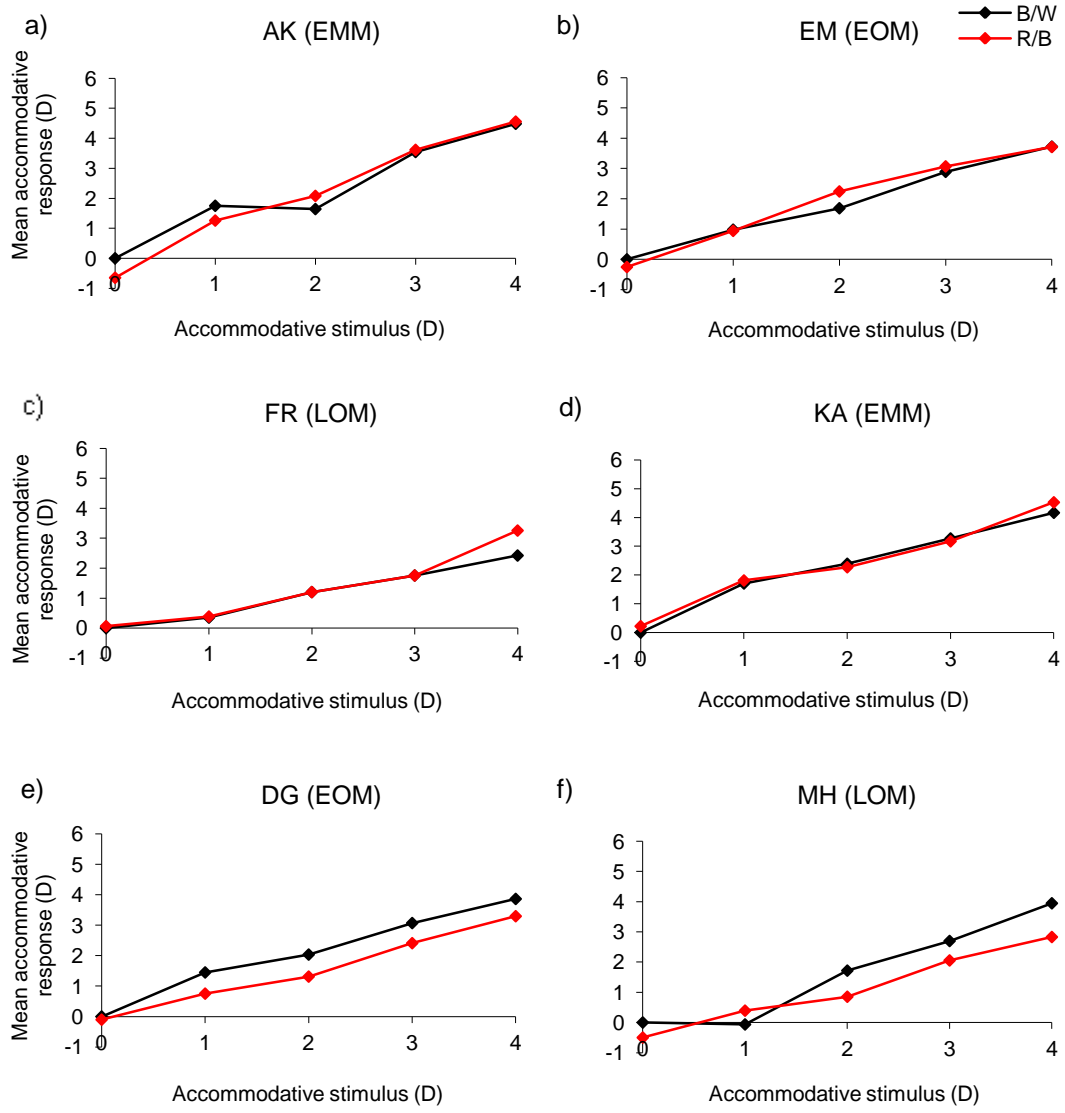


Figure A6.8. Individual post-task regression quotient values during the first 60 seconds post-task for the symptomatic group: a) 2 D task, b) 3 D task and c) 3.75 D task.

Appendix 7

Static accommodative response graphs



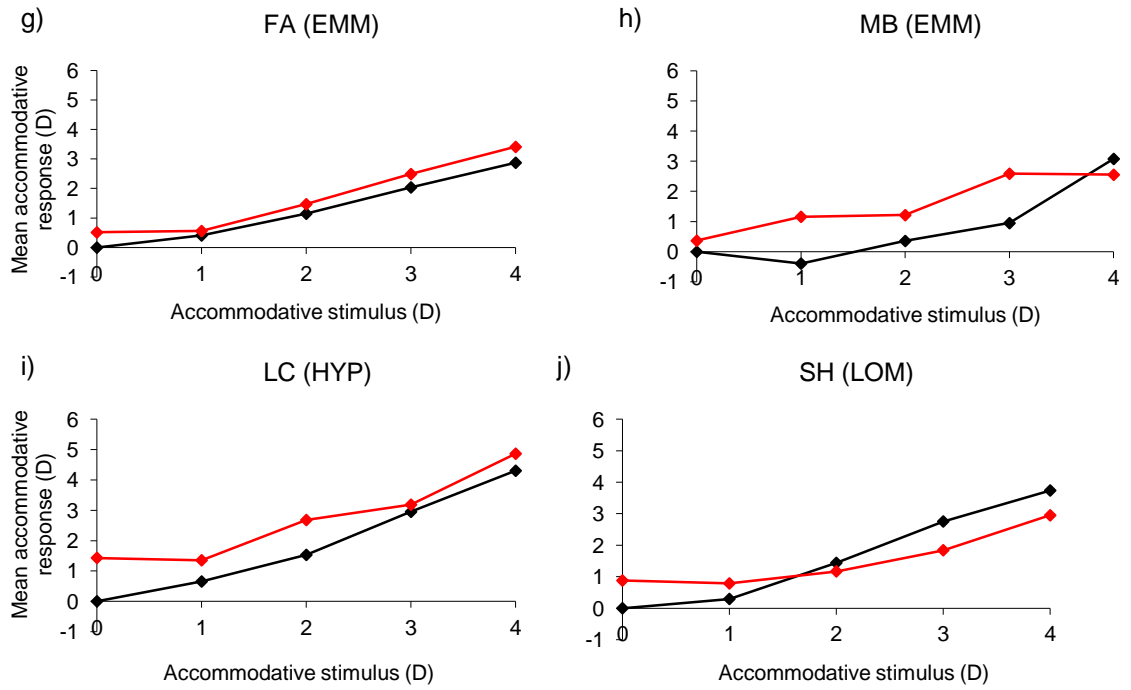


Figure A7.1. Graphs showing the normalised accommodative response for each accommodative stimulus for the B/W condition and the R/B condition. The graphs appear to show four different types of responses: group 1 (a,b,c and d) show little difference between their accommodative responses to a B/W stimulus and a R/B stimulus; group 2 (e and f) accommodate less to the R/B target than the B/W target; group 3 (g,h and i) accommodate more to the R/B target than the B/W target; group 4 (j) accommodates more to the R/B target below 2 D stimulus and less to the R/B target above a 2 D stimulus.

Supporting publications

Publications in peer-reviewed journals

Alderson, A., Mankowska, A., Cufflin, M.P., Mallen, E.A.H. Simultaneous measurement of objective refraction, accommodation response and axial length of the human eye. *Ophthalmic & Physiological Optics*, 2011; **31**: 100-108.

Refereed abstracts from conference proceedings

Alderson, A., Mallen, E.A.H. Temporal factors in nearwork-induced transient myopia. College of Optometrists Conference, York, 2010.

Alderson, A., Mallen, E.A.H. A longitudinal study of myopia progression in young adults and associated nearwork-induced transient myopia. 13th International Myopia Conference, Tübingen, 2010.

Alderson, A., Sheppard, A.L., Davies, L.N., Mallen, E.A.H. Application of high resolution low coherence reflectometry to track ocular biometric changes during disaccommodation. Association for Research in Vision & Ophthalmology Conference, Fort Lauderdale, 2011.