Higher Order Aberrations and Age-Related Cataract: a Pre- and Post- Operative Study

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## SUMMARY

The outcome of higher order aberrations (HOAs) prior to, and following, age-related cataract extraction and intra-ocular lens (IOL) implantation was explored using placido disc skiaoscopy aberrometry. Ninety-nine individuals (median age 73.0, IQR 67.0, 80.5) underwent comprehensive ophthalmic examination including contrast sensitivity, endothelial cell imaging and aberrometry (Nidek OPD ARK-10000) at approximately 4 weeks pre-operatively (median 3.9, IQR 2.9, 4.8) 10 weeks (median 7.1, IQR 5.64, 11.71) (67 individuals) and 80 weeks (median $85.1, \mathrm{IQR}$ 80.0, 89.6) (41 individuals) postoperatively. Linear relationships between thirteen demographical, functional and structural variables and each of three components, Total (TC), Corneal (CC) and Internal (IC), for each of eight HOAs, were separately explored, using Analysis of Variance, for each examination and for the pre- and post-operative differences, respectively. The TC and IC of all HOAs decreased post-operatively ( $\mathrm{p} \leq 68 \%$ ). Preoperatively, the TC and IC of the Total HOA decreased as the spherical equivalent (SE) became less negative (both $\mathrm{p}<0.001, \mathrm{R}^{2}=0.56$ and 0.53 ). Both components of the Total HOA also decreased as the difference in SE between baseline and each follow-up became less negative (all $\mathrm{p} \leq 0.008$, $R^{2}=0.45-0.61$ ); the magnitude of the reduction varied between IOL type ( $p \leq 0.008$ ). The IC of the Tilt, T.Sph and HiAstig HOAs increased with increase in severity of posterior subcapsular ( $\mathrm{p}=0.018$ ), of cortical ( $\mathrm{p}=0.013$ ) and of combined nuclear colour and cortical cataract ( $p=0.003$ ), respectively. The relationship between cataract type and severity and reduction in post-operative HOA was not statistically significant at either follow-up examination. Slight associations, presumably due to post-operative corneal oedema, were present between increase in CCs of five HOAs and decreasing endothelial cell density at the first follow-up, only, (all $\mathrm{p} \leq 0.030, \mathrm{R}^{2}=0.09-0.14$ ). Pre-operative TCs and ICs were larger, respectively, than those of 22 individuals with 'less severe' cataract and postoperatively than those of 49 individuals with clear media, obtained from retrospective data.

To Miri, the love of my life and my best friend.

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## LIST OF CONTENTS

Page
Title Page ..... i
Summary ..... ii
Dedication ..... iii
Acknowledgments ..... iv
Declaration ..... V
List of Contents ..... vi
List of Abbreviations ..... xxi
CHAPTER 1: INTRODUCTION ..... 1
1.1 Background ..... 1
1.1.1 Chromatic Aberrations ..... 2
1.1.1.1 Longitudinal Chromatic Aberrations ..... 2
1.1.1.2 Transverse chromatic aberration ..... 4
1.1.2 Monochromatic Aberrations ..... 5
1.1.2.1 Spherical Refractive Error ..... 5
1.1.2.1.1 Myopia ..... 5
1.1.2.1.2 Hyperopia ..... 7
1.1.2.2 Cylindrical Refractive Error - off-axis and on-axis ..... 9
1.1.2.3 Higher Order Aberrations (HOAs) ..... 13
1.1.2.3.1 Spherical Aberration ..... 13
1.1.2.3.2 Coma Aberration ..... 16
1.2 Wavefront Aberration ..... 18
1.2.1 Zernike Polynomials ..... 23
1.2.2 Root Mean Square (RMS) ..... 32
1.2.3 Point Spread Function (PSF) ..... 32
1.2.4 Modulation Transfer Function (MTF) ..... 38
1.2.5 Clinical Measurement of Higher Order Aberrations ..... 39
1.2.5.1 Aberrometry ..... 39
1.2.5.1.1 Wavefront Aberrometers ..... 40
1.2.5.1.2 Principle of Hartmann-Shack ..... 42Aberrometry
1.2.5.1.3 Principle of Tscherning Aberrometry ..... 45
1.2.5.1.4 Principle of Ray Tracing Aberrometry ..... 46
1.2.5.1.5 Principle of Spatially Resolved ..... 47 Refractometer
1.2.5.1.6 Principle of Retinoscope Double Pass ..... 49
Aberrometry
1.3 Clinical Implications of Wavefront Aberrometry ..... 52
1.3.1 The Normal Eye ..... 52
1.3.2 Refractive Error ..... 53
1.3.3 Aging ..... 56
1.3.4 Accommodation ..... 58
1.3.5 The Tear Film ..... 60
1.3.6 Visual Acuity ..... 61
1.3.7 Contrast Sensitivity Function (CSF) ..... 62
1.3.8 Pupil Diameter ..... 62
1.3.9 Refractive Surgery ..... 65
1.3.10 Orthokeratology/ Corneal Refractive Therapy (CRT) ..... 69
1.3.11 Wavefront-guided Refractive Surgery (WFG) ..... 70
1.3.12 Age-Related Cataract ..... 71
1.3.13 Cataract Surgery ..... 72
1.3.14 Intraocular Lenses ..... 73
1.3.15 Surgical Incision ..... 79
1.3.16 Keratoconus and Collagen Cross-Linking in Keratoconus ..... 80
1.3.17 Contact Lenses ..... 82
1.4 Miscellaneous ..... 83
1.4.1 Pellucid Marginal Corneal Degeneration ..... 83
1.4.2 Retinal and Macular Disease ..... 83
1.4.3 Corneal Thickness ..... 85
1.4.4 Intraocular Pressure ..... 85
1.4.5 Amblyopia ..... 86
CHAPTER 2: RATIONALE FOR RESEARCH ..... 87
2.1 Introduction ..... 87
2.2 Primary Aims of the Study ..... 90
2.3 Secondary Aims of the Study ..... 90
2.4 Clinical Studies and Outcomes ..... 91
2.4.1 Wavefront Aberrations in Age-Related Cataract ..... 91
2.4.2 The Change in Higher Order Aberrations Arising from ..... 92 Cataract Extraction and Intra-ocular Lens Implantation
2.4.3 Comparison of the Higher Order Aberrations Obtained ..... 93
Prior to, and Following IOL Implantation, with Those in Less Severe Cataract and in Eyes with Clear Media
2.5 Logistics ..... 94
CHAPTER 3: WAVEFRONT ABERRATIONS IN AGE-RELATED ..... 97
CATARACT
3.1 Introduction ..... 97
3.2 Aims ..... 98
3.3 Methods ..... 99
3.3.1 Case Series ..... 99
3.3.2 Recruitment and Experimental Procedures ..... 100
3.3.2.1 Objective Refraction ..... 101
3.3.2.2 Subjective Refraction ..... 101
3.3.2.3 Spherical Equivalent Refraction (SE) ..... 101
3.3.2.4 Contrast Sensitivity (CS) ..... 101
3.3.2.5 Corneal Endothelial Cell Density (CECD) ..... 103
3.3.2.6 Ophthalmological Evaluation ..... 104
3.3.2.7 Cataract Classification ..... 105
3.3.2.8 Measurement of Higher Order Aberrations, of ..... 106 Central Corneal Curvature and of Dilated Pupil Diameter
3.3.2.9 Dilated Pupil Diameter ..... 107
3.3.2.10 Biometry, Ocular Axial Length, Tonometry and ..... 108
Gonioscopy
3.4 Analysis ..... 109
3.5 Results ..... 111
3.5.1 Characteristics of the Case Series ..... 111
3.5.1.1 Age and Gender ..... 111
3.5.1.2 Cataract Type and Severity ..... 112
3.5.1.3 Spherical Equivalent Refraction ..... 112
3.5.1.4 Distance Visual Acuity ..... 114
3.5.1.5 Near Visual Acuity ..... 115
3.5.1.6 Contrast Sensitivity ..... 117
3.5.1.7 Dilated Pupil Diameter ..... 118
3.5.1.8 Mean Corneal Curvature ..... 118
3.5.1.9 Flattest Corneal Curvature ..... 119
3.5.1.10 Corneal Endothelial Cell Density ..... 120
3.5.1.11 Axial Length ..... 121
3.5.1.12 Higher Order Aberrations ..... 122
3.5.1.12.1 Total Component of the Total HOA ..... 122
3.5.1.12.2 Total Component of the Tilt (S1) HOA ..... 123
3.5.1.12.3 Total Component of the High HOA ..... 124
3.5.1.12.4 Total Component of the T.Coma HOA ..... 125
3.5.1.12.5 Total Component of the T.Trefoil HOA ..... 126
3.5.1.12.6 Total Component of the T.4Foil HOA ..... 127
3.5.1.12.7 Total Component of the T.Sph HOA ..... 128
3.5.1.12.8 Total Component of the HiAstig HOA ..... 129
3.5.2 Explanatory Analysis of Associations between the ..... 130
Demographic, Structural and Functional Variables and
each of the Three Components of each of the Eight HOAs
3.5.2.1 Age and Gender ..... 131
3.5.2.2 Distance Visual Acuity ..... 133
3.5.2.3 Near Visual Acuity ..... 133
3.5.2.4 Contrast Sensitivity ..... 133
3.5.2.5 Dilated Pupil Diameter ..... 138
3.5.2.6 Mean Corneal Curvature ..... 138
3.5.2.7 Flattest Corneal Curvature ..... 140
3.5.2.8 Corneal Endothelial Cell Density ..... 140
3.5.2.9 Spherical Equivalent Refraction ..... 141
3.5.2.10 Axial Length ..... 141
3.5.2.11 Cataract Type ..... 144
3.6 Discussion ..... 151
CHAPTER 4: THE CHANGE IN HIGHER ORDER ABERRATIONS ..... 159
ARISING FROM CATARACT EXTRACTION AND INTRAOCULAR
LENS IMPLANTATION
4.1 Introduction ..... 159
4.2 Aims ..... 160
4.2.1 Primary Aim ..... 160
4.2.2 Secondary Aims ..... 160
4.3 Methods ..... 161
4.3.1 Experimental Procedures ..... 161
4.4 Analysis ..... 162
4.5 Results ..... 163
4.5.1 Case Series ..... 163
4.5.2 Characteristics of Case Series at the First Follow-up ..... 165
Examination
4.5.2.1 Age and Gender ..... 165
4.5.2.2 IOL and Surgeon ..... 166
4.5.2.3 Spherical Equivalent Refraction ..... 167
4.5.2.4 Distance Visual Acuity ..... 168
4.5.2.5 Near Visual Acuity ..... 169
4.5.2.6 Contrast Sensitivity ..... 170
4.5.2.7 Dilated Pupil Diameter ..... 170
4.5.2.8 Mean Corneal Curvature ..... 172
4.5.2.9 Flattest Corneal Curvature ..... 173
4.5.2.10 Corneal Endothelial Cell Density ..... 175
4.5.2.11 Higher Order Aberrations ..... 175
4.5.2.11.1 Total Component of the Total HOA ..... 176
4.5.2.11.2 Total Component of the Tilt (S1) HOA ..... 177
4.5.2.11.3 Total Component of the High HOA ..... 177
4.5.2.11.4 Total Component of the T.Coma HOA ..... 178
4.5.2.11.5 Total Component of the T.Trefoil HOA ..... 179
4.5.2.11.6 Total Component of the T.4Foil HOA ..... 179
4.5.2.11.7 Total Component of the T.Sph HOA ..... 181
4.5.2.11.8 The Total Component of the HiAstig ..... 181
4.5.3 Explanatory Analysis of Associations between the ..... 182
Demographic, Structural and Functional Variables andeach of the Three Components of each of the Eight HOAsObtained at the First Follow-up Examination
4.5.3.1 Age ..... 183
4.5.3.2 Distance Visual Acuity ..... 183
4.5.3.3 Near Visual Acuity ..... 184
4.5.3.4 Contrast Sensitivity ..... 184
4.5.3.5 Dilated Pupil Diameter ..... 184
4.5.3.6 Mean Corneal Curvature ..... 186
4.5.3.7 Flattest Corneal Curvature ..... 187
4.5.3.8 Corneal Endothelial Cell Density ..... 188
4.5.3.9 Spherical Equivalent Refraction ..... 191
4.5.4 Characteristics of the Case Series for the Investigation of the ..... 191
Change in the HOAs from the Pre-operative to the First Follow-up Examinations
4.5.4.1 Spherical Equivalent Refraction ..... 191
4.5.4.2 Distance Visual Acuity ..... 192
4.5.4.3 Near Visual Acuity ..... 193
4.5.4.4 Contrast Sensitivity ..... 195
4.5.4.5 Dilated Pupil Diameter ..... 198
4.5.4.6 Mean Corneal Curvature ..... 199
4.5.4.7 Flattest Corneal Curvature ..... 201
4.5.4.8 Corneal Endothelial Cell Density ..... 203
4.5.4.9 Higher Order Aberrations ..... 204
4.5.4.9.1 Total Component of the Total HOA ..... 204
4.5.4.9.2 Total Component of the Tilt (S1) HOA ..... 204
4.5.4.9.3 Total Component of the High HOA ..... 206
4.5.4.9.4 Total Component of the T.Coma HOA ..... 208
4.5.4.9.5 Total Component of the T.Trefoil HOA ..... 208
4.5.4.9.6 Total Component of the T.4Foil HOA ..... 209
4.5.4.9.7 Total Component of the T.Sph HOA ..... 210
4.5.4.9.8 Total Component of the HiAstig HOA ..... 212
4.5.5 Explanatory Analysis of Associations between the ..... 214
Confounding Variables, the Change in the Appropriate
Demographic, Structural and Functional Variables from the
Pre-operative to the First Follow-up Examination and theCorresponding Change in each of the Three Components ofeach of the Eight HOAs
4.5.5.1 Age and Gender ..... 214
4.5.5.2 Surgeon ..... 214
4.5.5.3 Type of Intra Ocular Lens ..... 216
4.5.5.4 Interval from the Pre-operative Examination ..... 217 to the First Follow-up Examination
4.5.5.5 Interval from the Pre-operative Examination ..... 217to Surgery
4.5.5.6 Distance Visual Acuity ..... 220
4.5.5.7 Near Visual Acuity ..... 220
4.5.5.8 Contrast Sensitivity ..... 220
4.5.5.9 Dilated Pupil Diameter ..... 221
4.5.5.10 Mean Corneal Curvature ..... 224
4.5.5.11 Flattest Corneal Curvature ..... 230
4.5.5.12 Corneal Endothelial Cell Density ..... 235
4.5.5.13 Spherical Equivalent Refraction ..... 236
4.5.5.14 Cataract Type ..... 237
4.6 Discussion ..... 238
CHAPTER 5: THE HIGHER ORDER ABERRATIONS, DETERMINED ..... 248
AT THE SECOND FOLLOW-UP EXAMINATION, ARISING
FROM CATARACT EXTRACTION AND IOL IMPLANTATION
5.1 Introduction ..... 248
5.2 Aims ..... 248
5.2.1 Primary Aim ..... 248
5.2.2 Secondary Aims ..... 249
5.3 Methods ..... 249
5.3.1 Experimental Procedures ..... 249
5.4 Analysis ..... 250
5.5 Results ..... 250
5.5.1 Case Series ..... 250
5.5.2 Characteristics of Case Series at the Second Follow-up ..... 250
Examination
5.5.2.1 Age and Gender ..... 250
5.5.2.2 IOL and Surgeon ..... 253
5.5.2.3 Spherical Equivalent Refraction ..... 254
5.5.2.4 Distance Visual Acuity ..... 255
5.5.2.5 Near Visual Acuity ..... 255
5.5.2.6 Contrast Sensitivity ..... 257
5.5.2.7 Dilated Pupil Diameter ..... 259
5.5.2.8 Mean Corneal Curvature ..... 259
5.5.2.9 Flattest Corneal Curvature ..... 260
5.5.2.10 Corneal Endothelial Cell Density ..... 261
5.5.2.11 Higher Order Aberrations ..... 261
5.5.2.11.1 Total Component of the Total HOA ..... 262
5.5.2.11.2 Total Component of the Tilt (S1) HOA ..... 263
5.5.2.11.3 Total Component of the High HOA ..... 263
5.5.2.11.4 Total Component of the T.Coma HOA ..... 264
5.5.2.11.5 Total Component of the T.Trefoil HOA ..... 264
5.5.2.11.6 Total Component of the T.4Foil HOA ..... 265
5.5.2.11.7 Total Component of the T.Sph HOA ..... 265
5.5.2.11.8 Total Component of the HiAstig HOA ..... 267
5.5.3 Explanatory Analysis of Associations between the ..... 268Demographic, Structural and Functional Variables andeach of the Three Components of each of the Eight HOAsObtained at the Second Follow-up Examination
5.5.3.1 Age ..... 268
5.5.3.2 Distance Visual Acuity ..... 270
5.5.3.3 Near Visual Acuity ..... 271
5.5.3.4 Contrast Sensitivity ..... 272
5.5.3.5 Dilated Pupil Diameter ..... 273
5.5.3.6 Mean Corneal Curvature ..... 273
5.5.3.7 Flattest Corneal Curvature ..... 274
5.5.3.8 Corneal Endothelial Cell Density ..... 274
5.5.3.9 Spherical Equivalent Refraction ..... 275
5.5.4 Characteristics of the Case Series for the Investigation of the ..... 275
Change in the HOAs from the Pre-operative to the Second
Follow-up Examinations
5.5.4.1 Spherical Equivalent Refraction ..... 275
5.5.4.2 Distance Visual Acuity ..... 277
5.5.4.3 Near Visual Acuity ..... 278
5.5.4.4 Contrast Sensitivity ..... 279
5.5.4.5 Dilated Pupil Diameter ..... 282
5.5.4.6 Mean Corneal Curvature ..... 283
5.5.4.7 Flattest Corneal Curvature ..... 285
5.5.4.8 Corneal Endothelial Cell Density ..... 286
5.5.4.9 Higher Order Aberrations ..... 287
5.5.4.9.1 Total Component of the Total HOA ..... 288
5.5.4.9.2 Total Component of the Tilt (S1) HOA ..... 289
5.5.4.9.3 Total Component of the High HOA ..... 289
5.5.4.9.4 Total Component of the T.Coma HOA ..... 290
5.5.4.9.5 Total Component of the T.Trefoil HOA ..... 292
5.5.4.9.6 Total Component of the T.4Foil HOA ..... 292
5.5.4.9.7 Total Component of the T.Sph HOA ..... 293
5.5.4.9.8 Total Component of the HiAstig HOA ..... 295
5.5.5 Explanatory Analysis of Associations between the ..... 297
Confounding Variables, the Change in the Appropriate Demographic, Structural and Functional Variables from the Pre-operative to the Second Follow-up Examination and the Corresponding Change in each of the Three Components of each of the Eight HOAs
5.5.5.1 Age and Gender ..... 298
5.5.5.2 Surgeon ..... 298
5.5.5.3 Type of Intra Ocular Lens ..... 298
5.5.5.4 Interval from the Pre-operative Examination ..... 298to Surgery
5.5.5.5 Interval from the Pre-operative Examination ..... 301 to the Second Follow-up Examination
5.5.5.6 Distance Visual Acuity ..... 302
5.5.5.7 Near Visual Acuity ..... 302
5.5.5.8 Contrast Sensitivity ..... 302
5.5.5.9 Dilated Pupil Diameter ..... 308
5.5.5.10 Mean Corneal Curvature ..... 310
5.5.5.11 Flattest Corneal Curvature ..... 311
5.5.5.12 Corneal Endothelial Cell Density ..... 314
5.5.5.13 Spherical Equivalent Refraction ..... 314
5.5.5.14 Cataract Type ..... 316
5.6 Discussion ..... 317
CHAPTER 6: COMPARISON OF THE HIGHER ORDER ..... 324
ABERRATIONS, OBTAINED PRE-AND POST-OPERATIVELY, WITH
THOSE IN 'LESS SEVERE' CATARACT AND WITH THOSE
EXHIBITING CLEAR MEDIA
6.1 Introduction ..... 324
6.2 Aim ..... 325
6.3 Methods ..... 326
6.3.1 Case Series ..... 326
6.3.1.1 Pre- and Post-operative Case Series ..... 326
6.3.1.2 'Less Severe' Cataract Case series ..... 326
6.3.1.3 Clear Media Case Series ..... 327
6.3.2 Experimental Procedures ..... 327
6.4 Results ..... 329
6.4.1 Characteristics of Case Series ..... 329
6.4.1.1 Pre- and Post-Operative Case Series ..... 329
6.4.1.1.1 Pre-Operative Eyes ..... 329
6.4.1.1.1.1 Age and Gender ..... 329
6.4.1.1.1.2 Spherical Equivalent ..... 330
Refraction
6.4.1.1.1.3 Distance Visual Acuity ..... 331
6.4.1.1.1.4 Near Visual Acuity ..... 331
6.4.1.1.1.5 Mean Corneal ..... 333
Curvature
6.4.1.1.1.6 Flattest Corneal ..... 333Curvature
6.4.1.1.2 Post-Operative Eyes ..... 334
6.4.1.1.2.1 Spherical Equivalent ..... 334Refraction
6.4.1.1.2.2 Distance Visual Acuity ..... 334
6.4.1.1.2.3 Near Visual Acuity ..... 336
6.4.1.1.2.4 Mean Corneal ..... 336Curvature
6.4.1.1.2.5 Flattest Corneal ..... 337
Curvature
6.4.1.2 'Less Severe’ Cataract Case Series ..... 338
6.4.1.2.1 Age and Gender ..... 338
6.4.1.2.2 Cataract Type and Severity ..... 338
6.4.1.2.3 Spherical Equivalent Refraction ..... 339
6.4.1.2.4 Distance Visual Acuity ..... 340
6.4.1.2.5 Near Visual Acuity ..... 340
6.4.1.2.6 Mean Corneal Curvature ..... 341
6.4.1.2.7 Flattest Corneal Curvature ..... 342
6.4.1.3 Clear Media Case Series ..... 342
6.4.1.3.1 Age and Gender ..... 342
6.4.1.3.2 Spherical Equivalent Refraction ..... 343
6.4.1.3.3 Distance Visual Acuity ..... 343
6.4.1.3.4 Near Visual Acuity ..... 345
6.4.1.3.5 Mean Corneal Curvature ..... 345
6.4.1.3.6 Flattest Corneal Curvature ..... 346
6.4.2 Higher Order Aberrations ..... 346
6.4.3 Comparison of the HOAs between Case Series ..... 359
6.4.3.1 Pre- and Post-operative Case Series ..... 359
6.4.3.2 Pre-operative and 'Less Severe' Cataract ..... 359
Case Series
6.4.3.3 Post-operative and Clear Media Case Series ..... 361
6.4.3.4 Post-operative and 'Less Severe' Cataract ..... 362
Case Series
6.4.3.5 Pre-operative and Clear Media Case Series ..... 363
6.4.3.6 'Less Severe' Cataract and Clear Media ..... 363
Case Series
6.4.4 Explanatory Analysis of Associations between Corneal ..... 364 Curvature; Spherical Equivalent Refraction; Distance and Near Visual Acuity; and each of the Three Components of each of the Eight HOAs for the 'Less Severe' Cataract Case Series and the Clear Media Case Series
6.4.4.1 'Less Severe’ Cataract Case Series ..... 364
6.4.4.1.1 Distance Visual Acuity ..... 364
6.4.4.1.2 Near Visual Acuity ..... 365
6.4.4.1.3 Mean and Flattest Corneal Curvature ..... 365
6.4.4.1.4 Spherical Equivalent Refraction ..... 365
6.4.4.1.5 Cataract Type ..... 365
6.4.4.2 Clear Media Case Series ..... 367
6.4.4.2.1 Distance Visual Acuity ..... 368
6.4.4.2.2 Near Visual Acuity ..... 368
6.4.4.2 3 Mean and Flattest Corneal Curvature ..... 368
6.4.4.2.4 Spherical Equivalent Refraction ..... 368
6.5 Discussion ..... 369
CHAPTER 7: CONCLUSIONS AND FUTURE WORK ..... 374
REFERENCES ..... 385

## LIST OF ABBREVIATIONS

| ANOVA | Analyses of Variance |
| :---: | :---: |
| ARVO | Association for Research in Vision and Ophthalmology |
| ASA | Aberration Smart Ablation |
| ASC | Anterior subcapsular cataract |
| C | Cortical cataract |
| CC | Corneal Curvature |
| CCD | Charged Coupled Device |
| CECD | Corneal Endothelial Cell Density |
| COAS | Complete Ophthalmic Analysis System |
| cpd | Cycles per degree |
| CRT | Cathode Ray Tube |
| CS | Contrast Sensitivity |
| CSF | Contrast Sensitivity Function |
| Epi-LASIK | Epipolis Laser in Keratomileusis |
| FACT | Functional Acuity Contrast Test |
| HOA | Higher Order Aberration |
| ICL | Implantable Collamer Lens |
| IOL | Intraocular Lens |
| IOP | Intraocular Pressure |
| IQR | Inter-quartile Range |
| IR | Iris Recognition |
| LASEK | Laser Epithelial Keratomileusis |
| LASIK | Laser-Assisted in Situ Keratomileusis |
| LED | Light Emitting Diode |
| LOCS | Lens Opacity Classification System |
| Log | Logarithm |


| MAR | Minimum Angle of Resolution |
| :--- | :--- |
| MTF | Modulation Transfer Function |
| NC | Nuclear Colour cataract |
| NO | Nuclear Opalescence cataract |
| OPD | Optical Path Difference |
| P or PSC | Posterior subcapsular cataract |
| PMCD | Pellucid Marginal Corneal Degeneration |
| PRK | Photorefractive Keratotomy |
| PSD | Position Sensitive Detector |
| PSF | Rigid Gas Permeable |
| RGP | Radial Keratotomy |
| RK | Root Mean Square |
| RMS | Retinitis Pigmentosa |
| RP | Statistical Analysis Software |
| SAS | Subcapsular cataract |
| SC | Spherical Equivalent |
| SE | Spatial Light Modulator |
| SLM | Wavefront-Supported Corneal Ablation |
| WASCA | Wavefront Guided |
| WFG | Poren |

## CHAPTER ONE

## INTRODUCTION

The purpose of this chapter is threefold: firstly, to provide an overview of the basic geometrical optics associated with lower and with higher order aberrations, particularly those of wavefront aberrometry; secondly, to review common methods for measurement of these aberrations i.e., aberrometry; and thirdly, to review the clinical utility of wavefront aberrometry. The first part of the chapter draws heavily upon a number of standard texts (Roddier 1999; MacRae et al 2001; Ray 2002; Tsubota et al 3003; Krueger and Applegate 2003; Porter 2006; Melki and Azar 2006).

### 1.1 Background

The images seen by the eye are made up of light reflected from observed objects. Because light rays diverge in all directions from their source, the set of rays that reach the eye from each point on the source must be focused. The formation of focused images on the retina depends upon the refraction (bending) of light by the cornea and by the crystalline lens. Light enters the eye through, and is converged by, the cornea. The cornea is responsible for most of the refraction within the eye, creating an inverted image on the retina that is reverted by the brain. The crystalline lens has considerably less refractive power than the cornea; however, the power of the lens is adjustable. The lens changes shape, and therefore power, via the ciliary processes and the ciliary muscle, thereby, enabling the focusing of objects at different distances (accommodation). Once the image is focused on the retina, the image is relayed via the optic nerve to the brain. The tear film, the aqueous
humour and the vitreous humour are also considered to be optical components; however, their contribution to refraction by the eye is minimal.

The eye exhibits certain functional and structural imperfections in its optical components. These imperfections induce aberrations into the image (Howland and Howland 1976; Howland 2002). Optical aberrations are classified into chromatic and monochromatic aberrations.

### 1.1.1 Chromatic Aberrations

In general, the speed of light in a medium depends upon both the medium and the wavelength of the light; i.e. the refractive index of the medium varies with wavelength. A prism can be used to split a beam of white light into its constituent spectral colours. Each wavelength of light is refracted through a different angle causing a phenomenon known as dispersion. Chromatic aberrations are those departures from perfect imaging that are due to dispersion. There are two types of chromatic aberration: longitudinal and transverse chromatic aberration.

### 1.1.1.1 Longitudinal Chromatic Aberration

Longitudinal chromatic aberration, also known as axial colour, is the inability of a lens to focus different colours in the same focal plane (Thibos 1991). For any specific given point on the optical axis, the foci of the different wavelengths are displaced along the axis in the longitudinal direction. This leads to the image size and the focal point for each major wavelength group to appear slightly different. This behaviour is illustrated in Figure 1.1
for a distant light source. In this illustration, only the green wavelength is in sharp focus on the focal plane. The blue and red wavelengths have a circle of confusion in the focal plane and are not sharply imaged. Longitudinal chromatic aberration can be further minimized by using an achromatic lens, or achromat, in which materials with differing dispersions are assembled together to form a compound lens. The most common type is an achromatic doublet. A doublet is a type of lens made up of two simple lenses attached together. The lenses are made from glass with different refractive indices, usually Crown and Flint glass, and different amounts of dispersion. This design reduces the amount of chromatic aberration over a certain range of wavelengths, but does not produce a perfect correction.


Figure 1.1. Longitudinal chromatic aberration. The chromatic aberration of a single lens causes different wavelengths of light to have differing focal lengths. Each wavelength is refracted by the lens through a different angle causing dispersion. The focal planes of the various colours do not coincide at the same focal point on the optical axis, but are displaced along the axis in the longitudinal direction. Only the green wavelength is in sharp focus on the focal plane. The blue and red wavelengths each have a circle of confusion on the focal plane and are, therefore, not sharply imaged.

### 1.1.1.2 Transverse chromatic aberration

Transverse chromatic aberration is also known as lateral colour and refers to sideward displaced focus. Obliquely incident light causes transverse chromatic aberration. In the absence of axial colour, all colours are in focus in the same plane, but the image magnification depends upon the wavelength. This behaviour is illustrated in Figure 1.2.


Figure 1.2. Transverse chromatic aberration. Oblique light refracted by the lens causes different wavelengths to focus at different distances off-axis resulting in images of different size for the different wavelengths. The size of the image varies from one wavelength to the next; all images are in the same plane.

Lateral colour implies that the focal length depends upon the wavelength and is determined by the distance from the rear principal plane to the image plane. The focal length will depend upon the wavelength even when all the images are in the same plane.

### 1.1.2 Monochromatic Aberrations

Monochromatic aberrations can be subdivided into low order aberrations i.e., spherical refractive error, cylindrical refractive error and higher order aberrations i.e., spherical aberration, coma and more complex aberrations.

### 1.1.2.1 Spherical Refractive Error

Refractive error is a manifestation of the relationship between the optical components of the eye (i.e., the curvatures, refractive indices and the distances between the cornea, aqueous, crystalline lens and vitreous) and the overall axial length of the eye. Optical defocus occurs when light is focused in front of, or behind, the retina.

### 1.1.2.1.1 Myopia

Myopia is the visual condition in which only nearby objects appear in focus; distant objects appear blurred. In a 'normal' or emmetropic eye, distant objects are naturally in focus; i.e., the focal length of the optics of the eye is appropriate for the length of the eye along the optical axis. Parallel rays of light emerging from a distant object are refracted just enough to focus and form a clear image on the retina.

In a myopic eye, as illustrated in Figure 1.3, the essentially parallel rays from distant objects are refracted too strongly and form an image in front of the retina when accommodation is relaxed. In other words, the focal length of the optics of the relaxed eye is too short for the physical length of the eye. The more severe the myopia, the further the image is from the retina. Myopia is, itself, best thought of as the final consequence of
variations in a number of biological, sometimes pathological, factors influencing refraction in the eye (Atchison et al 2005). Myopia may result, for example, from an abnormally steep cornea, a crystalline lens with greater than average thickness and power, or an axial elongation of the globe. Alternatively, it may result from a mismatch of these optical components even though each individual component is in the normal range of values. When myopia is attributed to an increase in the axial length, it is called axial myopia. Myopia attributed to an anomaly of the refractive elements of the eye is called refractive myopia.


Figure 1.3. Myopia. The globe is too long, or the optical power of the relaxed eye is too great for its length, such that parallel rays of light entering the eye are focused at the focal point, F , in the vitreous rather than on the retina creating a blurred image of distant objects.

The most common way to correct myopia is through the use of negatively powered lenses which compensate for the excessive positive power of the myopic eye. It may also be corrected by refractive surgery such as photorefractive keratotomy (PRK), laser-assisted in situ keratomileusis (LASIK) or clear lens replacement therapy (Thompson et al 2002;

Hill 2003; Wutthiphan 2005; Li et al 2009; Iribarren et al 2010; Durrie et al 2010). Practitioners and advocates of alternative therapies often recommend eye exercises and relaxation techniques such as the Bates method. However, there is no evidence-base for the efficacy of these latter practices.

### 1.1.2.1.2 Hyperopia

Hyperopia is the visual condition in which distant objects are seen clearly, but close objects are blurred. In the hyperopic eye, as illustrated in Figure 1.4, parallel rays of light from a distant object converge to a focus behind the retina when accommodation is relaxed. Hyperopia can occur because the axial length of the eye is normal but the focal length is longer than normal, i.e., the refractive power of the eye is too weak, or because the focal length is normal but the axial length is shorter than normal, i.e., the length of the globe is too short (Moore et al 2006). As with myopia, low amounts of hyperopia can occur with axial lengths and focal powers within the normal ranges for emmetropic eyes. Moderate to high amounts of hyperopia are usually due to axial lengths shorter than the emmetropic eye (Llorente et al 2004).

Hyperopia is usually present at birth. The refractive status tends to emmetropia as the axial length increases during the growth process (Hung 2000). Young adults and children with mild to moderate hyperopia see close objects clearly because the crystalline lens is able to accommodate and, as a consequence of the change in shape of the lens, moves the focus back onto the retina thereby obtaining a clear image (Kliegman et al 2007).

As a person ages, the ability to accommodate lessens (presbyopia) and refractive correction is needed to facilitate focusing on close objects. The effect of hyperopia varies
greatly and depends upon the magnitude of the hyperopia, the age of the individual, the status of the accommodative and convergence system and the demands on the visual system.


Figure 1.4. Hyperopia. Parallel rays of light entering the eye reach a focal point, F, behind the plane of the retina, while accommodation is maintained in a state of relaxation. Hyperopia may occur because the refractive power of the eye is too weak and/ or because the axial length is too short.

Uncorrected hyperopia can cause asthenopia ('eye strain') (Jamali et al 2009). The most common way to correct hyperopia is through the use of positive lenses, which compensate for the lack of positive power of the hyperopic eye, or surgical correction such as PRK, LASIK, or clear lens replacement therapy (Thompson et al 2002; Hill 2003; Wutthiphan 2005; Li et al 2009; Iribarren et al 2010; Durrie et al 2010).

### 1.1.2.2 Cylindrical Refractive Error - off-axis and on-axis

When a given object lies an appreciable distance from the optical axis, the cone of rays will strike the lens in an asymmetrical way, causing an aberration known as astigmatism. The plane which contains both the optical axis and the chief ray, which is defined as a special ray emanating from an off-axis point source that passes through the centre of the lens, is called the meridional, or tangential, plane. The sagittal, or equatorial, plane is defined as the plane containing the chief ray which is also perpendicular to the tangential plane. The aberration is manifested by the off-axis image of a specimen point that will appear as a line, or ellipse, instead of a point. Depending upon the angle of the off-axis rays entering the lens, the line image may be formed in two different directions, tangentially (meridionally) or sagittally (equatorially). The image will diminish in definition, in detail and in contrast which all increase as the distance from the centre increases.

When the object is on the optical axis, the cone of rays is symmetrical with respect to the spherical surfaces of the lens. In this case, the meridional and the sagittal planes are the same, and the ray formation in all the planes containing the optical axis is identical. In the absence of any spherical aberration, all of the focal lengths are the same and all of the rays arrive at a single focus. When the object is located off-axis, the rays enter the lens at an oblique angle and the characteristics of the ray bundle will be different in the meridional and sagittal planes. Because of this, the focal lengths in these planes will be different. The difference in the focal lengths depends effectively on the power of the lens and the angle at which the rays are inclined. This is known as the astigmatic difference and it increases rapidly as the rays become more oblique.

Since there are two different focal lengths, the conical bundle of rays changes after being refracted. In Figure 1.5, the beam is initially circular as it leaves the lens, but gradually becomes elliptical with the major axis in the sagittal plane until, at the tangential focus, $F_{t}$, the ellipse becomes a line. All the rays from the object traverse this line which is known as the primary image. Beyond this image, the beam rapidly opens out to an elliptical form until it becomes circular again. At this latter location, the image is a circular blur known as the circle of least confusion. Moving further away from the lens, the cross section of the beam again deforms into a line, called the secondary image, in the meridional plane at the sagittal focus, $F_{s}$.

Figure 1.5 Overleaf. Astigmatic aberration. Off-axis light rays passing through the tangential and sagittal planes which are used to define the geometry of astigmatism aberration. At the circle of least confusion, positioned between the tangential line image and the sagittal line image, the major and minor axes of the ellipse are equal and the image approaches a circular geometry. Modified from:
http://www.google.co.il/imgres?imgurl=http://www.microscopyu.com/articles/optics/imag es/aberrations/astigfigure2.jpg\&imgrefurl=http://www.microscopyu.com/tutorials/java/ab errations/astigmatism/index.html\&usg=___knbhIQIITxTbReyAWh_1nsWew=\&h=309\& w=375\&sz=26\&hl=iw\&start=3\&zoom=1\&tbnid=CM11SJMcfI2TFM:\&tbnh=101\&tbnw =122\&ei=NLzMT9DIII3rOZn0jfkP\&prev=/images\%3Fq\%3Dcoma\%2Baberration\%2Bco rrection\%26hl\%3Diw\%26sa\%3DX\%26tbm\%3Disch\&itbs=1 Accessed 21.11.2011.


In the absence of spherical aberration and coma, a lens that is free of astigmatism offers stigmatic imaging, i.e., points in object space are imaged as true points in image space. Astigmatism, however, does not offer stigmatic imaging. The astigmatic lens forms a sharp image of either the sagittal or the tangential foci. The typical example of astigmatism, a spoked wheel, is illustrated in Figure 1.6. A distortion free lens forms a sharp image (left wheel) which is illustrated in Figure 1.6. An astigmatically aberrated lens may be focused to form a sharp image of the spokes (middle wheel) whilst the rims, which have a tangential orientation, remain blurred. When the rim is in focus, the spokes are blurred. The kind of astigmatism commonly encountered in the eye results from different corneal and/ or lens curvatures in different planes. The vertical and horizontal planes are identified as tangential and sagittal meridia. The optical system is incapable of forming a point image for a point object.

The corneal profile and refractive power in one meridian is greater than that of the perpendicular axis (Grosvenor 1989). A steeper curvature in the vertical meridian is defined as with-the-rule astigmatism and in the horizontal meridian as against-the-rule astigmatism.


Figure 1.6. A typical example of astigmatism illustrated by means of a spoked wheel. Offaxis rays refracted by an astigmatic lens cause radial and tangential lines in the object plane to focus sharply at different distances in the image planes. Light from different planes cannot be simultaneously focused clearly. The astigmatic lens can be focused to form a sharp image of either the sagittal or the tangential focus, but not both simultaneously. Left wheel: no astigmatism. Tangential and sagittal planes (spokes and rims) appear sharp and focused separately. In the presence of astigmatism (middle and right wheels) there is a differentiation between the sagittal and tangential foci. Modified from: http://toothwalker.org/about.html Accessed 21.11.2011.

Astigmatism causes difficulties in resolving fine detail. In some cases, vertical lines and objects such as walls may appear to be 'leaning over'. Regular astigmatism can usually be corrected by cylindrical lenses (lenses that have different radii of curvature in two different planes) or by refractive surgery.

Astigmatism is relatively common. A study on the refractive error and ocular development in children from four ethnic groups (African American, Asian, Hispanic and White) revealed that approximately one in three children suffer from at least 1.00 dioptre of
astigmatism (Kleinstein et al 2003). In another study, amongst public and private school children, astigmatism was present in $34 \%$ of cases (Garcia et al 2005). Astigmatism is affected by age: the prevalence of astigmatism increases, and the axis turns to against-therule, with increase in age. This arises from changes in the cornea, lens and vitreous (Gudmundsdottir et al 2000; Asano et al 2005; Morteza 2008; Sawada et al 2008).

Although an individual may not notice mild astigmatism, higher amounts of astigmatism cause symptomatic blurred vision, asthenopia, fatigue and/ or headaches (Xu et al 1996; Sheedy et al 2003).

### 1.1.2.3 Higher Order Aberrations (HOAs)

The more complex aberrations are termed the higher order aberrations.

### 1.1.2.3.1 Spherical Aberration

Spherical aberration is due to the spherical shape of a lens. The aberration for a single, positive lens is illustrated in Figure 1.7. Light passing through the lens close to the optical axis is focused at position, c . The light that traverses the margins of the lens is focused at position, a, closer to the lens and further away from the focal point of the lens. In this way, the focal position depends upon the zone in which the light enters the lens; as the light intersection moves away from the axial focus, the spherical aberration becomes larger. When the marginal focus is closer to the lens than the axial focus, such as exhibited by the positive lens in Figure 1.7, the aberration is called under-corrected spherical aberration. Conversely, when the marginal focus is located beyond the axial focus, the lens is said to exhibit over-corrected spherical aberration. From Figure 1.7, it appears that a spherically
aberrated lens has no well-defined focus. At any position behind the lens, intersected rays of light will create a finite circle of least confusion rather than a true image point. However, there is a geometrically "best" focus (Conrady 1985) which corresponds to the circle of least confusion at position, $b$. This position is where the ensemble of light rays has a minimum cross section. The image of a point formed by a lens with spherical aberration is usually a bright dot surrounded by a halo of light. The effect of spherical aberration on an extended image is to soften the contrast and to blur its details (Smith 2000).

An interesting phenomenon occurs when an artificial pin hole is placed next to the lens in Figure 1.7. If the aperture is closed so as to block the marginal rays, the best focus moves to the right. For small lens apertures, the best focus is found at position, c , and gives a better focus, i.e., the circle of least confusion is a smaller circle than the circle of least confusion at full aperture. The pupil size therefore plays an important role in the way spherical aberration affects vision (de Valois 1990)

Spherical aberration is uniform over the field in that the longitudinal focus difference between the lens margins and the centre does not depend upon the obliquity of the incident light and thus differs from monochromatic aberrations.

The crystalline lens develops continuously with age (Kuroda et al 2002). The growth takes place at the periphery where old tissue is pushed and compressed towards the centre of the lens, causing an increase in the refractive index of the lens from cortex to core. The variation of refractive index, with a possible consequent variation in lens asphericity, can affect spherical aberration. Light passing through the periphery of the lens has focal lengths that are longer than the paraxial beams and will result in negative or overcorrected spherical aberration and will compensate for, and reduce, spherical aberration.


Figure 1.7. Spherical aberration. Top: Illustration of under-corrected spherical aberration. The margins of the lens have a shorter focal length than the centre. Light entering the lens far from the optical axis of the lens intersects at position, a, closer to the lens. As light enters the lens closer to the optical axis of the lens, the intersection moves away to position, c. It, therefore, does not produce a perfect focal point. The geometrically best focus is obtained at position, $b$, forming a circle of least confusion. Bottom: A simulated illustration of spherical aberration in an optical system with a circular, unobstructed aperture admitting a monochromatic point source. Left to right, the focus moves from being inside focus to outside focus.

Bottom, from: http://en.wikipedia.org/wiki/File:Spherical-aberration-disk.jpg Accessed 21.11.2011.

The opposite case is positive or under-corrected spherical aberration. The average aberration varies from positive to negative. In the young eye, the optical characteristics of the young crystalline lens compensate for the positive spherical aberration of the cornea, thereby reducing total aberration (Artal et al 2001). With aging, the optical performance of the eye progressively declines (Guirao et al 1999). The amount of spherical aberration increases with age (Artal et al 1993); the magnitude of the spherical aberration of the aging eye changes significantly mainly because of the increase in the spherical aberration of the internal optics (Amano et al 2004), with a reduction in the negative spherical
aberration of the lens. This loss of balance between corneal and lenticular spherical aberration is largely responsible for the degradation of optical quality in the aging eye.

### 1.1.2.3.2 Coma Aberration

Coma aberration derives its name from the comet-like appearance of the aberrated image. Rays of light which pass through the centre of a lens can be focused to a point. If the light travels through the lens off-axis (at an oblique angle to the axis) the light will not focus to a point and resembles a 'fuzzy' circle. As illustrated in Figure 1.8, the further off-axis, the larger the circle, giving objects a trailing 'comet-like' blur directed away from the optic axis (hence the name 'coma'). In general, a bundle of parallel rays passing through the lens at an oblique angle and at a fixed distance from the centre of the lens are focused to a ring-shaped image on the focal plane, known as a comatic circle (Figure 1.9). Each concentric zone of a lens forms such a comatic circle. The sum of all these circles results in a V-shaped or comet-like flare known as a comatic patch. A lens with considerable coma produces a comparatively sharp image in the centre of the field which becomes increasingly blurred toward the edges. Even if spherical aberration is corrected and the lens brings all rays to a sharp focus on-axis, a lens may still exhibit coma off-axis.

As with spherical aberration, coma can be minimized (and in some cases eliminated) by choosing the curvature of the two lens surfaces to match the aberration. Lenses in which both spherical aberration and coma are minimized are called bestform lenses. Alternatively, a sharper image may be produced by placing, judiciously, an aperture in an optical system to eliminate the more marginal rays. Coma is often considered a problematic aberration due to the asymmetry it produces in images.


Figure 1.8. The geometry of formation of a comatic patch, C , by refraction through zones 1 and 2 of a lens. Light from an off-axis object travels through paraxial, zonal and marginal regions of the lens. The image produces a series of asymmetrical spot shapes of increasing size that result in a trailing "comet-like" blur directed away from the optic axis which appears as a fuzzy circle. The further off-axis, the larger the circle.


Figure 1.9. Coma aberration. The bundle of parallel rays of light passing through a lens at an oblique angle to the optical axis forms a ring-shaped image in the focal plane, known as a comatic circle. The sum of all these circles results in a V-shaped or comet-like flare. Modified from: http://en.wikipedia.org/wiki/Coma_(optics) Accessed 21.11.2011.

### 1.2 Wavefront Aberration

Higher order aberrations can be identified by the types of distortions acquired by a wavefront of light as it passes through any optical system including the eye.

Since light travels in bundles of rays, a common way to describe an individual wavefront involves considering a bundle of light rays as illustrated in Figure 1.10. This bundle is referred to as the emergent wavefront. The tip of each light ray in the bundle is represented by a specific point and the wavefront, or wavefront map, is created by lines perpendicular to each point and results in a surface which is perpendicular to all the rays in the bundle.


Figure 1.10. The shape of the wavefront is obtained from a perpendicular line to each ray of light in the bundle of light rays thereby creating a new surface. When the rays of light are parallel, the wavefront obtained is a flat straight line normal to the rays of light at any point of intersection (Left). If the rays of light are not parallel, the emerging wavefront will be spherical (Right). The types of deformation can be represented as 2D and/ or 3D topographical maps.

In any optical system, the entrance pupil is the image of the aperture formed by the optics in front of the aperture, while the exit pupil is the image of the aperture formed by the optics behind the aperture. The geometrical ray trace for a distant point object is shown in Figure 1.11. As seen in the Figure, light from the object initially moves toward the entrance pupil whilst the light exiting the optical system appears to come from the exit pupil. The ray trace in Figure 1.11 is given for a system with no aberrations so, after dispersing through the entire system, the wavefront is perfectly spherical and the rays converge to a point. Real optical systems, however, are not aberration free and, therefore, the wavefront (which is an envelope of rays with the same phase) deviates from sphericity. All aberrations introduce phase distortions into the light waves. The light forming the image in Figure 1.11 completely fills the exit pupil and, since the exit pupil is the aperture as seen from the image space in the optical system, all the effects caused by the aberrations in the system are fully contained in the distribution of the light at the exit pupil. The exit pupil, therefore, is the best location to define and to characterize the nature of the light in an image formed by an optical system. Once the distribution of light (including amplitude and phase) is known at the exit pupil, the characteristics of the wavefront can be calculated by different mathematical and optical techniques.

A wavefront is a physical representation of the optical quality of light rays. In traditional geometrical optics, light rays from an object are traced through an optical system to determine the image by computing the optical path of a set of parallel rays entering the optical system. In a perfect optical system, rays entering through different parts of the entrance pupil hit the image plane at the same location. Such light rays originate from one object point and provide information about one image point only (Dave 2004).

As was discussed earlier, when the light beam is 'perfect' in terms of optical quality, the wavefront is either planar (flat) or spherical, i.e., if a planar or spherical wavefront is imaged on the retina with no degradation, the emergent wavefront would again be planar or spherical, respectively, as illustrated in Figure 1.12. When light is degraded by an optical element, the corresponding wavefront is not planar, but has a disrupted shape, as illustrated in Figure 1.13.


Figure 1.11. Geometrical ray trace for an optical system with no aberrations. Light from the object initially heads toward the entrance pupil, while the light exiting the optical system appears to come from the exit pupil. After propagating through the entire system, the wavefronts are perpendicular to the geometrical rays and perfectly spherical and the rays converge to a point. Modified from:
http://scien.stanford.edu/pages/labsite/2003/psych221/projects/03/pmaeda/index.html Accessed 21.11.2011.

Most wavefront sensing devices that assess the lower and the higher order aberrations evaluate the deviations of the emerging wavefront from the regular or 'gold standard' (planar or spherical) wavefront at the exit pupil (Thibos 2000).

These deviations can be quantified in terms of the Optical Path Difference which refers to the difference between either the planar reference plane, or the radius of the reference sphere, and the radius of the aberrated wavefront measured at a given distance orthogonal to the planar surface or at the radius of curvature of the referenced sphere, respectively, multiplied by the index of the medium (Smith 2008).


Figure 1.12. The emergent wavefront of an eye with perfect optics, i.e. no lower and no higher order aberrations. In the absence of aberrations, the emergent wavefronts are planar or spherical.


Figure 1.13. An eye with higher order aberrations. When the eye exhibits a given type of aberration, the emergent wavefront is deformed. In an eye free of aberrations, rays of light (in red) entering the eye, reach a focal point at the fovea. The emerging wavefront will be planar or spherical (red wavefront). In an eye with aberrations, rays of light are distorted (in blue) and do not reach a focal point on the retina. As a consequence the emerging wavefront will be distorted (blue wavefront).

The differences of the aberrated wavefront from the ideal planar/ spherical wavefront (Figure 1.14 and Figure 1.15) are expressed as the wavefront aberration function $\mathrm{W}(\mathrm{x}, \mathrm{y})$ where x, y are transverse coordinates (Dave 2004; Nayori et al 2004; Stifter et al 2004).


Figure 1.14. The optical deviations of the wavefront (in blue) from a reference ('gold standard') planar or spherical wavefront (in red).

The deviations from the 'gold standard' reference wavefront are determined mathematically from the reconstructed emergent wavefront. Such computations reveal different types of deformation of the emerging wavefront caused by the different types of aberrations. Zernike polynomials are used as a common method for describing the different types of aberrations, particularly the higher order aberrations.


Figure 1.15. The Wave Aberration Function, W(x,y), for a distant point object measured along the ray as a function of the transverse coordinates ( $\mathrm{x}, \mathrm{y}$ ) of the ray intersection with a reference sphere centred at the ideal image point. The wave aberration function is the distance from the reference spherical wavefront to the aberrated wavefront in the exit pupil. Modified from:
http://scien.stanford.edu/pages/labsite/2003/psych221/projects/03/pmaeda/index.html Accessed 21.11.2011.

### 1.2.1 Zernike Polynomials

Optical aberrations have historically been characterized by power series expansions where the wave aberration is expressed as the weighted sum of the power series terms at the given corneal location referenced to the (exit) pupil (Thibos et al 2002; Campbell 2003; Dai 2006). Each term in the series is associated with a particular aberration.

Any aberrated wavefront has a complex three-dimensional surface. Zernike polynomials are used to describe such aberrated wavefronts in three-dimensions. Zernike polynomials are composed of a group of basic shapes usually called 'basis functions' or 'terms' or
'modes' (Figure 1.20). Each Zernike polynomial depicts a specific shape which corresponds to a specific optical aberration. Therefore, the whole aberrated wavefront function is described by a weighted sum of the appropriate Zernike basis functions. Each term in the sum is multiplied by an appropriate coefficient which expresses the contribution of the specific aberration. The coefficient, C , is used as a weighting factor which represents how much of a given aberration is included in the aberrated wavefront function, i.e., the coefficient describes the relative strength of the aberration contributed by the given specific term. Since Zernike polynomials are mutually orthogonal (i.e., mathematically independent), any change of the weighted sum (by adding or omitting a polynomial) has no affect on the other polynomials and their coefficients.

Zernike polynomials form a complete set of mathematical functions that are orthogonal over a circle of unit radius and are convenient for serving as a set of basis functions. The sum of the different polynomials describes, precisely, the characteristics of the wavefront. Zernike polynomials are graphically described by solving the Zernike equations at many points on a circular disc or 'unit circle'. The resulting graphs are colour-coded circles that exhibit elevations or depressions at each point (Thibos et al 2000; Applegate et al 2001; Thibos et al 2002).

Zernike polynomials are usually expressed in polar coordinates $(\rho, \theta)$ where $0 \leq \rho \leq 1,0 \leq \theta \leq 2 \pi$ relative to a given circle (of constant diameter) (Figure 1.16). (http://scien.stanford.edu/pages/labsite/2003/psych221/projects/03/pmaeda/index.html) Accessed 21.11.2011.

Pupil Coordinate system


$$
\begin{array}{r}
x=r \cos (\theta) \\
y=r \sin (\theta) \\
\theta=\tan ^{-1}(x / y) \\
r=\left(x^{2}+y^{2}\right)^{1 / 2}
\end{array}
$$

## Normalized Pupil Coordinate System



$$
\begin{array}{r}
\mathrm{x}=\rho \cos (\theta) \\
\mathrm{y}=\rho \sin (\theta) \\
\theta=\tan ^{-1}(\mathrm{x} / \mathrm{y}) \\
\rho=\mathrm{r} / \mathrm{a}=\left(\mathrm{x}^{2}+\mathrm{y}^{2}\right)^{1 / 2}
\end{array}
$$

Figure 1.16. The coordinate system of the unit circle. (Left) Pupil coordinate system and (Right) Normalized pupil coordinate system in which the given pupil radius, a, is normalized to 1.0 and all measurements are referred to the unit circle. The variable, $\rho$, represents the given normalized pupil radius. Modified from:
http://scien.stanford.edu/pages/labsite/2003/psych221/projects/03/pmaeda/index.html Accessed 21.11.2011.

The terms in the polynomial have two variables: $\rho$, the normalized distance from the pupil centre which represents the radial order; and $\theta$, the angular subtence of an imaginary line joining the pupil centre to the point of interest, referenced to the horizontal.

The wavefront error function $\mathrm{W}(\mathrm{x}, \mathrm{y})$ for two basic aberrations is illustrated in Figure 1.17 for defocus (Figure 1.17a) and for astigmatism (Figure 1.17b). An eye manifesting defocus, only, exhibits an aberration which in three-dimensions describes a parabola. This latter shape is defined mathematically in terms of the x , y coordinates of the rectangular coordinate system in the pupil plane (Figure 1.17a). An eye with astigmatism, which exhibits a saddle shape, is shown in polar coordinates $W(\rho, \theta)$ in Figure 1.17b.


Figure 1.17. Two wavefront aberration functions. (a) Defocus - the wavefront error for an eye with defocus, only, has a parabolic shape and is specified in rectangular coordinates.
(b) Astigmatism - an eye with astigmatism exhibiting a saddle-shaped wavefront and expressed in polar coordinates. (From: Thibos LN. Wavefront Data Reporting and Terminology
http://research.opt.indiana.edu/Library/WavefrontReporting/WavefrontReporting.html Accessed 21.11.2011).

The Zernike polynomials are mathematically defined as:

$$
\begin{gathered}
\mathrm{Z}(\rho, \theta)=\mathrm{N} \cdot \mathrm{R}(\rho) \cdot \cos (\theta) \\
\mathrm{Z}_{\mathrm{n}}{ }^{\mathrm{f}}(\rho, \theta)=\mathrm{N}_{\mathrm{n}}{ }^{\mathrm{f}} \cdot \mathrm{R}_{\mathrm{n}}{ }^{\mathrm{f}} \cdot(\rho) \cos (\mathrm{m} \theta) \quad \text { for } \mathrm{m} \geq 0,0 \leq \rho \leq 1,0 \leq \theta \leq 2 \pi \\
=-\mathrm{N}_{\mathrm{n}}{ }^{\mathrm{f}} \cdot \mathrm{R}_{\mathrm{n}}{ }^{\mathrm{f}} \cdot(\rho) \sin (\mathrm{m} \theta) \quad \text { for } \mathrm{m}<0,0 \leq \rho \leq 1,0 \leq \theta \leq 2 \pi
\end{gathered}
$$

Each Zernike polynomial is composed of three components: a normalization factor (N), a radial polynomial (R), and a sinusoid. Zernike polynomials are defined using a dual index notation $\mathrm{Z}_{\mathrm{n}}{ }^{\mathrm{f}}$ (Thibos et al 2000) which groups each term according to the radial order, n , in terms of $(\rho)$ and the meridional frequency, $f$, in terms of $(\theta)$. The indices, $f$ and $n$, indicate the complexity of the shape that the polynomial can describe and are independent of each other. The radial order is the value for the highest exponent in the Zernike polynomial radial function. It describes the order of the function that measures the wavefront aberration function along a given meridian. The radial order, n, shown in Figure 1.18, clearly illustrates the peaks and troughs along the $90^{\circ}-270^{\circ}$ meridian. The blue region represents a trough whilst the yellow-red region represents a peak. The meridional frequency (f) is the frequency of the sinusoidal component and represents the frequency with which the amplitude of the radial function increases and decreases from meridian to meridian. The change in amplitude from meridian to meridian is shown in Figure 1.19.

Zernike polynomials with higher indices can represent more complicated shapes and depict more detail with more peaks and troughs. The Zernike basis functions are usually layered to form a pyramid as shown in Figure 1.20 which illustrates, in three- and twodimensions, the individual Zernike polynomials up to the fifth order (Applegate et al 2002; Campbell 2003).

Each row of the pyramid corresponds to a given order of the polynomial whilst each column represents a different meridional frequency. The second-order functions, for example, include the defocus $\left(\mathrm{Z}_{2}{ }^{0}\right)$ and astigmatism aberrations $\left(\mathrm{Z}_{2}{ }^{-2}\right.$ and $\left.\mathrm{Z}_{2}{ }^{2}\right)$.


Figure 1.18. The radial order, n , describes the order of the function that measures the wavefront aberration function along a given meridian. In this example, the peak and trough are shown along the $90^{\circ}-270^{\circ}$ meridian. The blue region represents a trough and the yellow-red region represents a peak.


Figure 1.19. The meridional frequency, f, describes the frequency with which the amplitude of the radial function increases, then decreases and changes it's sign from meridian to meridian around the wavefront. Peaks and troughs of this circular cut correspond to the maximum negative amplitude and maximum positive amplitude of the radial function.

Both Figures modified from:
http://www.optikon.com/en/articles/keratron_023/media/TheAberrometers_2003_Tripoli \%20(Zernike\%20Polynomials).pdf Accessed 21.11.2011.

Three of the Zernike basis functions are associated with low order aberrations: Tilt, Defocus and Astigmatism. Tilt indirectly describes the angular position of the optical system. Sphere describes a radially symmetric curvature over the optical system. Cylinder describes a symmetric curvature for each of two perpendicular meridia of the optical system. The cylinder aberration is composed of two terms whose combination defines the axis. Zernike functions of third order, and above, are known as higher-order aberrations.

The Zernike polynomials along with their wavefront error map and the equivalent optical aberration are listed in Table 1.1. The astigmatism aberration with axis at $\pm 45^{\circ}$, for example, is represented by the third Zernike function: $\mathrm{Z}_{2}^{-2}$, for which the polynomial $\left[6 \rho^{2} \sin (2 \theta)\right]^{1 / 2}$ and the wavefront error map are described by mode 3 . This polynomial is composed of: a normalization factor, $(\sqrt{ } 6)$, a second-order polynomial, $\left(\rho^{2}\right)$, and a sinusoidal with a frequency of $2,(2 \theta)$.

The wave aberration function is expressed as the weighted sum of the Zernike polynomials where C represents each aberration coefficient and can be described as follows:

$$
\begin{gathered}
\mathrm{W}(\rho, \theta)=\mathrm{C}_{1}{ }^{-1} \mathrm{Z}_{1}^{-1}+\mathrm{C}_{1}{ }^{1} \mathrm{Z}_{1}{ }^{1}+\mathrm{C}_{2}^{-2} \mathrm{Z}_{2}^{-2}+\mathrm{C}_{2}{ }^{0} \mathrm{Z}_{2}^{-0}+\mathrm{C}_{2}{ }^{2} \mathrm{Z}_{2}{ }^{2}+\mathrm{C}_{3}^{-3} \mathrm{Z}_{3}^{-3}+ \\
\mathrm{C}_{3}{ }^{-1} \mathrm{Z}_{3}^{-1}+\mathrm{C}_{3}{ }^{1} \mathrm{Z}_{3}{ }^{1}+\mathrm{C}_{3}{ }^{3} \mathrm{Z}_{3}^{3}+\mathrm{C}_{4}^{-4} \mathrm{Z}_{4}^{-4}+\ldots \text { etc }
\end{gathered}
$$

Thus, the weighted sum of the Zernike basis functions represents the entire wavefront and, therefore, mathematically describes the total-eye aberrations. The ability to decompose a wavefront into weighted Zernike polynomials enables objective measurements of the optical properties of the eye.


Figure 1.20. Zernike basis functions represented in terms of wavefront error maps. Each row in the pyramid corresponds to a given order of the polynomial and each column corresponds to a different meridional frequency.

Top (three - dimensions):
http://voi.opt.uh.edu/voi/WavefrontCongress/2003/presentations/applegate/Understanding \%20the\%20Zernike\%20Expansion\%20w\%20notes.pdf Accessed 29.1.2012

Bottom (two - dimensions):
http://www.telescope-optics.net/monochromatic_eye_aberrations.htm Accessed 29.1.2012

| Optical Equivalent | Wavefront error map | Zernike Term (polar mode) | Frequency f | $\begin{aligned} & \text { Order } \\ & \mathrm{n} \end{aligned}$ | Mode <br> j |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Tilt in y - direction, Distortion |  | $\mathrm{Z}_{1}^{-1}=2 \rho \sin (\theta)$ | -1 | 1 | 1 |
| Tilt in x - direction, Distortion |  | $\mathrm{Z}_{1}{ }^{1}=2 \rho \cos (\theta)$ | 1 | 1 | 2 |
| Astigmatism with axis at $\pm 45^{\circ}$ | - | $\mathrm{Z}_{2}^{-2}=\left[6 \rho^{2} \sin (2 \theta)\right]^{1 / 2}$ | -2 | 2 | 3 |
| Field curvature, Defocus |  | $\mathrm{Z}_{2}{ }^{0}=\left[3\left(2 \rho^{2}-1\right)\right]^{1 / 2}$ | 0 | 2 | 4 |
| Astigmatism with axis at $0^{\circ}$ or $90^{\circ}$ |  | $\mathrm{Z}_{2}{ }^{2}=\left[6 \rho^{2} \cos (2 \theta)\right]^{1 / 2}$ | 2 | 2 | 5 |
| Coma along y axis |  | $\mathrm{Z}_{3}{ }^{-1}=\left[8\left(3 \rho^{3}-2 \rho\right) \sin (\theta)\right]^{1 / 2}$ | -1 | 3 | 7 |
| Coma along x axis |  | $\mathrm{Z}_{3}{ }^{1}=\left[8\left(3 \rho^{3}-2 \rho\right) \cos (\theta)\right]^{1 / 2}$ | 1 | 3 | 8 |
| Secondary Astigmatism | - | $\mathrm{Z}_{4}^{-2}=\left[10\left(4 \rho^{4}-3 \rho^{2}\right) \sin (2 \theta)\right]^{1 / 2}$ | -2 | 4 | 11 |
| Spherical Aberration, Defocus |  | $\mathrm{Z}_{4}{ }^{0}=\left[5\left(6 \rho^{4}-6 \rho^{2}+1\right)\right]^{1 / 2}$ | 0 | 4 | 12 |

Table 1.1. Different types of aberrations within Zernike's pyramid represented by Zernike polynomials along with their wavefront error map and the equivalent optical aberration.
(http://docs.google.com/viewer?a=v\&q=cache:HhGRugg_0JkJ:arapaho.nsuok.edu/~salmo nto/articles_resources_pdf/Handout.pdf+4State+Area+Symposium+ Lecture+2,+9:1010:00+AM,+Saturday,+March+4,+2006,+COPE+OE\%23+ 534930\&hl=iw\&gl=il\&pid=bl\&srcid=ADGEESiugz_f5S1DR5V7r0r_r6YtuJ96takIcsuaI DkLezbmoKSoyeQPasc5_PjZNwppWQpa0p6hGcTykPKoryLkLZ4BBKSkHHQPuFqcIWTKDAH3A5qgG60fYaqYsQ_EAchHd2gIR\&sig=AHIEtbRtIOdI mikpnckZCdFI-o8RKB1TCQ) Accessed 21.11.2011.

### 1.2.2 Root Mean Square (RMS)

The root mean square aberration is the expression of the magnitude of the wave aberration and represents the smoothness of the wavefront (Fisher et al 2008). It is the square root of the arithmetic mean of the squares of the wave aberration coefficients across the pupil aperture (i.e., the square of the function that defines the continuous waveform) (Bille et al 2004), and is calculated as:

$$
\text { RMS } \left.=\left[\left(\mathrm{C}_{2}^{-2}\right)^{2}+\left(\mathrm{C}_{2}{ }^{0}\right)^{2}+\left(\mathrm{C}_{2}^{2}\right)^{2}+\left(\mathrm{C}_{3}^{-3}\right)^{2}+\left(\mathrm{C}_{3}{ }^{-1}\right)^{2}+\left(\mathrm{C}_{3}{ }^{1}\right)^{2}+\left(\mathrm{C}_{3}{ }^{3}\right)^{2}+\ldots \mathrm{etc}\right]\right]^{1 / 2}
$$

Or in a general description:

$$
\operatorname{RMS}=\left[\Sigma\left(\mathrm{C}_{\mathrm{n}}^{\mathrm{f}}\right)^{2}\right]^{1 / 2}
$$

Where C represents each aberration coefficient specified in microns, n is the radial order number and f is the meridional frequency. The RMS aberration indicates the magnitude of the aberration but not the shape.

### 1.2.3 Point Spread Function (PSF)

When the wavefront that enters the eye comes from a point source, the intensity/ irradiance distribution that is imaged on the retina is called the Point Spread Function (PSF). It has become routinely possible to predict the extent of the blur on the retina by using objective techniques that measure the various aberrations and subsequently compute the PSF of the eye (Liang et al 1994; Applegate et al 1998). The PSF defines how an optical system (including the eye) images a point of light. It describes the response of an
imaging system to a point source or point object and is a tool for describing the visual stimulus.

When the relative intensity of the point source is plotted as a function of distance on the retina the resultant function can be illustrated as the dashed, vertical, green line in Figure 1.21. However, the eye's optics are not perfect, so the relative intensity of the point source is broadened and distributed across the retina, as shown in a two-dimensional illustration by the red curve in Figure 1.21. This curve is the PSF. The degree of spreading of the image of the point source is a measure of the quality of the optical system. Any object can be considered as an array of independent point sources, each one producing its own PSF. These individual PSFs all overlap to form an image of the object. The overlap of the PSFs from the array of points that make up the object is called convolution.


Figure 1.21. The relative intensity of a point source plotted as a function of distance on the retina to show the Point Spread Function (PSF). The maximum relative intensity is described by the dashed, vertical, green line. Eye aberrations and diffraction effects affect the relative intensity of the point of light which is broadened and distributed across the retina (red curve).

Two point sources whose PSFs overlap, but are sufficiently far apart, are shown in Figure 1.22. The two PSFs will yield a single relative intensity function with two distinct peaks. The vertical dashed lines represent the energy distributions of the stimuli. Such a display would probably be perceived as two closely separated points.


Figure 1.22. Two point sources whose PSFs overlap but are sufficiently far apart to be resolved as two separate sources. The vertical green dashed lines represent the maximum energy distribution of each stimulus and each red curve represents the corresponding relative intensity distributions over the retina. The two PSFs will form a single relative intensity function with two separate peaks. Such a display would probably be perceived as two closely separated points.

When the two point sources are very close together, the two PSFs summate to produce a curve with a single peak with incomplete summation of the two relative intensity distributions. The two points would then be perceived as a single point as illustrated in Figure 1.23.


Figure 1.23. Two point sources whose PSFs overlap and are very close together. The vertical green dashed lines represent the energy distributions of the stimuli and the red curves represent the relative intensity distribution over the retina. The PSFs incompletely summate to produce a curve with a single peak (red bold curve). These two points would be perceived as a single point.

When the optical system has a circular aperture and no aberrations, the PSF takes the shape of the Airy disk (Figure 1.24). With monochromatic light, the Airy disk consists of a central point of maximum intensity surrounded by alternate circles of light and darkness caused by the reinforcement and interference of diffracted rays. The diffraction disk forms a basis for determining the resolving power of an ideal lens system. The diameter of the disk depends largely upon the aperture of the lens. Due to diffraction, the smallest point to which a beam of light can be focused using a lens is the size of the Airy disk.

In the optimum imaging system, the image formation will be limited only by diffraction (expressed by the term diffraction-limited). Under these conditions, the light reaching the retina will have a spherical shape. The PSF for a diffraction-limited eye as function of pupil size and also for a typical eye with aberrations is shown in Figure 1.25.


Figure 1.24. A typical Airy disk illustrated in two- (left) and three-dimensions (right). The diameter of an Airy disk depends upon the wavelength of the radiation and the numerical aperture of the objective lens. The diameter of the first dark circle of the Airy disk is used to define the theoretical maximum resolution for an optical system.

From: http://www.cambridgeincolour.com/tutorials/diffractionphotography.htm Accessed 21.11.2011.

The diameter of the Airy disk decreases as pupil size increases. In a typical aberrated eye with small pupils, the PSF is an Airy disk, but, as the pupil size increases, aberrations impact upon the source and the PSF broadens and exhibits different irregular shapes.


Figure 1.25. The PSF as a function of increase in pupil size for a diffraction-limited ("perfect eye"). Top: Each PSF has the shape of an Airy disk; as the pupil size increases, the size of the Airy disk decreases. Bottom: The corresponding PSF in a typically aberrated eye. For small pupils, the PSF has the shape of an Airy disk but as the pupil size increases, the aberrations adversely influence the PSF creating different irregular shapes.

From: www.google.co.il/search?hl=iw\&q=RMS+aberration+equation\&start=30\&sa=N Accessed 21.11.2011.

Monochromatic aberrations, compared to those of white light, will cause differences in the appearance of the PSF (Wilson et al 2002).

The application of PSFs to the clinic can be useful for separating optical from neural attenuation of the perceived image (Jiang et al 2008; Ligabue et al 2009; Moreno et al 2010; Nanavaty et al 2011; McAnany et al 2011; Serrao et al 2011). The PSF of the eye can be calculated knowing the wave aberration, the transmission of the optical system and the shape and size of the pupil. The wavefront aberrations and the associated PSFs in three different eyes are illustrated in Figure 1.26.


Figure 1.26. Three wavefront aberration maps (left illustration in each pair) and associated point spread functions (right illustration in each pair) for three different eyes. Aberration and diffraction effects spread the image over a finite area. (From: Villegas et al 2008).

Additionally, once determined, the PSF can be minimized using an adaptive optics system thereby improving visual acuity. The use of adaptive optics, in conjunction with a charged couple device, could also be used to increase the resolution of anatomical structures such as the cone photoreceptors of the retina (Zhang et al 2006).

### 1.2.4 Modulation Transfer Function (MTF)

The modulation transfer function describes the image quality of an optical system and measures the transfer of modulation (contrast) from the object to the image, i.e., how authentically the optical system reproduces (transfers) different levels of detail (spatial frequencies) from the object to the image. Typically, it is represented as the reduction in contrast from object to image by the ratio of the image modulation to the object modulation of a grating at a given spatial frequency:

$$
\operatorname{MTF}(v)=\mathrm{M}_{\mathrm{i}} / \mathrm{M}_{0}
$$

Where, $v$, is the spatial frequency, $\mathrm{M}_{\mathrm{i}}$, is the contrast of the image and $\mathrm{M}_{0}$, is the contrast of the stimulus (object).

In this sense, it is analogous to the contrast sensitivity function of the eye, but does not include neural factors that also determine contrast sensitivity (Boreman 2001).

When the light is measured in terms of luminance (L), the modulation can be defined as:

$$
\text { Modulation }=\left(\mathrm{L}_{\max }-\mathrm{L}_{\min }\right) /\left(\mathrm{L}_{\max }+\mathrm{L}_{\min }\right)
$$

Where $\mathrm{L}_{\text {max }}$ and $\mathrm{L}_{\text {min }}$ are the maximum and minimum luminances of the stimulus, respectively. This function is known as the Michelson contrast.

The MTF can be determined for a potential correcting lens in isolation or for the lens and the eye, together (Artola et al 2007; Alió et al 2008; Ortiz et al 2008). With the latter, the MTF can be used to ascertain the retinal image quality. An understanding of the effect of
aberrations on the MTF is a useful clinical tool to evaluate clinical outcomes and intraocular optical performance.

### 1.2.5 Clinical Measurement of Higher Order Aberrations

The presence of higher-order aberrations can be measured clinically by commercially available wavefront technology (aberrometers) (Sachdev et al 2002; Won et al 2008; Maeda 2009; Saad et al 2010; Piñero et al 2011; Shen et al 2011).

### 1.2.5.1 Aberrometry

Wavefront analysis originated in astronomy where adaptive optics are necessary to reduce wavefront distortions in telescopic images arising, for example, from the atmosphere (Platt et al 2001).

The concept of adaptive optics was first proposed by Babcock (1953) whereby an optical system was designed to reduce unwanted wavefront distortions. This concept is used today in many areas in addition to astronomy.

Currently, a number of commercially avaliable devices, each based upon various different wavefront sensing techniques, are available to measure ocular aberrations, clinically, and the various techniques are described in the following section.

### 1.2.5.1.1 Wavefront Aberrometers

Wavefront sensors measure the aberrations generated by the entire eye; however, the principal source of the aberrations is the corneal surface and the crystalline lens. Since wavefront sensing light needs to pass through the cornea and lens, the pupil is the absolute limiting aperture for wavefront sensing.

All aberrometers developed for clinical use are based upon the same principle of focal shift and indirect measurement of local wavefront slopes and the reconstruction of the complete wavefront by integration of these slopes (Figures 1.27 and 1.28 ). The principle of focal shift derives from the basis that a perfect lens always refracts any incident light ray, parallel to the optical axis, and through the focal point. If the lens is aberrated, this principle no longer applies. Some of the rays are focused behind, or in front of, the focal point and the resultant intersection of the focal plane with the aberrated rays lies away from the focal point. This is called focal shift and can be measured by an aberrometer.


Figure 1.27. The focal shift principle. Any incident beam parallel to the optical axis of a lens is refracted by the lens through it's focal point. If the lens is aberrated, the beam is focused behind, or in front of, the focal point (dashed line). The intersection between the focal plane and the refracted beam lies away from the focal point (Rozema et al 2005).


Figure 1.28. The principle of measuring ocular aberrations with a wavefront aberrometer. The local wavefront slopes (caused by the focal shift) are measured and the complete wavefront shape is reconstructed from the measured slopes in the $x$ and $y$ directions at each sampling point. $F$ is the focal length of the focusing optics (Porter et al 2006).

When the incident rays are moved to another given location in the focusing optics, the focal shift will change as a function of the local aberrations at the new given location. Mapping the relationship between the various points of incidence and the corresponding focal shifts enables the reconstruction of the wavefront slope at each location from which the wavefront can be calculated.

Aberrometers can be classified as to whether the measurement is a subjective method requiring the patient to give some feedback during the measurement process or is an objective method in which the entire measurement is performed without the requirement for a response from the patient. Another classification is based upon whether the measurement is either serial or parallel, i.e., single measurements at successive locations or a simultaneous measurement at all locations. A third classification is based upon the single or double-pass principle which defines the number of times the measurement beam passes through the aberrated optics. A further classification is based upon either forward projection of the measurement (i.e., the measurement of the light entering the eye) or upon
backward projection (i.e., the measurement of the light exiting the eye) which requires a source on the retina (Rozema et al 2005; Cerviño et al 2007).

A more general concept classifies aberrometers into four different principles of wavefront analysis: outgoing reflection aberrometry (Hartmann-Shack aberrometry), retinal imaging aberrometry (Tscherning and ray tracing aberrometry), ingoing adjustable aberrometry (spatial resolved refractometer) and double pass aberrometry (slit skiascopy) (Wygledowska-Promieńska 2005; Cerviño et al 2007).

### 1.2.5.1.2 Principle of Hartmann-Shack Aberrometry

The Hartmann-Shack is an objective, parallel, double-pass method using backward projection (Rozema et al 2005). The aberrometer uses a narrow laser beam along the visual axis of the eye. The image at the fovea then becomes a point source which radiates light out of the eye and which serves as a secondary source that illuminates the pupil area, posteriorly. The outgoing light is guided, as soon as it passes through the cornea, through a set of relay lenses that project the pupil plane onto an array of smaller lenses (lenslets) that split the wavefront into a number of individually focused point images which are then focused on a charged coupled device (CCD) camera (Liang et al 1994). The CCD camera captures the displacement of the each image from the optical axis of each lenslet. After determining the slope at each lenslet in the x and y directions, the reconstructed wavefront slopes are simultaneously determined for the entire pupil plane at the given locations and the wavefront can be referenced to the level of the exit pupil (Thibos 2000; Cerviño et al 2007) as illustrated in Figure 1.29.


Figure 1.29. The principle of the Hartmann-Shack aberrometer. A laser beam passes along the visual axis. The image at the fovea is reflected and becomes a secondary light source that illuminates the pupil area posteriorly. The returning laser light (in red) is guided through a set of relay lenses that project the pupil plane onto an array of lenslets which subdivides the wavefront into smaller rays of light, thereby forming multiple images of the original foveal point source on a charged coupled device (CCD) camera. The CCD camera is used to capture the displacement of the foveal image from the optical axis of each lenslet. After examining the slope at each lenslet in the x and y directions, the entire wavefront can be plotted in a three-dimensional form (Rozema et al 2005).

For a perfect (i.e., aberration free) eye, each image will not exhibit any displacement from the optical axis of the lenslet and will contribute to a perfect lattice arrangement of point images (Figure 1.30). However, an aberrated eye produces a distorted wavefront (Figure 1.31) since, due to the focal shift; the returning beam is displaced by each lenslet compared to the optical axis of the lenslet. The local slope of the wavefront is different for each lenslet and, therefore, the wavefront will be focused into a disordered collection of images. By measuring the displacement of each image from its corresponding lenslet axis, the slope of the aberrated wavefront can be calculated and the shape of the aberrated wavefront subsequently derived.

Commercially available aberrometers based upon the Hartman-Shack principle include the LADARWave aberrometer (Alcon Laboratories Inc. Ft Worth, Tex), the VISIX Wavescan (Abbott Medical Optics) and the Zywave II Wavefront Aberrometer (Bausch \& Lomb, Rochester, NY).


Figure 1.30. The reflection of a plane wavefront on a Hartmann-Shack aberrometer sensor. The lenslet array subdivides the wavefront into multiple beams. The local slope of the wavefront formed by each lenslet determines the location of the image on the CCD camera thereby creating a perfect lattice arrangement of images (Modified from: Thibos et al 2000).


Figure 1.31. The reflection of an aberrated wavefront on a Hartmann-Shack aberrometer sensor. The aberrated wavefront distorts the lattice arrangement of images. The displacement of each image from the corresponding lenslet axis is a measure of the slope of the wavefront producing an irregular lattice of images on the CCD camera (Modified from: Thibos et al 2000).

### 1.2.5.1.3 Principle of Tscherning aberrometry

The Tscherning aberrometer uses a parallel, double-pass, method with forward projection and can be implemented in both an objective and a subjective manner (Rozema et al 2005). In principle, the Tscherning aberrometer consists of two different optical paths: the entrance and exit paths. The ingoing frequency doubled laser beam passes through a beam expander that illuminates a regular matrix of pinholes called a Tscherning screen. The light passing through the matrix forms a bundle of thin parallel rays that are projected by an aberroscope lens system into the eye (Figure 1.30). The aberroscope lens system consists of adjustable lenses which enlarge the resultant dot pattern in order to separate and identify the single images. The lens system changes the angle of incidence, but maintains the location of each single dot in the corneal plane and keeps the retinal image size constant regardless of refraction.

In a similar manner to the Hartman-Shack principle, an aberrated eye forms an irregular lattice of dots dependent upon the degree of the focal shift. Using the principle of indirect ophthalmoscopy, the returning beam passes through a beam splitter and a second lens system and aperture onto a CCD camera. The deviation of each image from the reference position is measured at the level of the eye's exit pupil and, from these values, the wavefront aberration is mathematically reconstructed (Mrochen et al 2000; Cerviño et al 2007).

Commercially available aberrometers based upon the Tscherning principle include the Allegro Analyzer (Alcon Laboratories Inc. Ft Worth, Tex) and the Allegretto Wave Analyzer (Wavelight Laser Technologie AG, Germany).


Figure 1.30. The principle of Tscherning aberrometry. An expanded laser beam passes through a Tscherning screen. The light passing the screen forms thin parallel rays that are projected by an aberroscope lens (L1) onto the retina. The degree of focal shift is dependent upon the magnitude of the aberrated eye. The returning light is retrieved (red rays) using a beam splitter and a second lens system and aperture (L2) onto a CCD camera (Rozema et al 2005).

### 1.2.5.1.4 Principle of Ray Tracing Aberrometry

Ray tracing is a serial, double pass, method which uses forward projection and can be implemented in both an objective and a subjective manner (Rozema et al 2005). It utilizes a laser beam and ray tracing technology to measure wavefront aberrations on a point-bypoint basis.

A laser beam is directed into the eye, parallel to the visual axis, by means of an $x, y$ scanner (Figure 1.31). After entering the eye, the local aberration corresponding to the given entry position of the beam causes a focal shift of the retinal image with respect to the reference position. The returning light from the retina is imaged on a position sensitive detector (PSD) via a beam splitter and a detector objective lens (L2) and is caught on a linear array of photodetectors. The laser beam is moved to a new position and the
sequence is repeated until sufficient measurements are available over the whole pupil area (Molebny et al 2000; Pallikaris et al 2000; Cerviño et al 2007).


Figure 1.31. The principle of Ray Tracing aberrometry. The laser beam, after passing through an $x-y$ scanner, is directed into the eye parallel to the visual axis and provides its own projection on the retina. The position sensitive detector (PSD) measures the focal shift of the laser spot on the retina magnified by the detector objective lens (L2) (rays in red) due to the given aberration. The laser beam is moved to a new position until measurements are available over the whole pupil area (Rozema et al 2005).

Commercially available aberrometers based upon the ray tracing principle include the iTrace Visual Function Analyzer (Tracey Technologies) and the iTrace Combo Visual Function Analyzer (Topcon Medical Systems, Inc.).

### 1.2.5.1.5 Principle of Spatially Resolved Refractometer

The Spatially Resolved Refractometer is a serial, double pass, subjective method using forward projection. It measures aberrations relative to the entire entrance pupil and is based upon the Scheiner disk principle. The principle differs from other methods in that it
provides the option for patients to interact during the measurement procedure. The spatially resolved refractometer has two light sources: a fixed source that serves as a reference (the light which passes through the centre of the pupil and projects a fixed reference cross hair reticule onto the retina) and a movable source (the light which is moved to different locations over the pupil and projects a measurement (spot) image onto the retina). The position of the point on the retina changes for each pupil entry position according to the magnitude of the given aberration(s). For each location of the movable source, the patient's task is to change the position of the test spot until it is aligned with the centre of the fixed reference reticule. The same task is repeated at different locations of the movable light source over the pupil plane. The angle required to null the aberrations at each pupil position represents the slope of the wavefront at that location (Webb et al 2003; Cerviño et al 2007).

The spot and the alignment reticule are delivered through two independent optical channels (the measurement channel and the reference channel) and are shown in Figure 1.32. A CCD camera occupies a third optical channel and determines fixation stability during the measurement procedure. The measurement channel generates the spot image via illumination of a spatial light modulator (SLM) of a small spot from a cathode ray tube (CRT). The CRT is located at a plane conjugate to the patient's entrance pupil, while the SLM is located at a plane conjugate to the patient's retina. The second channel projects the alignment reticule from the CRT (Burns 2000; Moreno-Barriuso et al 2001).

The InterWave (InView, Atlanta, GA) is a commercially available aberrometer based upon the Spatially Resolved principle.


Figure 1.32. The principle of the Spatially Resolved Refractometer. The planes defined by $\mathrm{C} 0, \mathrm{C} 1$ and C 2 represent the corneal plane and its two conjugate planes, respectively (rays in black). The planes defined by R0, R1 and R2 represent the retinal plane and its two conjugate planes, respectively (rays in red). The CRT is conjugate to the corneal plane; the spatial light modulator (SLM) is conjugate to the retinal plane. The light which passes through the centre of the pupil, projects a fixed reference cross hair reticule onto the retina (fixed source, (SLM)) and the light which is moved to different locations over the pupil projects a test spot onto the retina (movable source, (CRT)). For each location of the movable source, the patient's task is to change the position of the movable light source until it is aligned with the reference reticule. The measurement is repeated for multiple pupil locations. A CCD camera determines fixation stability during the measurement procedure (Rozema et al 2005).

### 1.2.5.1.6 Principle of Retinoscope Double Pass Aberrometry

Retinoscope Double Pass Aberrometry is an automated version of retinoscopy, implemented in an objective, serial, double pass manner (Rozema et al 2005). The retinal image of a light beam coming from a superior direction is located below the optical axis in a myopic eye and above the optical axis in a hyperopic eye. Since the retina can be considered as a spherically concave mirror, the beam is reflected back in approximately the original direction in a myopic eye and to the opposite direction across the pupil in a hyperopic eye. Moving the incident beam along a given meridian over the pupil will result in the reflected beam moving either in the same, or in the opposite direction, as the
incident beam. The difference in direction and in the ratio between the speed of movement of the incident beam and that of the reflected beam can be used to estimate the ocular refraction along the given meridian (Cerviño et al 2007).

The automatic retinoscope uses a light emitting diode (LED) source that is placed behind a screen incorporating a fast-moving slit and is shown in Figure 1.33. The image of the slit is projected onto the pupil plane using a lens where a portion of the light will pass through the pupil. According to the ocular refraction along the scanned meridian, the reflected light from the retina will move at a greater speed either with or against the motion of the slit, depending upon the refractive error. The reflected light from the retina returns through an aperture stop and is registered by projecting the pupil plane onto an array of photodetectors using a beam splitter and a lens. An ametropia map is obtained that can be transposed into a wavefront map (MacRae et al 2000; Cerviño et al 2007).

The light emitting diode and photodetectors are conjugate with the cornea whilst the aperture stop is conjugate with the retina in the emmetropic eye. In myopia, the aperture stop is in front of the retina and in hyperopia it is behind the retina.

As in retinoscopy, the positioning of the aperture stop results in the reflected light flashing simultaneously at all photosensors across the pupil in emmetropia; and movement 'with' or 'against' when compared to the movement of the projected slit of light in ametropic conditions as shown in Figures 1.34 (a) and (b) respectively (Corboy 2003). This causes time differences in the peak illumination between the reference and data photodetectors. By comparing the peak intensity of each data sensor with respect to the peak intensity in the reference sensor, the refractive error for each data point is determined and a map is generated.


Figure 1.33. The principle of Retinoscope Double Pass Aberrometry. A fast-moving slit is placed in front of a light emitting diode (LED) source. The image of the slit passes the pupil via a lens $\left(\mathrm{L}_{1}\right)$. The reflected light from the retina (in red) will appear as a flash if the eye is emmetropic or move either with or against the motion of the slit depending upon the refractive error. Using a beam splitter and a lens $\left(\mathrm{L}_{2}\right)$, the pupil plane is projected onto a photosensor array that captures the reflected high-speed scan of the retina through an aperture stop. This movement is compared to the movement of the projected slit of light in emmetropic conditions resulting from the time differences in the peak illumination between the reference and the measured data. By comparing the peak light intensity of each sensor with respect to the peak intensity in the reference sensor, the refractive error for each point is determined and a map is generated. (Rozema et al 2005).


Aperture stop
(a) Myopia


Aperture stop
(b) Hyperopia

Figure 1.34. Reflected light from the retina in retinoscopy. Reflected light from the retina flashes simultaneously at all photodetectors across the pupil in emmetropia, but moves 'with' or 'against' when compared to the movement of the projected slit of light in ametropic conditions. In myopia (illustration (a)), the aperture stop is in front of the retinal plane causing the projected slit of light (in red) to move faster and in the opposite direction as the projected slit (in black). In hyperopia (illustration (b)), the aperture stop is behind the retinal plane, causing the projected slit of light (in red) to move in the same direction as the projected slit (in black) (Rozema et al 2005).

Commercially available aberrometers based upon the Retinoscope Double Pass principle include the The Nidek-OPD Scan II (Nidek, Gamagori, Japan) and the OPD Scan III Refractive Power / Corneal Analyzer (Marco Ophthalmic, Inc.).

### 1.3 Clinical Implications of Wavefront Aberrometry

The goal of measuring wavefront aberrations is to accurately assess the quality of the image formed on the retina. Wavefront aberration technology is used to assist corneal refractive surgery and has also been applied to further the understanding of the wavefront quality of the eye resulting from alterations in a variety of parameters including age, accommodation, tear film abnormalties, corneal disease etc.

### 1.3.1 The Normal Eye

The amount and distribution of ocular aberrations vary significantly between normal individuals. The wave aberration was measured by a Hartmann-Shack wavefront sensor in 118 eyes of normal individuals aged 20 to 29 years. The waveferont aberrations were studied up to the $4^{\text {th }}, 5^{\text {th }}, 6^{\text {th }}, 7^{\text {th }}$ and $8^{\text {th }}$ order for $3,4,5,6$ and 7 mm zone diameters (Castejon-Mochon et al 2002). A large range was present for all the Zernike coefficients. The most prevalent aberrations were myopia and "with the rule" astigmatism ( $2^{\text {nd }}$ order). Comparison of wavefront aberrations between eyes of an individual exhibited good agreement for most of the $2^{\text {nd }}$ and $3^{\text {rd }}$ terms with a slight (but not strong) tendency for mirror symmetry between eyes.

A similar study of the frequency of HOAs was undertaken on 109 normal individuals (mean age 41) who underwent aberrometry using a modified Hartmann-Shack wavefront sensor for a 5.7 mm zone diameter (Porter et al 2001). Most Zernike modes were
relatively poorly correlated with each other. Zernike defocus ( $2^{\text {nd }}$ order) accounted for $80 \%$ of the total variance of the wave aberration and had the largest magnitude of any mode. The next largest contributors to the wave aberration were the astigmatic modes ( $2^{\text {nd }}$ order). Even though there appeared to be a random between-individual variation in the HOAs, most aberrations exhibited statistically significant between-eye correlations.

A study, using the Nidek OPD aberrometer, on 140 eyes of 140 individuals (age range 1777 years) described the distribution of total, corneal, and mainly internal HOAs (from the $3^{\text {rd }}$ to the $6^{\text {th }}$ order) (Goebels et al 2008). Internal, Corneal, and Total wavefront aberrations varied widely among individuals. A correlation was present between right and left eyes for total, spherical, and coma HOAs (all p<0.001) (Wang et al 2003). The between-eye relationship, for an individual, in wavefront aberration measured using a spatially resolved refractometer (Marcos et al 2000) is, in general, asymmetrical, suggesting that, contrary to the findings from other studies (Porter et al 2001; Goebels et al 2008), the development of aberrations occurs independently between the two eyes of an individual.

The effect of change in posture tends to affect HOAs. The total and spherical-like HOAs significantly increase while changing from a sitting position to a supine position, suggesting that the increase in the HOA may limit the improvements in visual performance after customized refractive surgery based on wavefront measurement (Kawamorita et al 2006).

### 1.3.2 Refractive Error

Several studies have measured HOAs as a function of refractive error. However, there is a notable lack of consensus in the findings from these studies. With the Tscherning method, HOAs increase as myopia and astigmatism increase (Hu et al 2004). Coma ( $3^{\text {rd }}$ order)

HOA is related to astigmatism, whilst, secondary spherical aberration ( $6{ }^{\text {th }}$ order), spherical ( $4^{\text {th }}$ order) and secondary coma ( $5^{\text {th }}$ order) HOAs are more common in high myopia (Hu et al 2004). However, according to a study, using the Complete Ophthalmic Analysis System (COAS) Wavefront Analyzer, highly myopic eyes exhibit significantly smaller secondary astigmatism ( $4^{\text {th }}$ order) and spherical ( $4^{\text {th }}$ order) HOAs than non-myopic eyes ( $\mathrm{p}=0.015$ and $\mathrm{p}=0.009$ respectively) (Kwan et al 2009). Spherical aberration ( $4^{\text {th }}$ order) is not significantly different in eyes with refractive errors, which range from +5.00 to -10.00 dioptres, compared to emmetropic eyes (Kwan et al 2009). In particular, the $3^{\text {rd }}, 4^{\text {th }}$ and total $\left(3^{\text {rd }}\right.$ to $\left.10^{\text {th }}\right)$ HOAs, measured with the Hartmann-Shack aberrometer, in myopic and hyperopic eyes are not correlated with refractive error, however, astigmatic eyes tend to have larger total HOAs than non-astigmatic eyes (Cheng et al 2003).

Optical quality, measured with a modified Hartmann-Shack method, decreases as myopic refractive error increases and as pupil size increases. Coma-like HOA is more frequent in high myopia, and spherical aberration is found more frequently in dilated pupils (Paquin et al 2002). However, it is not clear which exerts the greater influence on the HOAs, the pupil size or the degree of myopia.

Total ocular HOAs were examined three times across a 6.0 mm zone diameter in 61 myopic eyes using the Nidek OPD aberrometer. Total, T.Sphere, T.Coma and T.Trefoil HOAs increased slightly but not significantly with increase in myopia. The Total and T.Trefoil of the $3^{\text {rd }}$ measurement were significantly different from the $1^{\text {st }}$ to the $2^{\text {nd }}$ measurement ( $\mathrm{p}<0.05$ ), with an overall low correlation between the three measurements for the Total, T.Sphere, T.Coma and T.Trefoil HOAs (Zadok et al 2005). Nevertheless, a study using the psychophysical ray-tracing technique states that myopic individuals seem to have significantly greater HOAs from the $2^{\text {nd }}$ to the $7^{\text {th }}$ order, compared to emmetropic individuals (He et al 2002).

Total ocular spherical HOA is significantly higher in hyperopic eyes, when determined using a laser ray tracing technique but Internal spherical HOA is not significantly different between hyperopic and myopic eyes (Llorente et al 2004).

There is no correlation between total HOA, measured with the Zywave (Bausch \& Lomb, Rochester, NY), and myopia (mean -5.23 dioptres, SD 1.79 and cylinder mean -1.29 dioptres, SD 0.98) (Wei et al 2006). There is also no correlation between coma ( $3^{\text {rd }}$ order) HOA, measured with the LadarWave aberrometer (Hartmann-Shack type), and refractive error (Bisneto et al 2007). However, a moderate, but statistically significant positive correlation is present between spherical refractive error and spherical HOA ( $4^{\text {th }}$ order) ( $\mathrm{p}=0.0068$ ), and between spherical equivalent (with astigmatism <-0.75 dioptres) and spherical HOA ( $4^{\text {th }}$ order) $(\mathrm{p}=0.0065)$, indicating that spherical HOA increases as the refractive error changes from myopia to hyperopia. Same correlation is present between spherical refractive error and trefoil, quadrafoil, secondary astigmatism ( $4^{\text {th }}$ order) and other (up to $8^{\text {th }}$ order) HOAs ( $\mathrm{p}=0.0262$ ) and between spherical equivalent (with astigmatism $\geq-0.75$ dioptres) and trefoil, quadrafoil, secondary astigmatism and other (up to $8^{\text {th }}$ order) HOAs $(\mathrm{p}=0.0258)$ (Bisneto et al 2007). In a more recent study, using the Zywave II aberrometer (Hartmann-Shack type), HOAs were examined in 126 eyes of 63 individuals (mean age $26.4 \pm 5.9$ years) with myopic ( $-4.94 \pm 1.63$ dioptres) astigmatism ($0.96 \pm 1.06$ dioptres) (Karimian et al 2010). The predominant HOA was vertical trefoil ( $3^{\text {rd }}$ order) followed by spherical aberration ( $4^{\text {th }}$ order) and primary vertical coma ( $3^{\text {rd }}$ order). The contribution of the given HOA to the total ocular HOA seemed to decrease as the order of the HOA increased from $3^{\text {rd }}$ to $5^{\text {th }}$ order (by $53.9 \%$ for $3^{\text {rd }}$ order, $31.9 \%$ for $4^{\text {th }}$ order, and $14.2 \%$ for $5^{\text {th }}$ order). Significant correlations were present between spherical equivalent refractive error and primary horizontal coma ( $3^{\text {rd }}$ order) ( $\mathrm{r}=0.231, \mathrm{p}=0.022$ ), and spherical ( $4^{\text {th }}$ order) ( $\mathrm{r}=0.213, \mathrm{p}=0.031$ ) HOAs; between astigmatism and total
$(\mathrm{r}=0.251, \mathrm{p}=0.032)$ HOAs, $4^{\text {th }}$ order $(\mathrm{r}=0.35, \mathrm{p}<0.001)$, and primary vertical coma $(\mathrm{r}=0.314, \mathrm{p}=0.004)$ HOAs (Karimian et al 2010).

### 1.3.3 Aging

The natural process of aging induces changes in the ocular optics that tend to increase the magnitude of the HOAs (Guirao et al 1999; Calver et al 1999; McLellan et al 2001; Brunette et al 2003; Applegate et al 2007). The lower order aberrations, and the coma and spherical HOAs generally show a large degree of variability with age (Baskaran et al 2011).

The total HOA increases with increase in age (Kuroda et al 2002; Wang et al 2003). The rate of increase in the Total Total HOA and in the Corneal Total HOA, measured with a Hartmann-Shack aberrometer is 0.0032 microns per year and 0.0015 microns per year, respectively (Fujikado et al 2004; Berrio et al 2010). Alternatively, there is no correlation between age and total HOA (Wei et al 2006) or between age and each of the Internal, Corneal, or Total HOAs measured with the Nidek OPD aberrometer (Goebels et al 2008). Small but statistically significant positive correlations are present between age and vertical coma ( $3^{\text {rd }}$ order) $(\mathrm{p}=0.008)$, and spherical ( $4^{\text {th }}$ order) $(\mathrm{p}=0.012)$, and horizontal trefoil ( $3^{\text {rd }}$ order) ( $\mathrm{p}=0.042$ ) HOAs (Wei et al 2006). However, although coma HOA increases with increase in age (p<0.001) spherical HOA does not (Wang et al 2003). Statistically significant increases in T.Sph, and in Total and Internal Coma HOAs were present with the Nidek OPD aberrometer from the 26-35 year old to the 56 year and older age groups (Goebels et al 2008). The $3^{\text {rd }}$ order corneal coma (Fujikado et al 2004; Cermáková et al 2010) including that measured with the Tscherning wavefront aberrometer (Jahnke et al 2006) and $4^{\text {th }}$ order spherical HOAs increase with age (Fujikado et al 2004; Jahnke et al

2006; Radhakrishnan and Charman 2007; Cermáková et al 2010). The HOAs ( $5^{\text {th }}$ to $7^{\text {th }}$ ), using a spatially resolved refractometer, increase with increase in age ( $\mathrm{r}=0.57, \mathrm{p}<0.001$ ) which is independent of spherical equivalent refractive error (McLellan et al 2001). The apparent relationship between age and some HOAs would appear to be influenced by pupil diameter. For a 3.0 mm zone diameter, total ( $\mathrm{p}=0.103$ ) and spherical-like ( $\mathrm{p}=0.448$ ) HOAs do not change with aging, while coma-like HOA exhibits a weak, but statistically significant, correlation ( $p=0.004$ ). However, for a 7.0 mm zone diameter, total $(\mathrm{p}<0.001)$ and coma-like ( $\mathrm{p}<0.001$ ) HOAs increased significantly with aging, but spherical-like HOAs did not show any age-related change ( $\mathrm{p}=0.166$ ) (Oshika et al 1999).

Any increase in degradation with age may be explained by the loss of the balance between the aberrations of the corneal and the internal surfaces (Artal et al 2002). The aberrations of the anterior corneal surface increase only slightly with age. The corneal components of astigmatism, coma and spherical HOAs are larger than the total components in younger individuals whereas the opposite is true for older individuals (Keller et al 1996; Artal et al 1998; Guirao et al 2000; Artal et al 2001; Artal et al 2002; Kelly et al 2004; Atchison et al 2008). The internal ocular surfaces compensate, at least in part, for the aberrations associated with the anterior cornea in younger individuals when measured with the Hartmann-Shack sensor, but this compensation declines in older individuals (Artal et al 2002). Indeed, wavefront aberration measurements, combined with data from corneal topography, indicate that, in young eyes, the negative spherical HOA produced by the crystalline lens compensates for the positive spherical HOA produced by the cornea, thereby reducing the overall spherical HOA (Millodot et al 1997; Artal et al 2002). A partial compensation of coma and of other asymmetric HOAs also occurs, at least in young, low myopic eyes (Artal et al 2006; Tabernero et al 2007; Berrio et al 2010). The increase in horizontal coma with age can be explained by the decrease in the radii of
curvature of the crystalline lens which modifies the shape factor of the lens thereby reducing the compensation of lateral coma. This mechanism is also applicable to spherical HOA (el Hage et al 1973; Millodot et al 1997; Artal et al 1998; Smith et al 2001).

The increase in the Total coma with increase in age is, alternatively, considered to be mainly due to the increase in the Corneal coma (Guirao et al 2000; Karimian et al 2010). The increase in the Total spherical HOA, when measured with the Hartmann-Shack type wavefront aberrometer, with increase in age (Karimian et al 2010) can also be attributed to the increase in the spherical HOA of the internal optics (Amano et al 2004). However the Corneal spherical HOA may also increase with age (Cermáková et al 2010).

### 1.3.4 Accommodation

In the accommodating eye, wave aberrations are expected to change because ocular structures, particularly the shape, position, and refractive index gradient of the crystalline lens change during accommodation (Glasser and Campbell 1998; Koretz et al 2002; Alió et al 2005; Glasser 2008; Charman 2008; He and Applegate 2011). The total wavefront aberration, when measured with the spatially resolved refractometer, and the quality of the retinal image change with accommodation (He et al 2000; Iida et al 2008; Li et al 2011). These changes typically include a decrease in spherical HOA with increasing accommodation (Atchison et al 1995; He et al 2000; Cheng et al 2004) changes in astigmatism towards "with-the-rule" (Tsukamoto et al 2000; Mutti et al 2001; Radhakrishnan \& Charman 2007) and a possible increase in $3^{\text {rd }}$ order coma-like HOAs (Atchison et al 1995; Cheng et al 2004; Iida et al 2008).

Amongst all the aberrations, spherical-like HOAs exhibit the largest change with accommodation. Spherical ( $4^{\text {th }}$ order) HOA shows a phase shift from positive to negative
with increase in accommodation (Atchison et al 1995; Ninomiya et al 2002; Iida et al 2008; López-Gil et al 2008; Li et al 2011).

Using iTrace ray-tracing technology, positive spherical ( $4^{\text {th }}$ order) HOA has been found up to a 4.00 dioptre accommodation demand (Iida et al 2008) although others suggest that near-zero spherical HOA is present with accommodation of approximately 0.50 dioptres in young individuals (<20 years) and with 2-3 dioptres in individuals between 20 and 39 years (Radhakrishnan and Charman 2007). Alternatively, negative spherical HOA, when measured with the Hartmann-Shack type wavefront aberrometer, is present during 3 dioptres of accommodation (Ninomiya et al 2002. The rate of the phase shift in spherical HOA is greater in older individuals (López-Gil et al 2008). The change with age in the relationship between spherical HOA and accommodation can be interpreted in terms of the changing gradients of refractive index and surface curvatures of the crystalline lens with increasing age (Glasser and Campbell 1998; Radhakrishnan and Charman 2007).

Total HOA has also been shown to increase with accommodation over a range of 4.0 dioptres in young individuals (Iida et al 2008). Coma and Trefoil ( $3^{\text {rd }}$ order) HOAs are either unaffected (Iida et al 2008) or increase with increase in accommodation (Atchison et al 1995).

Changes in corneal parameters resulting from accommodation are small and generally insignificant (Read et al 2007). No significant change in the topography of the cornea was found with accommodation across a corneal zone of 8.0 to 9.0 mm . Small changes were found in the corneal cylinder axis, indicative of small cyclotorsional eye movements accompanying accommodation. However, steepened corneal curvatures (Yasuda et al 2003), central corneal steepening and increment in power due to contraction of the ciliary muscle during accommodation (Yasuda and Yamaguchi 2005) suggest that changes in
corneal curvature do participate in the mechanism of accommodation. Despite possible changes in the corneal shape and curvature, a very small positive shift of corneal spherical HOA occurs with accommodation (He et al 2003).

HOAs measured with the Hartmann-Shack aberrometer exhibit micro-fluctuations in magnitude, both within- and between-individuals, which are not associated with the coexisting micro-fluctuations in accommodation. The origin of the fluctuations in the higher order aberrations is not known (Hofer et al 2001).

### 1.3.5 The Tear Film

Changes in the tear volume and tear fluid dynamics can induce changes in the HOAs even if the remaining optical quality is 'ideal' (Albarran et al 1997). Higher-order aberrations (measured with the Hartmann-Shack aberrometer over a 4.0 mm zone) increased 1.44 fold following tear break-up compared to that before break-up and 1.23 fold (over a 6.0 mm zone) during scotopic vision (Koh et al 2002). Since any local change in tear-film thickness and tear-film regularity introduces additional aberrations to the cornea, patients with dry-eye can exhibit large optical aberrations compared to those of normal eyes and this can cause the blurred vision which can be present in such individuals. Total, spherical-like and coma-like HOAs, measured with the Hartmann-Shack aberrometer, are greater in dry eyed individuals both for 4.0 and 6.0 mm zones (Montes-Mico et al 2004(a)). These three HOAs, measured with the Hartmann-Shack aberrometer, reduce in magnitude following artificial tear instillation due to the improvement in optical quality (Montes-Mico et al 2004(a);(b); Montés-Micó 2007; Montes-Mico et al 2010).

Sequential changes in the Total HOA for those with a short tear-film break-up time are significantly higher than in those in whom blinking was suppressed for between 5 to 9 seconds (Koh et al 2008). Dynamic changes in HOAs are present after blinking and show variations even in normal individuals. Increased Total and coma-like HOAs are present in individuals who exhibit a saw-tooth pattern of sequential variation in HOA which suggests that an inferior-superior asymmetric change in tear film thickness is responsible (Koh et al 2006). Normal and dry eye individuals exhibit an increase in coma, trefoil, and the $3^{\text {rd }}$ to the $6^{\text {th }}$ order HOAs from post-blink through to the time of tear breakup which decreases with saline addition (Lin et al 2005).

### 1.3.6 Visual Acuity

High contrast acuity is not influenced by coma and spherical HOAs; however, it declines with increase in trefoil HOA (Villegas et al 2008) particularly for high values (FernándezSánchez et al 2008). Low contrast visual acuity is not influenced by either coma, trefoil or spherical HOAs (Villegas et al 2008) although large values of coma and trefoil HOAs (approximately 1 micron), significantly reduce both low and high contrast visual acuity (Fernández-Sánchez et al 2008). The degree of binocular vision declines as the betweeneye asymmetry in each of the three aberrations, total, coma, and spherical HOAs, increases (Piers et al 2007).

However, other studies claim that assessment of the distribution and contribution of the different HOAs is not totally appropriate to represent visual quality since the HOAs do not directly describe the quality of the retinal image (Chen et al 2005; Bühren et al 2009; Lombardo and Lombardo 2010).

### 1.3.7 Contrast Sensitivity Function (CSF)

Total HOA, spherical and $4^{\text {th }}$ order HOAs (quadrifoil, secondary astigmatism) attenuate, in myopic eyes, the area under the CSF defined as that between 1 and 18 cpd . (Feizi and Karimian 2009). CSF is optimum when spherical HOA is corrected by adaptive optics (Piers et al 2007). Alternatively, spherical-like HOAs measured for a 4.0 mm zone do not affect the area under the CSF defined as that between 3 and 18 cpd (Oshika et al 2006).

Coma-like HOAs ( $3^{\text {rd }}$ order) also attenuate the area under the CSF (Oshika et al 2006). Correction for monochromatic aberrations improves the CSF for mid to high spatial frequencies (de Gracia et al 2011).

Contrast sensitivity loss increases with cataract severity for cortical (p<0.001) (Lasa et al 1992; Maraini et al 1994) and for posterior sub-capsular (p<0.001) (Lasa et al 1992) cataract for all spatial frequencies ( $\mathrm{p}<0.001$ ) (Lasa et al 1992; Maraini et al 1994). Night and day glare sensitivity are each associated with increased severity of posterior subcapsular cataract ( $\mathrm{p} \leq 0.003$ ) and with decreased visual acuity ( $\mathrm{p}<0.001$ ) (Lasa et al 1992).

Contrast sensitivity and visual acuity remained similar between three types of aspheric IOLs (Tecnis Z9003- Abbott Medical Optics, Santa Ana, CA; AcrySof SN60WF- Alcon Laboratories Inc. Ft Worth, Tex; and Akreos Adapt AO- Bausch \& Lomb, Rochester, NY) following cataract extraction by phacoemulsification. However, post-operative spherical ( $4^{\text {th }}$ order) HOA, for 4.0, 5.0 and 6.0 mm zone diameters, declined (Nabh et al 2009).

### 1.3.8 Pupil Diameter

The relationship between the change in pupil diameter, and the corresponding change in the given HOA, varies between HOAs. Large increases in defocus ( $2^{\text {nd }}$ order), spherical
and quadrafoil ( $4^{\text {th }}$ order) HOAs were found with increasing pupil diameter (Fritzsch et al 2011).

All HOAs, in particular spherical ( $4^{\text {th }}$ order) and coma ( $3^{\text {rd }}$ order) HOAs, increase significantly as pupil diameter increases ( $\mathrm{p}<0.001$ ) (Liang and Williams 1997; Wang et al 2003; Hu et al 2004). Nevertheless, spherical HOA ( $4^{\text {th }}$ order) exhibits a larger increase from a 5.0 to a 6.0 mm than from a 4.0 to a 5.0 mm pupil diameter (Wang et al 2003). Compared with spherical HOA, coma ( $3^{\text {rd }}$ order) HOA had a less pronounced increase, and secondary coma ( $5^{\text {th }}$ order) and high astigmatism ( $4^{\text {th }}$ and $6^{\text {th }}$ order) HOAs a more pronounced increase, for the larger pupil diameter (Wang et al 2003). Total, coma, high astigmatism, spherical and trefoil HOAs increase significantly as pupil diameter increases from 2.0 to 4.0 mm in a relaxed accommodative state and is greatest for the total coma HOA (Wu et al 2008). The HOAs were independent of pupil diameter for 3.0 dioptres of induced accommodation. However, for 4.0 dioptres, and greater, of induced accommodation, spherical ( $4^{\text {th }}$ order) HOA decreased and changed from positive to negative and trefoil ( $3^{\text {rd }}$ order) HOA changed from negative to positive (Wu et al 2008). Spherical HOA changes more with accommodation than coma and trefoil HOAs. It becomes more negative with accommodative pupil constriction compared to that for a fixed 4.0 mm pupil. This change is larger in older individuals (López-Gil et al 2008).

The change in wavefront refraction, based on the $2^{\text {nd }}$ order Zernike coefficients (sphere and cylinder), between 3.0 and 6.0 mm zone diameters is correlated with the amount of $4^{\text {th }}$ and $6^{\text {th }}$ order spherical and $4^{\text {th }}$ and $6^{\text {th }}$ order astigmatism HOAs ( $\mathrm{p}<0.001$ ) (Iseli et al 2005).

Increased pupil diameter, under monocular conditions, produces higher Total HOA than those produced under the binocular condition, leading to worse retinal image quality.

Thus, individual eyes with large pupils will have exacerbated HOAs (Kawamorita et al 2006).

HOAs obtained through a pupil under cycloplegia differ from those obtained without cycloplegia. The mean horizontal and vertical coma ( $3^{\text {rd }}$ order) and horizontal secondary coma and secondary trefoil ( $5^{\text {th }}$ order) HOAs, were larger for a pupil dilated with 3 drops of $1 \%$ cyclopentolate than for a pupil dilated with one drop of $2.5 \%$ phenylephrine (Carkeet et al 2003).

Aberrometry and refractive measurements are different under physiological mydriasis compaired to pharmacological pupil dilation (Giessler et al 2002; Taneri et al 2010). Myopic refractive error measured by aberrometry is less than that determined subjectively depending upon the mydriatic (Giessler et al 2002): on average, the reduction in myopia was $0.19,0.35$ and 0.42 dioptres for phenylephrine, tropicamide and cyclopentolate respectively (Giessler et al 2002). In a similar study, the reduction in myopia was 0.19 dioptres (SD 0.3) for tropicamide $0.5 \%$ and 0.25 dioptres (SD 0.4) for tropicamide $0.5 \%$ and phenylephrine $2.5 \%$, combined (Taneri et al 2010). However, at a 6.0 mm pupil size, the total HOA is largest for phenylephrine $10 \%$, and larger for cyclopentolate $1 \%$ compared to tropicamide $1 \%(\mathrm{p}=0.002)$ ( Kim et al 2009). The magnitudes of the HOAs obtained following instillation of phenylephrine are similar to those obtained with the dark adapted pupil. However, tropicamide caused a reduction in the spherical ( $4^{\text {th }}$ order) HOA compared to the dark adapted pupil (Jurkutat et al 2007).

However, in a different study, the magnitudes of the defocus and astigmatism aberrations and of the total, $3^{\text {rd }}, 4^{\text {th }}$ and higher HOAs were similar for 3 drops of phenylephrine $5.0 \%$, 3 drops of tropicamide $0.5 \%, 3$ drops of Mydrin-P (phenylephrine $0.5 \%$ and tropicamide $0.5 \%$, combination) and 3 drops of the antibiotic Tarivid (ofloxacin) $0.3 \%$ (Yu et al 2005).

Similarly, HOAs and spherical equivalent refraction measured with the wavefrontsupported corneal ablation (WASCA) aberrometer are similar for a pupil dilated naturally under scotopic illumination levels, and that dilated using tropicamide (Yang and Wu 2007).

### 1.3.9 Refractive Surgery

Whilst the lower order aberrations, including astigmatism, are generally successfully corrected, refractive surgery tends to increase the total HOAs, primarily spherical and coma HOAs; with the increment being greater with increase in pupil size (Applegate et al 2000; Hong and Thibos 2000; Marcos 2001; Marcos et al 2001; Moreno-Barriuso et al 2001; Mrochen et al 2001; Tetsuro et al 2006; Queirós et al 2010). This increment results in symptoms of glare, halos, starbursts, and monocular diplopia (Chalita et al 2003; Chalita et al 2004).

There are numerous publications concerning HOAs following corneal refractive surgery and a detailed review is beyond the scope of this thesis. However, in individuals who have undergone LASIK (laser in situ keratomileusis) surgery, scotopic pupil diameter can be associated with an increase in starburst $(\mathrm{p}=0.001)$ and a reduction in diplopia ( $\mathrm{p}=0.011$ ) (Chalita et al 2004). For a 7.0 mm zone diameter, starburst was correlated with total coma ( $\mathrm{p}=0.004$ ) and diplopia with total and horizontal coma HOAs ( $p=0.014$ and $\mathrm{p}=0.024$ ). For the scotopic pupil, glare was correlated with spherical $(\mathrm{p}=0.010)$ and with total $(\mathrm{p}=0.041)$ HOAs; diplopia with horizontal coma HOA ( $\mathrm{p}=0.033$ ) and starburst with both spherical ( $\mathrm{p}=0.014$ ) and total ( $\mathrm{p}=0.004$ ) HOAs (Chalita et al 2004).

Corneal and Total coma-like and spherical-like HOAs, measured using a laser ray-tracing technique, increase after standard LASIK, custom LASIK, and corneal refractive therapy procedures by a factor of 50 for a zone diameter of 8.0 mm compared to a 3.0 mm diameter (Marcos et al 2001; Oshika et al 2002; Queirós et al 2010). Standard and custom LASIK induce less spherical-like HOAs than orthokeratology/ corneal refractive therapy (Queirós et al 2010). Corneal and Total HOAs (third-order and higher) showed a statistically significant increase after LASIK ( $\mathrm{p}<0.001$ ). However, the anterior Corneal spherical HOA increases more than the Total spherical HOA, suggesting a change in the spherical HOA of the posterior corneal surface (Marcos et al 2001). A reduction of two or more lines of baseline spectacle-corrected Snellen visual acuity is associated with increases in coma-like ( $\mathrm{p}=0.003$ ) and spherical-like ( $\mathrm{p}=0.009$ ) HOAs for a 3.0 mm zone diameter (Oshika et al 2002).

Third order, and beyond, HOAs increased by 1.9 fold ( $\mathrm{p}<0.001$ ) for a 6.5 mm zone diameter following LASIK surgery. The main contribution occurred from the fourfold increase in spherical HOA ( $\mathrm{p}<0.001$ ). Similar findings were present for a 3.0 mm zone diameter (Moreno-Barriuso et al 2001).

Myopic and hyperopic LASIK induce different patterns of $3^{\text {rd }}$ to $5^{\text {th }}$ HOAs (Kohnen et al 2005). Total HOA increased after myopic LASIK by 0.167 microns (SD 0.18) ( 1.53 fold) and after hyperopic LASIK by 0.341 microns (SD 0.34) ( 1.89 fold). Myopic LASIK induced positive spherical and positive secondary astigmatism ( $5^{\text {th }}$ order) HOAs whereas hyperopic LASIK induced negative spherical and negative secondary astigmatism HOAs. The extent of the increase in secondary astigmatism HOA was greater after myopic LASIK (Kohnen et al 2005). Similar results were obtained following hyperopic LASIK surgery for Total and for Corneal $3^{\text {rd }}, 4^{\text {th }}, 5^{\text {th }}$ and higher HOAs which became more negative ( $\mathrm{p}<0.001$ ) (Llorente et al 2004).

In another study, hyperopic LASIK significantly increased the $6^{\text {th }}$ month post-operative Corneal coma-like (by 172\%) and spherical-like (by $72 \%$ ) HOAs for a 3.0 mm zone diameter and by $182 \%$ and $223 \%$, respectively, for a 6.0 mm zone diameter (Nanba et al 2005).

Myopic LASIK flap creation either with a mechanical microkeratome or with femtosecond laser flap creation (IntraLase) causes an increase in anterior corneal HOAs (Muñoz et al 2010). The post-operative increase in spherical ( $4^{\text {th }}$ order), vertical and horizontal coma ( $3^{\text {rd }}$ order) HOAs for a 4.0 mm zone increased by a factor of 1.90 with both techniques. Similar results were obtained for a 6.0 mm zone diameter.

No statistically significant differences between three different types of LASIK ablations, Q-factor customized ablation (aberration smart ablation, ASA), wave-front guided ablation (WASCA) and ablation under wave-front guiding plus iris recognition system (IR+WASCA), were found in the post-operative spherical equivalent refraction, the change in the HOAs, including coma and spherical HOAs. Horizontal coma HOA accounted for the majority of the coma HOA. The post-operative increase in the various HOAs was still present 3 months after surgery (Mao et al 2011). A significant increase in the total HOA for a 6.0 mm zone diameter, measured with a Hartmann-Shack type aberrometer, occurs at one month post-operatively following myopic LASIK surgery (Benito et al 2011). Spherical HOA increases in myopic eyes greater than -5.0 dioptres during the first six months following surgery (Benito et al 2011).

A reduction in the contrast sensitivity function occurs with an increase in the spherical $\left(4^{\text {th }}\right.$ order) HOA following LASIK, commonly in myopic eyes, when the photopic pupil diameter is 4.0 mm or larger. An attenuation is also present with increase in coma ( $3^{\text {rd }}$
order) HOA when the photopic pupil size is smaller than 4.0 mm (Tetsuro et al 2006; Oshika et al 2006; Loukotová et al 2009).

Vertical secondary coma and oblique pentafoil ( $5^{\text {th }}$ order) HOAs increase after Epipolis laser in keratomileusis (Epi-LASIK) and after LASIK surgical techniques for 3.0 and 6.0 mm zone diameters (Yang et al 2011). The increase is significantly smaller for the EpiLASIK.

The total HOA increased by a factor of 17.65 ( $\mathrm{p}=0.001$ ) following photorefractive keratectomy (PRK) (Seiler et al 2000). Total HOA, for 3.50 and 6.00 mm zone diameters, increased after PRK for low (range -1.25 to -4.00 dioptres), high (range -4.10 to -9.00 dioptres) levels of myopia and myopia with a cylinder component ranging between -2.00 and -5.00 dioptres $(\mathrm{p}<0.05)$ (Serrao et at 2011). Spherical HOA increased for the low and high categories ( $\mathrm{p}<0.05$ ) whilst coma HOA increased only in the high myopia category ( $\mathrm{p}<0.05$ ), over a 6.00 mm zone diameter. One year after PRK, the anterior cornea HOAs remained stable (Serrao et at 2011).

Six months post-operative coma, trefoil ( $3^{\text {rd }}$ order) and spherical ( $4^{\text {th }}$ order) HOAs, measured using the CustomVue WaveScan, for a mean zone diameter of 6.0 mm were significantly increased compared with preoperative measurements but were similar between PRK and thin-flap LASIK (Hatch et al 2011).

Radial keratotomy (RK) causes an increase in Corneal spherical and coma-like HOAs (both $\mathrm{p}<0.001$ ) (Oliver et al 1997; Applegate et al 1998; Oshika et al 1999; Oliver et al 2001). The increase in HOAs for large pupils ( $\geq 7.0 \mathrm{~mm}$ ) was correlated with a decrease in contrast sensitivity (Applegate et al 1998). For large pupil diameters, LASIK induces a larger spherical HOA than PRK (Oshika et al 1999).

For myopia of between -6.00 to -9.00 dioptres, Implantable Collamer Lens implantation (ICL) induces Total vertical trefoil and spherical, Internal spherical and Corneal vertical trefoil HOAs whilst wavefront-guided laser epithelial keratomileusis (WFG-LASEK) induces total, Total and Corneal spherical, secondary astigmatism and tetrafoil HOAs. The ICL generated smaller induced Total and Corneal HOAs (Shin et al 2011). Similarly, for a 4-mm pupil, induced changes in ocular coma-like, spherical-like and total HOAs following ICL implantation are significantly less than those following WFG-LASIK (p< 0.001) (Igarashi et al 2009).

The 3 month post-operative increase ( 1.46 fold) in total and in vertical coma ( $3^{\text {rd }}$ order) HOAs following LASIK is greater than that after LASEK ( 1.25 fold) ( $\mathrm{p}=0.03$ ). One year post-operatively, a reduction in total HOA occurred in $13.8 \%$ of LASIK and in $48.5 \%$ of LASEK compared with preoperative levels (Kirwan and O'Keefe 2009).

### 1.3.10 Orthokeratology/ Corneal Refractive Therapy (CRT)

Orthokeratology/ CRT significantly reduce manifest refraction (Hiraoka et al 2005; Hiraoka et al 2006; Takahiro et al 2007; Hiraoka et al 2007; Hiraoka et al 2009). However, orthokeratology/ CRT induces coma-like ( $3^{\text {rd }}$ order) and spherical-like ( $4^{\text {th }}$ order) HOAs for a $3.0 \mathrm{~mm}(\mathrm{p}<0.001)$ and a $6.0 \mathrm{~mm}(\mathrm{p}<0.001)$ zone diameter (Stillitano et al 2007). Vertical coma changes from positive to negative ( $\mathrm{p}=0.032$ and $\mathrm{p}<0.001$, respectively). The increases in coma and in spherical HOAs are positively correlated with the magnitude of the pre-treatment myopia for a 3.0 mm ( $\mathrm{p}<0.001$ and $\mathrm{p}=0.002$, respectively) and a 6.0 mm ( $\mathrm{p}<0.001$ and $\mathrm{p}=0.001$, respectively) zone diameter (Hiraoka et al 2005; Hiraoka et al 2006). Orthokeratology/ CRT undertaken on myopic individuals with a mean refractive error of -3.33 dioptres (SD 1.26) and which resulted in a mean
reduction in myopia after one month of 3.08 dioptres (SD 0.93), produced an increase in the Total HOA, determined with a Hartmann-Shack aberrometer for both a 3.0 mm (by 2.66 fold; $\mathrm{p}=0.01$ ) and a 6.0 mm zone diameter (by 2.50 fold; $\mathrm{p}=0.005$ ). All HOAs increased by a factor ranging from 2.01 to 3.20 for a 3.0 mm zone diameter and by 2.52 to 2.98 for a 6.0 mm zone diameter. Spherical-like HOAs ( $4^{\text {th }}$ and $6^{\text {th }}$ order) increased by a factor of 1.79 for a 3.0 mm zone diameter and by 2.42 for a 6.0 mm zone diameter (Joslin et al 2003). The Corneal and Total HOAs, for a zone diameter of 5.0 mm , increased 3 month post-operatively for both CRT and LASIK (Anera et al 2009). For CRT, significant increases occurred in Corneal vertical trefoil ( $3^{\text {rd }}$ order) ( $\mathrm{p}=0.031$ ), Total vertical trefoil ( $\mathrm{p}=0.005$ ), and Corneal spherical HOAs ( $\mathrm{p}=0.001$ ) whilst Corneal vertical coma HOA became more negative ( $\mathrm{p}=0.041$ ). For LASIK, the Corneal ( $\mathrm{p}=0.005$ ) and Total ( $\mathrm{p}<0.001$ ) spherical HOA and the Total vertical trefoil HOA ( $\mathrm{p}=0.008$ ) increased 3 months post-operatively (Anera et al 2009). In a different study, the Total HOA did not change, for a 4.0 mm zone diameter, following CRT and LASIK; however, increases in Total and, in particular, spherical-like HOAs ( $\mathrm{p}=0.01$ ) occurred for a 6.0 mm zone diameter in those undergoing CRT (Goldstone et al 2010).

### 1.3.11 Wavefront-guided Refractive Surgery (WFG)

WFG refractive surgery has similar, or better, refractive accuracy, uncorrected visual acuity outcomes, improved contrast sensitivity and fewer visual symptoms, such as glare and halos at night, compared to conventional LASIK (Mrochen et al 2000; Nagy et al 2002; Wallerstein 2003; Doane et al 2003; Kim and Joo 2005; Kim and Chuck 2008; Schallhorn et al 2008). Although HOAs are generally increased after WFG LASIK, the
increase is less than that induced by conventional LASIK (Kim and Joo 2005; Schallhorn et al 2008).

WFG LASIK for hyperopia induces an increase in vertical coma and oblique trefoil ( $3^{\text {rd }}$ order) and a reduction in spherical ( $4^{\text {th }}$ order) and vertical trefoil ( ${ }^{\text {rd }}$ order) (all $\mathrm{p}<0.001$ ) HOAs (Keir et al 2011). WFG LASIK and wavefront-optimized LASIK produce equivalent post-operative total, coma, trefoil, tetrafoil and spherical HOAs in myopic eyes (Perez-Straziota et al 2010).

The 6 month post-operative increase in total HOA for WFG LASIK for myopia (1.22 fold) is less than that for WFG PRK (1.74 fold), (Moshirfar et al 2010).

### 1.3.12 Age-Related Cataract

Different types of lenticular opacities appear to induce different wavefront aberration profiles. However, the literature is sparse as to the relationship between cataract type and induced HOA.

Coma HOA predominates in cortical cataract and spherical HOA predominates in nuclear cataract (Rocha et al 2007; Lee et al 2008). In a case report, comprising a 22 year old woman with nuclear cataract and a 68 year old woman with mild cortical cataract, positive spherical-like HOAs, measured with the Hartmann-Shack type aberrometer, were greater than coma-like HOAs in the nuclear cataract and coma-like HOAs were greater than spherical-like HOAs in the cortical cataract (Kuroda et al 2002). In a study of 10 eyes with cortical cataract, 10 eyes with mainly nuclear cataract and a control group of 20 eyes without cataract, nuclear cataract exhibited greater spherical and tetrafoil HOAs, measured with the Hartmann-Shack (Zywave) aberrometer for a 6.0 mm zone diameter, than in the
control group ( $\mathrm{p}=0.001$ and $\mathrm{p}=0.004$, respectively) (Sachdev et al 2004). Cortical cataract exhibited a tendency for greater coma $(\mathrm{p}=0.06)$ and tetrafoil ( $\mathrm{p}=0.07$ ) HOAs. The increased tetrafoil HOA in both types of cataract may explain the presence of halos and other visual symptoms in individuals with early cataract who exhibit relatively good high contrast Snellen acuity (Sachdev et al 2004).

Spherical and trefoil HOAs were present in an eye with mild nuclear cataract causing monocular triplopia symptoms and complaints. Following cataract extraction and IOL implantation, the triplopia disappeared and the spherical and trefoil HOAs were markedly reduced (Fujikado et al 2004). Similar findings were present in six individuals who also complained of monocular triplopia and who exhibited mild nuclear cataract. These individuals also manifested increased spherical and trefoil HOAs (Kim et al 2006). Spherical and secondary astigmatism ( $4^{\text {th }}$ order) HOAs were present in an eye with cortical cataract causing monocular diplopia. After cataract surgery, the diplopia disappeared and the spherical and secondary astigmatism HOAs were considerably decreased (Fujikado et al 2006).

### 1.3.13 Cataract Surgery

Whilst light scatter is reduced following cataract extraction and IOL implantation, HOAs still remain within the eye. The positive spherical HOA of the corneal surfaces is highly corrected in the young eye by the negative spherical aberration of the lens (Artal et al 1998; Guirao et al 2000; Artal et al 2002; Fujikado et al 2004). Since spherical IOLs also have positive spherical aberration, the pseudophakic eye exhibits an overall increase in positive spherical aberration and in both vertical and horizontal coma HOAs (Iseli et al 2006). Conventional spherical IOLs with an anterior spherical surface cannot correct
residual HOAs, most of which originate in the anterior corneal surface (Barbero et al 2003; Vilarrodona et al 2004). Different IOL designs and materials are likely to result in different HOAs. An IOL which is decentred, tilted or deformed by compression can induce aberrations.

Even if perfectly positioned in the eye, IOLs tend to increase, rather than reduce, aberrations due to the inherent limitations of most designs (Holladay et al 2002; Moshirfar 2010; Taketani and Hara 2011).

The incision size and location can induce posterior corneal surface HOAs as a consequence of the healing process. However, it generally does not degrade the optical quality of the anterior corneal surface (Wang et al 2008). For example, the post-operative increase in total, spherical, coma, trefoil, $5^{\text {th }}$ and $6^{\text {th }}$ order HOAs of the anterior cornea did not reach significance ( $\mathrm{p}=0.22$ ) both for 3.0 and 6.0 mm zone diameters. However, the increases in the same HOAs for the posterior surface were highly significant ( $\mathrm{p}<0.001$ ) for both zone diameters (Wang et al 2008).

### 1.3.14 Intraocular Lenses

There is an extensive literature on HOAs following cataract extraction and IOL implantation. In some studies, the HOAs associated with the given IOL are compared to those in eyes with clear media. The majority of studies are concerned with the outcome of the comparison of HOAs between different types of IOLs. Such literature is of limited value particularly in that the multiplicity of IOL types is quickly superseded and the literature becomes dated. There are no studies comparing the pre- and post-operative HOAs.

The difference in the type and magnitude of any given HOA associated with any given IOL is also influenced by extraneous factors such as the location and magnitude of the incision, the success of the surgery and the integrity of the eye, itself.

The following concentrates on the generic properties of IOL design and material rather than that of any one given IOL. Factors associated with the IOL include the dioptric power, the design, and the material.

Increasing IOL power tends to increase the overall aberration profile (McKelvie et al 2009). In particular, the amount of induced spherical HOA increases with increase in the dioptric power of the IOL (Barbero et al 2003; Bellucci and Morselli 2006; Tabernero et al 2006; Padmanabhan et al 2006b). With low-powered lenses, the resulting Total spherical HOA is close to the corneal spherical HOA. With high-powered lenses, the increase in positive spherical HOA increases as the curvature of the anterior surface of the IOL steepens (Bellucci and Morselli 2006). Such an outcome is more apparent with IOLs of high refractive index. (Atchison 1991a). However, with aspheric IOLs, the induced spherical HOA in a modelled eye, declined with increase in the dioptric power of the IOL when determined by Hartmann-Shack type aberrometry (Taketani and Hara 2011).

A given IOL induces lower amounts of positive spherical HOA as the anterior surface of the IOL becomes steeper (Vilarrodona et al 2004). Therefore, for corneae with positive spherical HOA, an unequal biconvex or convex-plano IOL design with greater anterior curvature (i.e., that facing the posterior corneal surface) will provide less spherical HOA than an unequal biconvex design with a greater posterior curvature (i.e., that facing the retina) (Atchison 1991b; Vilarrodona et al 2004; Bellucci and Morselli 2006). The HOAs, associated with a more posteriorly curved biconvex shaped IOL (AcrySof MA30BA, Alcon Laboratories Inc. Ft Worth, Tex) are similar to those associated with a more
anteriorly curved biconvex shaped IOL (AcrySof MA30AC, Alcon Laboratories Inc. Ft Worth, Tex) for the cornea and for the whole eye when measured using the HartmannShack aberrometer at a 4.0 mm zone diameter (Taketani et al 2005a). For a 6.0 mm zone diameter, the MA30AC IOL exhibited smaller spherical-like aberrations than the MA30BA IOL; however, there were no differences between the two IOLs in Total and Corneal coma-like and total HOAs (Taketani et al 2005a; Padmanabhan et al 2006a).

Compared to spherical IOLs, aspheric IOLs decrease spherical ( $4^{\text {th }}$ order) (Holladay et al 2002; Denoyer et al 2007; Kim et al 2008; Mester and Kaymak 2008; Cui et al 2009; Kohnen et al 2009) and total HOAs (Holladay et al 2002; Denoyer et al 2007). Aspheric IOLs with a prolate anterior surface made of continuous aspherical surfaces across the entire optical zone reduce spherical HOAs by introducing negative spherical aberration to counter the typically positive spherical aberration of the cornea (Taketani et al 2004; Taketani et al 2005a; Padmanabhan et al 2006a; Padmanabhan et al 2006b). Aspheric IOLs offer no advantage compared to spherical IOLs in the reduction of coma and trefoil ( $3^{\text {rd }}$ order) HOAs (Bellucci et al 2004; Bellucci et al 2007; Lin et al 2008; Ohtani et al 2009). The aspheric Tecnis Z9000 IOL (Pharmacia Corporation, Peapack, NJ) which possesses a modified prolate surface, reduces spherical, total coma and vertical coma HOAs compared to the spherical acrylic Sensar Optiedge AR40e (Abbott Medical Optics) and Hydrophilic Acrylic Stabibag (Ioltech Laboratories) IOLs (Nanavaty et al 2010; Su et al 2009; Muñoz et al 2006; Holladay et al 2002). The Tecnis IOL also reduces secondary astigmatism HOA compared to the AR40e IOL (Kasper et al 2005; Kasper et al 2006). Similar results were obtained between the Tecnis Z9000 and the spherical AcrySof singlepiece SA60AT (Alcon Laboratories Inc. Ft Worth, Tex) (Su and Hu 2009), and the Acrysof MA60BM and Sensar Optiedge AR40e (Padmanabhan et al 2006), and the

CeeOn Edge 911 IOL (Abbott Medical Optics, Santa Ana, CA) (Rekas et al 2008; Denoyer et al 2006) IOLs.

In a comparison of the performance of a spherical (SoFlex SE, Bausch \& Lomb, Rochester, NY) IOL in one eye and an aspheric (SofPort AO, Bausch \& Lomb, Rochester, NY) IOL in the fellow eye, the aspheric IOL exhibited lower total HOAs (Morales et al 2011).

Spherical and coma HOAs are similar between the aspherical Tecnis Z9000 silicone (Abbott Medical Optics, Santa Ana, CA) and aspherical AcrySof IQ SN60WF acrylic (Alcon Laboratories Inc. Ft Worth, Tex) IOLs; however, vertical astigmatism, vertical trefoil, and vertical tetrafoil HOAs increased post-operatively ( $\mathrm{p}<0.0005$ ) resulting in a significantly increased overall corneal RMS wavefront error (based on ray tracing) for 10.0 mm and for 5.0 mm zone diameter (Marcos et al 2007).

The Implantable Collamer Toric IOL (STAAR Surgical, Monrovia, CA) and the irisfixated toric phakic Verisyse IOL (Abbott Medical Optics, Santa Ana, CA; Artisan, Ophtec) correct up to 2.00 dioptres of astigmatism and the AcrySof IQ Toric IOL (Alcon Laboratories Inc. Ft Worth, Tex) corrects up to 3.50 dioptres (Mertens et al 2008; Dick and Buchner 2007; Coskunseven et al 2007).

The total, spherical and tetrafoil (4th order) HOAs for a 6.0 mm zone diameter are smaller for the spherical 722C PMMA IOL (Pharmacia Corporation, Peapack, NJ) compared to two types of foldable acrylic IOLs, MA30BA AcrySof and MA60BM AcrySof (Alcon Laboratories Inc. Ft Worth, Tex). However, there was no difference between the three types of IOLs for a 3.5 mm zone diameter (Pesudovs et al 2005).

IOLs of high refractive index induce higher amounts of total HOAs and, in particular, spherical HOA (Marcos 2002).

IOLs can be made from PMMA, hydrophobic or hydrophilic acrylic, and silicone. Each material has a different refractive index which necessitates different curvatures for any given IOL power. The mechanical properties of the IOL (material and design) affect the magnitude of the HOAs induced following implantation, in particular spherical aberration. The acrylic IOLs have a more pliable nature than silicone IOLs, which are more elastic with rapid recovery of shape after folding, and PMMA lenses, which are rigid (Vilarrodona et al 2004).

The total, $3^{\text {rd }}$ and $4^{\text {th }}$ order HOAs are similar in normal phakic eyes and in eyes with the hydrophilic acrylic ACR6D (Corneal Laboratoire, Paris), the silicone-acrylic Acrysof Sensar AR40 (Allergan Surgical, Irvine, CA) and the acrylic/ silicone-PMMA MA60BM (Alcon Laboratories Inc. Ft Worth, Tex) IOLs, with the exception of trefoil HOA. The latter was greater for all IOL types compared to that of the phakic eye ( $\mathrm{p}<0.05$ ) (Choi et al 2005).

A comparative study was undertaken, using a Hartmann-Shack aberrometer, by Vilarrodona et al (2004) with the acrylic AcrySof MA30AC (Alcon Laboratories Inc. Ft Worth, Tex), the AcrySof MA30BA acrylic IOL (Alcon Laboratories Inc. Ft Worth, Tex), the silicone SI-30NB (Allergan Surgical, Irvine, CA) and the PMMA MZ30BD (Alcon Laboratories Inc. Ft Worth, Tex) IOLs. The two acrylic IOLs yielded similar HOAs and the silicone and PMMA IOLs produced similar HOAs. However, the coma, trefoil, spherical, secondary astigmatism, and tetrafoil HOAs were larger for the two high-refractive-index acrylic IOLs compared to the silicone and to the PMMA IOLs ( $\mathrm{p}<0.05$ ). The positive spherical HOA was lowest for the silicone IOL (Vilarrodona et al 2004).

A different study, using the iTrace Visual Function Analyzer for a zone diameter of 4.5 mm , compared the Collagen Collamer CC4205 IOL (STAAR Surgical, Monrovia, CA)
the silicone AA4204 (STAAR Surgical, Monrovia, CA), the acrylic Sensar AR40E (Abbott Medical Optics, Santa Ana, CA) and the acrylic AcrySof SA-60 IOL (Alcon Laboratories Inc. Ft Worth, Tex) (Martin and Sanders 2005). The AcrySof IOL induced larger total HOA than the Collamer IOL which, in turn, exhibited less $3{ }^{\text {rd }}$ order coma and trefoil, $4^{\text {th }}$ order tetrafoil and spherical, $5^{\text {th }}$ order pentafoil and $6^{\text {th }}$ order hexafoil HOAs than the Acrylic and silicone IOLs. The acrylic Sensar AR40E IOL exhibited less coma and spherical HOAs than the acrylic AcrySof IOL (Martin and Sanders 2005).

The Tilt(S1) and T.Coma HOAs, measured at least 1 month after cataract surgery for a 6.0 mm zone with the OPD aberrometer, were larger for the high index acrylic hydrophobic MA60AC (Alcon Laboratories Inc. Ft Worth, Tex) compared to the acrylic hydrophilic XLSTABI (Ioltech Laboratories) (Rohart et al 2006).

The post-operative vertical coma, horizontal coma and spherical HOAs, measured by the Tscherning Allegro Wave Analyzer, arising from an acrylic hydrophobic monofocal foldable IOL (Alcon Laboratories Inc. Ft Worth, Tex) were greater than those in normal young phakic eyes. These increases were attributed to the lack of compensation by the IOL; such compensation would, ordinarily, have been present in the crystalline lens (Iseli et al 2006). The hydrophilic acrylic expandable Acqua (Mediphacos, Belo Horizonte, Brazil) IOL, with a water content of $74 \%$, exhibits greater HOAs compared to the diffractive multifocal AcrySof ReSTOR (Alcon Laboratories Inc. Ft Worth, Tex) and the monofocal acrylic IOLs, Acrysof MA30AC (Alcon Laboratories Inc. Ft Worth, Tex) and Acrysof SA60AT (Alcon Laboratories Inc. Ft Worth, Tex) (Rocha et al 2005). The AcrySof ReSTOR multifocal IOL induced less spherical HOA compared to the two monofocal IOLs. In another study, similar HOAs were obtained for the spherical multifocal AcrySof SN60D3 and the spherical monofocal AcrySof SN60AT IOLs (both
from Alcon Laboratories Inc. Ft Worth, Tex) measured by the OPD aberrometer (Hida et al 2009).

The effect of IOL tilt and decentration, measured with the Scheimpflug videophotography, on HOAs has been described in a case presentation (Oshika et al 2005). The tilting angle was 28.87 degrees, and decentration was 1.78 mm .

The tilt and decentration induced a large amount of total coma-like HOAs but did not affect total spherical-like, corneal coma or corneal spherical HOAs. Repositioning surgery improved the IOL tilt and led to a reduction in the total coma-like HOAs (Oshika et al 2005; Taketani et al 2005b; Wang and Koch 2005). In eyes with a scleral-sutured posterior chamber IOL, tilting of the lens induces total coma-like HOAs (Oshika et al 2007).

### 1.3.15 Surgical Incision

Small-incision cataract surgery ( $3.5-\mathrm{mm}$ incision without suture) produces a small increase in post-operative corneal HOAs (Guirao et al 2004). Nasal small-incisions induce a larger total HOA compared with temporal small-incisions. The position of the incision influenced the orientation of the induced astigmatism and the magnitude of the trefoil HOA whereby the steepest curvature lay along the meridian of the incision. The trefoil HOA also showed a predominant pattern along this meridian (Guirao et al 2004).

Microincision cataract surgery performed through incisions smaller than 2.0 mm , using either biaxial microincision or microcoaxial phacoemulsification, generates statistically significantly less corneal astigmatism and better optical quality of the cornea compared to small-incision surgery (Denoyer et al 2008; Can et al 2010). However, there appears to be
no advantage over small-incision cataract surgery in the reduction of corneal HOAs, even for a 1.7 mm incision (Yao et al 2006).

### 1.3.16 Keratoconus and Collagen Cross-Linking in Keratoconus

The structural changes associated with keratoconus lead to a stretching and to a thinning of the cornea with a consequence progressive increase in distortion and reduction in visual performance (Sugar and Macsai 2012; Kok et al 2012; Agrawal 2010; Nordan 1997). Aberrometry is considered to be an efficient method for detecting, and monitoring keratoconus and as an aid in the management (Jafri et al 2007; Schwiegerling 1997; Langenbucher et al 1999).

As would, perhaps, be expected, corneal HOAs, especially coma-like, are significantly higher in keratoconic eyes compared to normal eyes (Alió and Shabayek 2006; Maeda et al 2002; Barbero et al 2002). In one study, the mean total anterior and the mean total posterior corneal surface HOAs were significantly higher ( $\mathrm{p}<0.001$ ) in keratoconic eyes (4.34 and 1.09 microns, respectively) than in normal eyes ( 0.46 and 0.15 microns, respectively) (Nakagawa et al 2009). In another study, the anterior and posterior surface trefoil, coma, tetrafoil, and secondary astigmatism ( $3^{\text {rd }}$ and $4^{\text {th }}$ order) HOAs were all significantly higher compared to normal eyes (p< 0.001) (Kosaki et al 2007; Nakagawa et al 2009). The anterior surface coma is approximately opposite to that of the posterior surface in the keratoconic eye. The posterior surface coma thus, at least partly, compensates for the anterior surface coma HOA (Nakagawa et al 2009). Indeed, an increase in anterior corneal surface vertical coma exhibits high diagnostic ability for the detection of subclinical keratoconus, yielding an area under the Receiver Operator curve of 0.980 (Bühren et al 2010).

Collagen cross-linking with administration of riboflavin and UV radiation may delay or halt the progression of keratoconus (Agrawal 2009; Baumeister et al 2009).

Individuals who received collagen cross-linking with riboflavin administration and 30 minutes of UV radiation at a wavelength of 365 nm exhibited little difference between the pre-operative and 6 months post-operative Total ( $\mathrm{p}=0.047$ ) and coma ( $\mathrm{p}=0.116$ ) HOAs for a zone diameter of 6.0 mm (Baumeister et al 2009).

Corneal collagen cross-linking reduces the HOAs compared with the control of the nontreated fellow eye. Twelve months after treatment, the post-operative anterior corneal total and coma-like HOAs were lower than the pre-operative values (both $\mathrm{p}<0.001$ ). No significant changes in the posterior corneal HOAs were found. The 12 month postoperative Total total HOAs, Total coma-like and Total spherical HOAs also declined $(\mathrm{p}=0.01)($ Greenstein et al 2012).

In another study, corneal wavefront analysis showed that at the 12 month follow-up examination, most Corneal HOAs were similar to those at the pre-operative base-line. However, the magnitude of the Corneal coma HOA was lower 6 months after treatment and remained stable throughout the follow-up period ( $\mathrm{p}=0.003$ ) (Agrawal 2009).

Two years after treatment, Corneal total, piston ( 0 order), defocus ( $2^{\text {nd }}$ order) and tertiary coma ( $7^{\text {th }}$ order) HOAs were all lower than the pre-operative base-line values ( $\mathrm{p} \leq 0.046$ ) (Vinciguerra et al 2009).

### 1.3.17 Contact Lenses

Aberrometry and corneal topography are useful techniques for assessing the optical performance of contact lenses, the outcome of contact lens fitting and the interaction of the contact lens with the tear film (Jeong et al 2005; Dorronsoro et al 2003). It may also be useful in the design of contact lenses such as customized soft contact lenses for keratoconus correction (Sabesan et al 2007).

Correction with rigid gas permeable (RGP) contact lenses exhibits significantly better optical quality than soft contact lenses or spectacle lens correction and is attributed to the reduction in Total HOAs, particularly positive spherical HOA (Hong et al 2001).

Spherical and toric soft contact lenses reduce positive spherical HOA ( $\mathrm{p}<0.0001$ ) compared to the non-contact lens wearing eye. Soft-toric contact lenses with prism-ballast designs exhibit higher amounts of vertical coma HOA than non-prism-ballasted lenses ( $\mathrm{p}<0.002$ ) (Berntsen et al 2009). Vertical coma HOA arising from RGP wear is dependent upon the riding position of the contact lens and/ or any pre-existing coma (Choi et al 2007). The total, total trefoil and total spherical HOAs arising from soft contact lens wear for myopia tend to be larger than for the non-contact lens wearing eye $(\mathrm{p}=0.01, \mathrm{p}=0.06$ and $p=0.036$, respectively) (Roberts et al 2006).

The magnitude of astigmatism is not altered by a spherical back-surface design whether lathe-cut, cast-molded or spun-cast when compared to the non-contact lens wearing eye. However, the cast-molded and the spun-cast contact lenses are particularly associated with an increase in coma and in spherical HOAs (Jiang et al 2006).

The Total HOA is lower in dry-eye symptomatic wearers of disposable Etafilcon A soft contact lenses which incorporate polyvinyl pyrrolidone (Koh et al 2008).

RGP contact lenses and toric soft contact lenses have been shown to reduce coma, trefoil, secondary astigmatism and cuadrifoil ( $4^{\text {th }}$ order) HOAs (all $\mathrm{p} \leq 0.015$ ) in keratoconus (Jinabhai et al 2012).

### 1.4 Miscellaneous

### 1.4.1 Pellucid Marginal Corneal Degeneration

Pellucid marginal corneal degeneration (PMCD) is a non-inflammatory corneal thinning disorder, the characteristics of which can be distinguished from keratoconus. Both conditions yield HOAs which are different to the normal eye. The mean axis of coma HOA in both conditions is opposite to that in the normal eye. However, the magnitude of the coma HOA is lower in PMCD ( 0.27 microns, SD 0.19 ) than in keratoconus $(0.70$ microns, SD 0.37) ( $\mathrm{p}<0.05$ ). Interestingly, the axis of the trefoil HOA in PMCD is similar to that in normal eyes but is approximately orthogonal to that in keratoconus. PMCD exhibits greater spherical HOA ( 0.086 microns, SD 0.10) than in keratoconus ( -0.030 microns, SD 0.13 ) $(\mathrm{p}<0.05)$ but the sign is opposite in polarity (Oie et al 2008).

A case report of a 59 year old with PMCD, who had been followed-up annually for 11 years, described a gradual 1.67 fold increase in the coma-like HOA. Spherical-like HOAs remained approximately stable (Kamiya et al 2003).

### 1.4.2 Retinal and Macular Disease

Wavefront aberrometry has been undertaken in Retinitis Pigmentosa (RP) as a quantitative method for detecting and monitoring associated changes in the crystalline lens,
particularly posterior subcapsular cataract (Rajagopalan et al 2005).

Wavefront aberrations were measured using the Hartmann-Shack method in individuals with RP and posterior sub-capsular cataract; in individuals with RP and minimal, or no, posterior sub-capsular cataract; and in age-matched normal individuals. For a 6.0 mm zone diameter, the total HOA was significantly larger for the individuals with RP than for the normal individuals (cataract, $\mathrm{p}<0.001$; minimal/ no cataract, $\mathrm{p}<0.05$ ). Similarly, the $4^{\text {th }}$ order (spherical, tetrafoil) HOAs were significantly larger for the individuals with RP ( $\mathrm{p}<0.01$ and $\mathrm{p}<0.05$ ). There were no significant differences in HOAs between groups for a 3.0mm zone diameter (Rajagopalan et al 2005). The two groups of individuals with RP generated similar HOAs, irrespective of the presence of posterior subcapsular cataract.

A similar utility for aberrometry has been proposed in diabetes where transient changes in the crystalline lens may be used as a biomarker for adequacy of metabolic control. Total HOAs in diabetic individuals with various stages of retinopathy were higher (mean 0.45 microns, SD 0.18) than in normal individuals (mean 0.34 microns, SD 0.14) ( $\mathrm{p}=0.03$ ) (Shahidi et al 2004).

In phakic eyes with macular disease (epi-retinal membrane, macular oedema or macular hole), the $3^{\text {rd }}$ order HOAs trefoil and coma were larger than those in normal eyes by $12 \%$ for a 5.0 mm and by $31 \%$ for a 3.0 mm zone diameter ( $\mathrm{p}<0.021$ ). In pseudophakic eyes, the difference in the $3^{\text {rd }}$ order HOAs was greater ( $57 \%$ for the 5.0 mm and $51 \%$ for the 3.0 mm zone diameters; $\mathrm{p}<0.031$ ). It was suggested that the increase in these HOAs could have resulted from irregular, or multiple, reflecting retinal surfaces (Bessho et al 2009).

Scleral buckling surgery increases HOAs at 2 weeks ( $p<0.001$ ), 1 month ( $p<0.005$ ), and 3 months (p<0.05) post-operatively compared with normal eyes. Encircling buckling
resulted in lower HOAs compared with segmental buckling ( $\mathrm{p}<0.05$ ) 3 months postoperatively (Okamoto et al 2008).

### 1.4.3 Corneal Thickness

Central and peripheral corneal thickness are not associated with either Corneal or Total HOAs for a case series with a group mean central corneal thickness of 550.5 microns, (SD 28.5) and a peripheral corneal thickness of 629.9 microns, (SD 32.1) (Mohamed et al 2009).

### 1.4.4 Intraocular Pressure

The association between intraocular pressure (IOP) and any given HOA is equivocal. In myopic eyes, Corneal defocus, Corneal spherical and Corneal secondary astigmatism HOAs are moderately correlated with IOP ( $\mathrm{r}=0.31$ to 0.36 ). Total spherical HOA increased with increase in IOP ( $\mathrm{r}=0.32$ ) and secondary astigmatism HOA declines with increase in IOP ( $\mathrm{r}=-0.37$ ) ( Qu et al 2007). Total trefoil is negatively correlated with IOP ( $\mathrm{r}=-0.31$ ) (Mohamed et al 2009). Alternatively, there is no association between IOP and any HOA (de Castro et al 2007).

The reduction in IOP in normal individuals between midday and afternoon ( $\mathrm{p}<0.01$ ) is associated with reductions in defocus ( $\mathrm{p}=0.013$ ), astigmatism ( $\mathrm{p}=0.013$ ), Total coma ( $\mathrm{p}=0.013$ ) and Total trefoil ( $\mathrm{p}=0.031$ ) HOAs (Asejczyk-Widlicka and Pierscionek 2007). It was suggested that the reduction in the HOAs was a compensatory mechanism to
stabilize vision. However, it is more likely that the reductions are secondary to the reduction in IOP.

### 1.4.5 Amblyopia

The total, coma, sphere, high astigmatism and trefoil HOAs were each slightly higher in 30 children with either strabismic or anisometropic amblyopia compared to normal children; however, these changes did not reach statistical significance, perhaps due to lack of statistical power (Kirwan and O'Keefe 2008). There was no difference in HOAs between those with strabismic amblyopia and those with anisometropic amblyopia. It was suggested that HOAs have no role in the development of amblyopia. In a study of children with idiopatic unilateral amblyopia, the HOAs were more pronounced in the amblyopic eye compared to the normal fellow eye for trefoil-like and coma-like HOAs (Prakash et al 2011). In a study of individuals with amblyopia in whom strabismus was not the aetiology for the amblyopia, the astigmatism and the total HOA were higher in the amblyopic eye compared to the fellow normal eye and this difference was greater for anisometric rather than isometric (idiopathic) amblyopia (Plech et al 2010).

Several other studies have investigated the association of HOA with amblyopia; however, it is not possible from these publications to determine the type of amblyopia and interpretation of the various findings is, therefore, difficult and superfluous (Prakash et al 2007; Yu et al 2009; Zhao et al 2010; Qiu et al 2011).

## CHAPTER 2

## RATIONALE FOR RESEARCH

### 2.1 Introduction

Age-related cataract is the leading cause of preventable blindness, worldwide. In Europe and the United States, cataract surgery is the most common surgical procedure in people older than 65 years of age (Hyman et al 2001; Sagoo and Tuft 2005; Cotter et al 2006). Visual quality decreases with the development of cataract, primarily because of the absorption and/ or scattering of light by the opacity. Patients with age-related cataract present with a history of gradual progressive deterioration and disturbance in vision including loss of acuity and contrast, increased glare, monocular diplopia/ polyopia etc. The visual symptoms largely depend upon the type of cataract present (Maraini et al 1994). Visual loss is traditionally assessed by visual acuity where the limit of resolution with high-contrast figures such as Snellen optotypes is measured. A cataract is considered to be clinically relevant if the reduction in visual acuity significantly affects the lifestyle of the patient (Chua et al 2004; Stifter et al 2004; Stifter et al 2005). Different types of cataract produce different effects on visual acuity. For example, a mild posterior subcapsular cataract can cause a severe reduction in visual acuity, affecting mostly near acuity, presumably as a result of pupil miosis. Nuclear sclerotic cataracts are often associated with decreased distance acuity and relatively good near acuity (Sperduto and Hiller 1984; Maraini et al 1994). A cortical cataract generally is not clinically relevant until late in its progression by which time the cortical spokes compromise the visual axis.

The HOAs resulting from an age-related cataract will also contribute to the deterioration of vision.

However, the effect of age-related cataract type and severity on the associated HOA is equivocal (Kuroda et al 2002; Sachdev et al 2004; Fujikado et al 2004; Kim et al 2006; Fujikado et al 2006; Rocha et al 2007; Lee et al 2008) largely due to the small number of individuals within the various case series and to the scarcity of individuals with a 'pure', i.e. homogenous, cataract type. The majority of patients with age-related cataract have nuclear opacities in conjunction with either, or both, anterior cortical and posterior subcapsular cataract.

Post-operative HOAs are not usually evaluated in terms of a pre- and post-operative comparison; the HOAs associated with the IOL are either compared to those in eyes with clear media or, most commonly, are compared with those of other given types of IOL. Various types of IOLs are available which correct, in part, astigmatism and spherical HOA. A significant reduction in spherical HOA was achieved, for example, after implantation of Tecnis Z9000 IOL (Pharmacia Corporation, Peapack, NJ) with a modified prolate surface design and AcrySof IQ IOL (Alcon Laboratories Inc. Ft Worth, Tex) (Su et al 2009, Muñoz et al 2006, Padmanabhan et al 2006b). The Implantable Collamer Toric IOL (STAAR Surgical, Monrovia, CA) corrects up to 2.00 dioptres of astigmatism and the AcrySof IQ Toric IOL (Alcon Laboratories Inc. Ft Worth, Tex) corrects up to 3.50 dioptres (Coskunseven et al 2007).

It can be speculated that different types and severity of age-related cataract will produce different wavefront aberrometry patterns. It is not inconceivable that, in the future, from knowledge of the pre-operative corneal HOAs, a custom IOL could be selected to minimize post-operative HOAs and maximize visual acuity (Negishi et al 2010). Such an outcome would, of course, depend upon a '(near) perfect' incision and healing process.

The idea and concept of this Doctoral thesis arose from the joint programme between the Cardiff School of Optometry and Vision Sciences, Cardiff University, Cardiff, Wales, U.K. and Pennsylvania College of Optometry (now Salus University), Philadelphia, Pennsylvania, USA. This programme was open to all graduates holding the degree of MSc in Clinical Optometry from the Pennsylvania College of Optometry. It enabled research carried out in countries other than the UK or the USA to be submitted for the Degree of PhD from Cardiff University. The research described in this thesis was undertaken in the Department of Ophthalmology, Soroka University Medical Centre, Beer-Sheva, Israel, (which is the teaching hospital associated with the Ben-Gurion University of the Negev, Beer-Sheva, Israel) and in the Enaim Refractive Clinic, Beer-Sheva, Israel.

Wavefront sensing technology is widely used in clinical ophthalmology especially in the refinement of corneal refractive surgery. The Candidate met Professor Tova Lifshitz, a cataract and refractive surgeon and Head of the Department of Ophthalmology at the Soroka University Medical Centre and Medical Manager of the Enaim Refractive Clinic. The clinical potential of aberrometry and its different clinical utilities and implications were discussed at the meeting. It was decided to investigate the HOAs associated with age-related cataract. It was fortunate that a NIDEK Optical Path Difference Scanning System ARK-10000 aberrometer (OPD) was situated at the Enaim Refractive Clinic. No cross-sectional or longitudinal studies have been performed in a large case series of agerelated cataract using Placido Disc and Dynamic Skiascopy, in particular with the OPD aberrometer.

### 2.2 Primary Aims of the Study

The Primary aims of the study were to explore:
i. the associations between specified demographic, functional and structural (including cataract type and severity) variables and the magnitude of each of the Total, Corneal and Internal components for each of eight HOAs obtained by the OPD aberrometer.
ii. the associations between specified demographic, functional and structural (including cataract type and severity) variables and the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs, obtained by the OPD aberrometer at approximately 10 weeks postoperatively and, again, at approximately 80 weeks post-operatively.

### 2.3 Secondary Aims of the Study

The secondary aims of the study were to determine:
i. the associations between the changes from the pre- to the post-operative examinations in the specified functional and structural variables and the corresponding changes in the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained by the OPD aberrometer.
ii. the associations between the demographic variables and the corresponding changes from the pre- to the post-operative examinations in the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained by the OPD aberrometer.

### 2.4 Clinical Studies and Outcomes

The study used a prospective design. All participants conformed to rigid inclusion/ exclusion criteria (Chapter 3.0) and were recruited from the Soroka University Medical Centre Ophthalmic Outpatient Clinic and from the Enaim Refractive Clinic. The study protocols were approved by the local Research and Ethics Committee and all participants provided written informed consent.

The experimental work was divided into four separate studies.

### 2.4.1 Wavefront Aberrations in Age-Related Cataract

The study, described in Chapter 3, involved the measurement of HOAs in individuals with age-related cataract in order to determine the relationship between the type and magnitude of the pre-operative HOAs obtained with the OPD aberrometer and the specified demographic, functional and structural variables.

The case series comprised 99 participants listed for cataract extraction and intra-ocular lens implantation. A comprehensive ophthalmic and optometric evaluation was performed pre-operatively by an ophthalmologist and by the Author. HOA evaluation and keratometry were measured using the OPD aberrometer. Root mean square (RMS) values were separately evaluated for the HOA components Total, Tilt S1, High, TComa, TTrefoil, T4foil, TSph and HiAstig. Cataract was graded using the Lens Opacity Classification System (LOCS) III (Chylack et al 1993) for type (Nuclear Opalescence, Nuclear Colour, Cortical and Posterior) and severity (Levels 0 to 6 ). This technique is an accepted classification and grading system, routinely used in ophthalmic research, which is based upon a set of standard colour photographs of cortical cataract (C), posterior
subcapsular cataract ( P ), nuclear colour ( NC ) and nuclear opalescence (NO). The majority of individuals had combined types of cataract which required more complex descriptions involving combinations of $\mathrm{N}, \mathrm{C}$ and P . The results of a preliminary analysis were described in a poster presented at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO) in 2007.

### 2.4.2 The Change in Higher Order Aberrations Arising from Cataract Extraction and Intra-ocular Lens Implantation

The studies, described in Chapters 4 and 5, involved the measurement of HOAs obtained by the OPD aberrometer at the first and second follow-ups, respectively, in order to determine the relationship between the type and magnitude of the HOAs and the demographic, functional and structural variables at the given follow-up and to determine the relationship between the change from the pre-operative examination in the type and magnitude of the HOAs at the given follow-up and the corresponding change in the demographic, functional and structural variables.

The case series at the first follow-up, undertaken at approximately 10 weeks postoperatively, comprised 67 of the 99 individuals. The case series at the second follow-up, undertaken at approximately 80 weeks post-operatively, comprised 41 of the 67 individuals.

The choice of IOL for any given patient was at the discretion of the given surgeon and depended upon the clinical circumstances and upon the availability of the given lens specifications.

The results of a preliminary analysis were described in a poster presented at the annual meeting of the ARVO in 2008.

### 2.4.3 Comparison of the Higher Order Aberrations Obtained Prior to, and Following IOL Implantation, with Those in Less Severe Cataract and in Those exhibiting a Clear Media

The pilot study, described in Chapter 6, arose from the need to compare three outcomes. Firstly, the type and magnitude of HOAs obtained pre-operatively, in the study described in Chapter 3, with those in eyes with cataract considered insufficient to warrant extraction (i.e., 'less severe' cataract). Secondly, to compare the type and magnitude of the postoperative HOAs obtained at the second follow-up (described in Chapter 5) with those exhibiting a clear media. Thirdly, to compare the type and magnitude of the postoperative HOAs obtained at the second follow-up (described in Chapter 5) with those in eyes with cataract considered insufficient to warrant extraction.

Given the time-constraints for the completion of this thesis, the data necessary for these comparisons could only be obtained retrospectively. The individuals for the case series of clear media were obtained from the medical records of 52 normal individuals, attending the Enaim Refractive Clinic, who were listed to undergo corneal refractive surgery for the correction of refractive error. The data for the eyes with cataract considered insufficient to warrant extraction were obtained retrospectively from the medical records of 29 individuals who were also attending the Enaim Refractive Clinic. All individuals conformed to the inclusion/ exclusion criteria described in Chapter 3.

The preliminary analyses were based upon the outcome obtained with Software Revision Version 1.129 (June 2005) of the OPD aberrometer, which described each of the HOAs in terms of one component, the Total, only. However, software became available to the Author in March 2011 which enabled each HOA to be described in terms of separate components, Total, Corneal and Internal. As a consequence, the results for each study were reanalyzed in terms of the outcomes for each of the three components of each of the eight HOAs.

The complexity of the various statistical analyses were such as to necessitate professional assistance. The analyses were undertaken by Mr. David Shaw, MSc, Senior Medical Statistician following extensive discussions with both the Author and Professor Wild.

### 2.5 Logistics

The various studies were undertaken in the ophthalmic outpatient clinic during normal clinic hours and were, therefore, dependent upon the goodwill and punctuality of the participants.

The individuals participating in the first study attended for one visit which lasted five hours. At this visit, the individuals were recruited, informed consent obtained and the preoperative clinical examination undertaken. Those participating in the second study and in the third study then attended for the respective post-operative visits, each of which lasted approximately three hours. The complete data collection for these studies was spread over two years.

A number of individuals declined to take part in the initial study. Other individuals either withdrew from, or failed to attend for, the post-operative visits necessary for the second
and third studies. Some individuals were unable to undergo cataract extraction or did not undergo phacoemulsification and some developed severe post-operative corneal oedema. Some developed additional health complications, and three patients died between followup visits.

It had been intended to recruit patients undergoing surgery by a single surgeon to limit the influence of potential between-surgeon differences on the outcomes. Unfortunately, due to the hospital requirements and routine, it was not possible to obtain a sufficient number of individuals within the time frame for the thesis who conformed to the inclusion criteria but were under the care of one surgeon, only. Similarly, it was not possible to restrict the IOL to one type. Patients in the second study underwent surgery by one of four surgeons, who all used the phacoemulsification technique, and received one of four types of foldable IOLs.

The data used in the fourth (pilot) study was obtained from the medical notes over a period of six months.

The Author was responsible for the compilation, and the quality control, of the data files which were required by the medical statistician. Extensive discussions were undertaken with the statistician, in this regard.

A number of delays were encountered during the project. The most significant delays were those arising from the applications to the local Research and Ethics Committee separately for each study protocol. The completion of the thesis was also delayed by the decision to re-analyze the datasets in terms of each of the three components of each of the eight HOAs. However, such a decision was felt to be justified in terms of the time/ novelty/ benefit.

In addition, this re-analysis benefited from experience gained at, and modifications arising from, the initial analysis.

It is estimated that the data collection for the thesis involved approximately 580 hours. As was mentioned previously, the study was performed in Beer-Sheva, Israel, by the Author and was supervised by Professor John Wild in Cardiff, Wales, UK. The supervision was, therefore, not local to the project and was undertaken via international telephone calls and meetings either at Cardiff University or in different European cities. Such necessity placed considerable strain on both the Author and the Supervisor.

Although the Author had had 23 years experience of optometric patient care in the private sector, the exposure to the hospital environment and to hospital patient care was an interesting and new experience. Wavefront aberrometry has become an important topic in ophthalmic practice. The Doctoral work has created an opportunity to become part of the research community. The experience and knowledge in the research field benefited the Author both academically and clinically and it is hoped that this knowledge can now be used for the benefit of patients and colleagues, alike.

## CHAPTER 3

## WAVEFRONT ABERRATIONS IN AGE-RELATED CATARACT

### 3.1 Introduction

As was discussed in Chapter 1, little work has been undertaken into the types and magnitudes of HOAs associated with age-related cataract. It was shown in Section 1.3.12 that different types of mild cataract induced different wavefront aberration profiles. An early publication showed that $4^{\text {th }}$ order spherical HOA was greater than $3^{\text {rd }}$ order coma HOA in a 22 year old woman with nuclear cataract and $3^{\text {rd }}$ order coma HOA was greater than $4^{\text {th }}$ order spherical HOA in a 68 year old woman with mild cortical cataract (Kuroda et al 2002). These results were confirmed in two larger case series studies of 20 patients (33 eyes) and 65 patients ( 105 eyes), respectively, in which coma predominated in cortical cataract and spherical aberration predominated in nuclear cataract (Lee et al 2008; Rocha et al 2007). Similar results were obtained in case-control studies (Sachdev et al 2004; Kuroda et al 2002; Wali et al 2009).

Cortical and nuclear cataract also appear to be associated with a higher amount of tetrafoil which, in itself, may explain the presence of significant visual symptoms in those patients with early cataract who exhibit relatively good high contrast Snellen acuity (Sachdev et al 2004). Monocular triplopia associated with nuclear cataract has been attributed to the combined effects of spherical and trefoil aberrations: following cataract surgery, the triplopia disappeared and the spherical and trefoil aberrations markedly decreased (Fujikado et al 2004; Kim et al 2006). A case of monocular diplopia in a patient with mild cortical cataract probably stemmed from the combined effects of spherical aberration and secondary astigmatism caused by the cortical cataract (Fujikado
et al 2006). Following cataract surgery, the diplopia disappeared and the spherical and secondary astigmatism aberrations were considerably reduced.

All the studies, discussed above, involved a limited number of individuals and possibly, quite rightly, concentrated on 'pure' types of cataract of mild to moderate severity. As a consequence, the characteristics of HOAs in patients with advanced age-related cataract, which consist of combined types of cataract remains unknown.

In addition, all the studies used the Hartmann-Shack principle, either with the commercially available Zywave aberrometer or the commercially available LADARWave aberrometer, to measure the aberrations. To the Author's knowledge, no measurements of HOAs have been undertaken on eyes with advanced cataract using the Placido Disc and Dynamic Skiascopy basis for aberrometry and, in particular, with the Nidek Optical Path Difference (OPD) Scanning System ARK-10000 aberrometer.

The relationship between cataract type and severity and each of the HOAs is unknown. Such knowledge could contribute to the understanding of the physiological mechanism of age-related cataract and would further the understanding of the visual experience associated with image degradation arising from the given HOAs and which occurs concomitantly with absorption and intraocular light scatter. It is also possible that knowledge of the type and magnitude of HOA for any given eye could be used to custom design IOLs.

### 3.2 Aims

The aim of the study described in this Chapter was to explore any association between the demographic variables, age and gender; the structural variables, corneal curvature,
endothelial cell density, spherical equivalent, axial length, and the primary cataract type and severity; the functional variables, distance and near visual acuity and contrast sensitivity; and the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained using Placido Disc and Dynamic Skiascopy by the OPD aberrometer, in individuals listed for cataract surgery and intra-ocular lens implantation.

### 3.3 Methods

### 3.3.1 Case Series

The case series comprised 99 consecutively presenting individuals, recruited from the Ophthalmic Outpatient Clinic of Soroka University Medical Centre of the Negev, who had fulfilled the pre-defined inclusion criteria, who had volunteered to take part in the study and who had provided written informed consent, after receiving an explanation of the study, in accordance with the ethical requirements of the Soroka University Medical Centre Ethics Committee.

According to the Israeli Health Care system, a patient is able to attend a local (neighbourhood) health clinic for different clinical examinations and evaluations. The patient is examined by a general physician, who, according to the patient's complaints or clinical findings refers the patient to a specialist doctor. Under this system, all patients with cataract undergo a full ophthalmic examination by an ophthalmologist following which, and when necessary, referral is made for cataract extraction. In most cases, the surgery is undertaken within several months. All patients recruited for the study were referred, prior to cataract surgery, to the Ophthalmic Outpatient Clinic of Soroka

University Medical Centre of the Negev by one of approximately fifteen ophthalmologists.

At enrolment in the study, all individuals had undergone a second ophthalmological examination and an optometric examination. One hundred individuals had originally been enrolled in the study; however, one individual withdrew from the study, for personal reasons, shortly after giving informed consent, and before the aberrometry had been undertaken. No suitable individuals declined to take part in the study.

The inclusion criteria comprised an age greater than 18 years; an eye with a cataract suitable for extraction by phakoemulcification and suitable for intraocular lens implantation; absence of corneal scarring and/ or pterygium in the eye designated for surgery; no ocular trauma in the designated eye; intraocular pressure less than 22 mmHg ; no previous or current ocular surgery or co-existing disease in the designated eye, including glaucoma, age-related macular degeneration or diabetic retinopathy, or any other retinal disease likely to cause a reduction in vision; lack of usage of topical ophthalmic drops; and a willingness to undergo cataract surgery.

### 3.3.2 Recruitment and Experimental Procedures

Following enrolment into the study, all individuals attended for one visit which lasted up to five hours. All individuals were assessed by the Author using the following procedures (3.3.2.1-3.3.2.5, 3.3.2.8):

### 3.3.2.1 Objective Refraction

An objective refraction was undertaken in each eye using a Canon RK-2 autokeratorefractor.

### 3.3.2.2 Subjective Refraction

Subjective refraction was then undertaken for distance and near. The vision and visual acuity at distance was obtained using a high contrast Snellen chart. Near visual acuity was assessed, with appropriate near correction, with a near point high contrast Snellen acuity card at 40 cm and was recorded in Jaeger notation.

### 3.3.2.3 Spherical Equivalent Refraction (SE)

The spherical equivalent refraction was calculated from the subjective refraction.

### 3.3.2.4 Contrast Sensitivity (CS)

Contrast sensitivity was determined using the Functional Acuity Contrast Test (FACT) 301, based upon Ginsburg (1984), at a distance of three meters (Figure 3.1). The FACT Test involves the assessment of the minimum contrast (assessed in 9 discrete steps) necessary for the detection of a grating at each of 5 spatial frequencies, $1.5,3,6,12$ and 18 cycles per degree (cpd). The contrast sensitivity values were taken from the conversion table within the manufacturer's instruction manual which converts the last seen value on the FACT chart (by row and column) to a contrast value (Table 3.1).


Figure 3.1. Top: The Functional Acuity Contrast Test (FACT) ${ }^{\text {TM }} 301$ at the Ophthalmic Outpatient Clinic of Soroka University Medical Centre, Beer-Sheva, Israel. Bottom: The chart for recording contrast sensitivity.

| Stimulus <br> (Patch <br> Letter) | Corresponding Spatial Frequency | Stimulus (Patch Number) |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| A | (1.5) | 7 | 9 | 13 | 18 | 25 | 36 | 50 | 71 | 100 |
| B | (3) | 10 | 15 | 20 | 29 | 40 | 57 | 80 | 114 | 160 |
| C | (6) | 12 | 16 | 23 | 33 | 45 | 64 | 90 | 128 | 180 |
| D | (12) | 8 | 11 | 15 | 22 | 30 | 43 | 60 | 85 | 120 |
| E | (18) | 4 | 6 | 8 | 12 | 17 | 23 | 33 | 46 | 65 |

Table 3.1. The conversion table, within the manufacturer's instruction manual, which transforms the combination of a given contrast (patch number) and a given spatial frequency (patch letter) to a contrast sensitivity value.

### 3.3.2.5 Corneal Endothelial Cell Density (CECD)

The corneal endothelial cell density was recorded, as a measure of corneal integrity, using the Topcon SP 2000P specular microscope (Figure 3.2). This non-contact specular microscope enables a magnified, direct view of the corneal endothelium.

Each individual was positioned with the chin on the cup and the forehead against the headband and was required to fixate on the internal fixation light. After proper positioning and alignment, the endothelial layer appeared on the screen. In order to quantify the endothelial cell density, a rectangular frame was drawn on the screen over the image using the computer mouse supplied with the unit. A dot was placed in each of 10 to 12 adjacent endothelial cells within the frame. After the cells had been marked, the "END" option was selected and the cell outcome within the frame appeared on the screen. The image and the results of the endothelial cell density measurement were then printed out (Figure 3.2).


Figure 3.2. Top: The Topcon SP 2000P specular microscope used at the Ophthalmic Outpatient Clinic of Soroka University Medical Centre, Beer-Sheva, Israel. Bottom: The print-out from the specular microscope.

### 3.3.2.6 Ophthalmological Evaluation

The pre-operative ophthalmological evaluation was then performed by one of three ophthalmologists (Jaime Levy MD; Aliona Petrov MD; and the late Pavel Poliakov MD). Anterior segment examination was undertaken using slit-lamp biomicroscopy. Fundal examination was undertaken with slit-lamp biomicroscpy using a Volk +90 dioptre lens through a pupil dilated with 1-2 drops of Tropicamide $0.5 \%$.

### 3.3.2.7 Cataract Classification

The type and severity of the cataract in each eye was assessed using the Lens Opacity Classification System (LOCS) III (Chylack et al 1993). This technique is an accepted classification and grading system, routinely used in research, which is based upon a set of standard colour photographs of cortical cataract (C), posterior subcapsular cataract (P), nuclear colour ( NC ) and nuclear opalescence ( NO ) graded in terms of increasing severity for type, i.e. C1-C5, P0-P5, NO0-NO6 and NC0-NC6 (Figure 3.3). The clinical appearance of the cataract viewed, through the dilated pupil, with the slit lamp is compared to that of each of the reference photographs to yield a monotonic increase in severity of cataract type and severity (Chylack et al 1993).


Figure 3.3. The reference photographs used in the Lens Opacity Classification System (LOCS) III to grade nuclear opalescence, nuclear colour, cortical cataract and posterior subcapsular cataract (from Chylack, et al 1993).

### 3.3.2.8 Measurement of Higher Order Aberrations, of Central Corneal Curvature and of Dilated Pupil Diameter

The measurement of the HOAs and of the central corneal curvature was then undertaken using the OPD aberrometer (Figure 3.4) through the dilated pupil.


Figure 3.4. The Nidek Optical Path Difference Scanning System ARK-10000 aberrometer used at the Ophthalmic Outpatient Clinic of Soroka University Medical Centre, Beer-Sheva, Israel.

The OPD aberrometer has two measurement modes: ARK mode and ARK/CT mode. In the ARK mode, AR represents the refractive power in the central area of the eye (equals to the data obtained by an auto refractometer) measured along the visual axis. K represents the radius of curvature, acquired using a placido ring image. In the ARK/CT mode, which was used in the study, CT represents the option for the measurement of corneal topography. The confirmation screen of the OPD aberrometer displays the results and the quality of which is required to be approved by the examiner. The results are then
stored in the hard drive to be printed-out later. The print-out from the OPD aberrometer (Figure 3.5) provides the Root Mean Square (RMS) value for each of the eight aberrations derived by the Zernike polynomials, namely, Total, Tilt (S1), High, T.coma, T.trefoil, T.4Foil, T.sph and High Astig. Each aberration is made up of various Zernike terms as follows:
"Total" $=0^{\text {th }}$ to $44^{\text {th }}$ terms.
"Tilt (S1)": $=1^{\text {st }}$ and $2^{\text {nd }}$ terms (Tip, Tilt).
"High": $=6^{\text {th }}$ to $44^{\text {th }}$ terms.
"T.Coma": $=7^{\text {th }}, 8^{\text {th }}, 17^{\text {th }}, 18^{\text {th }}, 31^{\text {st }}$ and $32^{\text {nd }}$ terms.
"T.Trefoil": $=6^{\text {th }}, 9^{\text {th }}, 16^{\text {th }}, 19^{\text {th }}, 30^{\text {th }}$ and $33^{\text {rd }}$ terms.
"T. 4 Foil": $=10^{\text {th }}, 14^{\text {th }}, 22^{\text {nd }}, 26^{\text {th }}, 38$ th and $42^{\text {nd }}$ terms.
"T.Sph": $=12^{\text {th }}, 24^{\text {th }}$ and $40^{\text {th }}$ terms.
"HiAstig": $=11^{\text {th }}, 13^{\text {th }}, 23^{\text {rd }}, 25^{\text {th }}, 39^{\text {th }}$ and $41^{\text {st }}$ terms.

Each individual underwent a single measurement, unless the quality of the image in terms of clarity and centration was inadequate. In such cases, the measurement procedure was repeated until a sufficient quality image was obtained.

### 3.3.2.9 Dilated Pupil Diameter

The magnitude of the dilated pupil diameter was that recorded by the OPD aberrometer and displayed on the print-out.


Figure 3.5. The print-out of the Nidek Optical Path Difference Scanning System ARK10000 aberrometer for the left eye of an individual in the study at the pre-operative evaluation.

### 3.3.2.10 Biometry, Ocular Axial Length, Tonometry and Gonioscopy

Tonometry, using the Goldmann applanation tonometer; biometry, including ocular axial length measurement, using the Nidek US-1800 Echoscan; and gonioscopy, with a Goldmann two mirror lens; were then all undertaken by the ophthalmologist following installation of two drops of Oxybuprocaine $0.4 \%$ (Localin 0.4\%).

### 3.4 Analysis

The aberrometry data for each individual was downloaded from the OPD aberrometer onto a CD and imported into Nidek OPD NAVEX Station software (Version 2.10) contained in a personal computer.

The NAVEX Station software partitioned each of the eight HOAs, referenced either to a 6 mm or to a 4 mm zone diameter, into a Total value and two sub-components: the Corneal component attributable to the anterior cornea and tear film, combined, and the Internal component attributable to the posterior cornea and to the ocular media, combined. The output from the NAVEX Station software was in Microsoft Excel (Microsoft Corporation, Redmond, WA) file format.

The NAVEX Station software yielded Total values of the eight HOAs, using the 6.0 mm diameter zone, for 90 of the 99 individuals. However, the software only derived the corresponding two sub-components (i.e., a complete data set) for any given HOA in a maximum of 18 individuals. The reason for these incomplete data sets could not be explained by Nidek. The NAVEX Station software yielded an almost complete data set for the 4.0 mm diameter zone for the Total and for each of the two sub-components for each HOA. As a consequence, the analysis was undertaken for the 4.0 mm diameter measurement zone.

The demographical and clinical data, including that of the aberrations, were then compiled into a master Excel file which was appropriately arranged such that the data could exported to Statistical Analysis Software (SAS, Version 9.1) (Marlow, Buckinghamshir, UK).

The demographic and clinical characteristics of the case series were described using measures of central tendency (i.e., mean and standard deviation and median and interquartile range (IQR)) and were tabulated accordingly. For reasons of brevity, the distribution of each of the HOAs are described in tabular format for the Total Component, only, (rather than in terms of each of the Total, Corneal and Internal components) i.e., eight tables rather than twenty-four tables.

The inferential analysis was undertaken using separate analyses of variance (ANOVA) for each of the three components of each of the eight HOAs whereby the influence of each independent variable on the magnitude of the dependent variable, the given HOA, was modeled. The independent variables were divided into three separate groups: demographic, structural and cataract characteristics. For the functional characteristics, distance visual acuity, near visual acuity and contrast sensitivity at each spatial frequency, were each considered as separate dependent variables and each component of each HOA as a separate independent variable. The distance visual acuity was considered in terms of LogMAR and followed the recommendation of Holladay (1997) in regards to the statistical handling of 'count fingers' and 'hand movements'. The near visual acuity was considered in terms of the ' $x$ height' (Bailey and Lovie 1980; Johnston 1985).

As discussed in Chapter 2.0, the inferential analysis was, a priori, considered to be an explanatory analysis of any potential associations with the given HOA. Accordingly, no $a$ priori attempt was made to adjust the level of significance to account for the presence of Type I errors arising from the numerous comparisons that were investigated.

### 3.5 Results

### 3.5.1 Characteristics of the Case Series

### 3.5.1.1 Age and Gender

The demography of the 99 individuals in the study ( 36 males and 63 females) stratified by age and gender and by the designated eye for cataract extraction and IOL implantation is given in Table 3.2.

| Age group (years) | Gender | Designated eye |  | Total |  | Total |  | Total |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | R | L | R | L | M | F |  |
| 21-30 | M | 1 | - | 1 | - | 1 | - | 1 |
|  | F | - | - |  |  |  |  |  |
| 31-40 | M | - | - | - | - | - | - | - |
|  | F | - | - |  |  |  |  |  |
| 41-50 | M | - | 1 | - | 1 | 1 |  | 1 |
|  | F | - | - |  |  |  |  |  |
| 51-60 | M | 1 | 2 | 2 | 3 | 3 | 2 | 5 |
|  | F | 1 | 1 |  |  |  |  |  |
| 61-70 | M | 6 | 6 | 12 | 19 | 12 | 19 | 31 |
|  | F | 6 | 13 |  |  |  |  |  |
| 71-80 | M | 5 | 6 | 22 | 14 | 11 | 25 | 36 |
|  | F | 17 | 8 |  |  |  |  |  |
| 81-90 | M | 1 | 7 | 10 | 15 | 8 | 17 | 25 |
|  | F | 9 | 8 |  |  |  |  |  |
| Total |  | 47 | 52 | 47 | 52 | 36 | 63 | 99 |

Table 3.2. The 99 individuals within the case series stratified by age, gender and the eye designated for cataract extraction and IOL implantation.

The mean age of the 99 individuals was 72.95 (SD 10.32) and the median 73.00 (IQR $67.00,80.50)$. The case series was composed of 92 individuals older than 60 years of age and 7 individuals who were aged less than 60 years of age. Amongst these 92 individuals, the majority were aged less than 80 years of age. One individual, aged 24 years, with
bilateral cataract of an unknown aetiology was included in the case series. The rationale for inclusion of this case in the series was that the cataract, in the initial eye designated for surgery, was a 'pure' bilateral posterior subcapsular cataract and was severe (Grade 4) in magnitude.

### 3.5.1.2 Cataract Type and Severity

The distribution of cataract type and severity by LOCS III classification as a function of the most commonly occurring cataract category in the series, namely, nuclear opalescence and nuclear colour, is given in Table 3.3.

### 3.5.1.3 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst the case series is shown in Table 3.4. Eighty-nine individuals were myopic. Sixty-one individuals manifested a spherical equivalent refraction between -4.00 dioptres and plano with the majority manifesting a spherical equivalent refraction between -2.00 dioptres and -0.1 dioptres; 25 between -4.01 dioptres and -10.00 dioptres; and two between -16.00 dioptres and -16.50 dioptres. Ten individuals had a positive spherical equivalent refraction between +0.01 dioptres and +5.00 dioptres.

Table 3.3 Overleaf. The distribution of cataract type and severity, by LOCS III classification, as a function of the most commonly occurring cataract category in the case series namely, nuclear opalescence (NO) and nuclear colour (NC) for the 99 individuals in the case series. (C) represents anterior cortical cataract and ( P ) represents posterior subcapsular cataract. The integer associated with the type of cataract represents the severity.

|  | C0P0 | C0P1-2 | C0P4-5 | Sub-group Total | C1P0 | C1P2 | C1P4 | Sub-group Total | Total |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| NO0NC0 |  |  | 1 | 1 |  |  |  |  |  |
| NO1NC1 | 1 |  |  | 1 |  |  |  |  |  |
| NO2NC2 |  |  |  |  |  |  |  |  |  |
| NO3NC3 |  | 1 | 1 | 2 |  |  | 2 | 2 |  |
| NO4NC2 |  |  |  |  |  |  |  |  |  |
| NO4NC3 |  |  |  |  |  |  |  |  |  |
| NO4NC4 | 3 | 1 |  | 4 | 1 | 1 |  | 2 |  |
| NO4NC5 |  | 1 |  | 1 |  |  |  |  |  |
| NO5NC3 |  |  |  |  |  |  |  |  |  |
| NO5NC4 |  |  |  |  |  |  |  |  |  |
| NO5NC5 | 3 |  | 2 | 5 |  |  |  |  |  |
| NO6NC6 | 1 |  |  | 1 |  | 1 |  | 1 |  |
| Total | 8 | 3 | 4 | 15 | 1 | 2 | 2 | 5 | 20 |
|  | C2P0-1 | C2P2-3 | C2P4-5 | Sub-group Total | C3P0 | C3P1-2-3 | C3P4-5 | Sub-group Total |  |
| NO0NC0 |  |  |  |  |  |  |  |  |  |
| NO1NC1 |  |  |  |  |  |  |  |  |  |
| NO2NC2 |  | 1 |  | 1 |  |  |  |  |  |
| NO3NC3 | 5 | 4 | 2 | 11 | 6 | 1 |  | 7 |  |
| NO4NC2 |  |  |  |  |  |  |  |  |  |
| NO4NC3 |  | 1 |  | 1 |  |  |  |  |  |
| NO4NC4 | 7 | 2 | 2 | 11 | 4 | 5 | 3 | 12 |  |
| NO4NC5 | 1 |  |  | 1 |  |  |  |  |  |
| NO5NC3 |  |  |  |  |  |  |  |  |  |
| NO5NC4 | 1 |  |  | 1 |  |  |  |  |  |
| NO5NC5 | 4 | 2 | 1 | 7 | 5 | 1 | 1 | 7 |  |
| NO6NC6 |  |  | 2 | 3 | 4 | 1 | 1 | 6 |  |
| Total | 18 | 10 | 7 | 35 | 19 | 8 | 5 | 32 | 67 |
|  | C4P0 | C4P1 | C4P4-5 | Sub-group Total | C5P0 | C5P2-3 | C5P4-5 | Sub-group Total |  |
| NO0NC0 |  |  |  |  |  |  |  |  |  |
| NO1NC1 |  |  |  |  |  |  |  |  |  |
| NO2NC2 |  |  |  |  |  |  | 1 | 1 |  |
| NO3NC3 | 2 |  |  | 2 | 1 |  |  | 1 |  |
| NO4NC2 |  |  | 1 | 1 |  |  |  |  |  |
| NO4NC3 |  |  |  |  |  |  |  |  |  |
| NO4NC4 | 1 |  |  | 1 |  |  |  |  |  |
| NO4NC5 |  |  |  |  |  |  |  |  |  |
| NO5NC3 |  |  |  |  |  |  | 1 | 1 |  |
| NO5NC4 |  |  |  |  |  |  |  |  |  |
| NO5NC5 |  | 1 | 2 | 3 |  |  |  |  |  |
| NO6NC6 |  |  | 1 | 1 | 1 |  |  | 1 |  |
| Total | 3 | 1 | 4 | 8 | 2 |  | 2 | 4 | 12 |
|  |  |  | Total | number of in | viduals |  |  |  | 99 |


| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than -10.00 | 3 | -14.17 | - | -16.00 | -16.50 | -10.00 | - |
| -9.0 to -9.99 | - | - | - | - | - | - | - |
| -8.0 to -8.99 | 6 | -8.50 | 0.27 | -8.50 | -8.75 | -8.00 | $-8.69,-8.50$ |
| -7.0 to -7.99 | 2 | -7.69 | - | - | -7.88 | -7.50 | - |
| -6.0 to -6.99 | 4 | -6.28 | - | -6.25 | -6.63 | -6.00 | $-6.53,-6.00$ |
| -5.0 to -5.99 | 7 | -5.21 | 0.22 | -5.25 | -5.50 | -5.00 | $-5.38,-5.00$ |
| -4.0 to -4.99 | 6 | -4.42 | 0.31 | -4.50 | -4.88 | -4.00 | $-4.50,-4.22$ |
| -3.00 to -3.99 | 15 | -3.36 | 0.30 | -3.35 | -3.88 | -3.00 | $-3.63,-3.06$ |
| -2.00 to -2.99 | 13 | -2.38 | 0.33 | -2.50 | -2.88 | -2.00 | $-2.50,-2.00$ |
| -1.00 to -1.99 | 19 | -1.27 | 0.25 | -1.25 | -1.88 | -1.00 | $-1.50,-1.00$ |
| 0.00 to -0.99 | 14 | -0.37 | 0.26 | -0.44 | -0.75 | 0.00 | $-0.50,-0.16$ |
| 0.01 to +0.99 | 3 | 0.38 | - | 0.25 | 0.13 | 0.75 | - |
| +1.00 to +1.99 | 2 | 1.63 | - | - | 1.50 | 1.75 | - |
| +2.00 to +2.99 | 2 | 2.25 | - | - | 2.00 | 2.50 | - |
| +3.00 to +3.99 | 1 | 3.63 | - | - | - | - | - |
| +4.00 to +4.99 | 2 | 4.00 | - | - | 4.00 | 4.50 | - |
| Group | 99 | -2.90 | 3.44 | -2.50 | -16.50 | 4.50 | $-4.50,-1.00$ |

Table 3.4. The summary statistics for the distribution, amongst the 99 individuals within the case series, of the spherical equivalent refraction.

### 3.5.1.4 Distance Visual Acuity

The distribution of distance visual acuity amongst the case series, shown in Figure 3.6, was approximately bimodal. Seventeen individuals exhibited a visual acuity of 6/120 or worse and 17 individuals a visual acuity of $6 / 12$ or better. The 'modal' visual acuities were $6 / 15$ (19 individuals, median age 77 years (IQR 72.5, 83.0)) and $6 / 60$ (20 individuals, median age 69 years, (IQR 64.75, 77.25)).


Figure 3.6. The distribution of distance visual acuity for the 99 individuals within the case series. The upper legend for the abscissa delineates the acuity in Snellen notation and the lower legend the acuity in MAR.

### 3.5.1.5 Near Visual Acuity

The distribution of near visual acuity amongst the case series is shown in Figure 3.7. Thirty-two individuals exhibited a near visual acuity between Jaeger 2 and Jaeger 3, 27 of between Jaeger 5 and Jaeger 6 and 13 of Jaeger 16 .


Figure 3.7. The distribution of near visual acuity in Jaeger notation for the 99 individuals in the case series.

### 3.5.1.6 Contrast Sensitivity

The distribution of the contrast sensitivity derived by the Functional Acuity Contrast Test (FACT) 301 for each of the five spatial frequencies is shown in Figure 3.8.

As would be expected, most individuals exhibited poor contrast sensitivity at each of the five spatial frequencies, particularly for 6 cycles per degree and higher.


Figure 3.8. The distribution, amongst the case series, of the contrast sensitivity derived by the Functional Acuity Contrast Test (FACT) 301 for spatial frequencies of 1.5 and 3 cycles per degree (Top and Bottom, respectively). Note the difference in the scaling of the abscissa for the various spatial frequencies.




Figure 3.8 Continued. The distribution, amongst the case series, of the contrast sensitivity derived by the Functional Acuity Contrast Test (FACT) 301 for spatial frequencies of 6,12 and 18 cycles per degree (Top, Middle and Bottom, respectively). Note the difference in the scaling of the abscissa for the various spatial frequencies.

### 3.5.1.7 Dilated Pupil Diameter

The distribution of the dilated pupil diameter, within the case series, as measured by the OPD aberrometer, is shown in Table 3.5. Eight individuals exhibited a dilated pupil diameter of between 4.0 and $5.0 \mathrm{~mm}, 32$ of between 5.01 and $6.0 \mathrm{~mm}, 45$ of between 6.01 and 7.0 mm and 14 of between 7.01 and 8.0 mm .

| Dilated Pupil Diameter <br> (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 4.01 to 4.50 | 3 | 4.45 | - | 4.48 | 4.36 | 4.50 | - |
| 4.51 to 5.00 | 5 | 4.74 | 0.15 | 4.76 | 4.52 | 4.95 | $4.71,4.78$ |
| 5.01 to 5.50 | 11 | 5.29 | 0.15 | 5.35 | 5.04 | 5.49 | $5.20,5.38$ |
| 5.51 to 6.00 | 21 | 5.84 | 0.13 | 5.88 | 5.60 | 6.00 | $5.70,5.93$ |
| 6.01 to 6.50 | 21 | 6.29 | 0.15 | 6.30 | 6.02 | 6.50 | $6.20,6.44$ |
| 6.51 to 7.00 | 24 | 6.70 | 0.13 | 6.68 | 6.53 | 6.99 | $6.59,6.75$ |
| 7.01 to 7.50 | 8 | 7.17 | 0.14 | 7.15 | 7.01 | 7.47 | $7.07,7.21$ |
| 7.51 to 8.00 | 4 | 7.67 | - | 7.58 | 7.52 | 8.00 | $7.57,7.69$ |
| 8.01 to 8.50 | 2 | 8.02 | - | - | 8.01 | 8.03 | - |
| Group | 99 | 6.21 | 0.80 | 6.28 | 4.36 | 8.03 | $5.74,6.70$ |

Table 3.5. The summary statistics for the distribution, amongst the 99 individuals within the case series, of the dilated pupil diameter as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer.

### 3.5.1.8 Mean Corneal Curvature

The distribution of mean corneal curvature, within the case series, as measured by the OPD aberometer, is shown in Table 3.6. Two individuals exhibited a mean corneal curvature of between 7.00 and $7.09 \mathrm{~mm}, 20$ of between 7.10 and $7.39 \mathrm{~mm}, 52$ of between 7.40 and $7.69 \mathrm{~mm}, 16$ of between 7.70 and $7.99 \mathrm{~mm}, 9$ of between 8.00 and 8.29 mm .

### 3.5.1.9 Flattest Corneal Curvature

The distribution of the flattest corneal curvature, within the case series, as measured by the OPD, is shown in Table 3.7. Five individuals exhibited a flattest corneal curvature of between 7.10 and 7.29 mm , 32 of between 7.30 and 7.59 mm , 38 of between 7.60 and 7.79 mm , 21 of between 7.80 and 8.29 mm and 3 individuals exhibited a flattest corneal curvature greater than 8.29 mm .

| Mean Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 7.00 to 7.09 | 2 | 7.07 | - | - | 7.06 | 7.08 | - |
| 7.10 to 7.19 | 2 | 7.10 | - | - | 7.10 | 7.10 | - |
| 7.20 to 7.29 | 9 | 7.25 | 0.03 | 7.26 | 7.22 | 7.29 | $7.23,7.28$ |
| 7.30 to 7.39 | 9 | 7.35 | 0.03 | 7.36 | 7.30 | 7.39 | $7.34,7.37$ |
| 7.40 to 7.49 | 18 | 7.45 | 0.04 | 7.46 | 7.40 | 7.49 | $7.42,7.48$ |
| 7.50 to 7.59 | 13 | 7.55 | 0.02 | 7.55 | 7.50 | 7.59 | $7.55,7.56$ |
| 7.60 to 7.69 | 21 | 7.65 | 0.03 | 7.66 | 7.60 | 7.69 | $7.63,7.67$ |
| 7.70 to 7.79 | 9 | 7.72 | 0.02 | 7.72 | 7.70 | 7.76 | $7.71,7.74$ |
| 7.80 to 7.89 | 2 | 7.84 | - | - | 7.84 | 7.84 | - |
| 7.90 to 7.99 | 5 | 7.94 | 0.03 | 7.93 | 7.91 | 7.98 | $7.92,7.97$ |
| 8.00 to 8.09 | 2 | 8.03 | - | - | 8.02 | 8.03 | - |
| 8.10 to 8.19 | 5 | 8.11 | 0.04 | 8.09 | 8.09 | 8.19 | $8.09,8.12$ |
| 8.20 to 8.29 | 2 | 8.23 | - | - | 8.20 | 8.27 | - |
| Group | 99 | 7.58 | 0.26 | 7.56 | 7.06 | 8.27 | $7.40,7.70$ |

Table 3.6. The summary statistics for the distribution, amongst the 99 individuals within the case series, of the mean corneal curvature as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer (OPD, Nidek).

| Flattest Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 7.10 to 7.19 | 3 | 7.15 | - | 7.17 | 7.11 | 7.18 | - |
| 7.20 to 7.29 | 2 | 7.27 | - | - | 7.25 | 7.29 | - |
| 7.30 to 7.39 | 10 | 7.33 | 0.03 | 7.32 | 7.3 | 7.39 | $7.31,7.36$ |
| 7.40 to 7.49 | 11 | 7.46 | 0.03 | 7.47 | 7.41 | 7.49 | $7.43,7.48$ |
| 7.50 to 7.59 | 11 | 7.54 | 0.03 | 7.54 | 7.51 | 7.59 | $7.53,7.56$ |
| 7.60 to 7.69 | 21 | 7.64 | 0.03 | 7.64 | 7.6 | 7.69 | $7.63,7.66$ |
| 7.70 to 7.79 | 17 | 7.75 | 0.03 | 7.75 | 7.7 | 7.79 | $7.73,7.76$ |
| 7.80 to 7.89 | 5 | 7.84 | 0.04 | 7.84 | 7.8 | 7.89 | $7.80,7.88$ |
| 7.90 to 7.99 | 4 | 7.92 | - | 7.92 | 7.9 | 7.94 | $7.91,7.93$ |
| 8.00 to 8.09 | 4 | 8.06 | - | 8.07 | 8.02 | 8.09 | $8.04,8.09$ |
| 8.10 to 8.19 | 6 | 8.12 | 0.03 | 8.105 | 8.1 | 8.17 | $8.10,8.12$ |
| 8.20 to 8.29 | 2 | 8.24 | - | - | 8.23 | 8.25 | - |
| Greater than 8.29 | 3 | 8.50 | - | 8.35 | 8.31 | 8.85 | - |
| Group | 99 | 7.68 | 0.29 | 7.65 | 7.11 | 8.85 | $7.49,7.79$ |

Table 3.7. The summary statistics for the distribution, amongst the 99 individuals within the case series, of the flattest corneal curvature as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer (OPD, Nidek).

### 3.5.1.10 Corneal Endothelial Cell Density

The corneal endothelial cell density was available for 97 individuals only; the distribution is given in Table 3.8. Four individuals exhibited a corneal endothelial cell density of less than 1300 cells $/ \mathrm{mm}^{2}$, 18 between 1300 and 1799 cells $/ \mathrm{mm}^{2}$, 35 between 1800 and 2199 cells $/ \mathrm{mm}^{2}, ~ 36$ between 2200 and 2699 cells $/ \mathrm{mm}^{2}, 7$ between 2700 and 3199 cells $/ \mathrm{mm}^{2}$ and one greater than 3199 cells $/ \mathrm{mm}^{2}$.

| Corneal Endothelial <br> Cell Density <br> $\left(\right.$ Cells $\left./ \mathrm{mm}^{2}\right)$ | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 1300 | 4 | 1270 | - | 1265 | 1254 | 1296 | 1261,1274 |
| 1300 to 1399 | 4 | 1365 | - | 1368 | 1342 | 1382 | 1356,1376 |
| 1400 to 1499 | 3 | 1437 | - | 1425 | 1409 | 1476 | - |
| 1500 to 1599 | 2 | 1559 | - | - | 1554 | 1563 | - |
| 1600 to 1699 | 4 | 1667 | - | 1674 | 1615 | 1700 | 1659,1684 |
| 1700 to 1799 | 5 | 1767 | 27.99 | 1770 | 1734 | 1795 | 1743,1793 |
| 1800 to 1899 | 4 | 1862 | - | 1866 | 1819 | 1898 | 1835,1893 |
| 1900 to 1999 | 9 | 1947 | 33.72 | 1956 | 1903 | 1998 | 1918,1958 |
| 2000 to 2099 | 13 | 2062 | 23.43 | 2059 | 2029 | 2099 | 2046,2082 |
| 2100 to 2199 | 5 | 2172 | 18.02 | 2179 | 2141 | 2187 | 2176,2179 |
| 2200 to 2299 | 10 | 2229 | 20.08 | 2230 | 2203 | 2264 | 2217,2235 |
| 2300 to 2399 | 8 | 2345 | 31.93 | 2345 | 18760 | 2386 | 2322,2367 |
| 2400 to 2499 | 6 | 2442 | 36.38 | 2439 | 2403 | 2482 | 2412,2474 |
| 2500 to 2599 | 8 | 2541 | 26.63 | 2538 | 2510 | 2586 | 2522,2550 |
| 2600 to 2699 | 4 | 2651 | - | 2655 | 2605 | 2690 | 2619,2687 |
| 2700 to 2799 | 1 | 2733 | - | - | - | - | - |
| 2800 to 2899 | 3 | 2822 | - | 2820 | 2812 | 2834 | - |
| 2900 to 2999 | 2 | 2931 | - | - | 2915 | 2947 | - |
| 3000 to 3099 | - | - | - | - | - | - | - |
| 3100 to 3199 | 1 | 3108 | - | - | - | - | - |
| Greater than 3199 | 1 | 3203 | - | - | - | - | - |
| Group | 97 | 2125 | 436.75 | 2141 | 1254 | 3203 | 1891,2412 |

Table 3.8. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement could be obtained, of the corneal endothelial cell density.

### 3.5.1.11 Axial Length

The ocular axial length was available for 88 individuals only; the distribution is given in
Table 3.9. Eight individuals exhibited an ocular axial length of between 21.00 and $21.99 \mathrm{~mm}, 53$ of between 22.00 and $23.99 \mathrm{~mm}, 19$ of between 24.00 and 24.99 mm and 7 of between 26.00 and 30.00 mm .

| Axial Length (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 21.00 to 21.99 | 8 | 21.65 | 0.27 | 21.70 | 21.18 | 21.97 | $21.49,21.86$ |
| 22.00 to 22.99 | 26 | 22.51 | 0.33 | 22.62 | 22.00 | 22.91 | $22.16,22.82$ |
| 23.00 to 23.99 | 27 | 23.49 | 0.28 | 23.41 | 23.01 | 23.99 | $23.30,23.66$ |
| 24.00 to 24.99 | 19 | 24.44 | 0.28 | 24.42 | 24.00 | 24.92 | $24.18,24.63$ |
| 25.00 to 25.99 | 1 | 25.18 | - | - | - | - |  |
| 26.00 to 26.99 | 5 | 26.51 | 0.24 | 26.50 | 26.20 | 26.79 | $26.38,26.69$ |
| Greater than 26.99 | 2 | 28.46 | - | - | 27.47 | 29.44 |  |
| Group | 88 | 23.54 | 1.42 | 23.36 | 21.18 | 29.44 | $22.65,24.17$ |

Table 3.9. The summary statistics for the distribution, amongst 88 of the 99 individuals within the case series in whom the measurement was available, of the axial length as measured by the the Nidek US-1800 Echoscan.

### 3.5.1.12 Higher Order Aberrations

The summary statistics of the distribution of the RMS value of the Total component for each of the eight HOAs, measured with the Nidek NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone, namely, Total, Tilt (S1), High, T.coma, T.trefoil, T.4Foil, T.sph and HiAstig are given in Tables 3.10-3.17, respectively.

### 3.5.1.12.1 Total Component of the Total HOA

The Total HOA is composed of the $0^{\text {th }}$ to the $44^{\text {th }}$ Zernike terms. Eight individuals exhibited RMS values for the Total component of the Total HOA of less than 1.000 microns, 53 of between 1.000 and 2.499 microns, 17 of between 2.500 and 3.499 microns, 18 of between 3.500 and 7.999 microns and one of 9.553 microns.

Total Component

| Total RMS <br> (microns) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 0.500 to 0.999 | 8 | 0.854 | 0.34 | 0.880 | 0.670 | 0.964 | $0.815,0.905$ |
| 1.000 to 1.499 | 16 | 1.286 | 0.57 | 1.286 | 1.064 | 1.470 | $1.185,1.381$ |
| 1.500 to 1.999 | 16 | 1.751 | 0.73 | 1.749 | 1.553 | 1.976 | $1.595,1.868$ |
| 2.000 to 2.499 | 21 | 2.198 | 0.78 | 2.161 | 2.011 | 2.494 | $2.089,2.321$ |
| 2.500 to 2.999 | 10 | 2.642 | 0.80 | 2.635 | 2.509 | 2.915 | $2.554,2.687$ |
| 3.000 to 3.499 | 7 | 3.259 | 1.03 | 3.256 | 3.065 | 3.480 | $3.114,3.381$ |
| 3.500 to 3.999 | 5 | 3.885 | 1.18 | 3.515 | 3.978 | 0.116 | $3.682,3.907$ |
| 4.000 to 4.499 | 3 | 4.357 | - | 4.389 | 4.243 | 4.435 | - |
| 4.500 to 4.999 | 3 | 4.645 | - | 4.621 | 4.519 | 4.790 | - |
| 5.000 to 5.499 | 4 | 5.087 | - | 5.078 | 5.066 | 5.126 | $5.073,5.092$ |
| 5.500 to 5.999 | - | - | - | - | - | - | - |
| 6.000 to 6.499 | 1 | 6.241 | - | - | - | - | - |
| 6.500 to 6.999 | - | - | - | - | - | - | - |
| 7.000 to 7.499 | 1 | 7.065 | - | - | - | - | - |
| 7.500 to 7.999 | 1 | 7.546 | - | - | - | - | - |
| Greater than 7.999 | 1 | 9.553 | - | - | - | - | - |
| Group | 97 | 2.979 | 3.60 | 2.103 | 0.670 | 9.553 | $1.553,3.090$ |

Table 3.10. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total Component of the Total HOA.

### 3.5.1.12.2 Total Component of the Tilt (S1) HOA

The Tilt (S1) HOA is composed of the $1^{\text {st }}$ and $2^{\text {nd }}$ Zernike terms (Tip, Tilt). Twenty-nine individuals exhibited an RMS value for the Total component of the Tilt (S1) HOA of between 0.050 and 0.449 microns, 37 of between 0.450 and 0.849 microns, 22 of between 0.850 and 1.149 microns and 7 individuals of between 1.450 and 2.049 microns. One individual exhibited an RMS value of 0.033 microns and one of 3.953 microns.

Total Component

| Tilt (S1) RMS <br> (microns) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.050 | 1 | 0.033 | - | - | - | - | - |
| 0.050 to 0.249 | 16 | 0.159 | 0.12 | 0.160 | 0.058 | 0.231 | $0.130,0.181$ |
| 0.250 to 0.449 | 13 | 0.308 | 0.14 | 0.314 | 0.242 | 0.341 | $0.294,0.332$ |
| 0.450 to 0.649 | 26 | 0.508 | 0.29 | 0.496 | 0.351 | 0.647 | $0.444,0.575$ |
| 0.650 to 0.849 | 11 | 0.736 | 0.29 | 0.716 | 0.654 | 0.827 | $0.698,0.777$ |
| 0.850 to 1.049 | 8 | 0.930 | 0.31 | 0.935 | 0.863 | 1.007 | $0.884,0.957$ |
| 1.050 to 1.249 | 6 | 0.162 | 0.34 | 1.173 | 1.083 | 1.213 | $1.131,1.199$ |
| 1.250 to 1.449 | 8 | 1.360 | 0.34 | 1.348 | 1.307 | 1.420 | $1.332,1.390$ |
| 1.450 to 1.649 | 2 | 1.535 | - | - | 1.530 | 1.540 | - |
| 1.650 to 1.849 | 3 | 1.755 | - | 1.757 | 1.704 | 1.804 | - |
| 1.850 to 2.049 | 2 | 1.993 | - | - | 1.987 | 2.000 | - |
| Greater than 2.049 | 1 | 3.953 | - | - | - | - | - |
| Group | 97 | 0.917 | 1.33 | 0.565 | 0.033 | 3.953 | $0.320,0.947$ |

Table 3.11. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the Tilt (S1) HOA.

### 3.5.1.12.3 Total Component of the High HOA

The High HOA is composed of the $6^{\text {th }}$ to the $44^{\text {th }}$ Zernike terms. Forty of the individuals exhibited an RMS value for the Total component of the High HOA of between 0.150 and 0.549 microns, 38 of between 0.550 and 0.949 microns and 18 of between 0.950 and 2.749 microns. One individual exhibited an RMS value greater than 5.000 microns.

Total Component

| High RMS <br> (microns) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 0.150 to 0.349 | 14 | 0.266 | 0.18 | 0.273 | 0.151 | 0.340 | $0.226,0.323$ |
| 0.350 to 0.549 | 26 | 0.462 | 0.23 | 0.460 | 0.367 | 0.543 | $0.410,0.516$ |
| 0.550 to 0.749 | 20 | 0.639 | 0.27 | 0.628 | 0.558 | 0.731 | $0.595,0.685$ |
| 0.750 to 0.949 | 18 | 0.825 | 0.31 | 0.826 | 0.758 | 0.944 | $0.783,0.877$ |
| 0.950 to 1.149 | 5 | 1.036 | 0.32 | 1.058 | 0.952 | 1.077 | $1.016,1.069$ |
| 1.150 to 1.349 | 4 | 1.235 | - | 1.222 | 1.163 | 1.327 | $1.192,1.263$ |
| 1.350 to 1.549 | 1 | 1.358 | - | - | - | - | - |
| 1.550 to 1.749 | 2 | 1.667 | - | - | 1.643 | 1.691 | - |
| 1.750 to 1.949 | 2 | 1.797 | - | - | 1.754 | 1.84 | - |
| 1.950 to 2.149 | 1 | 2.030 | - | - | - | - | - |
| 2.150 to 2.349 | 1 | 2.263 | - | - | - | - | - |
| 2.350 to 2.549 | 1 | 2.436 | - | - | - | - | - |
| 2.550 to 2.749 | 1 | 2.606 | - | - | - | - | - |
| Greater than 2.749 | 1 | 5.306 | - | - | - | - | - |
| Group | 97 | 1.029 | 1.74 | 0.608 | 0.151 | 5.306 | $0.441,0.869$ |

Table 3.12. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the High HOA.

### 3.5.1.12.4 Total Component of the T.Coma HOA

The T.Coma HOA is composed of the $7^{\text {th }}, 8^{\text {th }}, 17^{\text {th }}, 18^{\text {th }}, 31^{\text {st }}$ and $32^{\text {nd }}$ terms. Fifty-six individuals exhibited RMS values for the Total component of the T.Coma HOA of between 0.500 and 0.199 microns, 22 individuals of between 0.200 and 0.349 microns and 13 of between 0.350 and 0.599 microns. Two individuals exhibited an RMS value greater than 0.799 microns.

Total Component

| T.Coma RMS <br> (microns) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.050 | 2 | 0.041 | - | - | 0.031 | 0.048 | - |
| 0.050 to 0.099 | 16 | 0.088 | 0.50 | 0.088 | 0.051 | 0.099 | $0.065,0.091$ |
| 0.100 to 0.149 | 25 | 0.129 | 0.06 | 0.129 | 0.102 | 0.149 | $0.108,0.142$ |
| 0.150 to 0.199 | 15 | 0.177 | 0.08 | 0.188 | 0.150 | 0.199 | $0.160,0.194$ |
| 0.200 to 0.249 | 7 | 0.228 | 0.08 | 0.230 | 0.200 | 0.242 | $0.222,0.238$ |
| 0.250 to 0.299 | 5 | 0.272 | 0.10 | 0.265 | 0.256 | 0.299 | $0.261,0.277$ |
| 0.300 to 0.349 | 10 | 0.330 | 0.09 | 0.331 | 0.309 | 0.348 | $0.328,0.335$ |
| 0.350 to 0.399 | 3 | 0.369 | - | 0.359 | 0.353 | 0.395 | - |
| 0.400 to 0.449 | 3 | 0.434 | - | 0.433 | 0.430 | 0.438 | - |
| 0.450 to 0.499 | 1 | 0.498 | - | - | - | - | - |
| 0.500 to 0.549 | 4 | 0.527 | - | 0.527 | 0.508 | 0.549 | $0.515,0.540$ |
| 0.550 to 0.599 | 2 | 0.585 | - | - | 0.572 | 0.598 | - |
| 0.600 to 0.649 | - | - | - | - | - | - | - |
| 0.650 to 0.699 | - | - | - | - | - | - | - |
| 0.700 to 0.749 | 2 | 0.712 | - | - | 0.712 | 0.712 | - |
| 0.750 to 0.799 | - | - | - | - | - | - | - |
| Greater than 0.799 | 2 | 1.023 | - | - | 0.876 | 0.151 | - |
| Group | 97 | 1.011 | 0.42 | 0.164 | 0.031 | 1.151 | $0.108,0.326$ |

Table 3.13. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the T.Coma HOA.

### 3.5.1.12.5 Total Component of the T.Trefoil HOA

The T.Trefoil HOA is composed of the $6^{\text {th }}, 9^{\text {th }}, 16^{\text {th }}, 19^{\text {th }}, 30^{\text {th }}$ and $33^{\text {rd }}$ terms. Sixty-nine individuals exhibited an RMS value for the Total component of the T.Trefoil HOA of between 0.100 and 0.599 microns and 21 of between 0.600 and 1.199 microns. Five individuals exhibited an RMS value greater than 1.300 microns and 2 of less than 0.100 microns.

Total Component

| T.Trifoil RMS <br> (microns) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.100 | 2 | 0.057 | - | - | 0.012 | 0.083 | - |
| 0.100 to 0.199 | 15 | 0.152 | 0.09 | 0.144 | 0.104 | 0.194 | $0.127,0.177$ |
| 0.200 to 0.299 | 14 | 0.229 | 0.12 | 0.222 | 0.200 | 0.282 | $0.206,0.255$ |
| 0.300 to 0.399 | 14 | 0.352 | 0.15 | 0.344 | 0.307 | 0.399 | $0.323,0.375$ |
| 0.400 to 0.499 | 13 | 0.435 | 0.14 | 0.438 | 0.406 | 0.486 | $0.421,0.442$ |
| 0.500 to 0.599 | 13 | 0.541 | 0.17 | 0.541 | 0.506 | 0.591 | $0.526,0553$ |
| 0.600 to 0699 | 5 | 0.667 | 0.19 | 0.672 | 0.631 | 0.692 | $0.648,0.690$ |
| 0.700 to 0.799 | 7 | 0.456 | 0.21 | 0.754 | 0.713 | 0.795 | $0.738,0.777$ |
| 0.800 to 0.899 | 3 | 0.853 | - | 0.866 | 0.814 | 0.878 | - |
| 0.900 to 0.999 | 1 | 0.948 | - | - | - | - | - |
| 1.000 to 1.099 | 3 | 1.034 | - | 1.024 | 1.011 | 0.066 | - |
| 1.100 to 1.199 | 2 | 1.161 | - | - | 1.145 | 1.177 | - |
| 1.200 to 1.299 | - | - | - | - | - | - | - |
| 1.300 to 1.399 | 2 | 1.357 | - | - | 1.315 | 1.397 | - |
| 1.400 to 1.499 | 1 | 1.452 | - | - | - | - | - |
| Greater than 1.499 | 2 | 2.614 | - | - | 2.335 | 2.867 | - |
| Group | 97 | 0.672 | 1.02 | 0.421 | 0.012 | 2.867 | $0.230,0.648$ |

Table 3.14. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the T.Trifoil HOA.

### 3.5.1.12.6 Total Component of the T.4Foil HOA

The T.4Foil" HOA is composed of the $10^{\text {th }}, 14^{\text {th }}, 22^{\text {nd }}, 26^{\text {th }}, 38^{\text {th }}$ and $42^{\text {nd }}$ terms. Five individuals exhibited an RMS value for the Total component of the T.4Foil HOA of less than 0.050 microns, 60 of between 0.050 and 0.299 microns, 25 of between 0.300 and 0.699 microns and 4 of between 0.700 and 0.999 microns. Three individuals exhibited an RMS value greater than 0.999 microns.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.4Foil RMS (microns) | Number of Individuals | Mean | SD | Median | Min | Max | IQR |
| Less than 0.050 | 5 | 0.034 | 0.02 | 0.032 | 0.022 | 0.045 | 0.032, 0.034 |
| 0.050 to 0.099 | 18 | 0.074 | 0.05 | 0.070 | 0.052 | 0.096 | 0.061, .0860 |
| 0.100 to 0.149 | 19 | 0.125 | 0.05 | 0.124 | 0.107 | 0.145 | 0.117, 0.134 |
| 0.150 to 0.199 | 7 | 0.182 | 0.07 | 0.185 | 0.159 | 0.194 | 0.172, 0.192 |
| 0.200 to 0.249 | 6 | 0.212 | 0.07 | 0.206 | 0.200 | 0.230 | 0.203, 0.221 |
| 0.250 to 0.299 | 10 | 0.277 | 0.10 | 0.279 | 0.250 | 0.297 | 0.263, 0.291 |
| 0.300 to 0.349 | 3 | 0.332 | - | 0.335 | 0.313 | 0.349 | - |
| 0.350 to 0.399 | 3 | 0.382 | - | 0.384 | 0.376 | 0.385 | - |
| 0.400 to 0.449 | 5 | 0.425 | 0.43 | 0.427 | 0.410 | 0.438 | 0.421, 0.429 |
| 0.450 to 0.499 | 7 | 0.471 | 0.11 | 0.470 | 0.452 | 0.491 | 0.464, 0.476 |
| 0.500 to 0.549 | 2 | 0.519 | - | - | 0.500 | 0.538 | - |
| 0.550 to 0.599 | 1 | 0.571 | - | - | - | - | - |
| 0.600 to 0.649 | 2 | 0.617 | - | - | 0.602 | 0.631 | - |
| 0.650 to 0.699 | 2 | 0.681 | - | - | 0.667 | 0.696 | - |
| 0.700 to 0.749 | - | - | - | - | - | - | - |
| 0.750 to 0.799 | - | - | - | - | - | - | - |
| 0.800 to 0.849 | 1 | 0.814 | - | - | - | - | - |
| 0.850 to 0.899 | - | - | - | - | - | - | - |
| 0.900 to 0.949 | 3 | 0.939 | - | 0.939 | 0.931 | 0.945 | - |
| 0.950 to 0.999 | - | - | - | - | - | - | - |
| Greater than 0.999 | 3 | 2.163 | - | 1.033 | 1.016 | 3.455 | - |
| Group | 97 | 0.310 | 0.40 | 0.194 | 0.022 | 3.455 | 0.107, 0.421 |

Table 3.15. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the T. 4 Foil HOA.

### 3.5.1.12.7 Total Component of the T.Sph HOA

The T.Sph HOA is composed of the $12^{\text {th }}, 24^{\text {th }}$ and $40^{\text {th }}$ Zernike terms. Seventy-seven individuals exhibited an RMS value for the Total component of the T.Sph HOA of between 0.005 and 0.199 microns, 14 of between 0.200 and 0.349 microns, 4 individuals between 0.350 and 0.499 . One individual exhibited an RMS value of 1.026 microns and one of less than 0.005 microns.

## Total Component

| T.Sph RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.005 | 1 | 0.004 | - | - | - | - | - |
| 0.005 to 0.009 | 2 | 0.008 | - | - | 0.006 | 0.009 | - |
| 0.010 to 0.049 | 21 | 0.033 | 0.03 | 0.030 | 0.011 | 0.049 | $0.021,0.040$ |
| 0.050 to 0.099 | 22 | 0.078 | 0.05 | 0.073 | 0.053 | 0.099 | $0.064,0.089$ |
| 0.100 to 0.149 | 16 | 0.118 | 0.05 | 0.119 | 0.101 | 0.104 | $0.109,0.130$ |
| 0.150 to 0.199 | 16 | 0.174 | 0.07 | 0.172 | 0.151 | 0.195 | $0.160,0.187$ |
| 0.200 to 0.249 | 7 | 0.005 | 0.08 | 0.226 | 0.203 | 0.246 | $0.216,0.233$ |
| 0.250 to 0.299 | 5 | 0.268 | 0.08 | 0.263 | 0.260 | 0.289 | $0.261,0.264$ |
| 0.300 to 0.349 | 2 | 0.338 | - | 0.339 | 0.346 | - | - |
| 0.350 to 0.399 | 1 | 0.437 | - | - | - | - | - |
| 0.400 to 0.449 | 1 | 0.440 | - | - | - | - | - |
| 0.450 to 0.499 | 2 | 0.469 | - | - | 0.448 | 0.491 | - |
| Greater than 0.549 | 1 | 1.026 | - | - | - | - | - |
| Group | 97 | 0.139 | 0.14 | 0.106 | 0.004 | 1.026 | $0.053,0.186$ |

Table 3.16. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the T.Sph HOA.

### 3.5.1.12.8 Total Component of the HiAstig HOA

The HiAstig HOA is composed of the $11^{\text {th }}, 13^{\text {th }}, 23^{\text {rd }}, 25^{\text {th }}, 39^{\text {th }}$ and $41^{\text {st }}$ Zernike terms. Eighty-eight individuals exhibited an RMS value for the Total component of the HiAstig HOA of between 0.010 and 0.249 microns, 3 of between 0.400 and 0.649 microns, 5 of greater than 1.649 microns and one of less than 0.010 microns.

Total Component

| HiAstig RMS <br> (microns) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.010 | 1 | 0.009 | - | - | - | - | - |
| 0.010 to 0.049 | 36 | 0.036 | 0.02 | 0.037 | 0.014 | 0.049 | $0.029,0.046$ |
| 0.050 to 0.099 | 38 | 0.068 | 0.06 | 0.066 | 0.050 | 0.095 | $0.057,0.076$ |
| 0.100 to 0.149 | 6 | 0.116 | 0.05 | 0.113 | 0.102 | 0.132 | $0.105,0.124$ |
| 0.150 to 0.199 | 7 | 0.169 | 0.05 | 0.172 | 0.150 | 0.177 | $0.168,0.174$ |
| 0.200 to 0.249 | 1 | 0.244 | - | - | - | - | - |
| 0.250 to 0.299 | - | - | - | - | - | - | - |
| 0.300 to 0.349 | - | - | - | - | - | - | - |
| 0.350 to 0.399 | - | - | - | - | - | - | - |
| 0.400 to 0.449 | 1 | 0.446 | - | - | - | - | - |
| 0.450 to 0.499 | 1 | 0.491 | - | - | - | - | - |
| 0.500 to 0.549 | - | - | - | - | - | - | - |
| 0.550 to 0.599 | - | - | - | - | - | - | - |
| 0.600 to 0.649 | 1 | 0.621 | - | - | - | - | - |
| Greater than 0.649 | 5 | 1.230 | 0.92 | 1.079 | 0.951 | 1.736 | $1.049,1.170$ |
| Group | 97 | 0.139 | 0.27 | 0.058 | 0.009 | 1.736 | $0.041,0.086$ |

Table 3.17. The summary statistics for the distribution, amongst 97 of the 99 individuals within the case series, in whom the measurement was available, of the RMS values for the Total component of the HiAstig HOA.

### 3.5.2 Explanatory Analysis of Associations between the Demographic, Structural and Functional Variables and each of the Three Components of each of the Eight <br> HOAs

The results of the analysis are given for the demographic variables in Table 3.18, for the visual performance variables in Table 3.19, for the structural variables in Table 3.20 and for the type and severity of the cataract in Table 3.21.

### 3.5.2.1 Age and Gender

No association was present between gender and each of the three components for each of the eight HOAs (Table 3.18). However, some association was present between age as a categorical variable and the Total component of the T.Coma and of the T.Sph HOAs. Some association was also present between age as a continuous variable and the Total component of the Total and of the T.Coma HOAs. The reduction with age in the Total component of the Total HOA was 0.0360 microns per year $\left(R^{2}=0.057\right)$ and that of the Total component of the T.Coma was 0.0047 microns per year $\left(\mathrm{R}^{2}=0.066\right)$ (Figure 3.9).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorical | 0.093 | 0.179 | 0.720 | 0.024 | 0.811 | 0.869 | 0.036 | 0.599 |  |
| Age continuous | 0.018 | 0.295 | 0.498 | 0.011 | 0.722 | 0.970 | 0.056 | 0.607 |  |
| Gender | 0.243 | 0.490 | 0.879 | 0.793 | 0.760 | 0.903 | 0.604 | 0.159 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorical | 0.730 | 0.387 | 0.693 | 0.326 | 0.771 | 0.659 | 0.447 | 0.494 |  |
| Age continuous | 0.630 | 0.242 | 0.594 | 0.269 | 0.697 | 0.964 | 0.142 | 0.414 |  |
| Gender | 0.672 | 0.218 | 0.482 | 0.630 | 0.445 | 0.583 | 0.574 | 0.603 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorical | 0.295 | 0.864 | 0.801 | 0.075 | 0.865 | 0.827 | 0.102 | 0.817 |  |
| Age continuous | 0.106 | 0.904 | 0.667 | 0.056 | 0.833 | 0.638 | 0.216 | 0.800 |  |
| Gender | 0.110 | 0.800 | 0.579 | 0.416 | 0.907 | 0.760 | 0.557 | 0.072 |  |

Table 3.18. The probability value derived by ANOVA for the association between age, as a categorical variable and as a continuous variable, and between gender, and each of the three components of each of the eight HOAs (Top: Total Component. Middle: Corneal Component. Bottom: Internal Component). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.


Figure 3.9. The magnitude of the Total component of the Total, T.Coma and T.Sph HOAs as a function of age as a continuous variable amongst 97 of the 99 the individuals within the case series, in whom the HOAs were available, (Top, Middle and Bottom, respectively). Note the difference in the scaling of the ordinate between the three graphs.

### 3.5.2.2 Distance Visual Acuity

The distance visual acuity worsened with increase in the magnitude of the Total component of all the HOAs ( $\mathrm{R}^{2} \leq 11.4 \%$ ) with the exception of the T.Trefoil and HiAstig HOAs (Table 3.19). The reduction in acuity largely arose from the Internal component of each HOA.

### 3.5.2.3 Near Visual Acuity

Similarly, the near visual acuity worsened with increase in the magnitude of the Total component of all the HOAs ( $\mathrm{R}^{2} \leq 17.7 \%$ ) with the exception of the T.Trefoil, T.4Foil and HiAstig HOAs (Table 3.19) and this, again, largely arose from the Internal component of each respective HOA.

### 3.5.2.4 Contrast Sensitivity

Surprisingly, there seemed to be no general association between the magnitudes of the HOAs, particularly, as might be expected for the Total and Internal components, and the magnitude of the contrast sensitivity at each of the spatial frequencies (Table 3.19). There was some suggestion of an inverse association between the magnitude of the Total component of the Total HOA and the magnitude of the contrast sensitivity at 1.5 ( $\mathrm{p}=0.009$ ) and $3.0(\mathrm{p}=0.016)$ cycles per degree and the magnitude of the Total component of the T.Coma HOA and the magnitude of the contrast sensitivity at $3.0(\mathrm{p}=0.033)$ cycles per degree (Figure 3.10). Some inverse association was also present between the magnitude of the Internal component of the Total HOA and the magnitude of the contrast sensitivity at $1.5(\mathrm{p}=0.013)$ and $3.0(\mathrm{p}=0.016)$ cycles per degree and the magnitude of the

Internal component of the Tilt (S1) HOA and the magnitude of the contrast sensitivity at $3.0(\mathrm{p}=0.011)$ and $6.0(\mathrm{p}=0.048)$ cycles per degree (Figure 3.11).There was also a suggestion of an inverse association between the magnitude of the Corneal component of the High HOA and the magnitude of the contrast sensitivity at $1.5(\mathrm{p}=0.029)$ and 3.0 $(\mathrm{p}=0.029)$ cycles per degree (Figure 3.12).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.001 | 0.045 | 0.010 | 0.004 | 0.139 | 0.007 | 0.003 | 0.108 |  |
| NVA | 0.002 | 0.001 | 0.015 | 0.001 | 0.105 | 0.150 | 0.004 | 0.057 |  |
| CS 1.5 cpd | 0.009 | 0.180 | 0.331 | 0.054 | 0.518 | 0.200 | 0.251 | 0.958 |  |
| CS 3 cpd | 0.016 | 0.066 | 0.116 | 0.033 | 0.205 | 0.153 | 0.231 | 0.470 |  |
| CS 6 cpd | 0.073 | 0.214 | 0.083 | 0.092 | 0.133 | 0.177 | 0.583 | 0.274 |  |
| CS 12 cpd | 0.390 | 0.351 | 0.287 | 0.404 | 0.355 | 0.426 | 0.535 | 0.704 |  |
| CS 18 cpd | 0.432 | 0.548 | 0.429 | 0.613 | 0.486 | 0.511 | 0.644 | 0.840 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.212 | 0.317 | 0.267 | 0.457 | 0.240 | 0.361 | 0.058 | 0.215 |  |
| NVA | 0.914 | 0.636 | 0.611 | 0.483 | 0.568 | 0.868 | 0.566 | 0.469 |  |
| CS 1.5 cpd | 0.287 | 0.087 | 0.029 | 0.096 | 0.281 | 0.211 | 0.337 | 0.136 |  |
| CS 3 cpd | 0.326 | 0.107 | 0.029 | 0.052 | 0.439 | 0.272 | 0.417 | 0.127 |  |
| CS 6 cpd | 0.567 | 0.261 | 0.157 | 0.117 | 0.617 | 0.510 | 0.684 | 0.272 |  |
| CS 12 cpd | 0.797 | 0.685 | 0.503 | 0.412 | 0.784 | 0.724 | 0.904 | 0.701 |  |
| CS 18 cpd | 0.894 | 0.901 | 0.616 | 0.663 | 0.908 | 0.816 | 0.933 | 0.970 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Visual Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| DVA | 0.002 | 0.021 | 0.029 | 0.001 | 0.235 | 0.020 | 0.008 | 0.143 |  |  |
| NVA | 0.025 | 0.001 | 0.028 | 0.001 | 0.098 | 0.271 | 0.017 | 0.088 |  |  |
| CS 1.5 cpd | 0.013 | 0.076 | 0.278 | 0.058 | 0.466 | 0.201 | 0.258 | 0.943 |  |  |
| CS 3 cpd | 0.016 | 0.011 | 0.095 | 0.159 | 0.141 | 0.131 | 0.236 | 0.494 |  |  |
| CS 6 cpd | 0.068 | 0.048 | 0.107 | 0.282 | 0.115 | 0.176 | 0.468 | 0.299 |  |  |
| CS 12 cpd | 0.280 | 0.233 | 0.288 | 0.674 | 0.242 | 0.419 | 0.543 | 0.596 |  |  |
| CS 18 cpd | 0.324 | 0.436 | 0.427 | 0.802 | 0.325 | 0.518 | 0.826 | 0.706 |  |  |

Table 3.19. The probability value derived by ANOVA for the association between distance visual acuity, near visual acuity and each of the six spatial frequencies of the FACT 301 Test, and each of the three components of each of the eight HOAs (Top: Total Aberration. Middle: Corneal Aberration. Bottom: Internal Aberration). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.




Figure 3.10. The magnitude of the Total component of the Total HOA as a function of contrast sensitivity for spatial frequencies of 1.5 and 3 cycles per degree and of the T.Coma HOA for 3 cycles per degree amongst 97 of the 99 individuals within the case series, in whom the HOAs were available, (Top, Middle and Bottom, respectively). Note the difference in the scaling of the abscissa and ordinate between the three graphs.




Figure 3.11. The magnitude of the Internal component of the Total HOA as a function of contrast sensitivity for spatial frequencies of 1.5 and 3 cycles per degree and of the Tilt (S1) HOA for 3 cycles per degree amongst 83 of the 99 individuals within the case series, in whom the HOAs were available, (Top, Middle and Bottom, respectively).


Figure 3.11 Continued. The magnitude of the Internal component of the Tilt (S1) HOA as a function of contrast sensitivity for a spatial frequency of 6 cycles per degree amongst 83 of the 99 individuals within the case series, in whom the HOAs were available. Note the difference in the scaling of the abscissa and ordinate between the four graphs.


Figure 3.12. The magnitude of the Corneal component of the High HOA as a function of contrast sensitivity for spatial frequency of 1.5 cycles per degree amongst 85 of the 99 individuals within the case series, in whom the HOAs were available.


Figure 3.12 Continued. The magnitude of the Corneal component of the High HOA as a function of contrast sensitivity for spatial frequencies of 1.5 and 3 cycles per degree amongst 85 of the 99 individuals within the case series, in whom the HOAs were available, (Top and Bottom, respectively). Note the difference in the scaling of the abscissa between the two graphs.

### 3.5.2.5 Dilated Pupil Diameter

No association was present between the dilated pupil diameter and any of the three components for each of the eight HOAs (Table 3.20).

### 3.5.2.6 Mean Corneal Curvature

The magnitude of the mean corneal curvature showed some association with the Corneal component of T.Sph ( $\mathrm{p}=0.002$ ) HOA (Table 3.20) whereby the magnitude of T.Sph decreased as the mean corneal curvature increased (Figure 3.13); however, the magnitude of the association was highly influenced by some individuals with corneal curvatures in the normal range who manifested an HOA greater than approximately 0.150 microns (Figure 3.13).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.174 | 0.794 | 0.990 | 0.534 | 0.973 | 0.858 | 0.672 | 0.535 |  |
| CC Mean | 0.472 | 0.309 | 0.797 | 0.501 | 0.541 | 0.947 | 0.997 | 0.931 |  |
| CC Flattest | 0.707 | 0.526 | 0.651 | 0.669 | 0.355 | 0.956 | 0.800 | 0.806 |  |
| CECD | 0.287 | 0.567 | 0.104 | 0.289 | 0.113 | 0.318 | 0.595 | 0.159 |  |
| Sph Equiv | $<0.001$ | 0.783 | 0.382 | 0.481 | 0.051 | 0.913 | 0.680 | 0.417 |  |
| Axial Length | $<0.001$ | 0.160 | 0.033 | 0.415 | 0.004 | 0.373 | 0.561 | 0.112 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.400 | 0.330 | 0.436 | 0.377 | 0.493 | 0.676 | 0.320 | 0.437 |  |
| CC Mean | 0.078 | 0.065 | 0.388 | 0.086 | 0.515 | 0.793 | 0.002 | 0.249 |  |
| CC Flattest | 0.260 | 0.897 | 0.079 | 0.845 | 0.045 | 0.020 | 0.012 | 0.255 |  |
| CECD | 0.912 | 0.507 | 0.955 | 0.410 | 0.705 | 0.945 | 0.509 | 0.138 |  |
| Sph Equiv | 0.603 | 0.838 | 0.406 | 0.625 | 0.268 | 0.224 | 0.576 | 0.496 |  |
| Axial Length | 0.157 | 0.293 | 0.394 | 0.420 | 0.443 | 0.521 | 0.040 | 0.349 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.168 | 0.852 | 0.989 | 0.468 | 0.869 | 0.760 | 0.690 | 0.527 |  |
| CC mean | 0.596 | 0.413 | 0.823 | 0.816 | 0.790 | 0.890 | 0.702 | 0.955 |  |
| CC flattest | 0.946 | 0.183 | 0.440 | 0.381 | 0.293 | 0.649 | 0.675 | 0.959 |  |
| CECD | 0.244 | 0.233 | 0.062 | 0.118 | 0.102 | 0.134 | 0.401 | 0.151 |  |
| Sph Equiv | $<0.001$ | 0.788 | 0.365 | 0.862 | 0.379 | 0.665 | 0.313 | 0.205 |  |
| Axial Length | $<0.001$ | 0.129 | 0.039 | 0.007 | 0.007 | 0.266 | 0.370 | 0.117 |  |

Table 3.20. The probability value derived by ANOVA for the association between the magnitude of each of the structural variables [pupil size, mean central corneal curvature (CC), flattest central corneal curvature (CC), corneal endothelial cell density (CECD), and spherical equivalent refraction (SE), axial length] and each of the three components of each of the eight HOAs (Top: Total Aberration. Middle: Corneal Aberration. Bottom: Internal Aberration). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.


Figure 3.13. The magnitude of the Corneal Component of the T.Sph HOA as a function of the mean corneal curvature amongst 85 of the 99 individuals within the case series, in whom the HOA was available. The circled data points indicate those individuals with corneal curvatures in the normal range who manifested a HOA of more than 0.150 microns.

### 3.5.2.7 Flattest Corneal Curvature

The magnitude of the flattest corneal curvature showed some association with the Corneal component of the T.Trifoil ( $\mathrm{p}=0.045$ ), T.T4foil ( $\mathrm{p}=0.020$ ) and T.Sph ( $\mathrm{p}=0.012$ ) (Table 3.20). The magnitude of the former two HOAs increased with a flattening of the cornea but was heavily influenced by one outlying value (Figure 3.14). The latter HOA declined with a flattening of the cornea. Interestingly, the individual manifesting the outlying HOA for the T.Trifoil and T.T4foil HOAs exhibited a value for the T.Sph HOA which was more representative of the general trend (Figure 3.14).

### 3.5.2.8 Corneal Endothelial Cell Density

No association was present between corneal endothelial cell density and any of the three components for each of the eight HOAs (Table 3.20).

### 3.5.2.9 Spherical Equivalent Refraction

The spherical equivalent refraction was highly associated with both the Total ( $\mathrm{p}<0.001$ ) and the Internal ( $\mathrm{p}<0.001$ ) components of the Total HOA but was independent of the Corneal component $(\mathrm{p}=0.603)$. No association was the found between the spherical equivalent refraction and the Total, Corneal or Internal components of each of the remaining seven HOAs (Table 3.20 and Figure 3.15). Both (Total and Internal) components decreased with increase in the magnitude of the reduction in myopia/ increase in hyperopia ( $\mathrm{R}^{2}=0.562$ and $\mathrm{R}^{2}=0.530$, respectively).

### 3.5.2.10 Axial Length

The axial length was highly associated with both the Total and the Internal components of the Total HOA (both p 20.001 ) (Table 3.20 and Figure 3.16). Both components increased with increase in the axial length $\left(R^{2}=0.293\right.$ and $R^{2}=0.274$, respectively). The Corneal component of the Total HOA was independent of axial length ( $\mathrm{p}=0.157$, $\left.R^{2}=0.009\right)$.

Associations were also found between axial length and the Total and the Internal components of the High ( $\mathrm{p}=0.033$ and $\mathrm{p}=0.039$, respectively) and the T.Trefoil $(\mathrm{p}=0.004$ and $\mathrm{p}=0.007$, respectively) HOAs, and the Internal component of the T.Coma ( $\mathrm{p}=0.007$ ) and the Corneal component of the T.Sph HOAs $(\mathrm{p}=0.040)$ (Table 3.20).

As might be expected, the spherical equivalent refraction co-varied with the axial length $\left(\mathrm{R}^{2}=0.245\right)$ : myopia increased with increase in axial length.


Figure 3.14. The magnitude of the Corneal Component of the T.Trefoil and T.4Foil HOAs as a function of the flattest corneal curvature amongst 85 of the 99 individuals within the case series, in whom the HOAs were available (Top and Bottom). The circled data points indicate outlying values.


Figure 3.14 Continued. The magnitude of the Corneal Component of the T.Sph HOA as a function of the flattest corneal curvature amongst 85 of the 99 individuals within the case series, in whom the HOAs were available. Note the difference in the scaling of the ordinate between the three graphs. The circled data points indicate outlying values.


Figure 3.15. The magnitude of the Total component of the Total HOA as a function of the spherical equivalent refraction amongst 97 of the 99 individuals within the case series, in whom the HOAs were available, respectively. The circled data points indicate outlying values.



Figure 3.15 Continued. The magnitude of the Corneal and Internal components of the Total HOA as a function of the spherical equivalent refraction amongst 85 and 83 of the 99 individuals within the case series, in whom the HOAs were available, respectively (Top and Bottom). The circled data points indicate outlying values.

### 3.5.2.11 Cataract Type

The probability value for the association between the given type and severity of cataract and the given component of the given HOA is shown in Table 3.21. Associations were present between increase in severity of cortical cataract ( $\mathrm{p}=0.032$ ) and of posterior subcapsular cataract ( $\mathrm{p}=0.003$ ) and increase in the magnitude of the Total component of
the Tilt (S1) HOA (Table 3.21 and Tables 3.22, 3.23). However, no association was present when the two cataracts were considered together ( $\mathrm{p}=0.733$ ). The association with the Internal component of the Tilt (S1) HOA was maintained for posterior subcapsular cataract only ( $\mathrm{p}=0.018$ ) (Table 3.21 and Table 3.23). The association with the Corneal component was, as would be expected, negligible.

The Total component of the T.Coma HOA increased with increase in severity of posterior subcapsular ( $\mathrm{p}=0.037$ ) (Table 3.21 and Table 3.24). The association of posterior subcapsular and nuclear colour cataract, combined, with the magnitude of the Total component of the T.Coma HOA, almost reached significance ( $\mathrm{p}=0.053$ ) (Table 3.21). The association with the Corneal component was, as would be expected, negligible.

The Total component of the T.Sph HOA increased with increases in nuclear opalescence ( $\mathrm{p}=0.025$ ), nuclear colour ( $\mathrm{p}=0.037$ ) and cortical ( $\mathrm{p}=0.004$ ) cataract (Table 3.21 and Tables $3.25,3.26$ ). Cortical cataract was also associated with the Total component of the HiAstig HOA ( $(\mathrm{p}=0.018)$ (Table 3.21 and Table 3.29). The Internal components of the T.Sph ( $\mathrm{p}=0.013$ ) and HiAstig ( $\mathrm{p}=0.033$ ) HOAs increased with increase in the severity of cortical cataract. A strong positive association was present for cortical cataract in the presence of nuclear colour cataract and the Total and Internal components of both the T.Sph and the HiAstig HOAs (Table 3.21 and Tables 3.27, 3.29).

Some positive association was suggested for nuclear colour cataract and the Internal component of T.4Foil ( $\mathrm{p}=0.046$ ) (Table 3.21 and Table 3.28).


Figure 3.16. The magnitude of the Total, Corneal and Internal components of the Total HOA as a function of the axial length amongst 86, 77 and 75 of the 99 individuals within the case series, in whom the HOAs were available, respectively, (Top, Middle and Bottom, respectively).

|  |  | TOTAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| NO |  |  |  |  |  |  | 0.025 |  |  |
| NC |  |  |  |  |  |  | 0.037 |  |  |
| C |  | 0.032 |  |  |  |  | 0.004 | 0.018 |  |
| P |  | 0.003 |  | 0.037 |  |  |  |  |  |
| C |  |  |  |  |  |  | 0.002 | 0.012 |  |
| NC |  |  |  |  |  |  | 0.037 | 0.059 |  |
| C*NC |  |  |  |  |  |  | $<0.001$ | 0.001 |  |
| C |  | 0.043 |  |  |  |  |  |  |  |
| P |  | 0.002 |  |  |  |  |  |  |  |
| P |  | 0.733 |  |  |  |  |  |  |  |
| NC |  |  |  | 0.035 |  |  |  |  |  |
| $\mathrm{P}^{* N C}$ |  |  |  | 0.060 |  |  |  |  |  |


| INTERNAL |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |
| Cataract type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |
| NO |  |  |  |  |  | 0.046 |  |  |
| NC |  |  |  |  |  |  |  |  |
| C |  |  |  |  |  |  | 0.013 | 0.033 |
| P |  | 0.018 |  |  |  |  |  |  |
| C |  |  |  |  |  |  | 0.010 | 0.023 |
| NC |  |  |  |  |  |  | 0.083 | 0.058 |
| C*NC |  |  |  |  |  |  | 0.025 | 0.003 |
| NO |  |  |  |  |  |  |  |  |
| P |  |  |  |  |  |  |  |  |
| NO*P |  |  |  |  |  |  |  |  |
| P |  |  |  |  |  |  |  |  |
| NC |  |  |  |  |  |  |  |  |
| P*NC |  |  |  |  |  |  |  |  |

Table 3.21. The probability value derived by ANOVA for the association between the cataract type (Nuclear Opalescence, NO; Nuclear Colour, NC; Anterior Cortical, C; posterior subcapsular cataract, P) and each of the three components of each of the eight HOAs (Top: Total Aberration. Bottom: Internal Aberration). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

| TOTAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Tilt(S1) HOA |  |  |  |  |  |  |  |
| C Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.563 | 0.395 | -0.404 | 14 | 0.455 | 0.409 |  |
| 1 | 0.647 | 0.565 | -0.248 | 5 | 0.304 | 0.284 |  |
| 2 | 0.635 | 0.489 | -0.310 | 34 | 0.463 | 0.333 |  |
| 3 | 0.721 | 0.506 | 0.396 | 32 | 0.528 | 0.421 |  |
| 4 | 1.167 | 1.185 | 0.070 | 8 | 1.185 | 0.642 |  |
| 5 | 0.992 | 0.869 | -0.061 | 4 | 0.665 | 0.241 |  |

Table 3.22. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total component of the Tilt (S1) HOA, derived for a 4.0 mm zone diameter, as a function of increasing severity of Cortical cataract (C) amongst the 98 of the 99 individuals within the case series.

| ToTAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Tilt(S1) HOA |  |  |  |  |  |  |  |
| P Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.584 | 0.435 | -0.361 | 49 | 0.454 | 0.358 |  |
| 1 | 0.675 | 0.437 | -0.359 | 5 | 0.499 | 0.549 |  |
| 2 | 0.673 | 0.517 | -0.287 | 12 | 0.499 | 0.339 |  |
| 3 | 0.675 | 0.546 | -0.263 | 8 | 0.402 | 0.332 |  |
| 4 | 0.867 | 0.807 | -0.093 | 8 | 0.391 | 0.168 |  |
| 5 | 1.372 | 0.841 | -0.075 | 17 | 1.404 | 0.489 |  |


| INTERNAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Tilt(S1) HOA |  |  |  |  |  |  |  |
| P Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.766 | 0.614 | -0.212 | 45 | 0.575 | 0.284 |  |
| 1 | 0.724 | 0.488 | -0.312 | 5 | 0.540 | 0.489 |  |
| 2 | 0.727 | 0.485 | -0.315 | 10 | 0.573 | 0.491 |  |
| 3 | 0.885 | 0.550 | -0.260 | 6 | 0.803 | 0.509 |  |
| 4 | 1.124 | 1.098 | 0.041 | 5 | 0.260 | 0.106 |  |
| 5 | 2.394 | 1.278 | 0.106 | 12 | 3.79 | 0.452 |  |

Table 3.23. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total and Internal components of the Tilt (S1) HOA (Top and Bottom), derived for a 4.0 mm zone diameter, as a function of increasing severity of Posterior sub-capsular cataract ( P ) amongst the 98 and 84 of the 99 individuals within the case series, respectively.

| T.Coma HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | C Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals |  |
| 0 | 0.215 | 0.163 | -0.789 | 49 | 0.195 | 0.318 |  |
| 1 | 0.242 | 0.228 | -0.643 | 5 | 0.081 | 0.183 |  |
| 2 | 0.189 | 0.162 | -0.791 | 12 | 0.102 | 0.265 |  |
| 3 | 0.203 | 0.175 | -0.757 | 8 | 0.134 | 0.241 |  |
| 4 | 0.251 | 0.210 | -0.679 | 8 | 0.175 | 0.267 |  |
| 5 | 0.405 | 0.301 | -0.521 | 16 | 0.304 | 0.360 |  |

Table 3.24. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total component of the T.Coma HOA, derived for a 4.0 mm zone diameter, as a function of increasing severity of Posterior sub-capsular cataract ( P ) amongst the 98 of the 99 individuals within the case series.

| T.Sph HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| NO Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.110 | 0.110 | -0.960 | 1 | - | - |  |
| 1 | 0.028 | 0.028 | -1.547 | 1 | - | - |  |
| 2 | 0.051 | 0.050 | -1.299 | 2 | 0.016 | 0.134 |  |
| 3 | 0.127 | 0.099 | -1.005 | 24 | 0.093 | 0.333 |  |
| 4 | 0.135 | 0.102 | -0.990 | 34 | 0.089 | 0.374 |  |
| 5 | 0.100 | 0.058 | -1.237 | 24 | 0.106 | 0.518 |  |
| 6 | 0.385 | 0.220 | -0.657 | 12 | 0.431 | 0.515 |  |

Table 3.25. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total component of the T.Sph HOA, derived for a 4.0 mm zone diameter, as a function of increasing severity of Nuclear opalescence cataract (NO) amongst the 98 of the 99 individuals within the case series.

| TOTAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Sph HOA |  |  |  |  |  |  |  |
| NC Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.110 | 0.110 | -0.960 | 1 | - | - |  |
| 1 | 0.028 | 0.028 | -1.547 | 1 | - | - |  |
| 2 | 0.112 | 0.084 | -1.076 | 3 | 0.106 | 0.398 |  |
| 3 | 0.123 | 0.095 | -1.021 | 26 | 0.091 | 0.332 |  |
| 4 | 0.139 | 0.110 | -0.958 | 31 | 0.087 | 0.340 |  |
| 5 | 0.096 | 0.053 | -1.275 | 24 | 0.107 | 0.529 |  |
| 6 | 0.288 | 0.185 | -0.732 | 11 | 0.269 | 0.468 |  |

Table 3.26. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total component of the T.Sph HOA, derived for a 4.0 mm zone diameter, as a function of increasing severity of Nuclear colour cataract (NC) amongst the 98 of the 99 individuals within the case series.

| TOTAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Sph HOA |  |  |  |  |  |  |  |
| C Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.083 | 0.049 | -1.311 | 14 | 0.091 | 0.499 |  |
| 1 | 0.125 | 0.092 | -1.035 | 5 | 0.092 | 0.421 |  |
| 2 | 0.143 | 0.086 | -1.067 | 35 | 0.237 | 0.447 |  |
| 3 | 0.183 | 0.137 | -0.862 | 32 | 0.131 | 0.364 |  |
| 4 | 0.139 | 0.106 | -0.976 | 8 | 0.095 | 0.379 |  |
| 5 | 0.289 | 0.091 | -1.041 | 4 | 0.492 | 0.715 |  |


| INTERNAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Sph HOA |  |  |  |  |  |  |  |
| C Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.108 | 0.081 | -1.091 | 14 | 0.089 | 0.315 |  |
| 1 | 0.180 | 0.124 | -0.907 | 4 | 0.118 | 0.540 |  |
| 2 | 0.270 | 0.130 | -0.888 | 26 | 0.658 | 0.433 |  |
| 3 | 0.206 | 0.161 | -0.793 | 28 | 0.129 | 0.359 |  |
| 4 | 0.157 | 0.109 | -0.962 | 8 | 0.129 | 0.415 |  |
| 5 | 0.262 | 0.169 | -0.771 | 4 | 0.311 | 0.433 |  |

Table 3.27. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total and Internal components of the T.Sph HOA (Top and Bottom), derived for a 4.0 mm zone diameter, as a function of increasing severity of Cortical cataract (C) amongst the 98 and 84 of the 99 individuals within the case series, respectively.

| INTERNAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| NO Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.079 | 0.079 | -1.099 | 1 | - | - |  |
| 1 | 0.145 | 0.145 | -0.838 | 1 | - | - |  |
| 2 | 0.400 | 0.364 | -0.438 | 2 | 0.237 | 0.273 |  |
| 3 | 0.289 | 0.180 | -0.746 | 19 | 0.288 | 0.472 |  |
| 4 | 0.231 | 0.166 | -0.781 | 19 | 0.233 | 0.356 |  |
| 5 | 0.309 | 0.231 | -0.636 | 22 | 0.245 | 0.338 |  |
| 6 | 0.740 | 0.371 | -0.431 | 9 | 1.088 | 0.548 |  |

Table 3.28. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Internal component of the T.4Foil HOA, derived for a 4.0 mm zone diameter, as a function of increasing severity of Nuclear opalescence cataract (NO) amongst the 84 of the 99 individuals within the case series.

| TOTAL |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| HiAstig HOA |  |  |  |  |  |  |
| C Grade | Mean RMS | Geometric Mean | Log Mean | Number of Individuals | SD Mean | SD Log Mean |
| 0 | 0.063 | 0.050 | -1.301 | 14 | 0.056 | 0.281 |
| 1 | 0.078 | 0.072 | -1.140 | 5 | 0.034 | 0.186 |
| 2 | 0.079 | 0.056 | -1.255 | 34 | 0.104 | 0.333 |
| 3 | 0.206 | 0.091 | -1.043 | 32 | 0.372 | 0.487 |
| 4 | 0.191 | 0.084 | -1.077 | 8 | 0.36 | 0.49 |
| 5 | 0.346 | 0.135 | -0.871 | 4 | 0.550 | 0.653 |


| INTERNAL |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| HiAstig HOA |  |  |  |  |  |  |  |
| C Grade | Mean RMS | Geometric <br> Mean | Log Mean | Number of <br> Individuals | SD Mean | SD Log Mean |  |
| 0 | 0.078 | 0.059 | -1.230 | 14 | 0.071 | 0.318 |  |
| 1 | 0.075 | 0.068 | -1.165 | 4 | 0.034 | 0.232 |  |
| 2 | 0.085 | 0.059 | -1.229 | 25 | 0.123 | 0.308 |  |
| 3 | 0.230 | 0.094 | -1.028 | 28 | 0.427 | 0.503 |  |
| 4 | 0.204 | 0.085 | -1.069 | 8 | 0.396 | 0.502 |  |
| 5 | 0.408 | 0.155 | -0.808 | 4 | 0.654 | 0.662 |  |

Table 3.29. Arithmetic Mean (SD), Geometric Mean and Log Arithmetic Mean (SD) for the Total and Internal components of the HiAstig HOA (Top and Bottom), derived for a 4.0 mm zone diameter, as a function of increasing severity of Cortical cataract (C) amongst the 98 and 84 of the 99 individuals within the case series, respectively.

### 3.6 Discussion

The use of the OPD aberrometer, which is based upon the Retinoscope Double Pass principle, and with the NAVEX Station (Version 2.10) software permits partition of the given HOA into three components Total, Corneal and Internal HOAs. Such an approach affords a more rigorous study of the site of the given HOA which was not possible in the earlier literature.

The reduction with age, considered as a continuous variable in the Total Component of the Total HOA is not compatible with that of other studies. The reduction of 0.0358 microns per year in the current study is not compatible with the increase of 0.0018 microns per year of Fujikado et al (2004) and with that of 0.0032 microns per year of Berrio et al
(2010) both of which were obtained from studies of normal individuals. The reason for this discrepancy is most likely to be explained by two factors. Firstly, each of the two studies utilised a predominantly younger cohort than the current study. Secondly, the two studies were undertaken on 'normal' indivduals rather than on individuals with advanced cataract. However, it is also conceivable that the difference in the magnitudes of the slopes arises from differences in the measurement principles between the different types of aberometer: as noted above, the aberrometers used by Fujikado et al (2004) and Berrio et al (2010) were both based upon the Hartmann-Shack principle.

The reduction in the Total component of the T.Coma HOA with age ( 0.0047 microns per year) in the current study is contrary to increases of 0.0013 microns per year (Fujikado et al 2004) and 0.0017 microns per year (Berrio et al 2010) found in normal individuals and obtained with the Hartmann-Shack principle. It is also contrary to the qualitative increase with age in both the Corneal and the Total components of the coma HOA obtained with the Hartmann-Shack principle (Amano et al 2004) and in the anterior corneal surface coma (Wang et al 2003). Normally, the coma HOA in the cornea is compensated by the crystalline lens (Guirao et al 2000; Artal et al 2002; Kelly et al 2004; Tabernero et al 2007; Marcos et al 2008; Lu et al 2008). This compensation declines with age and therefore, the Total component of coma HOA consequently increases, in addition to that of the increase in the Corneal component, itself. It is clear from the results of the current study that the compensation mechanism breaks down in the presence of age-related cataract. The Corneal component increased by 0.0015 microns per year whilst that arising from the Internal component declined by 0.0052 microns per year resulting in a net reduction of the Total component with increase in age. The increase in the Corneal component of 0.0015 microns per year compares with that of 0.0004 microns per year obtained with the Hartmann-Shack aberrometer (Fujikado et al 2004). The decline in the

Total component of T.Coma HOA with age was most pronounced for posterior subcapsular cataract (Table 3.18).

The Total spherical HOA increases with age in normal individuals (Artal et al 2002; Vilarrodona et al 2004; Berrio et al 2010; Karimian et al 2010; Baskaran et al 2011). This increase arises from an increase in the spherical HOA of the crystalline lens, i.e., a loss of the compensation mechanism, rather than from an increase in the corneal spherical HOA, itself, which is either minimally (Fujikado et al 2004; Cermáková and Skorkovská 2010), or not, influenced by age (Wang et al 2003; Amano et al 2004; Athaide 2009). In the current study, the association between the Total component of the T.Sph HOA and age, as a continuous variable, just failed to reach statistical significance ( $\mathrm{p}=0.056$ ). Both the Corneal component and the Internal components of the T.Sph HOA were not associated with age ( $\mathrm{p}=0.142$ and $\mathrm{p}=0.216$ respectively). The lack of any association of the Internal component of the T.Sph HOA with age can be attributed to the presence of age-related cataract, particularly nuclear colour and cortical cataract.

In the current study, the extent of the attenuation of the contrast sensitivity at 1.5 and 3.0 cycles per degree increased with increase in the magnitude of the Total ( $\mathrm{p}=0.009$ and $\mathrm{p}=0.013$, respectively) and Internal ( $\mathrm{p}=0.016$ and $\mathrm{p}=0.016$, respectively) components of the Total HOA (Figure 3.9). No association was present for the Corneal component for both spatial frequencies ( $\mathrm{p}=0.208$ and 0.326 respectively). The former finding is compatible with that of Feizi and Karimian (2009) who found that, in the normal eye, the area under the CSF, defined as that between 1 and 18 cycles per degree, reduced as the Total HOA increased.

The attenuation of the contrast sensitivity at 1.5 and 3.0 cycles per degree also increased with increase in the magnitude of the Corneal component of the High HOA ( $\mathrm{p}=0.029$ ) (Figure 3.9).

An inverse association was also present in the current study between the magnitudes of the Total component of T.Coma HOA and the magnitude of the contrast sensitivity at 3.0 cycles per degree ( $\mathrm{p}=0.033$ ). The area under the CSF, defined as that between 3 and 18 cycles per degree, has also been shown to be reduced by the coma HOA (Oshika et al 2006). No association was present in the current study between the magnitudes of the Total and Internal components of the T.Sph HOA and the attenuation of the CSF. Such a finding is in agreement with that of Oshika et al (2006). Interestingly, CSF is optimum when either spherical HOA (Piers et al 2007) or Total HOA (de Gracia et al 2011) is corrected by adaptive optics.

Given the presence of age-related cataract in the current study, it was surprising that no association was found between the magnitudes of the Total and Internal components of each of the other HOAs and the magnitude of the contrast sensitivity at each of the spatial frequencies, particularly the higher frequencies (Rouhiainen et al 1996) (Table 3.19). The reason for this is unclear, but it is likely that the concomitant influences of absorption and, particularly, of (forward) intra-ocular light scatter arising from the age-related cataract degrade the retinal image to a greater extent than any induced HOA arising from the cataract. Absorption and light scatter exhibit a greater influence on the mid to high spatial frequencies than on the low frequencies (Hong et al 2010; de Gracia et al 2011; Owsley 2011). As a consequence, the adverse influence of any induced HOA from the age-related cataract only becomes apparent at the lowest spatial frequency.

The lack of an association in the current study between pupil size and any of the three components for each of the eight HOAs can be explained by the use of a 4.0 mm diameter measurement zone. All individuals achieved a pharmacologically dilated pupil of at least 4.0 mm in diameter.

The magnitudes of the Corneal components of the T.Trefoil, and T.4foil HOAs increased, and of the T.Sph HOA decreased, with increase in flattest corneal curvature ( $\mathrm{p}=0.045$, $\mathrm{p}=0.020$ and $\mathrm{p}=0.012$, respectively) (Table 3.20). The three associations were slight and, although the former two functions could have been influenced by one individual, suggest that the anterior cornea and tear film contribute to the presence of these aberrations. No associations were present between either the mean or the flattest corneal curvatures and the Total and Internal components and any of the eight HOAs.

In the current study, the group mean RMS of the Total component of the Total HOA for the individuals with myopia was 0.128 microns (SD 0.11 ) and that for the individuals with hyperopia 0.312 microns (SD 0.43). The Total and Internal components of the Total HOA increased with increase in myopic spherical equivalent refraction upto approxiamately 16.00 dioptres. The literature is equivocal as to the relationship between the spherical equivalent refractive error and each of the HOAs. In general, the magnitude of the various HOAs increase with increase in the myopia. For myopia of less than -6.00 dioptres, Total (Zadok et al 2005; Wei et al 2006), T.Spherical, T.Coma and T.Trefoil HOAs are not correlated with spherical equivalent refractive error (Zadok et al 2005). No correlation is present for spherical equivalent refractive error upto -10.00 dioptres and coma, spherical and Total HOAs (Cheng et al 2003).

Alternatively, secondary spherical ( $6^{\text {th }}$ order), spherical ( $4^{\text {th }}$ order) and secondary coma ( $5^{\text {th }}$ order) HOAs (Kwan et al 2009), $4^{\text {th }}$ order HOAs (Hu et al 2004) and coma ( $3^{\text {rd }}$ order)
(Paquin et al 2002) increase with increase in myopia over a range of upto approximately -10.00 dioptres.

The increase in spherical HOA (Hu et al 2004; Kwan et al 2009; Karimian et al 2010), and, additionally, primary horizontal coma ( $3^{\text {rd }}$ order) HOA (Karimian et al 2010) and secondary spherical ( $6^{\text {th }}$ order) HOA (Hu et al 2004) is also present for myopia upto aproximately -6.00 dioptres which is associated with astigmatism of less than aproximately -1.00 dioptre. However, trefoil HOA reduces in magnitude (Wei et al 2006). For astigmatism greater than aproximately -1.00 dioptres, Total, primary horizontal coma ( $3^{\text {rd }}$ order) and spherical ( $4^{\text {th }}$ order) HOAs (Karimian et al 2010). Hyperopic eyes upto approximately +3.00 dioptres tend to exhibit larger Total and corneal spherical HOAs and $3^{\text {rd }}$ order HOAs than myopic eyes of upto approximately -3.00 dioptres whereas the Internal HOAs are similar (Llorente et al 2004). In the current study, the Total spherical HOA increased with the magnitude of the hyperopic spherical equivalent refractive error $(\mathrm{r}=0.216)$. However, the limited number of eyes with a hyperopic spherical equivalent refractive error prevents a meaningful comparison of the results with those in the literature.

As might be expected from the co-variance of the spherical equivalent with axial length $\left(\mathrm{R}^{2}=0.245\right)$, the Total and Internal component of the Total HOA increased with increase in axial length. Modest positive associations were also present between the Total and Internal components of the High, T.Coma and T.Trefoil HOAs. These findings compare with with those of Cerviño et al (2008) who reported a weak correlation between axial length and both horizontal coma ( $\mathrm{r}=0.500 ; \mathrm{p}=0.005$ ) and spherical ( $\mathrm{r}=0.423$; $\mathrm{p}=0.020$ ) HOAs.

Cortical cataract can cause significant astigmatic and hyperopic shifts (Planter 1981; Brown 1993; Kuroda et al 2002) whilst nuclear cataract can cause significant myopic shifts (Brown et al 1987). The influence of such changes in refraction on the outcome of the various HOAs is unknown.

Positive associations were found between the Total component of the Tilt (S1) HOA and the severity of both cortical and posterior subcapsular cataract. These associations are a novel finding. The influence on the Tilt HOA was stronger for posterior subcapsular cataract than for cortical cataract (Table 3.21). The association with the Internal component of the Tilt (S1) HOA was maintained for posterior subcapsular cataract only.

The severity of posterior subcapsular cataract was positively associated with the magnitude of the Total component of the T.Coma HOA.

Cortical cataract was also associated with the Total and Internal components of the HiAsig HOA and this association was particularly apparent in the presence of nuclear colour cataract.

The association between T.coma HOA and cortical cataract (Kuroda et al 2002; Sachdev et al 2004; Rocha et al 2007; Lee et al 2008) was not present in the current study.

It has been reported that nuclear and cortical cataract produce a higher amount of tetrafoil and this finding has been proposed to account for the presence of significant visual symptoms in those patients with early cataract who exhibit relatively good high-contrast Snellen acuity (Sachdev et al 2004). Interestingly, an association was present in the current study between nuclear opalescence and the Internal component of the T.4Foil HOA (Table 3.21).

It should be noticed that no associations were found between cataract type and the Corneal component for any of the eight HOAs. Such an outcome supports the robustness of the modelling of the influence of cataract on the HOAs, in that cataract would not be expected to influence the Corneal component but would be expected, as was the case, to influence both the Internal and Total components.

In summary, the Corneal components of the T.Trefoil, T.4Foil and T.Sph HOAs increased with increase in flattest corneal curvature; however, the presence of outliers may have influenced the outcome. The Total and Internal components of the Tilt (S1) HOA increased with increase in severity of posterior subcapsular cataract. The Total component of the Tilt (S1) HOA also increased with increase in severity of cortical cataract. The Total and Internal components of both the T.Sph and the HiAstig HOAs increased with increase in severity of cortical cataract, particularly in the presence of increasing nuclear colour cataract. The Total Component of the T.Coma HOA increased with increase in severity of the posterior subcapsular cataract. Thus, it would be expected that such aberrations would reduce in magnitude following extraction of the associated cataract type. Such a hypothesis forms the basis of the study described in Chapter 4.

## CHAPTER 4

# THE CHANGE IN HIGHER ORDER ABERRATIONS ARISING FROM <br> CATARACT EXTRACTION AND INTRAOCULAR LENS IMPLANTATION 

### 4.1 Introduction

It was shown in Chapter 3 that the Total and Internal components of the Tilt (S1) HOA increased with increase in severity of posterior subcapsular cataract and that the Total component of the Tilt (S1) HOA also increased with increase in severity of cortical cataract. The Total and Internal components of both the T.Sph and the HiAstig HOAs increased with increase in severity of cortical cataract, particularly in the presence of increasing nuclear colour cataract. The Total Component of the T.Coma HOA increased with increase in severity of the posterior subcapsular cataract.

As discussed before in Chapter 1, the HOAs associated with the given IOL are usually compared with those of other given types of IOL. Other studies have compared postoperative HOAs with a given IOL to those in phakic eyes with clear media (Vilarrodona et al 2004; Pesudovs et al 2005; Choi et al 2005; Iseli at al 2006; Yao et al 2006). There are no comparative studies of pre- and post-operative HOAs and, by definition, no longitudinal studies of any potential post-operative change in HOAs. Furthermore, crosssectional studies of post-operative HOAs are seldom performed on a large case series. A comparison of the findings from Chapter 3 in regard to the HOAs with those obtained post-operatively would thus be a useful contribution to knowledge.

### 4.2 Aims

### 4.2.1 Primary Aim

The primary aim was to to explore any association between the demographic variables, age and gender; the structural variables, corneal curvature, corneal endothelial cell density, spherical equivalent and the primary cataract type and severity; the functional variables, distance and near visual acuity and contrast sensitivity and the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained using Placido Disc and Dynamic Skiascopy by the Nidek OPD Scanning System ARK10000 aberrometer in individuals who had undergone cataract surgery and intra-ocular lens implantation at approximately 10 weeks previously.

### 4.2.2. Secondary Aims

The secondary aims were twofold:

Firstly, to determine the associations between the changes from the pre- to the postoperative examinations in the specified and structural variables, corneal curvature, corneal endothelial cell density, spherical equivalent; functional variables, visual acuity and contrast sensitivity; and the corresponding changes in the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained by the OPD aberrometer.

Secondly, to determine the associations between the demographic variables, type of IOL, surgeon, the times from the Pre-operative examination to surgery and from the Preoperative examination to the First Follow-up examination; and the corresponding changes from the pre- to the post-operative examinations in the magnitude of each of the

Total, Corneal and Internal components for each of the eight HOAs obtained by the OPD aberrometer.

The primary cataract type and severity variable was to be referenced to the findings described in Chapter 3, i.e., it was hypothesized that a reduction in the Tilt (S1) HOA would occur following extraction of cortical and posterior subcapsular cataract; a reduction in the T.Coma HOA would occur following the extraction of posterior subcapsular cataract; and a reduction in the T.Sph and HiAstig HOAs would occur following the extraction of cortical and nuclear cataracts.

### 4.3 Methods

### 4.3.1 Experimental Procedures

The case series was drawn from the 99 consecutively presenting individuals, described in Chapter 3, who had attended the Ophthalmic Outpatient Clinic of Soroka University Medical Centre, Beer-Sheva, Israel, and who had been listed for cataract extraction and IOL implantation.

All individuals who attended each follow-up examination underwent an identical standard ophthalmlogical and optometric examination to that, and in the order, described in Chapter 3.3.2. The ophthalmic evaluation was performed by one of three ophthalmologists (Jaime Levi MD; Aliona Petrov MD and the late Pavel Poliakov MD). The optometric evaluation was performed by the Author in an identical manner to that described in section 3.3.2.

### 4.4 Analysis

The aberrometry data set for each individual at each follow-up examination was downloaded from the OPD aberrometer and partitioned into the Total, Corneal and Internal components for a 4 mm diameter zone using the NAVEX Station (Version 2.10) software, as described in Chapter 3.

The demographical and clinical data, including that of the aberrations, were again entered into a master Excel file which was appropriately formatted such that the data could exported to Statistical Analysis Software (SAS, Version 9.1) (Marlow, Buckinghamshir, UK).

The demographic and clinical characteristics of the case series were again described using measures of central tendency (i.e., mean and standard deviation and median and inter-quartile range) and were tabulated accordingly.

The inferential statistics for the analysis of the outcomes at the first follow-up examination (i.e., that of the first aim) were undertaken, as described in Chapter 3, using separate analyses of variance (ANOVA) for each HOA whereby the influence of the same given independent variable on the magnitude of the dependent variable, the given component of the given HOA, was determined. The independent variables were divided into two separate groups: demographic and structural. As before, the visual performance data were considered as dependant variables. As discussed in Chapter 3, the inferential analysis was, a priori, considered to be an explanatory analysis of any potential postoperative associations with the given HOA. Accordingly, no a priori attempt was made to adjust the level of significance to account for the presence of Type I errors arising from the numerous comparisons that were investigated.

A similar approach was adopted for the analysis of the secondary aims whereby the influence of the change in the given structural and/ or functional variable on the change in the given component of the given HOA, was determined using separate ANOVA. The influence of the conflicting variables (type of IOL, surgeon and the times from the Postoperative examination to surgery and from the Post-operative examination to the First Follow-up examination) and the magnitude of the change between the pre- and postoperative outcomes on the change in each of the three components of each of the eight HOAs was determined using separate ANOVA.

### 4.5 Results

### 4.5.1 Case Series

Of the 99 individuals, 11 were excluded (10 did not undergo surgery and one underwent extra-capsular extraction (Table 4.1 and Figure 4.1). The remaining 88 individuals (mean age 72.44 , SD 10.57 ; median 73.00 , IQR $66.75,80.00$ ) had undergone cataract surgery by phacoemulsification and IOL implantation by one of four surgeons (Tova Lifshitz MD, Itamar Klemperer MD, Yaron Finkelman MD and Nadav Belfer MD). For the purposes of the data display, these surgeons were randomly anonymised as Surgeons 1, 2, 3 or 4 . One of four types of spherical foldable IOLs were implanted during surgery, namely: Forelens (hydrophilic acrylic; Hanita, Israel), Triplens (hydrophilic acrylic; Hanita, Israel), B-lens (hydrophilic acrylic; Hanita, Israel), and Xcelence (hydrophilic foldable acrylic; Xcelens Co., Switzerland). The choice of IOL for any given individual was at the discretion of the given surgeon and depended upon the clinical circumstances and upon the availability of the given IOL specifications.


Figure 4.1. The number of individuals participating at each examination visit of the study.

Of the 88 individuals, 69 presented at the First Follow-up examination (Figure 4.1). Two of the 69 individuals were excluded from the study on the basis of severe post-operative corneal oedema. The reason for the withdrawal/ non-attendance of the remaining 19 individuals (Figure 4.1) is given in Table 4.2. The mean age of the 67 individuals was 72.73 years (SD 10.81; median 73.00, IQR 66.50, 80.00).

The First Follow-up examination took place approximately 10 weeks after surgery (mean 9.69, SD 6.50; median 7.14, IQR 5.64, 11.71).

| Case <br> number in <br> study | Gender | Reason for withdrawal |
| :---: | :---: | :--- |
| 10 | M | Decided not to undergo surgery; under public hospital care |
| 29 | F | Health complication - Unable to undergo surgery |
| 40 | M | Deceased |
| 48 | F | Health complication - Unable to undergo surgery |
| 50 | F | Health complication - Unable to undergo surgery |
| 59 | F | Decided not to undergo surgery; under public hospital care |
| 62 | M | Health complication - Unable to undergo surgery |
| 73 | F | Decided not to undergo surgery; under public hospital care |
| 90 | F | Extracapsular cataract extraction |
| 96 | F | Decided not to undergo surgery; under public hospital care |
| 98 | M | Surgery not undertaken by a surgeon participating in the study |

Table 4.1. The reason for withdrawal of the 11 individuals from the case series prior to cataract surgery.

### 4.5.2 Characteristics of Case Series at the First Follow-up Examination

### 4.5.2.1 Age and Gender

The distributions of age and gender, stratified by the operated eye, of the 67 individuals who attended the First Follow-up examination are given in Table 4.3.

The mean age was 72.73 years, SD 10.81; median 73.00 years, IQR 66.50, 80.00. The youngest individual in the case series was 24 years old and the eldest 90 years old. The group was composed of 25 males and 42 females. Cataract extraction and IOL implantation was undertaken on 33 right eyes and 34 left eyes.

| Case number in study | Gender | Reason for non-attendance |
| :---: | :---: | :---: |
| 24 | F | Refused to attend for follow up |
| 34 | F | Health complication - Unable to attend the clinic |
| 41 | F | Refused to attend for follow up |
| 49 | M | Health complication - Unable to attend the clinic |
| 51 | F | Refused to attend for follow up |
| 53 | F | Refused to attend for follow up |
| 54 | M | Refused to attend for follow up |
| 55 | F | Refused to attend for follow up |
| 68 | F | Health complication - Unable to attend the clinic |
| 70 | F | Moved from Beer-Sheva - Unable to attend the clinic |
| 80 | M | Refused to attend for follow up |
| 81 | F | Health complication - Unable to attend the clinic |
| 84 | F | Refused to attend for follow up |
| 85 | M | Refused to attend for follow up |
| 87 | F | Refused to attend for follow up |
| 89 | F | Health complication - Unable to attend the clinic |
| 91 | M | Refused to attend for follow up |
| 93 | F | Refused to attend for follow up |
| 100 | M | Refused to attend for follow up |

Table 4.2. The reason for non-attendance of the 19 individuals at the First Follow-up examination.

### 4.5.2.2 IOL and Surgeon

The numbers of eyes operated upon by each of the four surgeons stratified by eye, by gender and by type of IOL for the 67 individuals attending the First Follow-up examination are given in Table 4.4.

The Forelens IOL was used in 53 cases, the B-lens in 9, the Xcelens in 3 cases and the Triplens in 2 cases. Thirty-five individuals were operated upon by Surgeon 3, 24 by Surgeon 2, 16 by Surgeon 1 and 14 individuals by Surgeon 4.

| Age group (years) | Gender | Operated eye |  | Total |  | Total |  | Total |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | R | L | R | L | M | F |  |
| 21-30 | M | 1 | - | 1 | - | 1 | - | 1 |
|  | F | - | - |  |  |  |  |  |
| 31-40 | M | - | - | - | - | - | - | - |
|  | F | - | - |  |  |  |  |  |
| 41-50 | M | - | 1 | - | 1 | 1 | - | 1 |
|  | F | - | - |  |  |  |  |  |
| 51-60 | M | 1 | - | 1 | 1 | 1 | 1 | 2 |
|  | F | - | 1 |  |  |  |  |  |
| 61-70 | M | 5 | 5 | 9 | 15 | 10 | 14 | 24 |
|  | F | 4 | 10 |  |  |  |  |  |
| 71-80 | M | 5 | 2 | 16 | 7 | 7 | 16 | 23 |
|  | F | 11 | 5 |  |  |  |  |  |
| 81-90 | M | 1 | 4 | 5 | 11 | 5 | 11 | 16 |
|  | F | 5 | 6 |  |  |  |  |  |
| Total |  | 33 | 34 | 32 | 35 | 25 | 42 | 67 |

Table 4.3.The age of the 67 individuals attending the First Follow-up examination, stratified by gender and by the operated eye.

### 4.5.2.3 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst the 67 individuals at the First Follow-up examination is shown in Table 4.5. As expected, following cataract surgery and IOL implantation, the range of the spherical equivalent refraction reduced appreciably from the Pre-operative value. One individual manifested a spherical equivalent of - 3.00 dioptres. Fifty-eight individuals manifested a spherical equivalent between - 2.00 dioptres and Plano, with a majority manifesting a spherical equivalent
between -1.00 dioptres and Plano. Four individuals exhibited a positive spherical equivalent between Plano and +1.00 dioptres and 2 individuals between +1.00 dioptres and +3.00 dioptres.


Table 4.4. The numbers of eyes operated upon by each of the four surgeons stratified by eye, by gender and by type of IOL for the 67 individuals attending the First Follow-up examination.

### 4.5.2.4 Distance Visual Acuity

The distribution of distance visual acuity amongst the 67 individuals within the case series at the First Follow-up examination is shown in Figure 4.2. As expected, a considerable improvement in distance visual acuity occurred following cataract surgery. Sixteen individuals exhibited a visual acuity of $6 / 6,39$ of between $6 / 7.5$ and $6 / 9,8$ of between $6 / 10$ and $6 / 12$, and 4 of $6 / 15$.

| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $(-3.00)-(-3.99)$ | 1 | -3.00 | - | - | - | - | - |
| $(-2.00)-(-2.99)$ | 2 | -2.63 | - | - | -2.75 | -2.50 | - |
| $(-1.00)-(-1.99)$ | 20 | -1.37 | 0.26 | -1.38 | -1.75 | -1.00 | $-1.63,-1.13$ |
| $(0.00)-(-0.99)$ | 38 | -0.55 | 0.18 | -0.69 | -0.88 | 0.00 | $-0.75,-0.25$ |
| $(0.01)-(+0.99)$ | 4 | 0.34 | - | 0.38 | 0.25 | 0.50 | $0.25,0.50$ |
| $(+1.00)-(+1.99)$ | 1 | 1.13 | - | - | - | - | - |
| $(+2.00)-(+2.99)$ | 1 | 2.75 | - | - | - | - | - |
| Group | 67 | -0.76 | 0.83 | -0.75 | -3.00 | 2.75 | $-1.13,-0.50$ |

Table 4.5. The summary statistics for the distribution of the spherical equivalent refraction amongst the 67 individuals within the case series at the First Follow-up examination.


Figure 4.2. The distribution of visual acuity amongst the 67 individuals within the case series at the First Follow-up examination. The upper legend for the abscissa delineates the acuity in Snellen notation and the lower legend the acuity in MAR.

### 4.5.2.5 Near Visual Acuity

The distribution of near visual acuity amongst the 67 individuals within the case series is shown in Figure 4.3.

As with the distance visual acuity, all individuals exhibited a large improvement in near visual acuity following cataract surgery.

Thirty-three individuals exhibited a near visual acuity of Jaeger 1, 25 of Jaeger 2, 6 of Jaeger 3 and 3 of between Jaeger 4 and Jaeger 6.


Figure 4.3. The distribution of near visual acuity in Jaeger notation for the 67 individuals within the case series at the First Follow-up examination.

### 4.5.2.6 Contrast Sensitivity

The distribution of contrast sensitivity amongst the 67 individuals for each of the five spatial frequencies derived by the Functional Acuity Contrast Test (FACT) 301 at the First Follow-up examination is shown in Figure 4.4. Contrast sensitivity improved greatly for all spatial frequencies.




Figure 4.4. The distribution of the contrast sensitivity value for spatial frequencies of 1.5 , 3 and 6 cycles per degree, derived by the Functional Acuity Contrast Test (FACT) for the 67 individuals within the case series at the First Follow-up examination (Top, Middle and Bottom, respectively). Note the difference in the scaling of the abscissa.


Figure 4.4 Continued. The distribution of the contrast sensitivity value for spatial frequencies of 12 and 18 cycles per degree, derived by the Functional Acuity Contrast Test (FACT) for the 67 individuals within the case series at the First Follow-up examination (Top and Bottom, respectively). Note the difference in the scaling of the abscissa.

### 4.5.2.7 Dilated Pupil Diameter

The distribution of the dilated pupil diameter, within the case series, as measured by the OPD aberrometer, is shown in Table 4.6. One individual exhibited a dilated pupil diameter of $3.72 \mathrm{~mm}, 16$ of between 4.00 and $4.99 \mathrm{~mm}, 40$ of between 5.00 and 6.49 mm and 10 of between 6.50 and 8.00 mm .

| Dilated Pupil <br> Diameter (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 4.00 | 1 | 3.72 | - | - | - | - | - |
| 4.00 to 4.49 | 7 | 4.24 | 0.16 | 4.24 | 4.05 | 4.47 | $413,4.34$ |
| 4.50 to 4.99 | 9 | 4.79 | 0.08 | 4.78 | 4.70 | 4.98 | $4.73,4.78$ |
| 5.00 to 5.49 | 16 | 5.23 | 0.15 | 5.21 | 5.04 | 5.47 | $5.07,5.12$ |
| 5.50 to 5.99 | 13 | 5.83 | 0.14 | 5.85 | 5.54 | 5.99 | $5.68,5.80$ |
| 6.00 to 6.49 | 11 | 6.28 | 0.17 | 6.32 | 6.00 | 6.49 | $6.08,6.28$ |
| 6.50 to 6.99 | 6 | 6.77 | 0.17 | 6.86 | 6.54 | 6.96 | $6.68,6.93$ |
| 7.00 to 7.49 | 3 | 7.26 | - | 7.17 | 7.15 | 7.46 | - |
| 7.50 to 7.99 | 1 | 7.89 | - | - | - | - | - |
| Group | 67 | 5.60 | 0.90 | 5.54 | 3.72 | 7.89 | $5.01,6.22$ |

Table 4.6. The summary statistics for the distribution, amongst the 67 individuals within the case series, of the dilated pupil diameter as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer at the First Follow-up examination.

### 4.5.2.8 Mean Corneal Curvature

The distribution of the mean corneal curvature, within the case series, as measured by the OPD aberrometer, is shown in Table 4.7. Five individuals exhibited a mean corneal curvature of less than $7.20 \mathrm{~mm}, 6$ individuals of between 7.20 and $7.39 \mathrm{~mm}, 47$ of between 7.40 and 7.99 mm and 7 of between 8.20 and 8.39 mm . One individual exhibited an apparent mean corneal curvature of 12.78 mm . The measurement of corneal curvature was not available in one individual.

### 4.5.2.9 Flattest Corneal Curvature

The distribution of the flattest corneal curvature, amongst 66 of 67 individuals within the case series, as measured by the OPD aberrometer, is shown in Table 4.8. Three individuals exhibited a flattest corneal curvature of less than $7.20 \mathrm{~mm}, 7$ of between 7.20
and $7.39 \mathrm{~mm}, 52$ of between 7.40 and $8.19 \mathrm{~mm}, 2$ of between 8.20 and 8.39 mm and 2 exhibited a flattest corneal curvature greater than 8.39 mm . The latter included the outlier described above with a mean corneal curvature of 12.78 mm . The measurement of corneal curvature was not available in one individual.

| Mean Corneal <br> Curvature (mm) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 7.2 | 5 | 7.10 | 0.08 | 7.12 | 6.98 | 7.18 | $7.06,7.71$ |
| 7.20 to 7.39 | 6 | 7.30 | 0.06 | 7.32 | 7.20 | 7.35 | $7.277,7.34$ |
| 7.40 to 7.59 | 20 | 7.49 | 0.06 | 7.50 | 7.40 | 7.59 | $7.45,7.54$ |
| 7.60 to 7.79 | 21 | 7.69 | 0.05 | 7.70 | 7.60 | 7.79 | $7.64,7.73$ |
| 7.80 to 7.99 | 6 | 7.92 | 0.08 | 7.96 | 7.82 | 7.99 | $7.86,7.99$ |
| 8.00 to 8.19 | 4 | 8.04 | - | 8.03 | 8.00 | 8.10 | $8.01,8.05$ |
| 8.20 to 8.39 | 3 | 8.27 | - | 8.26 | 8.25 | 8.29 | - |
| Greater than 8.39 | 1 | 12.78 | - | - | - | - | - |
| Group | 66 | 7.70 | 0.69 | 7.62 | 6.98 | 12.78 | $7.46,7.74$ |

Table 4.7. The summary statistics for the distribution amongst 66 of the 67 individuals within the case series in whom the measurement was available, of the mean corneal curvature as measured by the Nidek Optical Path Difference Scanning System ARK10000 aberrometer at the First Follow-up examination.

| Flattest Corneal <br> Curvature (mm) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 7.2 | 3 | 7.12 | - | 7.11 | 7.05 | 7.19 | - |
| 7.20 to 7.39 | 7 | 7.30 | 0.07 | 7.30 | 7.21 | 7.38 | $7.25,7.34$ |
| 7.40 to 7.59 | 12 | 7.52 | 0.05 | 7.53 | 7.46 | 7.59 | $7.47,7.55$ |
| 7.60 to 7.79 | 18 | 7.67 | 0.06 | 7.66 | 7.60 | 7.77 | $7.63,7.72$ |
| 7.80 to 7.99 | 13 | 7.85 | 0.02 | 7.84 | 7.82 | 7.91 | $7.83,7.86$ |
| 8.00 to 8.19 | 9 | 8.09 | 0.06 | 8.07 | 8.03 | 8.19 | $8.06,8.12$ |
| 8.20 to 8.39 | 2 | 8.35 | - | - | 8.25 | 8.37 | - |
| Greater than 8.39 | 2 | 11.33 | - | - | 8.91 | 13.75 | - |
| Group | 66 | 7.80 | 0.81 | 7.69 | 7.05 | 13.75 | $7.54,7.86$ |

Table 4.8. The summary statistics for the distribution amongst 66 of the 67 individuals within the case series in whom the measurement was available, of the flattest corneal curvature as measured by the Nidek Optical Path Difference Scanning System ARK10000 aberrometer at the First Follow-up examination.

### 4.5.2.10 Corneal Endothelial Cell Density

The distribution of the corneal endothelial cell density amongst the 67 individuals within the case series is given in Table 4.9. Three individuals exhibited an apparent corneal endothelial cell density of between 300 and 599 cells $/ \mathrm{mm}^{2}$, 5 of between 600 and 899 cells $/ \mathrm{mm}^{2}, 17$ of between 900 and 1499 and 36 of between 1500 and 2399 cells $/ \mathrm{mm}^{2}$. Six individuals exhibited a corneal endothelial cell density greater than 2399 cells $/ \mathrm{mm}^{2}$.

| Corneal Endothelial <br> Cell Density <br> $\left(\right.$ Cells $\left./ \mathrm{mm}^{2}\right)$ | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 300 to 599 | 3 | 483 | - | 567 | 307 | 576 | - |
| 600 to 899 | 5 | 759 | 100.75 | 783 | 629 | 873 | 683,825 |
| 900 to 1199 | 9 | 1085 | 102.37 | 1144 | 936 | 1173 | 969,1166 |
| 1200 to 1499 | 8 | 1085 | 91.72 | 1144 | 1205 | 1461 | 1239,1405 |
| 1500 to 1799 | 11 | 1677 | 105.49 | 1736 | 1526 | 1784 | 1571,1764 |
| 1800 to 2099 | 13 | 1949 | 101.21 | 1946 | 1812 | 2085 | 1835,2037 |
| 2100 to 2399 | 12 | 2265 | 94.61 | 2268 | 2103 | 2399 | 2201,2357 |
| Greater than 2399 | 6 | 2463 | 54.36 | 2461 | 2402 | 2558 | 2430,2473 |
| Group | 67 | 1661 | 578.00 | 1777 | 307 | 2558 | 1189,2125 |

Table 4.9. The summary statistics for the distribution, amongst the 67 individuals within the case series, of corneal endothelial cell density at the First Follow-up examination.

### 4.5.2.11 Higher Order Aberrations

The summary statistics of the distribution of the RMS value of the Total component for each of the eight HOAs, measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone, namely, Total, Tilt (S1), High, T.coma, T.trefoil, T.4Foil, T.sph and HiAstig are given in Tables 4.10-4.17, respectively
for the 65 of the 67 individuals. A measure of the HOAs for the 2 remaining individuals could not be obtained. The reason for this is unknown.

### 4.5.2.11.1 Total Component of the Total HOA

Twenty individuals exhibited RMS values for the Total component of the Total HOA of between 0.500 and 0.899 microns, 29 of between 0.900 and 1.499 microns, 11 of between 1.500 and 2.099 microns and 5 greater than 2.099 , 1 of whom exhibited an RMS value of 10.070 microns.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.500 to 0.699 | 10 | 0.627 | 0.21 | 0.621 | 0.586 | 0.687 | $0.593,0.645$ |
| 0.700 to 0.899 | 10 | 0.833 | 0.30 | 0.843 | 0.714 | 0.891 | $0.803,0.875$ |
| 0.900 to 1.099 | 12 | 1.031 | 0.33 | 1.030 | 0.931 | 1.097 | $1.011,1.065$ |
| 1.100 to 1.299 | 6 | 1.187 | 0.39 | 1.183 | 1.115 | 1.277 | $1.135,1.224$ |
| 1.300 to 1.499 | 11 | 1.387 | 0.40 | 1.394 | 1.314 | 1.462 | $1.340,1.431$ |
| 1.500 to 1.699 | 4 | 1.591 | - | 1.593 | 1.519 | 1.656 | $1.569,1.615$ |
| 1.700 to 1.899 | 3 | 1.782 | - | 1.749 | 1.741 | 1.854 | - |
| 1.900 to 2.099 | 4 | 2.011 | - | 2.013 | 1.937 | 2.078 | $1982,2.041$ |
| Greater than 2.099 | 5 | 5.579 | 6.30 | 3.872 | 2.716 | 10.070 | $3.139,4.689$ |
| Group | 65 | 1.940 | 3.57 | 1.115 | 0.586 | 10.070 | $0.853,1.462$ |

Table 4.10. The summary statistics for the distribution, amongst 65 of the 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the Total HOA at the First Follow-up examination.

### 4.5.2.11.2 Total Component of the Tilt (S1) HOA

Twenty-four individuals exhibited an RMS value for the Total component of the Tilt (S1) HOA of between 0.050 and 0.199 microns, 28 of between 0.200 and 0.399 microns, 9 of between 0.400 and 0.549 microns and 5 individuals an RMS value greater than 0.549 microns.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Tilt (S1) RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.050 to 0.099 | 7 | 0.072 | 0.04 | 0.069 | 0.056 | 0.086 | $0.062,0.080$ |
| 0.100 to 0.149 | 6 | 0.122 | 0.06 | 0.121 | 0.106 | 0.145 | $0.114,0.124$ |
| 0.150 to 0.199 | 11 | 0.173 | 0.06 | 0.173 | 0.150 | 0.188 | $0.168,0.182$ |
| 0.200 to 0.249 | 6 | 0.231 | 0.07 | 0.235 | 0.215 | 0.240 | $0.226,0.236$ |
| 0.250 to 0.299 | 7 | 0.280 | 0.09 | 0.283 | 0.258 | 0.295 | $0.270,0.293$ |
| 0.300 to 0.349 | 8 | 0.331 | 0.09 | 0.335 | 0.308 | 0.345 | $0.324,0.339$ |
| 0.350 to 0.399 | 7 | 0.376 | 0.09 | 0.378 | 0.362 | 0.388 | $0.367,0.383$ |
| 0.400 to 0.449 | 3 | 0.419 | - | 0.423 | 0.405 | 0.428 | - |
| 0.450 to 0.499 | 3 | 0.470 | - | 0.473 | 0.463 | 0.473 | - |
| 0.500 to 0.549 | 3 | 0.538 | - | 0.543 | 0.516 | 0.553 | - |
| Greater than 0.549 | 5 | 2.275 | 2.71 | 1.384 | 0.742 | 4.237 | $0.821,2.190$ |
| Group | 65 | 0.691 | 1.51 | 0.274 | 0.056 | 4.237 | $0.168,0.383$ |

Table 4.11. The summary statistics for the distribution, amongst 65 of the 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the Tilt (S1) HOA at the First Follow-up examination.

### 4.5.2.11.3 Total Component of the High HOA

Forty-six individuals exhibited an RMS value for the Total component of the High HOA of between 0.100 and 0.399 microns, 14 of between 0.400 and 0.999 microns, 2 of
between 1.000 and 1.999 microns and 2 of between 2.000 and 4.000 microns. One individual exhibited an RMS value of 8.240 microns.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| High RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.100 to 0.199 | 12 | 0.161 | 0.09 | 0.169 | 0.100 | 0.197 | $0.142,0.180$ |
| 0.200 to 0.299 | 23 | 0.256 | 0.11 | 0.260 | 0.215 | 0.296 | $0.233,0.268$ |
| 0.300 to 0.399 | 11 | 0.115 | 0.13 | 0.345 | 0.302 | 0.371 | $0.322,0.354$ |
| 0.400 to 0.499 | 3 | 0.427 | - | 0.421 | 0.410 | 0.449 | - |
| 0.500 to 0.599 | 6 | 0.530 | 0.19 | 0.533 | 0.473 | 0.568 | $0.516,0.550$ |
| 0.600 to 0.699 | 2 | 0.626 | - | - | 0.605 | 0.648 | - |
| 0.700 to 0.799 | 2 | 0.770 | - | - | 0.753 | 0.786 | - |
| 0.800 to 0.899 | - | - | - | - | - | - | - |
| 0.900 to 0.999 | 1 | 0.968 | - | - | - | - | - |
| 1.000 to 1.999 | 2 | 1.389 | - | - | 1.061 | 1.653 | - |
| 2.000 to 4.000 | 2 | 3.283 | - | - | 2.832 | 3.680 | - |
| Greater than 4.000 | 1 | 8.240 | - | - | - | - | - |
| Group | 65 | 1.250 | 2.93 | 0.289 | 0.100 | 8.240 | $0.229,0.450$ |

Table 4.12. The summary statistics for the distribution, amongst 65 of the 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the High HOA at the First Follow-up examination. Note the difference in the scaling for the last 4 data cells.

### 4.5.2.11.4 Total Component of the T.Coma HOA

Thirty-eight individuals exhibited RMS values for the Total component of the T.Coma HOA of between 0.030 and 0.109 microns, 21 of between 0.110 and 0.209 microns, 2 of between 0.230 and 0.269 microns and 3 greater than 0.269 microns.

## Total Component

| T.Coma RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.030 | 1 | 0.029 | - | - | - | - | - |
| 0.030 to 0.049 | 2 | 0.046 | - | - | 0.043 | 0.048 | - |
| 0.050 to 0.069 | 5 | 0.060 | 0.030 | 0.060 | 0.053 | 0.068 | $0.054,0.064$ |
| 0.070 to 0.089 | 21 | 0.080 | 0.030 | 0.077 | 0.071 | 0.089 | $0.074,0.085$ |
| 0.090 to 0.109 | 10 | 0.099 | 0.030 | 0.099 | 0.091 | 0.107 | $0.095,0.103$ |
| 0.110 to 0.129 | 6 | 0.120 | 0.040 | 0.119 | 0.110 | 0.129 | $0.116,0.126$ |
| 0.130 to 0.149 | 4 | 0.143 | - | 0.144 | 0.137 | 0.147 | $0.412,0.146$ |
| 0.150 to 0.169 | 6 | 0.162 | 0.040 | 0.160 | 0.158 | 0.169 | $0.159,0.164$ |
| 0.170 to 0.189 | 3 | 0.184 | - | 0.183 | 0.183 | 0.186 | - |
| 0.190 to 0.209 | 2 | 0.200 | - | - | 0.195 | 0.204 | - |
| 0.210 to 0.229 | - | - | - | - | - | - | - |
| 0.230 to 249 | 1 | 0.240 | - | - | - | - | - |
| 0.250 to 0.269 | 1 | 0.263 | - | - | - | - | - |
| Greater than 0.269 | 3 | 0.539 | - | 0.551 | 0.417 | 0.627 | - |
| Group | 65 | 0.734 | 0.251 | 0.097 | 0.029 | 0.627 | $0.077,0.147$ |

Table 4.13. The summary statistics for the distribution, amongst 65 of the 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.Coma HOA at the First Follow-up examination.

### 4.5.2.11.5 Total Component of the T.Trefoil HOA

Forty-five individuals exhibited an RMS value for the Total component of the T.Trefoil HOA of between 0.030 and 0.269 microns, 10 of between 0.270 and 0.509 microns, 6 of between 0.510 and 0.749 microns and 4 greater than 0.749 microns.

### 4.5.2.11.6 Total Component of the T.4Foil HOA

Twelve individuals exhibited an RMS value for the Total component of the T.4Foil HOA of between than 0.010 and 0.049 microns, 40 of between 0.050 and 0.149 microns, 8 of between 0.150 and 0.249 microns and 5 greater than 0.249 microns.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Trifoil RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.030 to 0.089 | 6 | 0.047 | 0.04 | 0.044 | 0.025 | 0.067 | $0.029,0.057$ |
| 0.090 to 0.149 | 13 | 0.117 | 0.12 | 0.117 | 0.094 | 0.141 | $0.099,0.128$ |
| 0.150 to 0.209 | 15 | 0.177 | 0.08 | 0.174 | 0.150 | 0.209 | $0.158,0.186$ |
| 0.210 to 0.269 | 11 | 0.241 | 0.10 | 0.252 | 0.211 | 0.269 | $0.220,0.257$ |
| 0.270 to 0.329 | 3 | 0.305 | - | 0.303 | 0.292 | 0.318 | - |
| 0.330 to 0.389 | 2 | 0.374 | - | - | 0.362 | 0.386 | - |
| 0.390 to 0.449 | 2 | 0.414 | - | - | 0.407 | 0.422 | - |
| 0.450 to 0.509 | 3 | 0.481 | - | 0.482 | 0.459 | 0.501 | - |
| 0.510 to 0.569 | 1 | 0.510 | - | - | - | - | - |
| 0.570 to 0.629 | 2 | 0.600 | - | - | 0.598 | 0.603 | - |
| 0.630 to 0.689 | 2 | 0.672 | - | - | 0.672 | 0.672 | - |
| 0.690 to 0.749 | 1 | 0.740 | - | - | - | - | - |
| Greater than 0.749 | 4 | 2.495 | 3.08 | 1.293 | 1.015 | 4.515 | $1.024,2.298$ |
| Group | 65 | 0.682 | 1.59 | 0.203 | 0.025 | 4.515 | $0.137,0.362$ |

Table 4.14. The summary statistics for the distribution, amongst 65 of 67 the individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.Trefiol HOA at the First Follow-up examination.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.4Foil RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.010 to 0.029 | 6 | 0.021 | 0.01 | 0.021 | 0.013 | 0.027 | $0.017,0.025$ |
| 0.030 to 0.049 | 6 | 0.040 | 0.02 | 0.040 | 0.032 | 0.048 | $0.035,0.044$ |
| 0.050 to 0.069 | 9 | 0.060 | 0.02 | 0.059 | 0.053 | 0.067 | $0.058,0.063$ |
| 0.070 to 0.089 | 9 | 0.078 | 0.30 | 0.079 | 0.070 | 0.086 | $0.073,0.081$ |
| 0.090 to 0.109 | 11 | 0.099 | 0.03 | 0.099 | 0.091 | 0.106 | $0.097,0.102$ |
| 0.110 to 0.129 | 5 | 0.118 | 0.04 | 0.117 | 0.110 | 0.126 | $0.114,0.122$ |
| 0.130 to 0.149 | 6 | 0.143 | 0.30 | 0.141 | 0.140 | 0.149 | $0.141,0.144$ |
| 0.150 to 0.169 | 2 | 0.161 | - | - | 0.154 | 0.168 | - |
| 0.170 to 0.189 | 1 | 0.170 | - | - | - | - | - |
| 0.190 to 0.209 | 2 | 0.191 | - | - | 0.191 | 0.191 | - |
| 0.210 to 0.229 | 1 | 0.217 | - | - | - | - | - |
| 0.230 to 0.249 | 2 | 0.234 | - |  | 0.231 | 0.236 | - |
| Greater than 0.249 | 5 | 2.712 | 3.30 | 0.030 | 0.283 | 5.111 | $0.919,2.716$ |
| Group | 65 | 0.759 | 1.83 | 0.0969 | 0.013 | 5.111 | $0.059,0.141$ |

Table 4.15. The summary statistics for the distribution, amongst the 65 of 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.4Foil HOA at the First Follow-up examination.

### 4.5.2.11.7 Total Component of the T.Sph HOA

Five individuals exhibited an RMS value for the Total component of the T.Sph HOA of less than 0.010 microns, 46 of between 0.010 and 0.069 microns, 9 of between 0.070 and 0.109 microns, 3 of between 0.110 and 0.149 microns and 2 greater than 1.149 microns.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Sph RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| Less than 0.010 | 5 | 0.006 | 0.01 | 0.006 | 0.003 | 0.009 | $0.004,0.006$ |
| 0.010 to 0.029 | 18 | 0.018 | 0.01 | 0.019 | 0.011 | 0.026 | $0.013,0.022$ |
| 0.030 to 0.049 | 15 | 0.001 | 0.02 | 0.034 | 0.030 | 0.045 | $0.032,0.038$ |
| 0.050 to 0.069 | 13 | 0.060 | 0.03 | 0.056 | 0.052 | 0.069 | $0.053,0.065$ |
| 0.070 to 0.089 | 7 | 0.081 | 0.03 | 0.081 | 0.073 | 0.087 | $0.076,0.085$ |
| 0.090 to 0.109 | 2 | 0.098 | - | - | 0.091 | 0.104 | - |
| 0.110 to 0.129 | 2 | 0.126 | - | - | 0.126 | 0.129 | - |
| 0.130 to 0.149 | 1 | 0.132 | - | - | - | - | - |
| Greater than 0.149 | 2 | 0.247 | - | - | 0.200 | 0.287 | - |
| Group | 65 | 0.069 | 0.107 | 0.037 | 0.003 | 0.287 | $0.021,0.067$ |

Table 4.16. The summary statistics for the distribution, amongst 65 of the 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.sph HOA at the First Follow-up examination.

### 4.5.2.11.8 Total Component of the HiAstig HOA

Fifty-four individuals exhibited an RMS value for the Total component of the HiAstig HOA of between 0.010 and 0.089 microns, 6 of between 0.090 and 0.189 microns, 4 greater than 0.189 microns and one of less than 0.010 microns.

Total Component

| HiAstig RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.010 | 1 | 0.008 | - | - | - | - | - |
| 0.010 to 0.029 | 14 | 0.024 | 0.02 | 0.026 | 0.012 | 0.029 | $0.021,0.027$ |
| 0.030 to 0.049 | 23 | 0.039 | 0.02 | 0.038 | 0.030 | 0.047 | $0.034,0.044$ |
| 0.050 to 0.069 | 10 | 0.059 | 0.03 | 0.060 | 0.050 | 0.067 | $0.055,0.062$ |
| 0.070 to 0.089 | 7 | 0.081 | 0.03 | 0.081 | 0.073 | 0.086 | $0.078,0.084$ |
| 0.090 to 0.109 | 2 | 0.098 | - | - | 0.095 | 0.101 | - |
| 0.110 to 0.129 | 1 | 0.128 | - | - | - | - | - |
| 0.130 to 0.149 | 1 | 0.134 | - | - | - | - | - |
| 0.150 to 0.169 | 1 | 0.168 | - | - | - | - | - |
| 0.170 to 0.189 | 1 | 0.185 | - | - | - | - | - |
| Greater than 0.189 | 4 | - | 0.75 | 0.509 | 0.219 | 1.128 | $0.343,0.758$ |
| Group | 65 | 0.180 | 0.41 | 0.044 | 0.008 | 1.128 | $0.031,0.073$ |

Table 4.17. The summary statistics for the distribution, amongst 65 of the 67 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the HiAstig HOA at the First Follow-up examination.

### 4.5.3 Explanatory Analysis of Associations between the Demographic, Structural and Functional Variables and each of the Three Components of each of the Eight <br> HOAs Obtained at the First Follow-up Examination

The results of the explanatory analysis at the First Follow-up examination are given for the demographic variables in Table 4.18, for the visual performance variables in Table 4.19, and for the structural variables in Table 4.20 and Figures 4.5-4.7.

### 4.5.3.1 Age

No association was present between age and each of the three components for each of the eight HOAs (Table 4.18).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age continuous | 0.663 | 0.665 | 0.616 | 0.549 | 0.944 | 0.343 | 0.771 | 0.404 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age continuous | 0.800 | 0.128 | 0.159 | 0.113 | 0.130 | 0.818 | 0.682 | 0.601 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age continuous | 0.824 | 0.548 | 0.697 | 0.358 | 0.818 | 0.382 | 0.601 | 0.477 |  |

Table 4.18. The probability value derived by ANOVA at the First Follow-up examination for the association between age, as a continuous variable, and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 4.5.3.2 Distance Visual Acuity

Distance visual acuity declined with increase in all three components of the Total ( $\mathrm{p}=0.027, \mathrm{p}=0.014$ and $\mathrm{p}=0.036$, respectively) and the Tilt ( S 1 ) ( $\mathrm{p}=0.023, \mathrm{p}=0.004$ and $\mathrm{p}=0.008$, respectively) HOAs (Table 4.19). It also declined with increase in the Corneal component of all HOAs ( $\mathrm{R}^{2} \leq 15.4 \%$ ), with the exception of the T.Sph and the HiAstig HOAs (Table 4.19).

### 4.5.3.3 Near Visual Acuity

No associations were found between the near visual acuity and each of the components of each of the eight HOAs, with the exception of the Internal component of the Tilt (S1) HOA ( $\mathrm{p}=0.037$ ) (Table 4.19).

### 4.5.3.4 Contrast Sensitivity

No association was present between the magnitudes of the Total component and of the Internal component for each of the eight HOAs and the contrast sensitivity at each of the five spatial frequencies. However, an increase in the Corneal component of the Total, Tilt (S1), High and T.Trefoil HOAs was weakly associated ( $\mathrm{R}^{2} \leq 13.3 \%$ ) with a reduction in the magnitude of the contrast sensitivity at $1.5(\mathrm{p}=0.019, \mathrm{p}=0.023, \mathrm{p}=0.023$ and $\mathrm{p}=0.024$ respectively) and at $3(\mathrm{p}=0.036, \mathrm{p}=0.008, \mathrm{p}=0.017$ and $\mathrm{p}=0.028$ respectively) cycles per degree. In addition, the Corneal component of the Tilt (S1) also adversely influenced the magnitude of the contrast sensitivity at $6(\mathrm{p}=0.029)$ and $12(\mathrm{p}=0.028)$ cycles per degree (Table 4.19). However, these associations largely occurred as the result of one outlying value.

### 4.5.3.5 Dilated Pupil Diameter

No association was present between dilated pupil diameter and any of the three components for each of the eight HOAs (Table 4.20).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.027 | 0.023 | 0.137 | 0.108 | 0.053 | 0.308 | 0.623 | 0.202 |  |
| NVA | 0.162 | 0.064 | 0.271 | 0.871 | 0.140 | 0.414 | 0.387 | 0.324 |  |
| CS 1.5 cpd | 0.170 | 0.690 | 0.134 | 0.051 | 0.174 | 0.076 | 0.956 | 0.173 |  |
| CS 3 cpd | 0.875 | 0.641 | 0.739 | 0.113 | 0.940 | 0.487 | 0.466 | 0.750 |  |
| CS 6 cpd | 0.453 | 0.605 | 0.110 | 0.090 | 0.174 | 0.065 | 0.974 | 0.094 |  |
| CS 12 cpd | 0.781 | 0.876 | 0.463 | 0.229 | 0.622 | 0.357 | 0.827 | 0.511 |  |
| CS 18 cpd | 0.572 | 0.782 | 0.268 | 0.077 | 0.427 | 0.196 | 0.355 | 0.219 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| DVA | 0.014 | 0.004 | 0.013 | 0.042 | 0.008 | 0.014 | 0.624 | 0.061 |  |  |
| NVA | 0.115 | 0.194 | 0.147 | 0.085 | 0.229 | 0.105 | 0.258 | 0.800 |  |  |
| CS 1.5 cpd | 0.019 | 0.023 | 0.023 | 0.130 | 0.024 | 0.387 | 0.313 | 0.371 |  |  |
| CS 3 cpd | 0.036 | 0.008 | 0.017 | 0.013 | 0.028 | 0.788 | 0.940 | 0.959 |  |  |
| CS 6 cpd | 0.086 | 0.029 | 0.124 | 0.168 | 0.144 | 0.160 | 0.130 | 0.317 |  |  |
| CS 12 cpd | 0.578 | 0.028 | 0.092 | 0.077 | 0.183 | 0.703 | 0.632 | 0.661 |  |  |
| CS 18 cpd | 0.149 | 0.130 | 0.173 | 0.258 | 0.255 | 0.393 | 0.374 | 0.856 |  |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| DVA | 0.036 | 0.008 | 0.141 | 0.180 | 0.088 | 0.134 | 0.950 | 0.191 |  |  |
| NVA | 0.156 | 0.037 | 0.278 | 0.295 | 0.233 | 0.252 | 0.516 | 0.574 |  |  |
| CS 1.5 cpd | 0.460 | 0.823 | 0.336 | 0.152 | 0.387 | 0.313 | 0.389 | 0.498 |  |  |
| CS 3 cpd | 0.246 | 0.227 | 0.979 | 0.069 | 0.788 | 0.939 | 0.317 | 0.735 |  |  |
| CS 6 cpd | 0.359 | 0.987 | 0.131 | 0.221 | 0.159 | 0.130 | 0.959 | 0.205 |  |  |
| CS 12 cpd | 0.964 | 0.317 | 0.566 | 0.143 | 0.703 | 0.632 | 0.661 | 0.816 |  |  |
| CS 18 cpd | 0.718 | 0.674 | 0.347 | 0.862 | 0.393 | 0.374 | 0.856 | 0.504 |  |  |

Table 4.19. The probability value derived by ANOVA at the First Follow-up examination for the association between distance visual acuity, near visual acuity and each of the six spatial frequencies of the FACT 301 Test, and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.159 | 0.532 | 0.476 | 0.141 | 0.603 | 0.346 | 0.172 | 0.638 |  |
| CC Mean | 0.446 | 0.471 | 0.753 | 0.329 | 0.750 | 0.761 | 0.493 | 0.836 |  |
| CC Flattest | 0.513 | 0.579 | 0.790 | 0.347 | 0.621 | 0.954 | 0.263 | 0.871 |  |
| CECD | 0.510 | 0.270 | 0.386 | 0.784 | 0.214 | 0.578 | 0.302 | 0.370 |  |
| Sph Equiv | 0.049 | 0.214 | 0.830 | 0.219 | 0.723 | 0.958 | 0.569 | 0.997 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.595 | 0.810 | 0.990 | 0.988 | 0.971 | 0.623 | 0.490 | 0.750 |  |
| CC mean | 0.697 | 0.802 | 0.544 | 0.842 | 0.345 | 0.776 | 0.599 | 0.718 |  |
| CC flattest | 0.005 | 0.010 | 0.003 | 0.065 | 0.0006 | 0.523 | 0.393 | 0.823 |  |
| CECD | 0.005 | 0.010 | 0.009 | 0.030 | 0.012 | 0.158 | 0.251 | 0.245 |  |
| Sph Equiv | 0.617 | 0.310 | 0.455 | 0.298 | 0.443 | 0.959 | 0.969 | 0.765 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.274 | 0.760 | 0.539 | 0.717 | 0.623 | 0.499 | 0.750 | 0.507 |  |
| CC mean | 0.629 | 0.781 | 0.747 | 0.432 | 0.776 | 0.599 | 0.717 | 0.962 |  |
| CC flattest | 0.245 | 0.111 | 0.548 | 0.381 | 0.523 | 0.393 | 0.823 | 0.828 |  |
| CECD | 0.111 | 0.030 | 0.222 | 0.133 | 0.158 | 0.251 | 0.245 | 0.212 |  |
| Sph Equiv | 0.292 | 0.882 | 0.951 | 0.731 | 0.959 | 0.969 | 0.765 | 0.944 |  |

Table 4.20. The probability value derived by ANOVA at the First Follow-up examination for the association between the magnitude of each of the structural variables dilated pupil diameter, mean central corneal curvature (CC), flattest central corneal curvature (CC), corneal endothelial cell density (CECD), and spherical equivalent (SE), and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 4.5.3.6 Mean Corneal Curvature

No association was present between the mean corneal curvature and any of the three components for each of the eight HOAs (Table 4.20).

### 4.5.3.7 Flattest Corneal Curvature

No association was found between the flattest corneal curvature and the Total and Internal components of the eight HOAs. However, the magnitude of the Corneal component of the Total, Tilt (S1), High and T.Trefoil HOAs ( $\mathrm{p}=0.005, \mathrm{p}=0.010, \mathrm{p}=0.003$, $\mathrm{p}=0.0006$, respectively) increased with increase in the flatter corneal radius $\left(\mathrm{R}^{2} \leq 22.0 \%\right)$ due to the presence of one outlying value (Table 4.20 and Figure 4.5).


Figure 4.5. The magnitude of the Corneal component of the Total and the Tilt (S1) HOAs as a function of the flattest corneal curvature at the First Follow-up examination amongst 52 of 67 individuals within the case series in whom the measurement was available (Top and Bottom). The circled data points indicate outlying values.


Figure 4.5 Continued. The magnitude of the Corneal component of the High and the T.Trefoil HOAs as a function of the flattest corneal curvature at the First Follow-up examination amongst 52 of 67 individuals within the case series in whom the measurement was available (Top and Bottom). Note the differences in the scaling of the ordinate between the four graphs. The circled data points indicate outlying values.

### 4.5.3.8 Corneal Endothelial Cell Density

Weak negative associations ( $\mathrm{R}^{2} \leq 14.5 \%$ ) were present between the corneal endothelial cell density and the Corneal Component of Total, Tilt(S1), High, T.Coma and T.Trefoil HOAs $(\mathrm{p}=0.005, \mathrm{p}=0.010, \mathrm{p}=0.009, \mathrm{p}=0.030, \mathrm{p}=0.012$ respectively) (Table 4.20 and Figure 4.6).

A similar association was also present between corneal endothelial cell density and the Internal Component of Tilt (S1) HOA ( $\mathrm{p}=0.030$ ) (Table 4.20 and Figure 4.7). All associations were highly influenced by the presence of one outlying value (Figure 4.6 and Figure 4.7).



Figure 4.6. The magnitude of the Corneal component of the Total and Tilt (S1) HOAs as a function of the corneal endothelial cell density at the First Follow-up examination amongst 52 of 67 individuals within the case series in whom the measurement was available (Top and Bottom). The circled data points indicate outlying values.


Figure 4.6 Continued. The magnitude of the Corneal component of the High, T.Coma and T.Trefoil HOAs as a function of the corneal endothelial cell density at the First Follow-up examination amongst 52 of 67 individuals within the case series in whom the measurement was available (Top; Middle and Bottom, respectively). Note the difference in the scaling of the ordinate between the five graphs. The circled data points indicate outlying values.


Figure 4.7. The magnitude of the Internal component of the Tilt (S1) HOA as a function of the corneal endothelial cell density at the First Follow-up examination amongst 52 of 67 individuals within the case series in whom the measurement was available. Note the difference in the scaling of the ordinate between this and the previous graphs. The circled data points indicate outlying values.

### 4.5.3.9 Spherical Equivalent Refraction

No association was present between the spherical equivalent refraction and any of the three components of the eight HOAs.

### 4.5.4 Characteristics of the Case Series for the Investigation of the Change in the

## HOAs from the Pre-operative to the First Follow-up Examinations

### 4.5.4.1 Spherical Equivalent Refraction

The distribution of the change in the spherical equivalent refraction amongst the 67 individuals from the Pre-operative to the First Follow-up examinations is shown in Table 4.21 and in Figure 4.8. As would be expected, the general trend for the spherical
equivalent refraction from the Pre-operative examination to the First Follow-up examination was a reduction in myopia for the myopic eyes and a reduction in hyperopia for the hyperopic eyes. Of the 56 myopes within the case series of 67 individuals, 13 exhibited a reduction in myopia of between 0.00 to 1.00 dioptres, 17 of between 1.01 to 4.00 dioptres, 15 of between 4.01 to 8.00 dioptres, one of 14.50 dioptres and one of 15.75 dioptres. Eight individuals exhibited an increase in myopia of between 0.00 to 1.00 dioptres, and one of 1.18 dioptres. Of the 11 hyperopes within the case series, 3 exhibited a reduction in the hyperopia of between 0.50 to 1.00 dioptres, 4 of between 1.01 to 2.00 dioptres and 4 of between 2.01 to 5.25 dioptres. In total, 2 individuals exhibited an increasing myopic shift in spherical equivalent refraction of more than -5.25 dioptres, one of -4.88 dioptres and 17 of between -2.99 and 0.00 dioptres. Twenty-six individuals exhibited an increasing hyperopic shift of between 0.01 dioptres and 2.99 dioptres and 19 individuals of between 3.00 and 7.99 dioptres. One of the 2 individuals with high myopia exhibited an increasing hyperopic shift of 14.50 dioptres and the other of 15.75 dioptres.

### 4.5.4.2 Distance Visual Acuity

The change in complete lines of the distance visual acuity from the Pre-operative to the First Follow-up examinations, amongst the 67 individuals is shown in Figure 4.9.

Twenty-four individuals manifested an improvement of between 1 to 4 lines of distance visual acuity from the Pre-operative to the First Follow-up examinations, 28 of between 5 to 9 lines, 13 of between 10 to 12 lines and one individual manifested an improvement of 13 lines. One individual manifested no improvement.

| Difference in Spherical <br> Equivalent (Dioptres) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -5.25 | 2 | -5.19 | 0.08 | - | -5.25 | -5.13 | - |
| -4.0 to -4.99 | 1 | -4.88 | - | - | - | - | - |
| -3.00 to -3.99 | - | - | - | - | - | - | - |
| -2.00 to -2.99 | 1 | -2.75 | - | - | - | - | - |
| -1.00 to -1.99 | 7 | -1.35 | 0.35 | -1.25 | -1.88 | -1.00 | $-1.56,-1.09$ |
| 0.00 to -0.99 | 9 | -0.45 | 0.26 | -0.38 | -0.88 | -0.13 | $-0.63,-0.25$ |
| 0.01 to +0.99 | 11 | 0.60 | 0.22 | 0.63 | 0.25 | 0.88 | $0.50,0.75$ |
| +1.00 to +1.99 | 9 | 1.33 | 0.24 | 1.50 | 1.00 | 1.63 | $1.13,1.50$ |
| +2.00 to +2.99 | 6 | 2.33 | 0.31 | 2.31 | 2.00 | 2.75 | $2.06,2.56$ |
| +3.00 to +3.99 | 2 | 3.06 | - | - | 3.00 | 3.13 | - |
| +4.00 to +4.99 | 5 | 4.20 | 0.19 | 4.25 | 4.00 | 4.38 | $4.10,4.38$ |
| +5.00 to +5.99 | 5 | 5.08 | 0.11 | 5.00 | 5.00 | 5.25 | $5.0,5.13$ |
| +6.00 to +6.99 | 1 | 6.00 | - | - | - | - | - |
| +7.00 to +7.99 | 6 | 7.40 | 0.34 | 7.44 | 7.00 | 7.75 | $7.09,7.69$ |
| More than +7.99 | 2 | 15.13 |  |  | 14.50 | 15.75 | - |
| Group | 67 | 2.00 | 3.78 | 1.13 | -5.25 | 15.75 | $-0.25,4.13$ |

Table 4.21. The summary statistics for the distribution of the change in the spherical equivalent refraction from the Pre-operative to the First Follow-up examinations amongst the 67 individuals within the case series. A positive sign indicates a reduction in myopia or an increase in hyperopia. A negative sign indicates a reduction in hyperopia or an increase in myopia.

### 4.5.4.3 Near Visual Acuity

The change in lines of near visual acuity (Jaeger lines) from the Pre-operative to the First Follow-up examinations, amongst the 67 individuals is shown in Figure 4.10. Forty-one individuals manifested an improvement of between 1 to 6 lines (Jaeger notation) of near visual acuity from the Pre-operative to the First Follow-up examinations, 9 of between 7 to 9 lines, 6 of between 10 to 11 lines, 9 individuals manifested no improvement between the two examinations and 2 individuals manifested a reduction of one line.


Figure 4.8. The change in the spherical equivalent refraction from the Pre-operative to the First Follow-up examinations amongst the 67 individuals within the case series. Data points in the lower left quadrant between the ordinate and the line of unity represent myopic individuals who became less myopic at the First Follow-up examination. Data points in the lower left quadrant between the line of unity and the abscissa represent myopic individuals who became more myopic at the First Follow-up examination. Data points in the upper left quadrant represent hyperopic individuals who became myopic at the First Follow-up examination. Data points in the upper right quadrant represent hyperopic individuals who became less hyperopic at the First Follow-up examination.


|  | Improvement in Distance Visual Acuity (complete Snellen lines) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Lines of improvement | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
| Number of Individuals | 1 | 4 | 9 | 7 | 4 | 7 | 4 | 4 | 6 | 7 | 5 | 6 | 2 | 1 |

Figure 4.9. The change in distance visual acuity (complete Snellen lines) from the Preoperative to the First Follow-up examinations amongst the 67 individuals within the case series.


|  | Improvement in Near Visual Acuity (Jaeger lines) |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Lines of improvement | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
| Number of Individuals | 2 | 9 | 10 | 9 | 3 | 7 | 8 | 4 | 2 | 2 | 5 | 3 | 3 |

Figure 4.10. The change in lines of near visual acuity (lines of Jaeger notation) from the First Follow-up examination to the Pre-operative examination, amongst the 67 individuals. A negative number refers to a reduction in distance visual acuity at the First Follow-up examination.

### 4.5.4.4 Contrast Sensitivity

The distribution of the 67 individuals by the change in the contrast sensitivity from the Pre-operative to the First Follow-up examinations (defined as the change in the number of columns on the FACT chart) for each of the spatial frequencies $1.5,3,6,12$ and 18 cycles per degree, is shown in Table 4.22 and in Figure 4.11.

As would be expected, contrast sensitivity improved substantially for all spatial frequencies. For a spatial frequency of 1.5 cycles per degree, 10 individuals exhibited an improvement of between 7 to 8 columns, 30 of between 4 to 6 columns and 17 of between one to 3 columns. Seven individuals exhibited no improvement and 3 individuals a reduction in contrast sensitivity of one column.

For a spatial frequency of 3 cycles per degree, 26 individuals exhibited an improvement of between 5 to 8 columns and 24 of between one to 4 columns. Three individuals exhibited no improvement and 3 individuals a reduction in contrast sensitivity of between one to 4 columns.

For a spatial frequency of 6 cycles per degree, 32 individuals exhibited an improvement in contrast sensitivity of between 5 to 8 columns and 27 of one to 4 columns. Six individuals exhibited no improvement and 2 individuals a reduction in contrast sensitivity of between one to 4 columns.

For a spatial frequency of 12 cycles per degree, 24 individuals exhibited an improvement in contrast sensitivity of between 4 to 6 columns and 26 of 1 to 3 columns.

For a spatial frequency of 18 cycles per degree, 18 individuals exhibited an improvement in contrast sensitivity of between 3 to 4 columns and 23 of between one to 2 columns. Twenty-six individuals exhibited no improvement.

| Spatial Frequency (cpd) | Distribution of Individuals by the difference in Contrast Sensitivity (number of columns on the FACT chart) |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| 1.5 | - | - | - | 3 | 7 | 2 | 10 | 5 | 4 | 8 | 18 | 6 | 4 |
| 3 | 1 | - | - | 2 | 3 | 4 | 11 | 5 | 5 | 10 | 17 | 6 | 3 |
| 6 | 1 | - | - | 1 | 6 | 3 | 5 | 5 | 14 | 12 | 16 | 3 | 1 |
| 12 | - | - | - | - | 17 | 4 | 10 | 12 | 9 | 12 | 3 | - | - |
| 18 | - | - | - | - | 26 | 12 | 11 | 7 | 11 | - | - | - | - |

Table 4.22. The distribution of the change in the contrast sensitivity value (defined as the respective change in the number of columns) for spatial frequencies of $1.5,3,6,12$ and 18 cycles per degree from the Pre-operative to the First Follow-up examinations for the 67 individuals. A positive value represents an improvement in contrast sensitivity.


Figure 4.11. The change in contrast sensitivity from the Pre-operative to the First Followup examinations for spatial frequencies of $1.5,3$ and 6 cycles per degree for the 67 individuals within the case series (Top; Middle and Bottom, respectively). The data points below the line of unity represent an improvement in contrast sensitivity. Note that each data point represents more than one individual.


Figure 4.11 Continued. The change in contrast sensitivity from the Pre-operative to the First Follow-up examinations for spatial frequencies of 12 and 18 cycles per degree for the 67 individuals within the case series (Top and Bottom). The data points below the line of unity represent an improvement in contrast sensitivity. Note that each data point represents more than one individual. Note the difference in the scaling of the abscissa and the ordinate between the five graphs.

### 4.5.4.5 Dilated Pupil Diameter

The distribution of the change in the dilated pupil diameter, measured with the OPD aberrometer, from the Pre-operative to the First Follow-up examinations amongst the 67 individuals is shown in Figure 4.12. The summary statistics for the change in the dilated pupil diameter from the Pre-operative to the First Follow-up examinations is shown in Table 4.23. Fifty-five individuals exhibited a smaller dilated pupil diameter at the First

Follow-up examination compared to the Pre-operative examination. Of these, 7 individuals exhibited a reduction in dilated pupil diameter of between 2.00 and 1.21 mm , 47 of between 1.20 and 0.01 mm and one of 2.20 mm . Ten individuals exhibited an increase in dilated pupil diameter of between 0.00 and 0.39 mm and 2 an increase greater than 0.39 mm .


Figure 4.12. The change in dilated pupil diameter from the Pre-operative to the First Follow-up examinations for the 67 individuals as measured with the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. The data points above the line of unity represent a smaller dilated pupil diameter at the First Follow-up examination.

### 4.5.4.6 Mean Corneal Curvature

The change in the mean corneal curvature from the Pre-operative to the First Follow-up examinations, amongst 66 of the 67 individuals within the case series, as measured by the OPD aberrometer is shown in Figure 4.13. The summary statistics for the change in the mean corneal curvature from the Pre-operative to the First Follow-up examinations is shown in Table 4.24. Twenty-eight individuals exhibited a steepening of the mean corneal curvature of less than 0.149 mm and one individual exhibited a steepening of more than 0.149 mm .

Twenty-nine individuals exhibited a flattening of the mean corneal curvature of between
0.001 and $0.009 \mathrm{~mm}, 5$ of between 0.100 and 0.149 mm and 2 of more than 0.150 mm .

| Difference in Dilated <br> Pupil Diameter (mm) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -2.00 | 1 | -2.20 | - | - | - | - | - |
| -2.00 to -1.61 | 2 | -1.81 | - | - | -1.98 | -1.64 | - |
| -1.60 to -1.21 | 5 | -1.39 | 0.13 | -1.33 | -1.59 | -1.30 | $-1.44,-1.29$ |
| -1.20 to -0.81 | 13 | -1.01 | 0.09 | -1.00 | -1.20 | -0.91 | $-1.04,-0.94$ |
| -0.80 to -0.41 | 23 | -0.63 | 0.14 | -0.60 | -0.88 | -0.41 | $-0.73,-0.54$ |
| -0.40 to -0.01 | 11 | -0.24 | 0.14 | -0.32 | -0.40 | -0.04 | $-0.36,-0.13$ |
| 0.00 to 0.39 | 10 | 0.14 | 0.10 | 0.11 | 0.02 | 0.31 | $0.06,0.19$ |
| More than 0.39 | 2 | 1.09 | - | - | 0.95 | 1.24 | - |
| Group | 67 | -0.59 | 0.61 | -0.59 | -2.20 | 1.24 | $-0.94,-0.27$ |

Table 4.23. The summary statistics for the distribution of the change in the dilated pupil diameter, as measured by the Nidek Optical Path Difference Scanning System ARK10000 aberrometer, from the Pre-operative to the First Follow-up examinations amongst the 67 individuals within the case series. A negative value represents a reduction in the dilated pupil diameter at the First Follow-up examination.


Figure 4.13. The change in the mean corneal curvature from the Pre-operative to the First Follow-up examinations, amongst 66 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. The line indicates that of unity.

| Difference in Mean <br> Corneal Curvature <br> $(\mathrm{mm})$ | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -0.149 | 1 | -0.36 | - | - | - | - | - |
| -0.149 to -0.100 | 5 | -0.12 | 0.02 | -0.12 | -0.14 | -0.1 | $-0.14,-0.11$ |
| -0.099 to -0.050 | 12 | -0.07 | 0.01 | -0.07 | -0.09 | -0.05 | $-0.08,-0.06$ |
| -0.049 to 0.000 | 11 | -0.01 | 0.01 | -0.01 | -0.04 | 0 | $-0.02,0.00$ |
| 0.001 to 0.049 | 13 | 0.03 | 0.01 | 0.02 | 0.01 | 0.04 | $0.02,0.03$ |
| 0.050 to 0.099 | 16 | 0.06 | 0.01 | 0.06 | 0.05 | 0.09 | $0.05,0.07$ |
| 0.100 to 0.149 | 5 | 0.13 | 0.01 | 0.13 | 0.12 | 0.14 | $0.13,0.13$ |
| 0.150 to 0.199 | 2 | 0.32 | - | - | 0.17 | 0.47 | - |
| Group | 66 | 0.09 | 0.65 | 0.02 | -0.36 | 5.23 | $-0.05,0.06$ |

Table 4.24. The summary statistics for the change in the mean corneal curvature from the Pre-operative to the First Follow-up examinations, amongst 66 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. A negative value represents a steepening in the mean corneal curvature at the First Follow-up examination.

### 4.5.4.7 Flattest Corneal Curvature

The change in the flattest corneal curvature from the Pre-operative to the First Follow-up examinations, amongst 66 of the 67 individuals within the case series, as measured by the OPD aberrometer is shown in Figure 4.14. The summary statistics for the change in the flattest corneal curvature from the Pre-operative to the First Follow-up examinations is shown in Table 4.25. Twenty-seven individuals exhibited a steepening of the flattest corneal curvature at the First Follow-up examination. Of these, 3 exhibited a steepening of the flattest corneal curvature of more than $0.149 \mathrm{~mm}, 6$ a steepening of between 0.100 and 0.149 mm and 18 of between 0.099 and 0.000 mm . Twenty-four individuals exhibited a flattening of the flattest corneal curvature at the First Follow-up examination of between 0.001 and 0.100 mm and 12 a flattening of between 0.101 and 0.200 mm . Three individuals exhibited a flattening of the flattest corneal curvature of more than 0.200 at the First Follow-up examination.


Figure 4.14. The change in the flattest corneal curvature from the Pre-operative to the First Follow-up examinations, amongst 66 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. The line indicates that of unity.

| Difference in Flattest <br> Corneal Curvature <br> $(\mathrm{mm})$ | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -0.149 | 3 | -0.61 | - | -0.63 | -1.03 | -0.17 | - |
| -0.100 to -0.149 | 6 | -0.11 | 0.001 | -0.11 | -0.12 | -0.10 | $-0.11,-0.11$ |
| -0.099 to -0.050 | 7 | -0.08 | 0.01 | -0.08 | -0.09 | -0.06 | $-0.08,-0.07$ |
| -0.049 to 0.000 | 11 | -0.02 | 0.02 | -0.01 | -0.04 | 0.00 | $-0.02,-0.01$ |
| 0.001 to 0.050 | 16 | 0.03 | 0.02 | 0.03 | 0.01 | 0.05 | $0.02,0.02$ |
| 0.051 to 0.100 | 8 | 0.08 | 0.01 | 0.07 | 0.06 | 0.10 | $0.07,0.07$ |
| 0.101 to 0.150 | 8 | 0.12 | 0.01 | 0.12 | 0.11 | 0.13 | $0.11,0.12$ |
| 0.151 to 0.200 | 4 | 0.17 | - | 0.17 | 0.16 | 0.18 | $0.17,0.17$ |
| More than 0.200 | 3 | 2.54 | - | 1.26 | 0.33 | 6.03 | - |
| Group | 66 | 0.11 | 0.78 | 0.03 | -1.03 | 6.03 | $0.04,0.09$ |

Table 4.25. The summary statistics for the change in the flattest corneal curvature from the Pre-operative to the First Follow-up examinations, amongst 66 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. A negative value represents a steepening in the flattest corneal curvature at the First Follow-up examination.

### 4.5.4.8 Corneal Endothelial Cell Density

The change in the corneal endothelial cell density (cells $/ \mathrm{mm}^{2}$ ) from the Pre-operative to the First Follow-up examinations, amongst the 67 individuals within the case series, as measured by the Topcon SP 2000P specular microscope is shown in Figure 4.15. Fiftytwo individuals exhibited a reduction in corneal endothelial cell density (mean -685 cells $/ \mathrm{mm}^{2}$, SD 500) from the Pre-operative to the First Follow-up examination whilst 15 individuals exhibited an increase in corneal endothelial cell density (mean 234 cells $/ \mathrm{mm}^{2}$, SD 273).


| Check-up | Number of <br> individuals | Mean <br> $\left(\right.$ Cells $\left./ \mathrm{mm}^{2}\right)$ | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pre-operative | 67 | 2140 | 457 | 2176 | 457 | 3203 | 1895,2480 |
| First Follow-up | 67 | 1161 | 578 | 1777 | 307 | 2258 | 1189,2126 |
| Difference | 67 | -479 | 598 | -441 | -2371 | 1120 | $-783,-58$ |
| Reduction | 52 | -685 | 500 | -621 | -2371 | -9 | $-994,-278$ |
| Increase | 15 | 234 | 273 | 164 | 11 | 1120 | 112,203 |

Figure 4.15. The change in the corneal endothelial cell density from the Pre-operative to the First Follow-up examinations, amongst the 67 individuals within the case series as measured by the Topcon SP 2000P specular microscope. Negative values represent a reduction in CECD and positive values an increase in CECD. The line indicates that of unity.

### 4.5.4.9 Higher Order Aberrations

The change in the RMS value of the Total component for each of the eight HOAs; namely, Total, Tilt (S1), High, T.coma, T.trefoil, T.4Foil, T.sph and HiAstig, respectively, from the Pre-operative to the First Follow-up examinations as measured with the OPD NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0mm zone are given in Figures 4.16-4.23, respectively.

### 4.5.4.9.1 Total Component of the Total HOA

The change in the Total component of the Total HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.16. Forty-nine individuals exhibited a reduction of the Total component of the Total HOA (mean - 2.546 microns, SD 3.51) from the Pre-operative to the First Follow-up examination and 15 individuals exhibited an increase (mean 1.044 microns, SD 1.55). The ratio of the pre-operative median to the post-operative median was 1.899 for the Total component, 0.855 for the Corneal component and 1.974 for the Internal component (where a value of less than 1.0 indicates a larger HOA at the Preoperative examination).

### 4.5.4.9.2 Total Component of the Tilt (S1) HOA

The change in the Total component of the Tilt (S1) HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.17. Fifty-one individuals exhibited a reduction in the Total component
of the Tilt (S1) HOA (mean -0.834 microns, SD 1.42) from the Pre-operative to the First Follow-up examinations and 13 individuals exhibited an increase (mean 0.645 microns, SD 0.92). The ratio of the pre-operative median to the post-operative median was 2.069 for the Total component, 0.837 for the Corneal component and 2.024 for the Internal component.


| Total component of Total HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 3.091 | 3.86 | 2.100 | 0.670 | 9.553 | $1.412,3.163$ |  |
| First Follow-up | 64 | 1.496 | 1.85 | 1.106 | 0.586 | 4.689 | $0.853,1.461$ |  |
| Difference | 64 | -2.284 | 3.32 | -0.845 | -7.897 | 3.031 | $-2.051,-0.067$ |  |
| Reduction | 49 | -2.546 | 3.51 | -1.411 | -7.897 | -0.027 | $-2.776,-0.753$ |  |
| Increase | 15 | 1.044 | 1.55 | 0.254 | 0.069 | 3.031 | $0.165,1.010$ |  |

Figure 4.16. The change in the RMS value of the Total component of the Total HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.


| Total component of Tilt(S1) HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 0.933 | 1.42 | 0.561 | 0.033 | 3.953 | $0.312,0.990$ |  |
| First Follow-up | 64 | 0.452 | 0.80 | 0.271 | 0.056 | 2.190 | $0.168,0.379$ |  |
| Difference | 64 | -0.799 | 1.36 | -0.300 | -3.798 | 1.701 | $-0.715,-0.044$ |  |
| Reduction | 51 | -0.834 | 1.42 | -0.502 | -3.798 | -0.002 | $-0.827,-0.158$ |  |
| Increase | 13 | 0.645 | 0.92 | 0.070 | 0.007 | 1.701 | $0.034,0.709$ |  |

Figure 4.17. The change in the RMS value of the Total component of the Tilt (S1) HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 4.5.4.9.3 Total Component of the High HOA

The change in the Total component of the High HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.18. Fifty-three individuals exhibited a reduction of the Total component of the High HOA (mean - 0.950 microns, SD 1.87) from the Pre-operative to the First Follow-up examination and 11 individuals exhibited an increase (mean 1.246 microns, SD 1.86). The ratio of the pre-operative median to the post-operative median
was 2.348 for the Total component, 0.688 for the Corneal component and 2.462 for the
Internal component.


| Total component of High HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 1.080 | 1.90 | 0.671 | 0.151 | 5.306 | $0.447,0.859$ |  |
| First Follow-up | 64 | 0.725 | 1.40 | 0.286 | 0.100 | 3.680 | $0.228,0.428$ |  |
| Difference | 64 | -1.007 | 1.86 | -0.267 | -5.003 | 3.313 | $-0.615,-0.074$ |  |
| Reduction | 53 | -0.950 | 1.87 | -0.388 | -5.003 | -0.003 | $-0.658,-0.192$ |  |
| Increase | 11 | 1.246 | 1.86 | 0.186 | 0.053 | 3.313 | $0.127,0.660$ |  |

Figure 4.18. The change in the RMS value of the Total component of the High HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 4.5.4.9.4 Total component of the T.Coma HOA

The change in the Total component of the T.Coma HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.19. Fifty-one individuals exhibited a reduction of the Total component of the T.Coma HOA (mean -0.250 microns, SD 0.35 ) fromn the Pre-operative to the First Follow-up examination and 13 individuals exhibited an increase (mean 0.119 microns, SD 0.15). The ratio of the pre-operative median to the post-operative median was 1.646 for the Total component, 0.815 for the Corneal component and 2.009 for the Internal component.

### 4.5.4.9.5 Total Component of the T.Trefoil HOA

The change in the Total component of the T.Trefoil HOA from the Pre-operative to the First Follow-up examination, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.20. Forty-six individuals exhibited a reduction of the Total component of the T.Trefoil HOA (mean -0.6.38 microns, SD 1.03) from the Pre-operative to the First Follow-up examination and 18 individuals exhibited an increase (mean 0.338 microns, SD 0.53). The ratio of the pre-operative median to the post-operative median was 2.149 for the Total component, 0.677 for the Corneal component and 3.216 for the Internal component.


| Total component of T.Coma HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 0.303 | 0.37 | 0.048 | 0.876 | 0.048 | $0.110,0.331$ |  |
| First Follow-up | 64 | 0.166 | 0.25 | 0.097 | 0.029 | 0.627 | $0.077,0.149$ |  |
| Difference | 64 | -0.166 | 0.14 | -0.140 | -0.108 | -0.084 | $-0.216,-0.098$ |  |
| Reduction | 51 | -0.250 | 0.35 | -0.106 | -0.607 | -0.002 | $-0.241,-0.053$ |  |
| Increase | 13 | 0.119 | 0.15 | 0.054 | 0.010 | 0.458 | $0.029,0.096$ |  |

Figure 4.19. The change in the RMS value of the Total component of the T.Coma HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 4.5.4.9.6 The Total Component of the T.4Foil HOA

The change in the Total component of the T.4Foil HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.21. Forty-nine individuals exhibited a reduction of the Total component of the T.4Foil HOA (mean -0.576 microns, SD 1.27) from the Pre-operative to the First Follow-up examination and 15 individuals exhibited an increase (mean 0.802 microns, SD 1.36). The ratio of the pre-operative median to the post-operative median
was 2.243 for the Total component, 0.684 for the Corneal component and 1.939 for the
Internal component.


| Total component of T.Trefoil HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 0.696 | 1.04 | 0.436 | 0.012 | 2.867 | $0.207,0.697$ |  |
| First Follow-up | 64 | 0.392 | 0.60 | 0.203 | 0.025 | 1.559 | $0.135,0.329$ |  |
| Difference | 64 | -0.570 | 0.96 | -0.127 | -2.612 | 1.012 | $-0.475,0.008$ |  |
| Reduction | 46 | -0.638 | 1.03 | -0.239 | -2.612 | -0.013 | $-0.598,-0.080$ |  |
| Increase | 18 | 0.338 | 0.53 | 0.091 | 0.004 | 1.012 | $0.031,0.200$ |  |

Figure 4.20. The change in the RMS value of the Total component of the T.Trefoil HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 4.5.4.9.7 Total Component of the T.Sph HOA

The change in the Total component of the T.Sph HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is
shown in Figure 4.22. Forty-six individuals exhibited a reduction of the Total component of the T.Sph HOA (mean -0.158 microns, SD 0.20 ) from the Pre-operative to the First Follow-up examination and 18 individuals exhibited an increase (mean 0.054 microns, SD 0.08). The ratio of the pre-operative median to the post-operative median was 2.732 for the Total component, 1.150 for the Corneal component and 2.249 for the Internal component.


| Total component of T.4Foil HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 0.322 | 0.46 | 0.213 | 0.032 | 3.455 | $0.107,0.384$ |  |
| First Follow-up | 64 | 0.174 | 0.39 | 0.095 | 0.013 | 2.716 | $0.059,0.141$ |  |
| Difference | 64 | -0.636 | 1.29 | -0.128 | -3.354 | 2.653 | $-0.268,-0.018$ |  |
| Reduction | 49 | -0.576 | 1.28 | -0.208 | -3.354 | -0.014 | $-0.704,-0.067$ |  |
| Increase | 15 | 0.802 | 1.37 | 0.044 | 0.001 | 2.653 | $0.012,0.151$ |  |

Figure 4.21. The change in the RMS value of the Total component of the T.4Foil HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.


| Total component of T.Sph HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 0.161 | 0.20 | 0.101 | 0.009 | 0.448 | $0.055,0.187$ |  |
| First Follow-up | 64 | 0.065 | 0.10 | 0.037 | 0.003 | 0.287 | $0.021,0.065$ |  |
| Difference | 64 | -0.137 | 0.17 | -0.061 | -0.433 | 0.170 | $-0.139,0.007$ |  |
| Reduction | 46 | -0.158 | 0.20 | -0.094 | -0.433 | -0.021 | $-0.162,-0.057$ |  |
| Increase | 18 | 0.054 | 0.08 | 0.028 | 0.005 | 0.170 | $0.009,0.054$ |  |

Figure 4.22. The change in the RMS value of the Total component of the T.Sph HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement weas avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 4.5.4.9.8 Total Component of the HiAstig HOA

The change in the Total component of the HiAstig HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series, is shown in Figure 4.23. Forty-two individuals exhibited a reduction of the Total component of the HiAstig HOA (mean -0.384 microns, SD 0.71) from the Pre-operative to the First Follow-up examinations and 22 individuals exhibited an increase (mean 0.147 microns,

SD 0.26). The ratio of the pre-operative median to the post-operative median was 1.353 for the Total component, 0.809 for the Corneal component and 1.192 for the Internal component.


| Total component of HiAstig HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 64 | 0.336 | 0.67 | 0.058 | 0.009 | 1.736 | $0.041,0.085$ |  |
| First Follow-up | 64 | 0.083 | 0.14 | 0.044 | 0.008 | 0.635 | $0.031,0.069$ |  |
| Difference | 64 | -0.323 | 0.64 | -0.014 | -1.705 | 0.559 | $-0.044,0.017$ |  |
| Reduction | 42 | -0.384 | 0.71 | -0.028 | -1.705 | -0.002 | $-0.066,-0.015$ |  |
| Increase | 22 | 0.147 | 0.26 | 0.030 | 0.000 | 0.559 | $0.017,0.055$ |  |

Figure 4.23. The change in the RMS value of the Total component of the HiAstig HOA from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

# 4.5.5 Explanatory Analysis of Associations between the Confounding Variables, the Change in the Appropriate Demographic, Structural and Functional Variables from the Pre-operative to the First Follow-up Examination and the Corresponding 

## Change in each of the Three Components of each of the Eight HOAs

The results of the explanatory analysis of the change from the Pre-operative to the First Follow-up examinations are given for the appropriate demographic and conflicting variables in Table 4.26 and Figures 4.24, 4.25, for the visual performance variables in Table 4.28 and Figures 4.26, 4.27, for the structural variables in Table 4.29 and Figures 4.28-4.34 respectively and for the type and severity of the cataract in Table 4.30.

### 4.5.5.1 Age and Gender

No association was present between either gender or the change in age and the change in each of the three components for each of the eight HOAs from the Pre-operative examination to the First Follow-up examination (Table 4.26).

### 4.5.5.2 Surgeon

No association was present between each of the four surgeons and the change in each of the three components for each of the eight HOAs from the Pre-operative examination to the First Follow-up examination (Table 4.26).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorize | 0.247 | 0.589 | 0.662 | 0.401 | 0.940 | 0.408 | 0.235 | 0.573 |  |
| Age continuous | 0.089 | 0.745 | 0.666 | 0.170 | 0.176 | 0.636 | 0.851 | 0.589 |  |
| Gender | 0.351 | 0.283 | 0.607 | 0.949 | 0.780 | 0.557 | 0.498 | 0.149 |  |
| Surgeon | 0.847 | 0.902 | 0.630 | 0.870 | 0.360 | 0.848 | 0.885 | 0.849 |  |
| Type of IOL | $<0.001$ | 0.416 | 0.983 | 0.443 | 0.886 | 0.978 | 0.430 | 0.606 |  |
| Time Pre-op to <br> First Follow-up | 0.760 | 0.965 | 0.549 | 0.842 | 0.360 | 0.704 | 0.716 | 0.453 |  |
| Time Pre-op to <br> Surgery | 0.842 | 0.957 | 0.040 | 0.483 | 0.030 | 0.065 | 0.935 | 0.066 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorize | 0.232 | 0.693 | 0.246 | 0.388 | 0.199 | 0.793 | 0.904 | 0.303 |  |
| Age continuous | 0.541 | 0.763 | 0.671 | 0.709 | 0.635 | 0.701 | 0.663 | 0.257 |  |
| Gender | 0.965 | 0.855 | 0.917 | 0.325 | 0.930 | 0.296 | 0.163 | 0.406 |  |
| Surgeon | 0.108 | 0.123 | 0.142 | 0.095 | 0.229 | 0.345 | 0.597 | 0.204 |  |
| Type of IOL | 0.981 | 0.989 | 0.996 | 0.908 | 0.997 | 0.775 | 0.763 | 0.794 |  |
| Time Pre-op to <br> First Follow-up | 0.315 | 0.197 | 0.457 | 0.631 | 0.408 | 0.887 | 0.702 | 0.519 |  |
| Time Pre-op to <br> Surgery | 0.945 | 0.998 | 0.922 | 0.788 | 0.985 | 0.146 | 0.321 | 0.239 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorize | 0.197 | 0.941 | 0.582 | 0.519 | 0.907 | 0.384 | 0.644 | 0.772 |  |
| Age continuous | 0.182 | 0.839 | 0.494 | 0.372 | 0.299 | 0.766 | 0.891 | 0.966 |  |
| Gender | 0.644 | 0.660 | 0.730 | 0.885 | 0.826 | 0.682 | 0.345 | 0.364 |  |
| Surgeon | 0.314 | 0.929 | 0.998 | 0.476 | 0.931 | 0.990 | 0.123 | 0.863 |  |
| Type of IOL | $<0.001$ | 0.889 | 0.659 | 0.963 | 0.195 | 0.856 | 0.302 | 0.988 |  |
| Time Pre-op to <br> First Follow-up | 0.193 | 0.179 | 0.659 | 0.935 | 0.681 | 0.646 | 0.457 | 0.443 |  |
| Time Pre-op to <br> Surgery | 0.779 | 0.752 | 0.023 | 0.376 | 0.029 | 0.023 | 0.075 | 0.002 |  |

Table 4.26. The probability value derived by ANOVA for the associations between gender; the change in age as a categorical variable and as a continuous variable, from the Pre-operative examination to the First Follow-up examination; the conflicting variables (surgeon, type of IOL, time from the Pre-operative examination to the First Follow-up examination and the time from the Pre-operative examination to surgery); and the corresponding change in each of the three components for each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey. Note the independent variable gender was treated as such and not as a change in gender.

### 4.5.5.3 Type of Intraocular Lens

The magnitude of the change in the Total and Internal components of the Total HOA from the Pre-operative to the First Follow-up examinations varied between the type of IOL (Table 4.26). As would be expected, all four types of IOL reduced the Total and Internal components of the Total HOA (Table 4.27).

| Total component of Total HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |
| Forelens | 50 | -1.997 | 2.79 | -0.862 | -6.955 | 3.031 | $-1.954,-0.192$ |
| B Lens | 9 | -1.707 | 2.56 | -0.516 | -4.494 | 1.162 | $-0.837,-0.027$ |
| Xcelens | 3 | -2.144 | - | -2.376 | -2.378 | -1.578 | - |
| Triplens | 2 | -7.014 | - | - | -7.897 | -6.003 | - |


| Internal component of Total HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |
| Forelens | 39 | -2.109 | 2.74 | -0.848 | -6.065 | 3.158 | $-1.932,-0.083$ |
| B Lens | 4 | -0.890 | - | -0.524 | -1.602 | 0.051 | $-0.911,-0.263$ |
| Xcelens | 0 | - | - | - | - | - | - |
| Triplens | 2 | -7.224 | - | - | -8.365 | -5.865 | - |

Table 4.27. The change in the RMS value of the Total and Internal components of the Total HOA from the Pre-operative to the First Follow-up examinations, measured with the NAVEX Station software (Version 2.10), and described by the Zernike polynomials for a 4.0 mm zone (Top and Bottom). The data for the Total component of the Total HOA are based upon 64 individuals, and those for the Internal component upon 45 individuals, of the 67 individuals within the case series in whom the measurement was available.

### 4.5.5.4 Interval from the Pre-operative Examination to the First Follow-up

## Examination

No association was present between the interval from the Pre-operative examination to the First Follow-up examination and the change in each of the three components for each of the eight HOAs (Table 4.26).

### 4.5.5.5 Interval from the Pre-operative Examination to Surgery

Some association was present, based upon 64 of the 67 individuals, between the interval from the Pre-operative examination to Surgery and the change, between the Pre-operative and the First Follow-up examinations, in the Total component of the High and T.Trefoil HOAs (Table 4.26 and Figure 4.24). Some association was also present, based upon 45 of the 67 individuals, between the interval from the Pre-operative examination to Surgery and the change, between the Pre-operative and the First Follow-up examinations, in the Internal component of the High, T.Trefoil, T.4Foil and HiAstig HOAs (Table 4.26 and Figure 4.25). The slope of the regression lines between the given HOA and the interval from the Pre-operative examination to the First Follow-up examination is, in general, influenced by the 5 individuals with the longest interval (50-70 days) of whom at least 3 generally exhibited a large improvement in the given HOA, thereby exacerbating any negative trend of the slope. Simultaneously, the negativity of the slope is also influenced by 3 outlying individuals with intervals of between 15 to 35 days prior to surgery, 2 of whom exhibited large increases, and one a large reduction, in the given HOA at the First Follow-up examination. Of the 2 individuals who exhibited a worsening at the given HOA at the First Follow-up examination, one had undergone surgery by Surgeon 1 and
the other by Surgeon 2. The individual manifesting an improvement in the given HOA was operated upon by Surgeon 3.


Figure 4.24. The change in the Total component of the Total and of the T.Trefoil HOAs from the Pre-operative to the First Follow-up examinations, amongst 64 of the 67 individuals in whom the measurement was avaliable, as a function of the interval between the Pre-operative examination and Surgery (Top and Bottom). A negative value indicates a reduction in the magnitude of the HOA at the First Follow-up examination. Note the difference in the scaling of the ordinate between the two graphs.


Figure 4.25. The change in the Total component of the High, T.Trefoil and T.4Foil HOAs from the Pre-operative to the First Follow-up examinations, amongst 45 of the 67 individuals in whom the measurement was avaliable, as a function of the interval between the Pre-operative examination and Surgery (Top; Middle and Bottom). A negative value indicates a reduction in the magnitude of the HOA at the First Follow-up examination.

### 4.5.5.6 Distance Visual Acuity

The improvement in the distance visual acuity from the Pre-operative to the First Followup examinations was associated with a reduction in the Total component of the Total HOA $\left(\mathrm{R}^{2}=16.8 \% ; \mathrm{p}<0.001\right)$ and to some extent with the Total component of the T.Coma HOA ( $\mathrm{R}^{2}=7.9 \% ; \mathrm{p}=0.025$ ) (Table 4.28). No associations were present for the Corneal and the Intenal components of each of the eight HOAs (Table 4.28).

### 4.5.5.7 Near Visual Acuity

The improvement in the near visual acuity from the Pre-operative to the First Follow-up examinations was weakly associated $\left(\mathrm{R}^{2} \leq 7.4 \%\right)$ with reductions in the Total component of the Total, Tilt (S1) and T.Coma HOAs (Table 4.28). No associations were present for the Corneal and the Intenal components of each of the eight HOAs (Table 4.28).

### 4.5.5.8 Contrast Sensitivity

Surprisingly, the only associations between the reductions in the magnitude of the HOAs from the Pre-operative to the First Follow-up examinations and the corresponding improvement in contrast sensitivity occurred for the Total component of the Total HOA at spatial frequencies of $1.5(\mathrm{p}=0.022)$ and $3.0(\mathrm{p}=0.026)$ cycles per degree, and for the Internal component of the Total HOA at 1.5 cycles per degree ( $\mathrm{p}=0.023$ ) (Table 4.28). The improvement in contrast sensitivity increased as the magnitude of the difference on the given HOA increased (Figures 4.26 and 4.27).


Figure 4.25 Continued. The change in the Total component of the HiAstig HOAs from the Pre-operative to the First Follow-up examinations, amongst 45 of the 67 individuals in whom the measurement was avaliable, as a function of the interval between the Preoperative examination and Surgery. A negative value indicates a reduction in the magnitude of the HOA at the First Follow-up examination. Note the difference in the scaling of the ordinate between the four graphs.

### 4.5.5.9 Dilated Pupil Diameter

Some association was present between the change from the Pre-operative to the First Follow-up examinations, in the Corneal component of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs $(\mathrm{p}=0.010, \mathrm{p}=0.002, \mathrm{p}=0.011, \mathrm{p}=0.0008, \mathrm{p}=0.028$, respectively) and the corresponding change in the dilated pupil diameter. Associations were also present between the difference in the Internal component of the Total ( $\mathrm{p}=0.048$ ) and T.Trefoil ( $\mathrm{p}=0.022$ ) HOAs and the corresponding change in the dilated pupil diameter (Table 4.29 and Figures 4.28 and 4.29).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | $<0.001$ | 0.209 | 0.136 | 0.025 | 0.470 | 0.087 | 0.049 | 0.107 |  |
| NVA | 0.030 | 0.036 | 0.517 | 0.032 | 0.928 | 0.482 | 0.121 | 0.247 |  |
| CS 1.5 cpd | 0.022 | 0.216 | 0.778 | 0.454 | 0.480 | 0.814 | 0.440 | 0.630 |  |
| CS 3 cpd | 0.026 | 0.279 | 0.609 | 0.202 | 0.344 | 0.777 | 0.998 | 0.954 |  |
| CS 6 cpd | 0.093 | 0.159 | 0.293 | 0.514 | 0.089 | 0.509 | 0.451 | 0.295 |  |
| CS 12 cpd | 0.123 | 0.303 | 0.538 | 0.360 | 0.326 | 0.741 | 0.490 | 0.286 |  |
| CS 18 cpd | 0.824 | 0.998 | 0.569 | 0.190 | 0.822 | 0.452 | 0.538 | 0.950 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.780 | 0.983 | 0.852 | 0.890 | 0.958 | 0.814 | 0.876 | 0.948 |  |
| NVA | 0.224 | 0.465 | 0.103 | 0.369 | 0.123 | 0.091 | 0.653 | 0.184 |  |
| CS 1.5 cpd | 0.457 | 0.314 | 0.499 | 0.773 | 0.471 | 0.278 | 0.140 | 0.979 |  |
| CS 3 cpd | 0.288 | 0.142 | 0.265 | 0.303 | 0.276 | 0.972 | 0.673 | 0.648 |  |
| CS 6 cpd | 0.311 | 0.193 | 0.418 | 0.462 | 0.416 | 0.200 | 0.082 | 0.707 |  |
| CS 12 cpd | 0.266 | 0.133 | 0.302 | 0.180 | 0.398 | 0.500 | 0.507 | 0.876 |  |
| CS 18 cpd | 0.644 | 0.620 | 0.709 | 0.514 | 0.822 | 0.221 | 0.309 | 0.532 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.055 | 0.514 | 0.449 | 0.266 | 0.886 | 0.273 | 0.501 | 0.274 |  |
| NVA | 0.306 | 0.122 | 0.656 | 0.309 | 0.932 | 0.728 | 0.200 | 1.000 |  |
| CS 1.5 cpd | 0.023 | 0.373 | 0.979 | 0.986 | 0.879 | 0.656 | 0.330 | 0.457 |  |
| CS 3 cpd | 0.058 | 0.534 | 0.757 | 0.678 | 0.473 | 0.709 | 0.576 | 0.529 |  |
| CS 6 cpd | 0.174 | 0.410 | 0.887 | 0.996 | 0.511 | 0956 | 0.466 | 0.733 |  |
| CS 12 cpd | 0.301 | 0.397 | 0.773 | 0.708 | 0.609 | 0.982 | 0.891 | 0.774 |  |
| CS 18 cpd | 0.465 | 0.318 | 0.049 | 0.036 | 0.059 | 0.158 | 0.442 | 0.320 |  |

Table 4.28. The probability value derived by ANOVA for the association between the changes in distance visual acuity, near visual acuity and contrast sensitivity for the six spatial frequencies, from the Pre-operative to the First Follow-up examinations and the corresponding changes in each of the three components for each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.


Figure 4.26. The change in the Total component of the Total HOA from the Pre-operative to the First Follow-up examinations as a function of the corresponding change in contrast sensitivity for spatial frequencies of 1.5 and 3 cycles per degree amongst the 67 individuals (Top and Bottom). The negative slope indicates that as the magnitude of the reduction in the HOA between the First Follow up examination and the Pre-operative examination increases (improves), the corresponding change in contrast sensitivity increases (improves). Note the difference in the scaling of the abscissa between the two graphs.

These apparent inverse associations indicate that the magnitude of the various HOAs declined with increase in dilated pupil diameter. However, the relationship for each of the HOAs appears to be markedly influenced by the presence of up to 4 outlying data points which arise from 6 individuals across each of the HOAs. If such outliers are ignored, there is no relationship between the two variables.

A similar influence of outliers was present for the Internal component of the Total and T.Trefoil HOAs, although, the between-individual variability was greater than for the corresponding Corneal components.


Figure 4.27. The change in the Internal component of the Total HOA from the Preoperative to the First Follow-up examinations as a function of the corresponding change in contrast sensitivity for spatial frequency of 1.5 cycles per degree amongst the 67 individuals. The negative slope indicates that as the magnitude of the reduction in the HOA between the First Follow up examination and the Pre-operative examination increases (improves), the corresponding change in contrast sensitivity increases (improves). Note the difference in the scaling of the abscissa between this and the previous graphs.

### 4.5.5.10 Mean Corneal Curvature

An association was present for the change in the Corneal component of the Total ( $\mathrm{p}=0.040$ ), High ( $\mathrm{p}=0.050$ ) and T.Trefoil $(\mathrm{p}=0.011)$ HOAs from the Pre-operative to the First Follow-up examinations and the corresponding change in the mean corneal curvature (Table 4.29 and Figure 4.30). The magnitude of the Corneal component of the

Total, High and T.Trefoil HOAs seemingly increased as the mean corneal curvature flattened. However, the apparent relationships were markedly influenced by the presence of 2 outlying data points which arose from the same 2 individuals across each of the HOAs. If such outliers are ignored, there is no relationship between the two variables.

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.500 | 0.396 | 0.385 | 0.844 | 0.331 | 0.389 | 0.182 | 0.474 |  |
| CC Mean | 0.756 | 0.941 | 0.792 | 0.476 | 0.635 | 0.841 | 0.559 | 0.352 |  |
| CC Flattest | 0.340 | 0.815 | 0.819 | 0.795 | 0.899 | 0.909 | 0.900 | 0.693 |  |
| CECD | 0.705 | 0.270 | 0.931 | 0.337 | 0.666 | 0.808 | 0.264 | 0.405 |  |
| Sph Equiv | $<0.0001$ | 0.620 | 0.544 | 0.106 | 0.208 | 0.763 | 0.581 | 0.750 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.010 | 0.002 | 0.011 | 0.0008 | 0.028 | 0.697 | 0.456 | 0.237 |  |
| CC mean | 0.040 | 0.089 | 0.050 | 0.990 | 0.011 | 0.280 | 0.081 | 0.741 |  |
| CC flattest | $<0.0001$ | $<0.0001$ | $<0.0001$ | 0.0008 | $<0.0001$ | 0.157 | 0.390 | 0.859 |  |
| CECD | 0.184 | 0.180 | 0.122 | 0.018 | 0.226 | 0.386 | 0.605 | 0.593 |  |
| Sph Equiv | 0.192 | 0.275 | 0.287 | 0.491 | 0.191 | 0.275 | 0.559 | 0.983 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.048 | 0.483 | 0.120 | 0.133 | 0.022 | 0.372 | 0.879 | 0.374 |  |
| CC mean | 0.571 | 0.108 | 0.194 | 0.173 | 0.644 | 0.910 | 0.915 | 0.138 |  |
| CC flattest | 0.023 | 0.0021 | 0.035 | 0.016 | 0.021 | 0.037 | 0.792 | 0.469 |  |
| CECD | 0.281 | 0.987 | 0.575 | 0.659 | 0.225 | 0.902 | 0.117 | 0.576 |  |
| Sph Equiv | $<0.0001$ | 0.695 | 0.852 | 0.377 | 0.734 | 0.966 | 0.201 | 0.726 |  |

Table 4.29. The probability value derived by ANOVA for the association between the change in the magnitude of each of the structural variables pupil size, mean central corneal curvature (CC), flattest central corneal curvature (CC), corneal endothelial cell density (CECD), and spherical equivalent (SE), from the Pre-operative to the First Follow-up examinations and the corresponding changes in each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.


Figure 4.28. The change in the Corneal component of the Total, Tilt (S1) and High HOAs from the Pre-operative to the First Follow-up examinations as a function of the corresponding change in the dilated pupil diameter amongst 46 of the 67 individuals in whom the measurement was avaliable. A negative change in dilated pupil diameter refers to a smaller pupil at the First Follow-up examination and a negative change in HOA refers to a smaller HOA at the First Follow-up examination. The circled data points indicate outlying values.


Figure 4.28 Continued. The change in the Corneal component of the T.Coma and the T.Trefoil HOAs from the Pre-operative to the First Follow-up examinations as a function of the corresponding change in the dilated pupil diameter amongst 46 of the 67 individuals in whom the measurement was available (Top and Bottom). A negative change in dilated pupil diameter refers to a smaller pupil at the First Follow-up examination and a negative change in HOA refers to a smaller HOA at the First Followup examination. Note the difference in the scaling of the ordinate between the five graphs. The circled data points indicate outlying values.


Figure 4.29. The difference in the Internal component of the Total and the T.Trefoil HOAs between the Pre-operative and the First Follow-up examinations as a function of the corresponding change in dilated pupil diameter amongst 45 of the 67 individuals. A negative change in dilated pupil diameter refers to a smaller pupil at the First Follow-up examination and a negative change in HOA refers to a smaller HOA at the First Followup examination. Note the difference in the scaling of the ordinate between these and the previous graphs. The circled data points indicate outlying values.


Figure 4.30. The change in the Corneal component of the Total, High and T.Trefoil HOAs from the Pre-operative to the First Follow-up examinations as a function of the corresponding change in the mean corneal curvature amongst 46 of the 67 individuals in whom the measurement was available (Top; Middle and Bottom). A negative change in mean corneal curvature indicates a steeper curvature at the First Follow-up examination and a negative change in HOA refers to a smaller RMS at the First Follow-up examination. Note the difference in the scaling of the ordinate between the three graphs. The circled data points indicate outlying values.

### 4.5.5.11 Flattest Corneal Curvature

The magnitude of the change in the flattest corneal curvature from the Pre-operative to the First Follow-up examinations was associated with the corresponding difference in the Corneal component of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs ( $\mathrm{p}<0.0001$, $\mathrm{p}<0.0001, \mathrm{p}<0.0001, \mathrm{p}=0.0008, \mathrm{p}<0.0001$, respectively) and the corresponding difference in the Internal component of Total, Tilt (S1), High, T.Coma, T.Trefoil and T.4Foil HOAs ( $\mathrm{p}=0.023, \mathrm{p}=0.0021, \mathrm{p}=0.035, \mathrm{p}=0.016, \mathrm{p}=0.021$ and $\mathrm{p}=0.037$ respectively) (Table 4.29 and Figures 4.31, 4.32, respectively).

The magnitude of the Corneal component of the Total, High and T.Trefoil HOAs seemingly increased with increase in the radius of the flatter meridian. However, the apparent relationships were markedly influenced by the presence of 2 outlying data points which arose from the same 2 individuals across each of the HOAs. If such outliers are ignored, there is no relationship between the two variables.

The relationship for the Internal component was influenced by the same two outliers, by generally upto a further 3 outliers, depending upon the given HOA, and by a greater between-individual variability. The additional 3 outliers arose from 5 individuals. If the outliers are ignored, there is no relationship for any of the components.


Figure 4.31. The change in the Corneal component of the Total, Tilt (S1) and High HOAs from the Pre-operative and the First Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 46 of the 67 individuals in whom the measurement was available (Top; Middle and Bottom). A negative change in flattest corneal curvature indicates a steeper curvature at the First Follow-up examination and a negative change in HOA refers to a smaller RMS at the First Follow-up examination. The circled data points indicate outlying values.


Figure 4.31 Continued. The change in the Corneal component of the T.Coma and the T.Trefoil HOAs from the Pre-operative and the First Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 46 of the 67 individuals in whom the measurement was available (Top and Bottom). A negative change in flattest corneal curvature indicates a steeper curvature at the First Follow-up examination and a negative change in HOA refers to a smaller RMS at the First Follow-up examination. Note the difference in the scaling of the abscissa between the five graphs. The circled data points indicate outlying values.


Figure 4.32. The change in the Internal component of the Total, Tilt (S1) and High HOAs from the Pre-operative and the First Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 45 of the 67 individuals in whom the measurement was available (Top; Middle and Bottom). A negative change in flattest corneal curvature indicates a steeper curvature at the First Follow-up examination and a negative change in HOA refers to a smaller RMS at the First Follow-up examination. The circled data points indicate outlying values.


Figure 4.32 Continued. The change in the Internal component of the T.Coma, T.Trefoil and T.4Foil HOAs from the Pre-operative and the First Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 45 of the 67 individuals in whom the measurement was available (Top; Middle and Bottom). A negative change in flattest corneal curvature indicates a steeper curvature at the First Follow-up examination and a negative change in HOA refers to a smaller RMS at the First Follow-up examination. Note the difference in the scaling of the abscissa between the six graphs. The circled data points indicate outlying values.

### 4.5.5.12 Corneal Endothelial Cell Density

No association was present between the change in the corneal endothelial cell density from the Pre-operative to the First Follow-up examinations and the corresponding change of any of the three components for each of the eight HOAs except for the Corneal component of T.Coma HOA ( $\mathrm{p}=0.018$ ) (Table 4.29 and Figure 4.33). The magnitude of the Corneal component of the T.Coma HOA increased at the First Follow-up examination as the corresponding corneal endothelial cell density decreased.


Figure 4.33. The change in the Corneal component of the T.Coma HOA from the Preoperative to the First Follow-up examinations as a function of the corresponding change in the corneal endothelial cell density amongst 46 of the 67 individuals in hom the measurement was avaliable. A negative change in corneal endothelial cell density indicates a reduction in density at the First Follow-up examination and a negative change in HOA refers to a smaller HOA at the First Follow-up examination. The circled data point indicates an outlying value.

### 4.5.5.13 Spherical Equivalent Refraction

An association was present between the change in the Total and Internal components of the Total HOA (both p <0.001) from the Pre-operative to the First Follow-up examinations and the corresponding change in the spherical equivalent refraction (Table 4.29 and Figure 4.34). Both components decreased with increase in the magnitude of the reduction in myopia/ increase in hyperopia.


Figure 4.34. The change in the Total and the Internal components of the Total HOA from the Pre-operative to the First Follow-up examinations as a function of the corresponding change in the spherical equivalent refraction amongst 64 and 45 of the 67 individuals, respectively in whom the measurement was available (Top and Bottom). A negative change in the spherical equivalent refraction indicates a reduction in myopia/ increase in hyperopia at the First Follow-up examination and a negative change in HOA refers to a smaller RMS at the First Follow-up examination.

### 4.5.5.14 Cataract Type

Surprisingly, given the apparent associations between cataract type and some HOAs, no association was present between the cataract type and the change in any of the three components for each of the eight HOAs from the Pre-operative to the First Follow-up examinations (Table 4.30).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| NO | 0.402 | 0.578 | 0.482 | 0.446 | 0.585 | 0.152 | 0.083 | 0.117 |  |
| NC | 0.285 | 0.588 | 0.403 | 0.556 | 0.610 | 0.108 | 0.117 | 0.113 |  |
| C | 0.982 | 0.211 | 0.117 | 0.465 | 0.204 | 0.136 | 0.156 | 0.054 |  |
| P | 0.758 | 0.068 | 0.617 | 0.064 | 0.761 | 0.767 | 0.773 | 0.806 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| NO | 0.813 | 0.780 | 0.837 | 0.693 | 0.883 | 0.177 | 0.136 | 0.344 |  |
| NC | 0.887 | 0.792 | 0.997 | 0.912 | 0.959 | 0.235 | 0.168 | 0.568 |  |
| C | 0.144 | 0.110 | 0.234 | 0.204 | 0.192 | 0.342 | 0.089 | 0.211 |  |
| P | 0.143 | 0.194 | 0.253 | 0.416 | 0.299 | 0.804 | 0.423 | 0.289 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| NO | 0.765 | 0.401 | 0.902 | 0.339 | 0.729 | 0.865 | 0.193 | 0.555 |  |  |
| NC | 0.614 | 0.365 | 0.833 | 0.465 | 0.771 | 0.756 | 0.303 | 0.595 |  |  |
| C | 0.121 | 0.544 | 0.595 | 0.770 | 0.892 | 0.505 | 0.124 | 0.061 |  |  |
| P | 0.982 | 0.545 | 0.380 | 0.664 | 0.284 | 0.685 | 0.728 | 0.236 |  |  |

Table 4.30. The probability value derived by ANOVA for the association between the cataract type at the Pre-operative examination (Nuclear Opalescence, NO; Nuclear Colour, NC; Anterior Cortical, C; posterior subcapsular cataract, P) and the change in each of the three components of each of the eight HOAs from the Pre-operative to the First Follow-up examinations (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 4.6 Discussion

Based on the induced corneal changes following cataract surgery (Das et al 2006; Soto Ruiz et al 2008; Wang et al 2008; Li et al 2011; Walters 2011) it would be expected that some association would be present for the Corneal component at the First Follow-up examination.

In the current study, both the Total $\left(\mathrm{R}^{2}=0.45\right)$ and the Internal $\left(\mathrm{R}^{2}=0.51\right)$ components of the Total HOA declined with reduction in myopia/ increase in hyperopia from the Preoperative examination to the First Follow-up examination. Such findings, as would be expected, implicate the association of the (cataractous) crystalline lens/ IOL with the magnitude of the Total HOA. The findings confirm the results from Chapter 3 whereby, for those with a myopic spherical equivalent refraction, the magnitude of both components of the Total HOA declined as a function of the decline in the magnitude of the absolute myopic spherical equivalent refraction. It is interesting to note that the slope of the magnitude of the Total and Internal components of the Total HOA for those with a myopic spherical equivalent refraction prior to cataract surgery was -0.413 and -0.423 microns per dioptre of myopia, respectively, whilst that for the change in spherical equivalent refraction from the Pre-operative examination to the First-Follow-up examination was -0.333 and -0.366 microns per dioptre of reduction in myopia, respectively. The consistency of the results for both the Total and Internal components of the Total HOA between those of Chapter 3 and those of the current study provide strong evidence for the association between increase in the Total HOA with increase in myopic spherical equivalent refraction particularly that arising from the crystalline lens. The similarity of the outcome of the results of the current study to those of Chapter 3 can be placed in the context of the literature which has already been discussed in Chapter 3. The
findings refute, at least in the context of the current case series, the presence of other measurable HOAs arising from age-related cataract.

The normal corneal endothelial cell count declines with age. In the young, it is in the region of $3500-4000$ cells $/ \mathrm{mm}^{2}$ and in the last decades of life it is typically 1500-2000 cells $/ \mathrm{mm}^{2}$ (Higa et al 2010; Waring et al 1982; Sugar 1979). The range of CECD in the current study is compatible with these figures but several instances of appreciably lower CECDs were encountered compared to those of the literature. In the current study, the group mean corneal endothelial cell density at the First Follow-up examination was 1661 cells $/ \mathrm{mm}^{2}$ (SD 578.05) and the median (IQR) was $1777(1189,2125)$ compared with 2140 cells $/ \mathrm{mm}^{2}$ (SD 456.66 ) and $2176(1895,2480)$ respectively, at the Pre-operative examination. The summary statistics for the proportionate reduction in corneal endothelial cell density at the First Follow-up were mean 21\% (SD 28.0); median (IQR) $18 \%(39 \%, 29 \%)$. This reduction is greater than that of other post-operative studies following cataract surgery and IOL implantation. A $9 \%$ reduction, 1 year postoperatively, has been reported following uncomplicated phacoemulsification surgery (Werblin 1993). Similar reductions, of $9.5 \%$ after microincision cataract surgery (Wilczynski et al 2006), of $7.6 \%$ after standard phacoemulsification (Wilczynski et al 2006), of $9.5 \%$ after coaxial 1.8 mm microincision cataract surgery (Wilczynski et al 2009) and $9.3 \%$ after bimanual 1.7 mm microincision cataract surgery (Wilczynski et al 2009) have also been reported. A reduction of $5.4 \%$ was found following phacoemulsification with a non-specified incision and implantation of a non-foldable intraocular lens (George et al 2005). Anterior chamber IOL implantation results in a greater reduction in corneal endothelial cell density ( $20 \%$ ) compared to posterior chamber implantation (12\%) (Werblin 1993). The reason for the greater endothelial cell loss in the current study is unknown.

Within the limits of the data set, there seem to be some difference in the reduction in the Post-operative corneal endothelial cell density between the four surgeons (Surgeon 1 mean $45 \%$, SD 24.1 ; median $47 \%$, IQR $57 \%$, $31 \%$, Surgeon 2 mean $18 \%$ SD 12.0 ; median $15 \%$, IQR $27 \%$, 8\%, Surgeon 3 mean $31 \%$ SD 20.6; median 31\%, IQR 46\%, 13\% and Surgeon 4 maen $24 \%$ SD 13.4; median $26 \%$, IQR 30\%, 26\%). Individuals with relatively few corneal endothelial cells, and therefore reduced corneal endothelial function, who undergo cataract surgery, require extended post-operative periods to resolve the post-operative corneal oedema (Ravalico et al 1997; Diaz-Valle et al 1998; Bourne et al 2004). However, it will be shown in Chapter 5 that the reduction in corneal endothelial cell density at the Second Follow-up examination for the 41 individuals who remained in the study was still high ( mean $18 \%$, SD 29.2) and median (IQR) $16 \%$ (43\%, $7.1 \%)$.

The magnitude of the change in the Corneal component of the T.Coma HOA from the Pre-operative to the First Follow-up examinations increased linearly as the corresponding corneal endothelial cell density decreased $\left(\mathrm{R}^{2}=12 \%\right)$. This finding is novel. The explanation for the finding is not immediately clear. However, it is known that the case series exhibited a relatively profound loss of corneal endothelial cell density as a consequence of the surgical intervention. The maintenance of corneal transparency is largely dependent upon the monolayer of corneal endothelial cells which act both as a barrier and a sight for the ionic pump. Since the magnitude of corneal oedema is inversely proportional to corneal endothelial cell density, the relationship between increase in the T.Coma HOA with reduction in corneal endothelial cell density may have resulted from transient post-operative corneal oedema rather than from a low corneal endothelial cell density, per se.

As stated previously, it is known that individuals with relatively few corneal endothelial cells require extended post-operative periods following cataract extraction to resolve the post-operative corneal oedema (Ravalico et al 1997; Diaz-Valle et al 1998; Bourne et al 2004). Thus it is likely that, in some individuals, the induced decrease in corneal endothelial cell density was such as to cause difficulties not only in the magnitude, but also in the time course, of the reduction in the corneal oedema arising from the surgery. It was possible that those individuals manifesting, at the First Follow-up examination, either low endothelial cell densities or large proportionate reductions in corneal endothelial cell density may have had a shorter follow-up interval than those with larger endothelial cell densities and, thus, manifest greater amounts of corneal oedema. However, no association was present between either absolute, or absolute or proportionate, changes in corneal endothelial cell density at the First Follow-up examination and the Total component of the T.Coma. The mechanism which influences the latter is unknown.

The magnitude of the contrast sensitivity at spatial frequencies of 1.5 and 3.0 cycles per degree improved as the Corneal components of the Total, High and T.Trefoil HOAs declined. A similar association was also present at a spatial frequency of 3.0 cycles per degree for the Corneal component of the T.Coma HOA and for the Corneal component of the Tilt (S1) HOA at spatial frequencies of $1.5,3.0,6.0$ and 12.0 cycles per degree (Table 4.19). Given that these associations were not present at the Second Follow-up examination (Chapter 5), the most likely explanation for the results at this First Followup examination lies in the presence of post-operative corneal oedema. Such an explanation is compatible with the increase at the First Follow-up examination in the T.Coma HOA with decline in corneal endothelial cell density which, itself, was attributed to corneal oedema.

In the current study, no association was present between the change in the contrast sensitivity from the Pre-operative examination to the First Follow-up examination and the corresponding change in any of the three components for each of the eight HOAs. This lack of an association can be explained by the extensive improvement in contrast sensitivity for all spatial frequencies at the First Follow-up examination and poor values at the base-line of the Pre-operative examination. The extent of this improvement masks any subtle (adverse) influences on contrast sensitivity arising either directly from any post-operative increase in the Corneal component of the given HOA, itself, or from the underlying post-operative corneal oedema, only, or from the increase in the HOA as a consequence of the oedema.

In the current study, the association between both the mean and the flattest corneal curvatures and the Corneal components of the various HOAs was influenced by the presence of upto 4 outlying data points emanating from up to 6 individuals. It is not known whether such data points represent 'true' values and thereby implicate corneal curvature in the generation of HOAs or whether such points are artifactual and the corneal curvature is not implicated in HOAs. The latter theory is compatible with that of Guirao et al (2004) who reported that corneal aberrations were similar in degree, or slightly larger, following cataract surgery using a 3.5 mm incision and that, in general, any increase in aberrations did not systematically degrade the optical quality of the cornea (Guirao et al 2004). If so, it would appear that the hypothesized sub-clinical corneal oedema would occur without the involvement of the anterior corneal curvature.

In addition to the presence of outliers in the distribution of the absolute values, and the change in absolute values for the distribution, of the two measures of corneal curvature, outliers were also present in the corresponding distributions for the interval between the

Pre-operative examination and the surgery, dilated pupil diameter, corneal endothelial cell density and spherical equivalent refraction. The characteristics of the individuals exhibiting outlying data points were evaluated. Six individuals exhibited outlying values in two or more of the distributions of the 6 structural variables. Of the 6 individuals, two (numbers 6 and 43) exhibited outlying values for 4 and 5 of the structural variables respectively. However, no particular trend in structure could be found amongst the 6 individuals.

The size and position of the incision determines a predominant pattern of induced astigmatism (Steinert et al 1991; Beltrame et al 2001; Naeser et al 2002), arising from a flattening of the surgical meridian during wound healing (Zemaitiene et al 2003; Guirao et al 2004; Khokhar et al 2006; Borasio et al 2006; Hayashi et al 2009; Amesbury and Miller 2009; Hayashi et al 2010). It also determines the magnitude of the trefoil (Guirao et al 2004; Kissner et al 2007; Kim et al 2011) and total HOAs (Kim et al 2011). In the current study, the incision was between $2.5-2.7 \mathrm{~mm}$ and was made superiorly. Twentyeight of the 67 individuals (42.4\%) exhibited an 'against the rule' flattening of the cornea post-operatively (i.e., a flattening of the vertical axis as a consequence of the surgical incision and resultant wound healing).

Small superior incisions induce consistent and significant increases in corneal vertical astigmatism, corneal vertical trefoil, and corneal vertical tetrafoil (Marcos et al 2007). Corneal total HOA ( $p=0.002$ ), $3^{\text {rd }}$ order trefoil $(p<0.001)$, trefoil-like $(p<0.001)$ and $5^{\text {th }}$ order HOAs ( $\mathrm{p}<0.001$ ) are larger following a 2.8 mm incision compared to a 1.7 mm incision (Denoyer et al 2008). Vertical coma ( $\mathrm{p}=0.002$ ), vertical trefoil ( $\mathrm{p}<0.001$ ) and primary trefoil ( $\mathrm{p}=0.042$ ) are larger postoperatively following a 1.89 mm incision (Can et al 2012). Trefoil and tetrafoil, oblique astigmatism ( $\mathrm{p}<0.0001$ ), secondary oblique
astigmatism ( $\mathrm{p}=0.001$ ), and vertical tetrafoil $(\mathrm{p}=0.001)$ also increase after a 3.0 mm incision (Tong et al 2008).

Interestingly, the findings from the current study indicate that the Corneal components of the Total ( $\mathrm{p}=0.005$ ), Tilt (S1) $(\mathrm{p}=0.010)$, High ( $\mathrm{p}=0.003$ ) and T.Trefoil ( $\mathrm{p}=0.0006$ ) HOAs at the First Follow-up examination decline with increase in the flattest corneal radius. The findings also indicate that the magnitude of the increase in the Corneal components of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs (all p<0.001) from the Pre-operative examination to the First Follow-up examination increase with increase (flattening) in the change in the radius of the flatter meridian. However, the latter were attributed to the presence of 2 obvious outliers in the magnitude of the change in corneal curvature. Nevertheless, it would appear from the literature that the two previously designated outliers in the current study may, in fact, be 'true' data points.

The association in the current study between the change from the Pre-operative to the First Follow-up examinations both in the Corneal component of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs $(\mathrm{p}=0.010, \mathrm{p}=0.002$, $\mathrm{p}=0.011, \mathrm{p}=0.0008, \mathrm{p}=0.028$ respectively, and in the Internal component of the Total $(\mathrm{p}=0.048)$ and T.Trefoil ( $\mathrm{p}=0.022$ ) HOAs, and the corresponding change in dilated pupil diameter, implies that the magnitude of the given HOAs declines with increase in the dilated pupil diameter. This association is not compatible with the literature. All HOAs, in particular, spherical (4 ${ }^{\text {th }}$ order) and coma ( $3^{\text {rd }}$ order) (Liang and Williams 1997; Wang et al 2003; Hu et al 2004) and defocus ( $2^{\text {nd }}$ order), spherical and quadrafoil ( $4^{\text {th }}$ order) (Fritzsch et al 2011). The reduction in the magnitude of the various HOAs with increase in the dilated pupil diameter in the current study seems to stem from the presence of 4 outliers from up to 6 individuals across each of the HOAs.

Indeed, given that the HOAs determined in the current study were referenced to a 4.0 mm diameter central zone and given that only one individual manifested a dilated pupil diameter of less than 4.00 mm (in this instance at the First Follow-up examination) the apparent relationship between change in dilated pupil diameter and the change in HOA would appear to be artefactual.

In the current study, 55 individuals ( $82 \%$ ) exhibited smaller dilated pupil diameters at the First Follow-up examination compared to the Pre-operative examination. This postoperative reduction in dilated pupil diameter is compatible with other studies. The maximal amplitude, constriction velocity and dilatation velocity decreases post-operatively (Komatsu et al 1999). The impaired dynamics of pupil constriction following either extra capsular extraction or phacoemulsification techniques have been attributed to reduced sphincter pupillae function arising from the trauma during surgery (Möller et al 2000). This latter conclusion might be relevant to the mechanical manipulation of the iris during cataract operation. The damage to the dilator muscle during surgery leads to temporary or permanent changes in pupillary function despite the latter appearing to be normal on postoperative slit-lamp examination (Möller et al 2000). In addition, a lower corneal metabolism has been reported following phacoemulsification which results in a statistically significant reduction in the maximal pharmacologically dilated pupil (Hooman et al 2000; Lohmann et al 1996). This finding was confirmed by Möller et al (2000) in that pupillary responses to neosynephrine and to pilocarpine were decreased following phacoemulsification. Such a finding indicates damage to both the dilator and sphincter muscles, respectively. An increased epithelial permeability occurs following phacoemulsification and implies a temporary impairment of the corneal barrier function which has been attributed to neural damage from the surgery (Lohmann et al 1996).

In Chapter 3, an increase in the Total and the Internal components of the Tilt (S1) HOA was found to be associated with an increase in severity of posterior subcapsular and cortical cataracts. An association was also found for the increase in the Total and the Internal components of both the T.Sph and the HiAstig HOAs and increase in severity of cortical cataract, particularly in the presence of increasing nuclear colour cataract. The increase in the Total Component of the T.Coma HOA was associated with increase in severity of the posterior subcapsular cataract. Contrary to these findings, no association was found between cataract type and severity at the Pre-operative examination and the change in HOA from the Pre-operative to the First Follow-up examination. The reason for such a discrepancy again lies in the profound change from base-line in the given HOA which, in this instance, masks the influence on the given post-operative HOA arising from any pre-operative differences in cataract type and severity.

The lack of statistical difference between the 4 surgeons in terms of any of the components for any of the eight HOAs overcame the necessity of partitioning the post-operative HOAs by the given surgeon. Although the use of the Forelens IOL resulted in smaller Total and Internal components of the Total HOA compared with the other types of IOL, the proportion of individuals with the Forelens was $78 \%$ of 64 individuals at the First Followup examination and $87 \%$ of 45 individuals at the Second Follow-up examination. Although the results for the HOAs could have been stratified by type of IOL, the small number of individuals manifesting one of the remaining three types of IOLs was such as to have rendered the partitioning to be of little value. Alternatively, those individuals who had received one of the remaining three types of IOL could have been excluded from the analysis. However, such an approach would have resulted in a loss of statistical power. Another approach would have been to have compiled the case series from individuals who had received one type of IOL, only; perhaps the Forelens.

In summary, it is clear that the magnitude of the Total and Internal components of the Total HOA increase linearly with increase in myopia which coexists with age-related cataracts. In addition, some evidence, namely the increase in the Corneal component of T.Coma with reduction in corneal endothelial cell density suggests the presence of postoperative (sub-clinical) corneal oedema in some individuals even at a median postoperative follow-up of 50 days after surgery. The magnitude in contrast sensitivity, particularly for spatial frequencies of 1.5 and 3.0 cycles per degree, increased with reduction in the Corneal components of the Total, Tilt (S1), High, T.Coma and T,Trefoil HOAs. Such a finding indicates a considerable between-individual variation in both the reduction in HOA and in the improvement in contrast sensitivity. The presence and magnitude of this variation suggests that, in some individuals, the underlying cause of the Pre-operative increase in HOA is not resolved by the IOL implantation. The reason for the lack of post-operative improvement in the given HOA is unknown but could involve the presence of post-operative (sub-clinical) corneal oedema. The measurement of the Corneal component of certain HOAs could, therefore, be used as a bio-marker for this condition whatever the aetiology. However, the hypothesis that such transient corneal oedema influences the magnitude of the Corneal component of the various HOAs depends upon the resolution of the corneal oedema. Such an outcome will be discussed in Chapter 5 in the context of its resolution at a longer (Second Follow-up) examination.

## CHAPTER 5

## THE HIGHER ORDER ABERRATIONS, DETERMINED AT THE SECOND FOLLOW-UP EXAMINATION, ARISING FROM CATARACT EXTRACTION

## AND IOL IMPLANTATION

### 5.1 Introduction

Chapter 5 describes the Second Follow-up examination which took place approximately 80 weeks following surgery. The results from this Second Follow-up examination were analysed, again, in terms of the absolute outcomes and also by the change in the outcomes relative to baseline.

### 5.2 Aims

The aims of the study were similar to those of Chapter 4 since the current Chapter is a natural continuation of the previous study with the exception that it provides an analysis of the same measurements and procedures following a healing period of approximately 80 weeks.

### 5.2.1 Primary Aim

The primary aim was to determine for each of the three components of the eight HOAs, obtained at approximately 80 weeks post-operatively, any association with the demographic variable, age; the structural variables, corneal curvature, corneal endothelial cell density, spherical equivalent and the primary type and severity of the age-related cataract; the functional variables, visual acuity and contrast sensitivity; and the magnitude of each of the Total, Corneal and Internal components for each of the eight

HOAs obtained using Placido Disc and Dynamic Skiascopy by the NIDEK OPD Scanning System ARK-10000 aberrometer in individuals who had undergone cataract surgery and intra-ocular lens implantation at approximately 80 weeks previously.

### 5.2.2 Secondary Aims

The secondary aims were twofold:

Firstly, to determine the associations between the changes from the pre- to the second post-operative examinations in the specified and structural variables, corneal curvature, Corneal endothelial cell density, spherical equivalent; the functional variables, visual acuity and contrast sensitivity; and the corresponding changes in the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained by the OPD aberrometer.

Secondly, to determine the associations between the demographic variables, type of IOL, surgeon, the times from the Pre-operative examination to surgery and from the Preoperative examination to the Second Follow-up examination, and the corresponding changes from the pre- to the second post-operative examinations in the magnitude of each of the Total, Corneal and Internal components for each of the eight HOAs obtained by the OPD aberrometer.

### 5.3 Methods

### 5.3.1 Experimental Procedures

All individuals who attended the Second Follow-up examination underwent an identical standard ophthalmological and optometric examination as described in Chapters 3 and 4.

The former was performed by one of the same three ophthalmologists as on the previous two examinations and the latter by the Author.

### 5.4 Analysis

The analysis was identical to that described in Chapter 4.

### 5.5 Results

### 5.5.1 Case Series

The Case series comprised 41 (mean age 73.39 , SD 8.68; median 71.00 , IQR 68.00, 81.00) of the 67 individuals who had attended the First Follow-up examination. Twentyseven individuals were excluded from the study and one individual (number 49 in the case study) who failed to attend the First Follow-up examination attended the Second Follow-up examination. The reason for withdrawal from the study of the 27 individuals is given in Table 5.1. The number of individuals participating at each phase of the study is shown in Figure 5.1. The 41 individuals attended a Second Follow-up examination approximately 80 weeks after surgery (mean 80.19, SD 17.61; median 85.14, IQR 80.00, 89.57).

### 5.5.2 Characteristics of Case Series at the Second Follow-up Examination

### 5.5.2.1 Age and Gender

The distributions of age and gender, stratified by the operated eye, of the 41 individuals attending the Second Follow-up examination are given in Table 5.2.

As mentioned before, the mean age was 73.39 , SD 8.68, median 71.00, IQR 68.00, 81.00. The youngest individual in the case series was 56 years old and the eldest 90 years old. The group was composed of 17 males and 24 females. Cataract extraction and IOL implantation had been undertaken on 21 right eyes and 20 left eyes.


Figure 5.1. The number of individuals participating at each examination phase of the study.

| Case Number in study | Gender | Reason for withdrawal |
| :---: | :---: | :---: |
| 2 | M | Deceased |
| 4 | F | Refused to attend for follow up |
| 8 | M | Unable to attend the clinic - Health complication |
| 12 | M | Deceased |
| 13 | M | Refused to attend for follow up |
| 15 | L | Unable to attend the clinic - Health complication |
| 17 | F | Posterior Capsular Opacification (had Yag lazer treatment) |
| 18 | F | Data acquisition not possible |
| 19 | F | Refused to attend for follow up |
| 20 | F | Data acquisition not possible |
| 21 | F | Refused to attend for follow up |
| 22 | F | Moved from Beer-Sheva - Unable to attend the clinic |
| 23 | F | Refused to attend for follow up |
| 25 | F | Unable to attend the clinic - Health complication |
| 31 | F | Unable to attend the clinic - Moved from Beer-Sheva |
| 33 | M | Unable to attend the clinic - Health complication |
| 58 | F | Posterior Capsular Opacification (had Yag lazer treatment) |
| 60 | M | Unable to attend the clinic - Health complication |
| 64 | M | Posterior Capsular Opacification (had Yag lazer treatment) |
| 71 | M | Unable to attend the clinic - Health complication |
| 75 | F | Refused to attend for follow up |
| 78 | F | Refused to attend for follow up |
| 82 | F | Unable to attend the clinic - Health complication |
| 86 | F | Unable to attend the clinic - Moved from Beer-Sheva |
| 92 | F | Refused to attend for follow up |
| 94 | M | Deceased |
| 97 | M | Refused to attend for follow up |

Table 5.1. The reason for withdrawal of the 27 individuals from the study prior to the Second Follow-up examination.

| Age group (years) | Gender | Operated eye |  | Total |  | Total |  | Total |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | R | L | R | L | M | F |  |
| 21-30 | M | - | - | - | - | - | - | - |
|  | F | - | - |  |  |  |  |  |
| 31-40 | M | - | - | - | - | - | - | - |
|  | F | - | - |  |  |  |  |  |
| 41-50 | M | - | - | - | - | - | - | - |
|  | F | - | - |  |  |  |  |  |
| 51-60 | M | 2 | - | 1 | 1 | 2 | - | 2 |
|  | F | - | - |  |  |  |  |  |
| 61-70 | M | 4 | 5 | 6 | 11 | 9 | 8 | 17 |
|  | F | 2 | 6 |  |  |  |  |  |
| 71-80 | M | 3 | - | 9 | 3 | 3 | 9 | 12 |
|  | F | 6 | 3 |  |  |  |  |  |
| 81-90 | M | 1 | 2 | 4 | 6 | 3 | 7 | 10 |
|  | F | 3 | 4 |  |  |  |  |  |
| Total |  | 21 | 20 | 20 | 21 | 17 | 24 | 41 |

Table 5.2. The age of the 41 individuals attending the Second Follow-up examination, stratified by gender and by the operated eye.

### 5.5.2.2 IOL and Surgeon

The numbers of eyes operated upon by each of the four surgeons stratified by eye, by gender and by type of IOL for the 41 individuals attending the Second Follow-up examination are given in Table 5.3. The Forelens IOL was used in 32 cases, the B-lens in 7, the Xcelens in one case and the Triplens in one case. Nineteen individuals were operated upon by Surgeon 3, 11 by Surgeon 2, 7 by Surgeon 1, 4 individuals by Surgeon 4.

|  |  |  | Type of IOL |  |  |  |  |  |  |  | Total |  | Total Surgeon |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | Forelens |  | B Lens |  | Xcelens |  | Triplens |  |  |  |  |
|  |  |  | M | F | M | F | M | F | M | F | R | L |  |
| Surgeon and Operated eye | Surgeon 1 | R | 3 | 1 | - | - | - | - | - | - | 4 | - | 7 |
|  |  | L | 1 | 2 | - | - | - | - | - | - | - | 3 |  |
|  | Surgeon 2 | R | 1 | 1 | 1 | 1 | - | 1 | - | - | 5 | - | 11 |
|  |  | L | 2 | 2 | 1 | - | - | - | - | 1 | - | 6 |  |
|  | Surgeon 3 | R | 1 | 6 | 1 | - | - | - | - | - | 8 | - | 19 |
|  |  | L | 3 | 6 | - | 2 | - | - | - | - | - | 11 |  |
|  | Surgeon 4 | R | 2 | 1 | - | - | - | - | - | - | 3 | - | 4 |
|  |  | L | - | - | 1 | - | - | - | - | - | - | 1 |  |
| Total |  |  | 13 | 19 | 4 | 3 | - | 1 | - | 1 | 20 | 21 | 41 |
| Total |  |  | 32 |  | 7 |  | 1 |  | 1 |  | 41 |  |  |

Table 5.3. The number of eyes operated upon by each of the four surgeons stratified by eye, by gender and by type of IOL for the 41 individuals attending the Second Follow-up examination.

### 5.5.2.3 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst 40 of the 41 individuals who attended the Second Follow-up examination is shown in Table 5.4. The range of the spherical equivalent refraction reduced considerably at the First-Follow-up examination following cataract surgery. The improvement was maintained at the Second Follow-up examination. One individual manifested a spherical equivalent refraction of between -3.00 and -3.99 dioptres, 6 of between -2.00 and -2.99 dioptres and 26 of between -1.00 dioptres and Plano. Six individuals exhibited a positive spherical equivalent refraction of between 0.01 and +1.99 dioptres and one of between +2.00 and +2.99 dioptres. The spherical equivalent refraction could not be obtained in one individual.

| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $(-3.00)-(-3.99)$ | 1 | -3.88 | - | - | -3.88 | -3.13 | - |
| $(-2.00)-(-2.99)$ | 6 | -2.27 | 0.30 | -2.19 | -2.75 | -2.00 | $-2.44,-2.03$ |
| $(-1.00)-(-1.99)$ | 9 | -1.39 | 0.32 | -1.25 | -1.75 | -1.00 | $-1.75,-1.13$ |
| $(0.00)-(-0.99)$ | 17 | -0.38 | 0.27 | -0.25 | -0.88 | 0.00 | $-0.50,-0.25$ |
| $(0.01)-(+0.99)$ | 4 | 0.38 | - | 0.25 | 0.25 | 0.75 | $0.25,0.38$ |
| $(+1.00)-(+1.99)$ | 2 | 1.44 | - | - | 1.13 | 1.75 | - |
| $(+2.00)-(+2.99)$ | 1 | 2.00 | - | - | - | - | - |
| Group | 40 | -0.75 | 1.18 | -0.50 | -3.88 | 2.00 | $-1.66,-0.19$ |

Table 5.4. The summary statistics for the distribution of the spherical equivalent refraction amongst 40 of the 41 individuals within the case series, at the Second Followup examination. The spherical equivalent refraction could not be obtained in one individual.

### 5.5.2.4 Distance Visual Acuity

The distribution of distance visual acuity amongst 40 of the 41 individuals within the case series at the Second Follow-up examination is shown in Figure 5.2. As would be expected, a considerable improvement occurred in distance visual acuity following cataract surgery and this improvement was maintained at the Second Follow-up examination. Twenty individuals exhibited a visual acuity of 6/6, 10 of $6 / 7.5,7$ of $6 / 9$ and 3 of between 6/10 and 6/15.

### 4.5.2.5 Near Visual Acuity

The distribution of near visual acuity amongst 40 of the 41 individuals within the case series at the Second Follow-up examination is shown in Figure 5.3. As with the distance visual acuity, all individuals exhibited a considerable improvement in near visual acuity following cataract surgery and it was maintained at the Second Follow-up examination.

Twelve individuals exhibited a near visual acuity of Jaeger 1, 22 of Jaeger 2 and 7 of Jaeger 3.


Figure 5.2. The distribution of visual acuity amongst 40 of the 41 individuals within the case series at the Second Follow-up examination. The upper legend for the abscissa delineates the acuity in Snellen notation and the lower legend the acuity in MAR.


Figure 5.3. The distribution of near visual acuity in Jaeger notation for 40 of the 41 individuals within the case series at the Second Follow-up examination.

### 5.5.2.6 Contrast Sensitivity

The distribution of contrast sensitivity amongst the 41 individuals for each of the five spatial frequencies derived by the Functional Acuity Contrast Test (FACT) 301 at the Second Follow-up examination is shown in Figure 5.4. The improvement in contrast sensitivity for all spatial frequencies at the First Follow-up examination was maintained at the Second Follow-up examination.


Figure 5.4. The distribution of the contrast sensitivity value for spatial frequencies of 1.5 and 3 cycles per degree, derived by the Functional Acuity Contrast Test (FACT) for the 41 individuals within the case series at the Second Follow-up examination (Top and Bottom).




Figure 5.4 Continued. The distribution of the contrast sensitivity value for spatial frequencies of 6,12 and 18 cycles per degree, derived by the Functional Acuity Contrast Test (FACT) for the 41 individuals within the case series at the Second Follow-up examination (Top, Middle and Bottom). Note the difference in the scaling of the abscissa.

### 5.5.2.7 Dilated Pupil Diameter

The distribution of the dilated pupil diameter, within the case series, as measured by the OPD aberrometer, is shown in Table 5.5. Two individuals exhibited a dilated pupil diameter of between 4.00 and $4.99 \mathrm{~mm}, 20$ of between 4.50 and 5.99 mm , 14 of between 6.00 and 6.99 mm and 4 of between 7.0 and 7.49 mm . The pupil diameter for one individual could not be measured by the OPD aberrometer. The reason for the lack of measurement is unknown.

| Dilated Pupil <br> Diameter (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 4.00 to 4.49 | 2 | 4.37 | - | - | 4.24 | 4.49 | - |
| 4.50 to 4.99 | 4 | 4.88 | 0.06 | 4.89 | 4.80 | 4.93 | $4.35,4.92$ |
| 5.00 to 5.49 | 6 | 5.24 | 0.14 | 5.24 | 5.05 | 5.43 | $5.15,5.33$ |
| 5.50 to 5.99 | 10 | 5.81 | 0.12 | 5.86 | 5.56 | 5.94 | $5.73,5.90$ |
| 6.00 to 6.49 | 9 | 6.28 | 0.09 | 6.29 | 6.13 | 6.43 | $6.26,6.34$ |
| 6.50 to 6.99 | 5 | 6.74 | 0.11 | 6.75 | 6.57 | 6.88 | $6.74,6.77$ |
| 7.00 to 7.49 | 4 | 7.19 | 0.20 | 7.15 | 7.02 | 7.45 | $7.04,7.29$ |
| Group | 40 | 5.92 | 0.78 | 5.91 | 4.24 | 7.45 | $5.33,6.42$ |

Table 5.5. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series, of the dilated pupil diameter as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer at the Second Follow-up examination.

### 5.5.2.8 Mean Corneal Curvature

The distribution of the mean corneal curvature, within the case series, as measured by the OPD, is shown in Table 5.6. Amongst the case series, 2 individuals exhibited a mean corneal curvature of less than $7.20 \mathrm{~mm}, 9$ individuals of between 7.20 and $7.39 \mathrm{~mm}, 26$ of between 7.40 and 7.99 mm and 4 of between 8.00 and 8.19 mm .

| Mean Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 7.2 | 2 | 7.17 | - | - | 7.16 | 7.17 | - |
| 7.20 to 7.39 | 9 | 7.29 | 0.05 | 7.29 | 7.22 | 7.37 | $7.26,7.32$ |
| 7.40 to 7.59 | 9 | 7.53 | 0.05 | 7.53 | 7.43 | 7.58 | $7.49,7.56$ |
| 7.60 to 7.79 | 14 | 7.67 | 0.06 | 7.66 | 7.60 | 7.79 | $7.63,7.72$ |
| 7.80 to 7.99 | 3 | 7.92 | - | 7.94 | 7.85 | 7.98 | - |
| 8.00 to 8.19 | 4 | 8.08 | - | 8.08 | 8.01 | 8.15 | $8.05,8.11$ |
| Group | 41 | 7.59 | 0.26 | 7.60 | 7.16 | 8.15 | $7.37,7.72$ |

Table 5.6. The summary statistics for the distribution amongst 41 individuals within the case series, of the mean corneal curvature as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer at the Second Follow-up examination.

### 5.5.2.9 Flattest Corneal Curvature

The distribution of the flattest corneal curvature, within the case series, as measured by the OPD aberrometer, is shown in Table 5.7. Amongst the case series, 7 individuals exhibited a flattest corneal curvature of between 7.20 and $7.39 \mathrm{~mm}, 27$ of between 7.40 and $7.99 \mathrm{~mm}, 6$ of between 8.00 and 8.19 mm and one greater than 8.19 mm .

| Flattest Corneal <br> Curvature (mm) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 7.20 to 7.39 | 7 | 7.30 | 0.04 | 7.31 | 7.23 | 7.34 | $7.29,7.33$ |
| 7.40 to 7.59 | 8 | 7.50 | 0.06 | 7.50 | 7.43 | 7.58 | $7.44,7.55$ |
| 7.60 to 7.79 | 13 | 7.70 | 0.07 | 7.69 | 7.61 | 7.79 | $7.65,7.77$ |
| 7.80 to 7.99 | 6 | 7.87 | 0.05 | 7.85 | 7.82 | 7.95 | $7.83,7.90$ |
| 8.00 to 8.19 | 6 | 8.08 | 0.07 | 8.07 | 8.01 | 8.18 | $8.01,8.13$ |
| Greater than 8.19 | 1 | 8.23 | - | - | - | - | - |
| Group | 41 | 7.68 | 0.27 | 7.66 | 7.23 | 8.23 | $7.48,7.84$ |

Table 5.7. The summary statistics for the distribution amongst the 41 individuals within the case series, of the flattest corneal curvature as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer at the Second Follow-up examination.

### 5.5.2.10 Corneal Endothelial Cell Density

The distribution of the corneal endothelial cell density amongst the 41 individuals within the case series is given in Table 5.8. Four individuals exhibited a corneal endothelial cell density of between 500 and 799 cells $/ \mathrm{mm}^{2}, 10$ of between 800 and 1399 cells $/ \mathrm{mm}^{2}, 17$ of between 1400 and 2299 cells $/ \mathrm{mm}^{2}$, 7 of between 2300 and 2899 cells $/ \mathrm{mm}^{2}$. Three individuals exhibited a corneal endothelial cell density greater than 2899 cells $/ \mathrm{mm}^{2}$.

| Corneal Endothelial <br> Cell Density <br> (cells $/ \mathrm{mm}^{2}$ ) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 500 to 799 | 4 | 701 | - | 646 | 596 | 782 | 634,781 |
| 800 to 1099 | 6 | 1016 | 38.10 | 1009 | 952 | 1067 | 1001,1047 |
| 1100 to 1399 | 4 | 1313 | - | 1319 | 1302 | 1343 | 1308,1382 |
| 1400 to 1699 | 7 | 1555 | 76.73 | 1589 | 1456 | 1637 | 1486,1627 |
| 1700 to 1999 | 6 | 1789 | 95.84 | 1764 | 1700 | 1957 | 1722,1821 |
| 2000 to 2299 | 4 | 2168 | - | 2166 | 2048 | 2293 | 2134,2199 |
| 2300 to 2599 | 5 | 2455 | 69.91 | 2430 | 2405 | 2575 | 2410,2455 |
| 2600 to 2899 | 2 | 2776 | - | - | 2668 | 2883 | - |
| Greater than 2899 | 3 | 3069 | - | 2976 | 2975 | 3257 | - |
| Group | 41 | 1744 | 696.42 | 1637 | 596 | 3257 | 1302,2293 |

Table 5.8. The summary statistics for the distribution, amongst the 41 individuals within the case series, of corneal endothelial cell density at the Second Follow-up examination.

### 5.5.2.11 Higher Order Aberrations

The summary statistics of the distribution of the RMS value of the Total component for each of the eight HOAs, measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone, namely, Total, Tilt (S1), High, T.coma, T.trefoil, T.4Foil, T.sph and HiAstig are given in Tables 5.9-5.16, respectively
for the 40 of the 41 individuals. A measure of the HOAs for the remaining individual could not be obtained. The reason for this is unknown.

### 5.5.2.11.1 Total Component of the Total HOA

Four individuals exhibited RMS values for the Total component of the Total HOA of between 0.500 and 0.799 micron, 21 of between 0.800 and 1.099 microns, 11 of between 1.400 and 2.299 microns, 2 of between 2.600 and 2.899 microns and 2 individuals exhibited RMS values greater than 2.899 (Table 5.9).

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.500 to 0.799 | 4 | 0.622 | 0.36 | 0.594 | 0.530 | 0.744 | $0.584,0.676$ |
| 0.800 to 1.099 | 11 | 0.958 | 0.38 | 0.937 | 0.874 | 1.092 | $0.896,1.010$ |
| 1.100 to 1.399 | 10 | 1.224 | 0.45 | 1.189 | 1.112 | 1.361 | $1.174,1.281$ |
| 1.400 to 1699 | 5 | 2.527 | 0.59 | 1.484 | 1.405 | 1.694 | $1.457,1.577$ |
| 1.700 to 1.999 | 3 | 1.843 | - | 1.83 | 1.746 | 1.947 | - |
| 2.000 to 2.299 | 3 | 0.662 | - | 2.079 | 2.066 | 2.248 | - |
| 2.300 to 2.599 | - | - | - | - | - | - | - |
| 2.600 to 2.899 | 2 | 2.8 | - | - | 2.694 | 2.895 | - |
| Greater than 2.899 | 2 | 3.24 | - | - | 3.14 | 3.336 | - |
| Group | 40 | 1.571 | 1.60 | 1.189 | 0.530 | 3.336 | $0.937,1.707$ |

Table 5.9. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the Total HOA at the Second Follow-up examination.

### 5.5.2.11.2 Total Component of the Tilt (S1) HOA

Sixteen individuals exhibited an RMS value for the Total component of the Tilt (S1) HOA of between 0.040 and 0.279 microns, 14 of between 0.280 and 0.499 microns, 7 of between 0.440 and 0.709 microns and 3 individuals an RMS value greater than 0.709 microns (Table 5.10).

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Tilt (S1) RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.040 to 0.119 | 6 | 0.079 | 0.06 | 0.085 | 0.042 | 0.095 | $0.061,0.093$ |
| 0.120 to 0.199 | 4 | 0.146 | 0.07 | 0.144 | 0.129 | 0.167 | $0.134,0.155$ |
| 0.200 to 0.279 | 6 | 0.244 | 0.10 | 0.247 | 0.205 | 0.265 | $0.233,0.261$ |
| 0.280 to 0.359 | 6 | 0.319 | 0.13 | 0.319 | 0.287 | 0.353 | $0.297,0.337$ |
| 0.360 to 0.439 | 8 | 0.406 | 0.13 | 0.402 | 0.366 | 0.437 | $0.395,0.423$ |
| 0.440 to 0.519 | 2 | 0.508 | - | - | 0.498 | 0.517 | - |
| 0.520 to 0.629 | 3 | 0.538 | - | 0.536 | 0.530 | 0.547 | - |
| 0.630 to 0.709 | 2 | 0.681 | - | - | 0.655 | 0.706 | - |
| Greater than 0.709 | 3 | 1.323 | - | 1.132 | 1.039 | 1.701 | - |
| Group | 40 | 0.500 | 0.71 | 0.336 | 0.042 | 1.701 | $0.196,0.452$ |

Table 5.10. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the Tilt (S1) HOA at the Second Follow-up examination.

### 5.5.2.11.3 Total Component of the High HOA

Six individuals exhibited an RMS value for the Total component of the High HOA of between 0.100 and 0.199 microns, 22 of between 0.400 and 0.299 microns, 6 of between 0.500 and 0.799 microns and 2 individuals of between 0.800 and 0.999 . Five individuals exhibited an RMS value greater than 0.999 microns (Table 5.11).

Total Component

| High RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 0.100 to 0.199 | 6 | 0.169 | 0.08 | 0.175 | 0.129 | 0.186 | $0.163,0.103$ |
| 0.200 to 0.299 | 11 | 0.242 | 0.11 | 0.232 | 0.203 | 0.283 | $0.224,0.256$ |
| 0.300 to 0.399 | 6 | 0.348 | 0.16 | 0.336 | 0.306 | 0.393 | $0.326,0.373$ |
| 0.400 to 0.499 | 4 | 0.464 | 0.17 | 0.470 | 0.422 | 0.490 | $0.447,0.486$ |
| 0.500 to 0.599 | 1 | 0.521 | - | - | - | - | - |
| 0.600 to 0.699 | 3 | 0.606 | - | 0.601 | 0.601 | 0.617 | - |
| 0.700 to 0.799 | 2 | 0.726 | - | - | 0.420 | 0.731 | - |
| 0.800 to 0.899 | 1 | 0.809 | - | - | - | - | - |
| 0.900 to 0.999 | 1 | 0.993 | - | - | - | - | - |
| Greater than 0.999 | 5 | 1.776 | 0.15 | 1.643 | 1.128 | 2.581 | $0.252,1.891$ |
| Group | 40 | 0.746 | 1.11 | 0.336 | 0.129 | 2.581 | $0.228,0.605$ |

Table 5.11. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the High HOA at the Second Follow-up examination.

### 5.5.2.11.4 Total Component of the T.Coma HOA

Ten individuals exhibited RMS values for the Total component of the T.Coma HOA of between 0.030 and 0.069 microns, 23 of between 0.070 and 0.149 microns and 4 of between 0.170 and 0.209 microns. Three individuals exhibited an RMS value greater than 0.209 microns (Table 5.12).

### 5.5.2.11.5 Total Component of the T.Trefoil HOA

Five individuals exhibited an RMS value for the Total component of the T.Trefoil HOA of between 0.030 and 0.109 microns, 22 of between 0.110 and 0.349 microns, 6 of between 0.350 and 0.589 microns and of between 0.670 and 0.909 microns. Three individuals exhibited an RMS value greater than 0.909 microns (Table 5.13).

### 5.5.2.11.6 Total Component of the T.4Foil HOA

Nine individuals exhibited an RMS value for the Total component of the T.4Foil HOA of between 0.000 and 0.049 microns, 16 of between 0.050 and 0.149 microns, 9 of between 0.150 and 0.299 microns and 2 of between 0.400 and 0.649 microns. Four individuals exhibited an RMS value greater than 0.649 microns (Table 5.14).

### 5.5.2.11.7 Total Component of the T.Sph HOA

Four individuals exhibited an RMS value for the Total component of the T.Sph HOA of less than 0.010 . Twenty-four individuals exhibited an RMS value of between 0.010 and 0.089 microns, 5 of between 0.090 and 0.169 microns, 2 of between 0.210 and 0.249 and 4 individuals of between 1.250 and 0.289 microns (Table 5.15).

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Coma RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.030 to 0.049 | 5 | 0.038 | 0.12 | 0.036 | 0.031 | 0.045 | $0.035,0.041$ |
| 0.050 to 0.069 | 5 | 0.060 | 0.03 | 0.059 | 0.053 | 0.068 | $0.056,0.064$ |
| 0.070 to 0.089 | 9 | 0.082 | 0.03 | 0.084 | 0.074 | 0.087 | $0.078,0.087$ |
| 0.090 to 0.109 | 6 | 0.096 | 0.03 | 0.093 | 0.091 | 0.104 | $0.093,0.098$ |
| 0.110 to 0.129 | 4 | 0.122 | 0.04 | 0.124 | 0.113 | 0.125 | $0.121,0.125$ |
| 0.130 to 0.149 | 4 | 0.140 | 0.04 | 0.139 | 0.135 | 0.148 | $0.136,0.143$ |
| 0.150 to 0.169 | - | - | - | - | - | - | - |
| 0.170 to 0.189 | 2 | 0.173 | - | - | 0.170 | 0.176 | - |
| 0.190 to 0.209 | 2 | 0.199 | - | - | 0.192 | 0.205 | - |
| Greater than 0.209 | 3 | 0.507 | - | 0.544 | 0.265 | 0.636 | - |
| Group | 40 | 0.172 | 0.28 | 0.091 | 0.031 | 0.636 | $0.073,0.135$ |

Table 5.12. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.Coma HOA at the Second Follow-up examination.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.Trifoil RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.030 to 0.109 | 5 | 0.080 | 0.07 | 0.092 | 0.036 | 0.107 | $0.040,0.097$ |
| 0.110 to 0.189 | 12 | 0.153 | 0.09 | 0.140 | 0.122 | 0.188 | $0.129,0.180$ |
| 0.190 to 0.269 | 7 | 0.232 | 0.12 | 0.236 | 0.195 | 0.265 | $0.197,0.261$ |
| 0.270 to 0.349 | 3 | 0.302 | - | 0.287 | 0.275 | 0.341 | - |
| 0.350 to 0.429 | 4 | 0.392 | 0.11 | 0.389 | 0.376 | 0.412 | $0.384,0.397$ |
| 0.430 to 0.509 | - | - | - | - | - | - | - |
| 0.510 to 0.589 | 2 | 0.537 | - | - | 0.531 | 0.544 | - |
| 0.590 to 0.669 | - | - | - | - | - | - | - |
| 0.670 to 0.749 | 1 | 0.679 | - | - | - | - | - |
| 0.750 to 0.829 | 2 | 0.810 | - | - | 0.799 | 0.820 | - |
| 0.830 to 0.909 | 1 | 0.852 | - | - | - | - | - |
| Greater than 0.909 | 3 | 1.251 | - | 1.208 | 1.140 | 1.392 | - |
| Group | 40 | 0.484 | 0.65 | 0.218 | 0.036 | 1.392 | $0.136,0.397$ |

Table 5.13. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.Trefiol HOA at the Second Follow-up examination.

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T.4Foil RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| 0.000 to 0.049 | 9 | 0.032 | 0.03 | 0.027 | 0.015 | 0.019 | $0.024,0.037$ |
| 0.050 to 0.099 | 8 | 0.073 | 0.05 | 0.071 | 0.054 | 0.091 | $0.058,0.084$ |
| 0.100 to 0.149 | 8 | 0.114 | 0.03 | 0.114 | 0.106 | 0.123 | $0.112,0.116$ |
| 0.150 to 0.199 | 3 | 0.172 | - | - | 0.156 | 0.184 | - |
| 0.200 to 0.249 | 4 | 0.229 | 0.07 | 0.229 | 0.216 | 0.242 | $0.223,0.235$ |
| 0.250 to 0.299 | 2 | 0.269 | - | - | 0.255 | 0.283 | - |
| 0.300 to 0.349 | - | - | - | - | - | - | - |
| 0.350 to 0.399 | - | - | - | - | - | - | - |
| 0.400 to 0.449 | 1 | 0.444 | - | - | - | - | - |
| 0.450 to 0.499 | - | - | - | - | - | - | - |
| 0.500 to 0.549 | - | - | - | - | - | - | - |
| 0.550 to 0.599 | - | - | - | - | - | - | - |
| 0.600 to 0.649 | 1 | 0.630 | - | - | - | - | - |
| Greater than 0.649 | 4 | 1.082 | 0.85 | 0.974 | 0.767 | 1.470 | $0.823,1.197$ |
| Group | 40 | 0.383 | 0.64 | 0.113 | 0.015 | 1.470 | $0.056,0.227$ |

Table 5.14. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.4Foil HOA at the Second Follow-up examination.

Total Component

| T.Sph RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than 0.010 | 4 | 0.007 | 0.00 | 0.006 | 0.006 | 0.007 | $0.006,0.007$ |
| 0.010 to 0.049 | 13 | 0.031 | 0.03 | 0.031 | 0.014 | 0.046 | $0.016,0.040$ |
| 0.0 .50 to 0.089 | 11 | 0.074 | 0.04 | 0.072 | 0.059 | 0.089 | $0.062,0.083$ |
| 0.090 to 0.129 | 3 | 0.118 | - | 0.126 | 0.101 | 0.127 | - |
| 0.130 to 0.169 | 2 | 0.146 | - | - | 0.135 | 0.157 | - |
| 0.170 to 0.209 | 1 | 0.192 | - | - | - | - | - |
| 0.210 to 0.249 | 2 | 0.223 | - | - | 0.215 | 0.230 | - |
| 0.250 to 0.289 | 4 | 0.277 | 0.09 | 0.277 | 0.264 | 0.289 | $0.266,0.288$ |
| Group | 40 | 0.123 | 0.16 | 0.062 | 0.006 | 0.289 | $0.029,0.126$ |

Table 5.15. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the T.Sph HOA at the Second Follow-up examination.

### 5.5.2.11.8 Total Component of the HiAstig HOA

One individual exhibited an RMS value for the Total component of the HiAstig HOA of less than 0.010 microns, 33 of between 0.010 and 0.089 microns, 2 of between 0.130 and 0.149 microns and 4 individuals an RMS value greater than 0.189 microns (Table 5.16).

| Total Component |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| HiAstig RMS <br> (microns) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| Less than 0.010 | 1 | 0.009 | - | - | - | - | - |
| 0.010 to 0.029 | 5 | 0.022 | 0.01 | 0.021 | 0.019 | 0.027 | $0.021,0.023$ |
| 0.030 to 0.049 | 14 | 0.039 | 0.02 | 0.038 | 0.030 | 0.049 | $0.035,0.043$ |
| 0.050 to 0.069 | 8 | 0.059 | 0.03 | 0.058 | 0.051 | 0.069 | $0.053,0.063$ |
| 0.070 to 0.089 | 6 | 0.080 | 0.03 | 0.080 | 0.071 | 0.088 | $0.077,0.085$ |
| 0.090 to 0.109 | - | - | - | - | - | - | - |
| 0.110 to 0.129 | - | - | - | - | - | - | - |
| 0.130 to 0.149 | 2 | 0.136 | - | - | 0.136 | 0.137 | - |
| 0.150 to 0.169 | - | - | - | - | - | - | - |
| 0.170 to 0.189 | - | - | - | - | - | - | - |
| Greater than 0.189 | 4 | 0.723 | 0.67 | 0.617 | 0.384 | 1.071 | $0.464,0.826$ |
| Group | 40 | 0.236 | 0.45 | 0.050 | 0.009 | 1.071 | $0.036,0.077$ |

Table 5.16. The summary statistics for the distribution, amongst 40 of the 41 individuals within the case series in whom the measurement was available, of the RMS values for the Total Component of the HiAstig HOA at the Second Follow-up examination.

### 5.5.3 Explanatory Analysis of Associations between the Demographic, Structural and Functional Variables and eeach of the Three Components of each of the Eight

## HOAs Obtained at the Second Follow-up Examination

The results of the explanatory analysis at the Second Follow-up examination are given for the demographic variables in Table 5.17 and in Figure 5.5, for the visual performance variables in Table 5.18 and for the structural variables in Table 5.19 in Figure 5.6 and in Figure 5.7.

### 5.5.3.1. Age

No association was present between age as a continuous variable and each of the three components for each of the eight HOAs (Table 5.17) with the exceptions of the Corneal component of the Total HOA and the Internal component of the Tilt (S1) and T.Trefoil

HOAs (Figure 5.5). The magnitude of these three components each increased with increase in age.

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| Demography | Total | Tilt |  |  |  |  |  |  |  |
| Age continuous | 0.189 | 0.227 | 0.201 | 0.214 | 0.068 | 0.515 | 0.922 | 0.586 |  |


| CORNEAL |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |
| Age continuous | 0.016 | 0.365 | 0.159 | 0.663 | 0.154 | 0.220 | 0.219 | 0.952 |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age continuous | 0.065 | 0.043 | 0.117 | 0.126 | 0.032 | 0.348 | 0.939 | 0.758 |  |

Table 5.17. The probability value derived by ANOVA at the Second Follow-up examination for the association between age, as a continuous variable, and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.


Figure 5.5. The magnitude of the Corneal component of the Total HOA as a function of age at the Second Follow-up examination amongst 35 of the 41 individuals within the case series in whom the measurement was available.


Figure 5.5 Continued. The magnitude of the Internal component of the Tilt (S1) (Top) and the T.Trefoil (Bottom) HOAs at the Second Follow-up examination as a function of age amongst 35 of 41 individuals within the case series. Note the differences in the scaling of the ordinate between the three graphs.

### 5.5.3.2 Distance Visual Acuity

No association was present between distance visual acuity and any of the three components for each of the eight HOAs measured at the Second Follow-up examination with exeption of an inverse association for the Total component of the Tilt (S1) HOA ( $\mathrm{p}=0.043$ ) (Table 5.18).

### 5.5.3.3 Near Visual Acuity

An inverse association was present between the Total component of the Total, Tilt (S1)
and the T.Trefoil HOAs and the near visual acuity $\left(\mathrm{R}^{2} \leq 17.7 \%\right)$ (Table 5.18).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.209 | 0.043 | 0.236 | 0.110 | 0.085 | 0.322 | 0.133 | 0.882 |  |
| NVA | 0.008 | 0.017 | 0.081 | 0.066 | 0.020 | 0.284 | 0.634 | 0.763 |  |
| CS 1.5 cpd | 0.202 | 0.448 | 0.494 | 0.586 | 0.161 | 0.814 | 0.335 | 0.901 |  |
| CS 3 cpd | 0.257 | 0.122 | 0.193 | 0.281 | 0.076 | 0.370 | 0.500 | 0.632 |  |
| CS 6 cpd | 0.179 | 0.136 | 0.249 | 0.286 | 0.108 | 0.443 | 0.579 | 0.408 |  |
| CS 12 cpd | 0.265 | 0.289 | 0.427 | 0.370 | 0.103 | 0.985 | 0.325 | 0.456 |  |
| CS 18 cpd | 0.201 | 0.241 | 0.328 | 0.291 | 0.079 | 0.951 | 0.855 | 0.668 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.858 | 0.387 | 0.603 | 0.925 | 0.420 | 0.487 | 0.948 | 0.363 |  |
| NVA | 0.940 | 0.225 | 0.364 | 0.597 | 0.410 | 0.205 | 0.730 | 0.271 |  |
| CS 1.5 cpd | 0.997 | 0.497 | 0.848 | 0.980 | 0.924 | 0.534 | 0.994 | 0.651 |  |
| CS 3 cpd | 0.957 | 0.458 | 0.671 | 0.941 | 0.608 | 0.605 | 0.990 | 0.479 |  |
| CS 6 cpd | 0.535 | 0.636 | 0.978 | 0.974 | 0.999 | 0.659 | 0.281 | 0.825 |  |
| CS 12 cpd | 0.308 | 0.912 | 0.565 | 0.929 | 0.443 | 0.971 | 0.198 | 0.743 |  |
| CS 18 cpd | 0.415 | 0.905 | 0.668 | 0.682 | 0.503 | 0.966 | 0.264 | 0.732 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.894 | 0.395 | 0.388 | 0.227 | 0.140 | 0.592 | 0.384 | 0.869 |  |
| NVA | 0.101 | 0.493 | 0.228 | 0.360 | 0.085 | 0.474 | 0.805 | 0.549 |  |
| CS 1.5 cpd | 0.719 | 0.618 | 0.999 | 0.741 | 0.823 | 0.963 | 0.439 | 0.927 |  |
| CS 3 cpd | 0.735 | 0.263 | 0.547 | 0.282 | 0.492 | 0.620 | 0.396 | 0.743 |  |
| CS 6 cpd | 0.546 | 0.375 | 0.522 | 0.549 | 0.386 | 0.582 | 0.416 | 0.522 |  |
| CS 12 cpd | 0.461 | 0.291 | 0.597 | 0.733 | 0.233 | 0.965 | 0.186 | 0.458 |  |
| CS 18 cpd | 0.404 | 0.373 | 0.448 | 0.814 | 0.142 | 0.840 | 0.727 | 0.639 |  |

Table 5.18. The probability value derived by ANOVA at the Second Follow-up examination for the association between distance visual acuity, near visual acuity and each of the six spatial frequencies of the FACT 301 Test, and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 5.5.3.4 Contrast Sensitivity

No association was present between the contrast sensitivity at each of the five spatial
frequencies and any of the three components of each for the eight HOAs measured at the
Second Follow-up examination (Table 5.18).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.302 | 0.103 | 0.176 | 0.233 | 0.149 | 0.521 | 0.728 | 0.305 |  |
| CC Mean | 0.175 | 0.027 | 0.619 | 0.721 | 0.441 | 0.819 | 0.421 | 0.812 |  |
| CC Flattest | 0.080 | 0.013 | 0.628 | 0.632 | 0.529 | 0.781 | 0.402 | 0.977 |  |
| CECD | 0.427 | 0.076 | 0.757 | 0.924 | 0.640 | 0.951 | 0.506 | 0.808 |  |
| Sph Equiv | 0.156 | 0.999 | 0.161 | 0.291 | 0.386 | 0.126 | 0.881 | 0.936 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.978 | 0.554 | 0.496 | 0.622 | 0.340 | 0.931 | 0.898 | 0.748 |  |
| CC mean | 0.380 | 0.618 | 0.336 | 0.202 | 0.434 | 0.642 | 0.982 | 0.920 |  |
| CC flattest | 0.978 | 0.984 | 0.662 | 0.444 | 0.684 | 0.990 | 0.300 | 0.759 |  |
| CECD | 0.741 | 0.419 | 0.987 | 0.778 | 0.739 | 0.622 | 0.673 | 0.571 |  |
| Sph Equiv | 0.796 | 0.733 | 0.383 | 0.769 | 0.505 | 0.340 | 0.489 | 0.970 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Pupil | 0.760 | 0.132 | 0.216 | 0.105 | 0.187 | 0.647 | 0.566 | 0.489 |  |
| CC mean | 0.474 | 0.286 | 0.882 | 0.983 | 0.725 | 0.938 | 0.272 | 0.784 |  |
| CC flattest | 0.237 | 0.118 | 0.764 | 0.769 | 0.678 | 0.958 | 0.218 | 0.986 |  |
| CECD | 0.968 | 0.681 | 0.923 | 0.664 | 0.553 | 0.981 | 0.326 | 0.840 |  |
| Sph Equiv | 0.427 | 0.715 | 0.100 | 0.149 | 0.287 | 0.068 | 0.756 | 0.673 |  |

Table 5.19. The probability value derived by ANOVA at the Second Follow-up examination for the association between the magnitude of each of the structural variables pupil size, mean central corneal curvature (CC), flattest central corneal curvature (CC), Corneal endothelial cell density (CECD), and spherical equivalent (SE), and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 5.5.3.5 Dilated Pupil Diameter

No association was present between dilated pupil diameter and any of the three components for each of the eight HOAs measured at the Second Follow-up examination (Table 5.19).

### 5.5.3.6 Mean Corneal Curvature

No association was present between the mean corneal curvature and any of the three components for each of the eight HOAs measured at the Second Follow-up examination with the exception of an association between the Total component of the Tilt (S1) HOA and the mean corneal curvature (Table 5.19 and Figure 5.6). The magnitude of the Tilt (S1) HOA increased as the mean corneal curvature increased (i.e., flattened).


Figure 5.6. The magnitude of the Total component of the Tilt (S1) HOA as a function of the mean corneal curvature at the Second Follow-up examination amongst 40 of 41 individuals within the case series in whom the measurement was available.

### 5.5.3.7 Flattest Corneal Curvature

No association was found between the magnitude of the flattest corneal curvature and any of the three components for each of the eight HOAs with the exception of the Total component of the Tilt (S1) HOA (Table 5.19 and Figure 5.7). The latter increased with increase in the flattest corneal radius.


Figure 5.7. The magnitude of the Total component of the Tilt (S1) HOA as a function of the flattest corneal curvature at the Second Follow-up examination amongst 40 of 41 individuals within the case series in whom the measurement was available.

### 5.5.3.8 Corneal Endothelial Cell Density

No association was present between the corneal endothelial cell density and any of the three components for each of the eight HOAs at the Second Follow-up examination (Table 5.19).

### 5.5.3.9 Spherical Equivalent Refraction

No association was present between the spherical equivalent refraction and any of the three components for each of the eight HOAs at the Second Follow-up examination (Table 5.19).

### 5.5.4 Characteristics of the Case Series for the Investigation of the Change in the HOAs from the Pre-operative to the Second Follow-up Examinations

### 5.5.4.1 Spherical Equivalent Refraction

The distribution of the difference in the spherical equivalent refraction amongst 40 of the 41 individuals within the case series from the Pre-operative to the Second Follow-up examinations is shown in Table 5.20 and in Figure 5.8. The change in the spherical equivalent refraction from the Pre-operative examination to the Second Follow-up examination manifested as a reduction in myopia for the myopic eyes and a reduction in hyperopia for the hyperopic eyes. The majority of eyes became less myopic. Nine individuals exhibited a myopic change in spherical equivalent refraction. Amongst them, 1 individual exhibited a myopic change of -5.25 dioptres and 8 of between -1.00 dioptres and Plano. Twenty individuals exhibited a hyperopic change in spherical equivalent refraction of between 0.01 and 2.99 dioptres, and 8 of between 4.00 and 7.99 dioptres. Three individuals exhibited a hyperopic change of more than 7.99 dioptres, one of them of 14.00 dioptres. The spherical equivalent refraction could not been obtained in one individual.

| Difference in Spherical <br> Equivalent (Diopres) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -1.99 | 1 | -5.25 | - | - | - | - | - |
| -1.00 to -1.99 | 4 | -1.51 | 0.26 | -1.46 | -1.88 | -1.25 | $-1.59,-1.38$ |
| 0.00 to -0.99 | 4 | -0.31 | 0.13 | -0.25 | -0.5 | -0.25 | $-0.31,-0.25$ |
| 0.01 to +0.99 | 9 | 0.67 | 0.28 | 0.75 | 0.25 | 0.99 | $0.50,0.88$ |
| +1.00 to +1.99 | 6 | 1.52 | 0.20 | 1.50 | 1.25 | 1.75 | $1.41,1.69$ |
| +2.00 to +2.99 | 5 | 2.30 | 0.36 | 2.13 | 2.00 | 2.75 | $2.00,2.62$ |
| +3.00 to +3.99 | - | - | - | - | - | - | - |
| +4.00 to +4.99 | 2 | 4.19 | - | - | 4.00 | 4.38 | - |
| +5.00 to +5.99 | 1 | 5.63 | - | - | - | - | - |
| +6.00 to +6.99 | 3 | 6.71 | - | 6.75 | 6.50 | 6.88 | - |
| +7.00 to +7.99 | 2 | 7.31 | - | - | 7.25 | 7.38 | - |
| More than +7.99 | 3 | 10.00 | - | 8.00 | 8.00 | 14 | - |
| Group | 40 | 2.32 | 3.58 | 1.44 | -5.25 | 14.00 | $0.25,4.09$ |

Table 5.20. The summary statistics for the distribution of the change in the spherical equivalent refraction from the Pre-operative to the Second Follow-up examinations amongst 40 of the 41 individuals within the case series. A positive sign indicates a reduction in myopia or an increase in hyperopia. A negative sign indicates a reduction in hyperopia or an increase in myopia.


Figure 5.8. The change in the spherical equivalent refraction amongst 40 of the 41 individuals within the case series between the Second Follow-up examination and the Pre-operative examination. Data points in the lower left quadrant between the ordinate and the line of unity represent myopic individuals who became less myopic at the Second Follow-up examination. Data points in the lower left quadrant between the line of unity and the abscissa represent myopic individuals who became more myopic at the Second Follow-up examination. Data points in the upper left quadrant represent hyperopic individuals who became myopic at the Second Follow-up examination. Data points in the upper right quadrant represent hyperopic individuals who became less hyperopic at the Second Follow-up examination.

### 5.5.4.2 Distance Visual Acuity

The change in complete lines of the distance visual acuity from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series is shown in Figure 5.9. Sixteen individuals manifested an improvement in distance visual acuity of between 1 to 5 lines on the Snellen chart from the Pre-operative examination to the Second Follow-up examination, 27 of between 7 to 11 lines and 5 of between 12 to 13 lines. One individual manifested no improvement and one a reduction of 1 line.


|  | Improvement in Distance Visual Acuity (complete Snellen lines) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Lines of improvement | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
| Number of Individuals | 1 | 1 | 1 | 3 | 3 | 5 | 4 | 0 | 3 | 2 | 3 | 4 | 5 | 3 | 2 |

Figure 5.9. The change in distance visual acuity (complete Snellen lines) from the Preoperative to the Second Follow-up examinations amongst 40 of the 41 individuals within the case series. A negative number refers to a reduction in distance visual acuity at the Second Follow-up examination.

### 5.5.4.3 Near Visual Acuity

The change in lines of near visual acuity (Jaeger lines) from Pre-operative to the Second Follow-up to examinations, amongst 40 of the 41 individuals within the case series is shown in Figure 5.10. Twenty-three individuals manifested an improvement of between 1 to 5 lines (Jaeger notation) of near visual acuity from the Pre-operative to the Second Follow-up examinations, 5 of between 6 to 11 lines and 6 individuals of between 14 to 15 lines. Five individuals manifested no improvement and 2 individuals manifested a reduction of one line.


|  | Improvement in Near Visual Acuity (Jaegen lines) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Lines of improvement | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| Number of Individuals | 2 | 5 | 6 | 7 | 5 | 3 | 2 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 4 | 1 |

Figure 5.10. The change in lines of near visual acuity (lines of Jaeger notation) from the Pre-operative to the Second Follow-up examinations amongst 40 of the 41 individuals within the case series. A negative number refers to a reduction in distance visual acuity at the Second Follow-up examination.

### 5.5.4.4 Contrast Sensitivity

The distribution of the 41 individuals by the change in contrast sensitivity from the Preoperative to the Second Follow-up examinations (defined as the change in the number of columns on the FACT chart), for each of the spatial frequencies $1.5,3,6,12$ and 18 cycles per degree, is shown in Figure 5.11 and in Table 5.21. After the cataract was removed, the individual's ability to define contrast improved greatly for all spatial frequencies. This improvement was maintained at the Second Follow-up examination. For a spatial frequency of 1.5 cycles per degree, 23 individuals exhibited an improvement of between 4 to 7 columns, 15 of between one to 3 columns and one of 9 columns. One individual exhibited a reduction in contrast sensitivity of one column and one of 4 columns.

For a spatial frequency of 3 cycles per degree, 19 individuals exhibited an improvement in contrast sensitivity of between 6 to 9 columns, 20 of between one to 5 columns, one exhibited no change and one a reduction in contrast sensitivity of 2 columns. For a spatial frequency of 6 cycles per degree, 33 individuals exhibited an improvement in contrast sensitivity of between 3 to 7 columns, 2 of one column, one of 9 columns, 2 exhibited no change and 3 a reduction in contrast sensitivity of between one to 4 columns. For a spatial frequency of 12 cycles per degree, 21 individuals exhibited an improvement in contrast sensitivity of between 3 to 6 columns, 13 of between 1 to 2 columns, one of 9 columns, 4 exhibited no change in contrast sensitivity and 2 a reduction in contrast sensitivity of one column. For a spatial frequency of 18 cycles per degree, 29 individuals exhibited an improvement in contrast sensitivity of between one to 4 columns, 2 of between 6 columns, one of 8 columns, 8 exhibited no change in contrast sensitivity and one exhibited a reduction of one column.


Figure 5.11. The change in contrast sensitivity from the Pre-operative to the Second Follow-up examinations for spatial frequencies of $1.5,3$ and 6 cycles per degree for 40 of the individuals within the case series (Top; Middle and Bottom, respectively). The data points below the line of unity represent an improvement in contrast sensitivity. Note that each data point represents more than one individual.


Figure 5.11 Continued. The change in contrast sensitivity from the Pre-operative to the Second Follow-up examinations for spatial frequencies of $1.5,3$ and 6 cycles per degree for 40 of the individuals within the case series (Top and Bottom). The data points below the line of unity represent an improvement in contrast sensitivity. Note that each data point represents more than one individual. Note the difference in the scaling of the abscissa and the ordinate between the five graphs.

| Spatial Frequency (cpd) | Distribution of Individuals by the difference in Contrast Sensitivity (number of columns on the FACT chart) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 1.5 | 1 | - | - | 1 | - | 3 | 6 | 5 | 5 | 5 | 9 | 5 | - | 1 |
| 3 | - | - | 1 | - | 1 | 4 | 3 | 4 | 6 | 3 | 10 | 6 | 2 | 1 |
| 6 | 1 | 1 | - | 1 | 2 | 2 | - | 9 | 6 | 5 | 8 | 5 | - | 1 |
| 12 | - | - | - | 2 | 4 | 6 | 7 | 3 | 10 | 5 | 3 | - | - | 1 |
| 18 | - | - | - | 1 | 8 | 12 | 5 | 8 | 4 | - | 2 | - | 1 | - |

Table 5.21. The distribution of the change in the contrast sensitivity value (defined as the respective change in the number of columns) for spatial frequencies of $1.5,3,6,12$ and 18 cycles per degree from the Pre-operative to the Second Follow-up examinations for 40 of the 41 individuals within the case series. A positive value represents an improvement in contrast sensitivity.

### 5.5.4.5 Dilated Pupil Diameter

The distribution of the change in the dilated pupil diameter, measured with the OPD aberrometer, from the Pre-operative to the Second Follow-up examinations amongst 40 of the 41 individuals within the case series, is shown in Figure 5.12. The summary statistics for the change in the dilated pupil diameter from the Pre-operative to the Second Follow-up examinations is shown in Table 5.22. Thirty-one individuals exhibited smaller dilated pupil diameters at the Second Follow-up examination compared to the Preoperative examination. Of these, one individual exhibited a reduction in dilated pupil diameter of $2.13 \mathrm{~mm}, 13$ of between 1.21 and 0.41 mm and 17 of between 0.40 and 0.01 mm . Seven individuals exhibited an increase in dilated pupil diameter of between 0.00 and 0.79 mm and 2 exhibited an increase greater than 0.79 mm . The measurement of dilated pupil diameter was not available in one individual.


Figure 5.12. The change in the dilated pupil diameter from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. The data points above the line of unity represent a smaller dilated pupil diameter at the Second Follow-up examination.

| Difference in Dilated <br> Pupil Diameter $(\mathrm{mm})$ | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -2.00 | 1 | -2.13 | - | - | - | - | - |
| -2.00 to -1.61 | - | - | - | - | - | - | - |
| -1.60 to -1.21 | 1 | -1.27 | - | - | - | - | - |
| -1.20 to -0.81 | 3 | -1.10 | - | -1.12 | -1.17 | -1.00 | - |
| -0.80 to -0.41 | 9 | -0.61 | 0.15 | -0.56 | -0.87 | -0.42 | $-0.72,-0.52$ |
| -0.40 to -0.01 | 17 | -0.20 | 0.08 | -0.20 | -0.34 | -0.05 | $-0.26,-0.13$ |
| 0.00 to 0.39 | 4 | 0.23 | - | 0.24 | 0.06 | 0.37 | $0.18,0.28$ |
| 0.40 to 0.79 | 3 | 0.59 | - | 0.51 | 0.49 | 0.78 | - |
| More than 0.79 | 2 | 0.95 | - | - | 0.82 | 1.08 | - |
| Group | 40 | -0.27 | 0.60 | -0.24 | -2.13 | 1.08 | $-0.54,-0.07$ |

Table 5.22. The summary statistics for the change in the dilated pupil diameter from the Pre-operative to the Second Follow-up examinations amongst 40 of the 41 individuals within the case series, as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. A negative value represents a smaller dilated pupil diameter at the Second Follow-up examination. The measurement of dilated pupil diameter was not available in one individual.

### 5.5.4.6 Mean Corneal Curvature

The change in the mean corneal curvature from the Pre-operative to the Second Followup examinations, amongst 41 individuals within the case series, as measured by the OPD aberrometer is shown in Figure 5.13. The summary statistics for the change in the mean corneal curvature from the Pre-operative to the Second Follow-up examinationsis shown in Table 5.23. Two individuals exhibited a steepening of the mean corneal curvature of more than 0.149 mm and 19 of between 0.149 and 0.000 mm . Seventeen individuals exhibited a flattening of the mean corneal curvature of between 0.001 and 0.099 mm and 3 of more than 0.099 mm .


Figure 5.13. The change in the mean corneal curvature from the Pre-operative to the Second Follow-up examinations, amongst the 41 individuals within the case series, as measured with the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. The line indicates that of unity.

| Difference in Mean <br> Corneal Curvature <br> (mm) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -0.149 | 2 | -0.34 |  | - | -0.50 | -0.19 | - |
| -0.149 to -0.100 | 3 | -0.11 | - | -0.11 | -0.12 | -0.10 | - |
| -0.099 to -0.050 | 5 | -0.06 | 0.01 | -0.06 | -0.08 | -0.05 | $-0.08,-0.05$ |
| -0.049 to 0.000 | 11 | -0.02 | 0.01 | -0.02 | -0.04 | 0.00 | $-0.03,-0.01$ |
| 0.001 to 0.049 | 10 | 0.03 | 0.01 | 0.03 | 0.01 | 0.04 | $0.02,0.03$ |
| 0.050 to 0.099 | 7 | 0.07 | 0.01 | 0.07 | 0.06 | 0.09 | $0.06,0.09$ |
| more than 0.099 | 3 | 0.14 | - | 0.13 | 0.16 | 0.15 | - |
| Group | 41 | -0.01 | 0.11 | 0.00 | -0.50 | 0.15 | $-0.04,0.04$ |

Table 5.23. The summary statistics for the change from the Pre-operative to the Second Follow-up examinations, amongst the 41 individuals, as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer (OPD, Nidek). A negative value represents a steepening in the mean corneal curvature at the Second Follow-up examination.

### 5.5.4.7 Flattest Corneal Curvature

The change in the flattest corneal curvature from the Pre-operative to the Second Followup examinations, amongst 41 individuals within the case series, as measured by the OPD aberrometer is shown in Figure 5.14. The summary statistics for the change in the flattest corneal curvature from the Pre-operative to the Second Follow-up examinations, amongst the 41 individuals, is shown in Table 5.24. Sixteen individuals exhibited a steepening of the flattest corneal curvature at the Second Follow-up examination. Of these, one of more than $0.699 \mathrm{~mm}, 2$ of between 0.699 and 0.300 mm and 13 of between 1.99 and 0.00 mm . Twenty-five individuals exhibited a flattening of the flattest corneal curvature at the Second Follow-up examination. Twenty-four of them of between 0.001 and 0.200 mm and one of more than 0.200 mm .


Figure 5.14. The change in the flattest corneal curvature from the Pre-operative to the Second Follow-up examinations, amongst the 41 individuals within the case series, as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. The line indicates that of unity.

| Difference in Flattest <br> Corneal Curvature <br> (mm) | Number of <br> individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| More than -0.699 | 1 | -1.31 | - | - | - | - | - |
| -0.600 to -0.699 | - | - | - | - | - | - | - |
| -0.500 to -0.599 | 1 | -0.58 | - | - | - | - | - |
| -0.400 to -0.499 | - | - | - | - | - | - | - |
| -0.300 to -0.399 | 1 | -0.33 | - | - | - | - | - |
| -0.200 to -0.299 | 1 | -0.22 | - | - | - | - | - |
| -0.100 to -0.199 | - | - | - | - | - | - | - |
| 0.000 to -0.099 | 12 | -0.03 | 0.03 | -0.03 | -0.09 | 0.00 | $-0.04,-0.11$ |
| 0.001 to 0.100 | 18 | 0.05 | 0.03 | 0.05 | 0.01 | 0.10 | $-0.08,-0.04$ |
| 0.101 to 0.200 | 6 | 0.14 | 0.04 | 0.12 | 0.11 | 0.20 | $0.02,0.06$ |
| More than 0.200 | 1 | 0.22 | - | - | - | - | - |
|  | 41 | -0.02 | 0.25 | 0.02 | -1.31 | 0.22 | $-0.12,0.00$ |

Table 5.24. The summary statistics for the change from the Pre-operative to the Second Follow-up examinations amongst the 41 individuals, as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer. A negative value represents a steepening of the flattest corneal curvature at the Second Follow-up examination.

### 5.5.4.8 Corneal Endothelial Cell Density

The change in the corneal endothelial cell density (cells/mm²), from the Pre-operative to the Second Follow-up examinations amongst the 41 individuals within the case series, as measured by the Topcon SP 2000P specular microscope is shown in Figure 5.15. Twentynine individuals exhibited a reduction in corneal endothelial cell density (mean -773 cells $/ \mathrm{mm}^{2}$, SD 573) from the Pre-operative to the Second Follow-up examination whilst 12 individuals exhibited an increase in corneal endothelial cell density (mean 361 cells $/ \mathrm{mm}^{2}$, SD 251).


| Check-up | Number of <br> individuals | Mean <br> $\left(\right.$ Cells $\left./ \mathrm{mm}^{2}\right)$ | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pre-operative | 41 | 2157 | 487 | 2179 | 1263 | 3203 | 1903,2465 |
| Second Follow-up | 41 | 1744 | 696 | 1637 | 596 | 3257 | 1302,2293 |
| Difference | 41 | -413 | 708 | -265 | -2167 | 780 | $-935,172$ |
| Reduction | 29 | -733 | 573 | -611 | -2167 | -1630 | $-1027,-252$ |
| Increase | 12 | 361 | 251 | 250 | 105 | 780 | 202,463 |

Figure 5.15. The change in the corneal endothelial cell density from the Pre-operative to the Second Follow-up examination, amongst the 41 individuals within the case series, as measured by the Topcon SP 2000P specular microscope. Negative values represent a reduction in CECD and positive values an increase in CECD. The line indicates that of unity.

### 5.5.4.9 Higher Order Aberrations

The change in the RMS value of the Total component for each of the eight HOAs; namely, Total, Tilt (S1), High, T.coma, T.trefoil, T.4Foil, T.sph and HiAstig, respectively, from the Pre-operative to the Second Follow-up examinations as measured with the NAVEX Station software (Version2.10) and described by the Zernike polynomials for a 4.0 mm zone, are given in Tables 5.16-5.23, respectively. A measure of the HOAs for one individual could not be obtained. The reason for this is unknown.

### 5.5.4.9.1 Total Component of the Total HOA

The change in the Total component of the Total HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.16. Twenty-nine individuals exhibited a reduction of the Total component of the Total HOA (mean - 2.478 microns, SD 2.49) from the Pre-operative to the Second Follow-up examinations and 11 individuals exhibited an increase (mean 0.684 microns, SD 0.88 ). The ratio of the pre-operative median to the post-operative median was 1.732 for the Total component, 0.994 for the Corneal component and 1.800 for the Internal component (where a value of less than 1.0 indicates a larger HOA at the Preoperative examination).

### 5.5.4.9.2 Total Component of the Tilt (S1) HOA

The change in the Total component of the Tilt (S1) HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.17. Twenty-nine individuals exhibited a reduction of the Total component of the Total HOA (mean - 0.547 microns, SD 0.66) from the Pre-operative to the Second Follow-up examination and 11 individuals exhibited an increase (mean 0.445 microns, SD 0.57). The ratio of the pre-operative median to the post-operative median was 1.354 for the Total componenet, 1.074 for the Corneal component and 1.659 for the Internal component.


| Total component of Total HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 2.600 | 1.77 | 2.060 | 0.841 | 9.553 | $1.461,2.748$ |  |
| Second Follow-up | 40 | 1.420 | 0.68 | 1.189 | 0.530 | 3.336 | $0.937,1.707$ |  |
| Difference | 40 | 2.140 | 3.26 | -0.727 | -7.806 | 1.516 | $-1.992,0.015$ |  |
| Reduction | 29 | -2.478 | 2.49 | -1.087 | -7.806 | -0.011 | $-2.162,-0.659$ |  |
| Increase | 11 | 0.684 | 0.88 | 0.233 | 0.002 | 1.516 | $0.068,0.724$ |  |

Figure 5.16. The change in the RMS value of the Total component of the Total HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 5.5.4.9.3 Total Component of the High HOA

The change in the Total component of the High HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.18. Twenty-seven individuals exhibited a reduction of the Total component of the High HOA (mean - 0.895 microns, SD 1.60) from the Pre-operative to the Second Follow-up examinations and 13 individuals exhibited an increase (mean 0.680 microns, SD 0.99). The ratio of the pre-operative median to the post-operative median

Internal component.


| Total component of Tilt (S1) HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.595 | 0.43 | 0.455 | 0.033 | 1.804 | $0.305,0.829$ |  |
| Second Follow-up | 40 | 0.388 | 0.32 | 0.336 | 0.042 | 1.701 | $0.196,0.452$ |  |
| Difference | 40 | -0.521 | 0.64 | -0.143 | -1.306 | 1.054 | $-0.464,0.029$ |  |
| Reduction | 29 | -0.547 | 0.66 | -0.277 | -1.306 | -0.013 | $-0.622,-0.105$ |  |
| Increase | 11 | 0.445 | 0.57 | 0.263 | 0.029 | 1.054 | $0.102,0.499$ |  |

Figure 5.17. The change in the RMS value of the Total component of the Tilt (S1) HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 5.5.4.9.4 Total Component of the T.Coma HOA

The change in the Total component of the T.Coma HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series,
is shown in Figure 5.19. Thirty-one individuals exhibited a reduction of the Total component of the High HOA (mean -0.184 microns, SD 0.24) from the Pre-operative to the Second Follow-up examination and 9 individuals exhibited an increase (mean 0.232 microns, SD 0.33 ). The ratio of the pre-operative median to the post-operative median was 1.623 for the Total component, 0.820 for the Corneal component and 1.952 for the Internal component.


| Total component of High HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.808 | 0.82 | 0.686 | 0.152 | 5.306 | $0.499,0.849$ |  |
| Second Follow-up | 40 | 0.542 | 0.52 | 0.336 | 0.129 | 2.581 | $0.228,0.601$ |  |
| Difference | 40 | -0.831 | 1.47 | -0.307 | -3.663 | 1.054 | $-0.513,0.077$ |  |
| Reduction | 27 | -0.895 | 1.60 | -0.446 | -3.663 | -0.013 | $-0.623,-0.307$ |  |
| Increase | 13 | 0.680 | 0.99 | 0.175 | 0.007 | 1.821 | $0.083,0.448$ |  |

Figure 5.18. The change in the RMS value of the Total component of the High HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 5.5.4.9.5 Total Component of the T.Trefoil HOA

The change in the Total component of the T.Trefoil HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.20. Twenty-seven individuals exhibited a reduction of the Total component of the High HOA (mean -0.596 microns, SD 0.90) from the Pre-operative to the Second Follow-up examinations and 13 individuals exhibited an increase (mean 0.410 microns, SD 0.49). The ratio of the pre-operative median to the post-operative median was 1.978 for the Total componenet, 0.738 for the Corneal component and 2.401 for the Internal component.

### 5.5.4.9.6 Total Component of the T.4Foil HOA

The change in the Total component of the T.4Foil HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.21. Twenty-six individuals exhibited a reduction of the Total component of the High HOA (mean -0.566 microns, SD 1.03) from the Pre-operative to the Second Follow-up examination and 9 individuals exhibited an increase (mean 0.392 microns, SD 0.62 ). The ratio of the pre-operative median to the post-operative median was 2.331 for the Total componenet, 0.722 for the Corneal component and 2.607 for the Internal component.


| Total component of T.Coma HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.204 | 0.13 | 0.148 | 0.048 | 0.598 | $0.109,0.277$ |  |
| Second Follow-up | 40 | 0.126 | 0.12 | 0.091 | 0.031 | 0.636 | $0.073,0.135$ |  |
| Difference | 40 | -0.196 | 0.27 | -0.069 | -0.512 | 0.557 | $-0.166,-0.013$ |  |
| Reduction | 31 | -0.184 | 0.24 | -0.094 | -0.512 | -0.008 | $-0.193,-0.052$ |  |
| Increase | 9 | 0.232 | 0.33 | 0.039 | 0.000 | 0.557 | $0.014,0.108$ |  |

Figure 5.19. The change in the RMS value of the Total component of the T.Coma HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 5.5.4.9.7 Total Component of the T.Sph HOA

The change in the Total component of the T.Sph HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.22. Twenty-five individuals exhibited a reduction of the Total component of the High HOA (mean -0.104 microns, SD 0.14) from the Pre-operative to the Second Follow-up examinations and 9 individuals exhibited an increase (mean 0.111 microns, SD 0.13 ). The ratio of the pre-operative median to the post-operative median


| Total component of T.Trefoil HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.538 | 0.49 | 0.430 | 0.012 | 2.867 | $0.212, .690$ |  |
| Second Follow-up | 40 | 0.356 | 0.33 | 0.218 | 0.036 | 1.392 | $0.136,0.397$ |  |
| Difference | 40 | -0.542 | 0.82 | -0.140 | -2.047 | 0.834 | $-0.429,0.058$ |  |
| Reduction | 27 | -0.596 | 0.90 | -0.300 | -0.404 | -0.005 | $-0.585,-0.140$ |  |
| Increase | 13 | 0.410 | 0.49 | 0.260 | 0.010 | 0.834 | $0.089,0.382$ |  |

Figure 5.20. The change in the RMS value of the Total component of the T.Trefoil HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.


| Total component of T.4Foil HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.366 | 0.54 | 0.263 | 0.032 | 3.455 | $0.102,0.435$ |  |
| Second Follow-up | 40 | 0.225 | 0.31 | 0.113 | 0.015 | 1.470 | $0.056,0.227$ |  |
| Difference | 40 | -0.512 | 0.94 | -0.076 | -2.349 | 1.200 | $-0.328,0.032$ |  |
| Reduction | 26 | -0.566 | 1.03 | -0.234 | -2.349 | -0.018 | $-0.369,-0.082$ |  |
| Increase | 14 | 0.392 | 0.62 | 0.065 | 0.023 | 1.200 | $0.032,0.347$ |  |

Figure 5.21. The change in the RMS value of the Total component of the T.4Foil HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

### 5.5.4.9.8 Total Component of the HiAstig HOA

The change in the Total component of the HiAstig HOA from the Pre-operative to the Second Follow-up examinations, amongst 40 of the 41 individuals within the case series, is shown in Figure 5.23. Nineteen individuals exhibited a reduction of the Total component of the High HOA (mean -0.446 microns, SD 0.81) from the Pre-operative to the Second Follow-up examination and 21 individuals exhibited an increase (mean 0.275 microns, SD 0.49). The ratio of the pre-operative median to the post-operative median


| Total component of T.Sph HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.110 | 0.09 | 0.092 | 0.012 | 0.448 | $0.049,0.155$ |  |
| Second Follow-up | 40 | 0.090 | 0.08 | 0.062 | 0.006 | 0.289 | $0.029,0.126$ |  |
| Difference | 40 | -0.107 | 0.14 | -0.018 | -0.322 | 0.233 | $-0073,0.020$ |  |
| Reduction | 25 | -0.104 | 0.14 | -0.070 | -0.322 | -0.003 | $-0.093,-0.034$ |  |
| Increase | 15 | 0.111 | 0.13 | 0.033 | 0.000 | 0.233 | $0.014,0.155$ |  |

Figure 5.22. The change in the RMS value of the Total component of the T.Sph HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.

Figure 5.23 Overleaf. The change in the RMS value of the Total component of the HiAstig HOA from the Pre-operative to the Second Follow-up examination, amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, as measured with the NAVEX Station software (Version 2.10) and described by the Zernike polynomials for a 4.0 mm zone. The values above the line of unity represent a reduction in the HOA. A negative value in the Table represents a reduction in the HOA.


| Total component of HiAstig HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Examination | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Pre-operative | 40 | 0.135 | 0.31 | 0.051 | 0.009 | 1.071 | $0.036,0.085$ |  |
| Second Follow-up | 40 | 0.115 | 0.21 | 0.050 | 0.009 | 1.071 | $0.036,0.077$ |  |
| Difference | 40 | -0.367 | 0.69 | 0.000 | -1.659 | 1.013 | $-0.021,0.026$ |  |
| Reduction | 19 | -0.446 | 0.81 | -0.021 | -1.659 | -0.005 | $-0.069,-0.015$ |  |
| Increase | 21 | 0.275 | 0.49 | 0.026 | 0.000 | 1.013 | $0.010,0.041$ |  |

### 5.5.5 Explanatory Analysis of Associations between the Confounding Variables, the Change in the Appropriate Demographic, Structural and Functional Variables from the Pre-operative to the Second Follow-up Examination and the Corresponding <br> Change in each of the Three Components of each of the Eight HOAs

The results of the explanatory analysis of the change from the Pre-operative to the Second Follow-up examinations are given for the appropriate demographic and conflicting variables in Table 5.25 and Tables 5.26-5.28, for the visual performance variables in Table 5.29 and Figures 5.24-5.26, for the structural variables in Table 5.30 and Figures 5.27-5.31, respectively and for the type and severity of the cataract in Table 5.31.

### 5.5.5.1 Age and Gender

No association was present between age as a categorical variable and between gender and the change in each of the three components for each of the eight HOAs from the Preoperative examination to the Second Follow-up examination, amongst 40 of 41 individuals within the case series (Table 5.25). A measure of the HOAs for one individual could not be obtained. The reason for this is unknown.

### 5.5.5.2 Surgeon

No association was present between the four surgeons and the change in each of the three components for each of the eight HOAs from the Pre-operative examination to the Second Follow-up examination (Table 5.25).

### 5.5.5.3 Type of Intraocular Lens

An association was present between the type of IOL and the change in the Total and Internal components of the Total and HiAstig HOAs from the Pre-operative examination to the Second Follow-up examination (Table 5.25). An association was also present between the type of IOL and the change in the Total component of the Tilt (S1) HOA from the Pre-operative examination to the Second Follow-up examination (Table 5.25). Within the remit of the limited data set, the Forelens produced a greater reduction in these HOAs than did the B Lens (Table 5.26, Table 5.27 and Table 5.28).

### 5.5.5.4 Interval from the Pre-operative Examination to Surgery

No association was present between the interval from the Pre-operative examination to Surgery and the change in each of the three components for each of the eight HOAs from the Pre-operative examination to the Second Follow-up examination (Table 5.25).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorize | 0.137 | 0.810 | 0.634 | 0.438 | 0.702 | 0.531 | 0.071 | 0.880 |  |
| Gender | 0.336 | 0.631 | 0.153 | 0.433 | 0.217 | 0.291 | 0.248 | 0.440 |  |
| Surgeon | 0.728 | 0.887 | 0.707 | 0.664 | 0.765 | 0.709 | 0.542 | 0.612 |  |
| Type of IOL | 0.0005 | 0.045 | 0.382 | 0.167 | 0.482 | 0.209 | 0.528 | 0.0072 |  |
| Interval - Pre-op to <br> Second Follow-up | 0.848 | 0.378 | 0.815 | 0.835 | 0.569 | 0.980 | 0.380 | 0.781 |  |
| Interval - Pre-op to <br> Surgery | 0.788 | 0.724 | 0.842 | 0.822 | 0.723 | 0.670 | 0.632 | 0.341 |  |


| CORNEAL |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |
| Age categorize | 0.287 | 0.601 | 0.291 | 0.481 | 0.287 | 0.326 | 0.470 | 0.524 |
| Gender | 0.643 | 0.603 | 0.606 | 0.480 | 0.570 | 0.657 | 0.457 | 0.826 |
| Surgeon | 0.236 | 0.409 | 0.306 | 0.157 | 0.379 | 0.249 | 0.179 | 0.548 |
| Type of IOL | 0.998 | 0.972 | 0.998 | 0.865 | 0.983 | 0.989 | 0.958 | 0.946 |
| Interval - Pre-op to <br> Second Follow-up | 0.417 | 0.570 | 0.181 | 0.116 | 0.149 | 0.160 | 0.696 | 0.453 |
| Interval - Pre-op to <br> Surgery | 0.599 | 0.514 | 0.597 | 0.613 | 0.574 | 0.602 | 0.277 | 0.539 |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Demography | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Age categorize | 0.156 | 0.598 | 0.931 | 0.374 | 0.867 | 0.815 | 0.464 | 0.730 |  |
| Gender | 0.582 | 0.872 | 0.264 | 0.356 | 0.437 | 0.374 | 0.349 | 0.587 |  |
| Surgeon | 0.244 | 0.173 | 0.431 | 0.120 | 0.334 | 0.728 | 0.957 | 0.759 |  |
| Type of IOL | 0.0082 | 0.254 | 0.572 | 0.308 | 0.828 | 0.472 | 0.360 | 0.0002 |  |
| Interval - Pre-op to <br> Second Follow-up | 0.967 | 0.799 | 0.988 | 0.352 | 0.882 | 0.889 | 0.462 | 0.974 |  |
| Interval - Pre-op to <br> Surgery | 0.994 | 0.232 | 0.391 | 0.264 | 0.433 | 0.382 | 0.279 | 0.118 |  |

Table 5.25. The probability value derived by ANOVA for the associations between age as a categorical variable, from the Pre-operative examination to the Second Follow-up examination; gender; the conflicting variables (surgeon, type of IOL, time from the Preoperative examination to the Second Follow-up examination and the time from the Preoperative examination to surgery); and the corresponding change in each of the three components of each of the eight HOAs HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey. Note the independent variable gender was treated as such and not as a change in gender.

| Total component of Total HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |
| Forelens | 32 | -1.888 | 2.440 | -0.727 | -4.853 | 1.516 | $-3.260,-0.076$ |
| B Lens | 6 | -0.773 | 0.76 | -0.372 | -1.362 | 0.883 | $-0.801,0.321$ |
| Xcelens | 1 | -2.153 | - | - | - | - | - |
| Triplens | 1 | -7.806 | - | - | - | - | - |


| Total component of HiAstig HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |
| Forelens | 32 | -0.302 | 0.70 | -0.002 | -1.659 | 0.361 | $-1.154,-0.144$ |
| B Lens | 6 | 0.493 | 0.65 | 0.032 | -0.076 | 1.013 | $0.196,0.741$ |
| Xcelens | 1 | -0.999 | - | - | - | - | - |
| Triplens | 1 | -0.009 | - | - | - | - | - |

Table 5.26. The change in the RMS value of the Total component of the Total and HiAstig HOAs from the Pre-operative to the Second Follow-up examination amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, measured with the NAVEX Station software (Version 2.10), and described by the Zernike polynomials for a 4.0 mm zone (Top and Bottom).

| Internal component of Total HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |
| Forelens | 23 | -2.461 | 3.00 | -1.139 | -5.910 | 2.991 | $-3.684,0.766$ |
| B Lens | 5 | -0.880 | 1.01 | -0.279 | -0.790 | 1.591 | $-0.195,0.966$ |
| Xcelens | 1 | -2.027 | - | - | - | - | - |
| Triplens | 1 | -8.466 | - | - | - | - | - |

Table 5.27. The change in the RMS value of the Internal component of the Total HOA from the Pre-operative to the Second Follow-up examination amongst 27 of the 41 individuals within the case series in whom the measurement was avaliable, measured with the NAVEX Station software (Version 2.10), and described by the Zernike polynomials for a 4.0 mm zone.

| Internal component of HiAstig HOA |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |  |
| Forelens | 20 | 0.116 | 0.230 | 0.000 | -0.150 | 0.482 | $0.008,0.324$ |  |
| B Lens | 5 | 0.631 | 0.760 | 0.009 | -0.064 | 1.135 | $0.236,0.835$ |  |
| Xcelens | 1 | -1.158 | - | - | - | - | - |  |
| Triplens | 1 | -0.034 | - | - | - | - | - |  |

Table 5.27 Continued. The change in the RMS value of the Internal component of the HiAstig HOA from the Pre-operative to the Second Follow-up examination amongst 27 of the 41 individuals within the case series in whom the measurement was avaliable, measured with the NAVEX Station software (Version 2.10), and described by the Zernike polynomials for a 4.0 mm zone (Top and Bottom).

| Total component of Tilt (S1) HOA |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of IOL | Number of <br> individuals | Mean RMS <br> (microns) | SD | Median | Min | Max | IQR |
| Forelens | 32 | -0.474 | 0.57 | -0.122 | -1.127 | 0.597 | $-0.696,0.166$ |
| B Lens | 6 | 0.489 | 0.66 | -0.092 | -0.450 | 1.054 | $-0.074,0.678$ |
| Xcelens | 1 | -1.306 |  |  |  |  | - |
| Triplens | 1 | -0.733 |  |  |  |  | - |

Table 5.28. The change in the RMS value of the Total component of the Tilt (S1) HOA from the Pre-operative to the Second Follow-up examination amongst 40 of the 41 individuals within the case series in whom the measurement was avaliable, measured with the NAVEX Station software (Version 2.10), and described by the Zernike polynomials for a 4.0 mm zone.

### 5.5.5.5 Interval from the Pre-operative Examination to the Second Follow-up

## Examination

No association was present between the interval from the Pre-operative examination to the Second Follow-up examination and the corresponding change in each of the three components for each of the eight HOAs (Table 5.25).

### 5.5.5.6 Distance Visual Acuity

The improvement in the distance visual acuity from the Pre-operative to the SecondFollow-up examinations was associated with a reduction in the Total and the Internal components of the Total, High, T.Coma and T.4Foil HOAs $\left(\mathrm{R}^{2} \leq 17.6 \%\right.$ and $\mathrm{R}^{2} \leq 24.0 \%$, respectively) (Table 5.29 ). No associations were present for the visual acuity and the Corneal component of each of the eight HOAs (Table 5.29).

### 5.5.5.7 Near Visual Acuity

A weak association was present between the improvement in the near visual acuity and the Internal component of the T.Coma HOA $(\mathrm{p}=0.046)$ (Table 5.29).

### 5.5.5.8 Contrast Sensitivity

Consistent associations were present, from the Pre-operative examination to the Second Follow-up examinations, between the reduction in the magnitudes of the Total and Internal components of the Total HOA and the improvement, over the corresponding interval, in contrast sensitivity at spatial frequencies of $1.5(\mathrm{p}=0.023$ and $\mathrm{p}=0.013), 3$ (both $\mathrm{p}=0.002$ ) and 6 cycles per degree $(\mathrm{p}=0.008$ and $\mathrm{p}=0.007$ ) (Table 5.29 and Figures 5.24-5.26). An association was also present for the Total component of the Trefoil HOA and the improvement, over the corresponding interval, in contrast sensitivity at a spatial frequency of 18 cycles per degree $(\mathrm{p}=0.050)$ and for the Corneal component of the T.Sph HOA at a spatial frequency of 6 cycles per degree $(p=0.050)$ and HiAstig HOA at a spatial frequency of 1.5 cycles per degree ( $\mathrm{p}=0.047$ ).

| TOTAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| DVA | 0.008 | 0.395 | 0.026 | 0.012 | 0.142 | 0.010 | 0.438 | 0.710 |  |  |
| NVA | 0.082 | 0.353 | 0.344 | 0.071 | 0.613 | 0.337 | 0.737 | 0.822 |  |  |
| CS 1.5 cpd | 0.023 | 0.262 | 0.377 | 0.237 | 0.304 | 0.328 | 0.630 | 0.773 |  |  |
| CS 3 cpd | 0.002 | 0.055 | 0.267 | 0.090 | 0.326 | 0.146 | 0.522 | 0.925 |  |  |
| CS 6 cpd | 0.008 | 0.058 | 0.170 | 0.162 | 0.140 | 0.138 | 0.609 | 0.526 |  |  |
| CS 12 cpd | 0.051 | 0.096 | 0.364 | 0.590 | 0.114 | 0.614 | 0.989 | 0.616 |  |  |
| CS 18 cpd | 0.057 | 0.102 | 0.158 | 0.376 | 0.050 | 0.417 | 0.995 | 0.051 |  |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.403 | 0.514 | 0.606 | 0.605 | 0.671 | 0.649 | 0.222 | 0.456 |  |
| NVA | 0.834 | 0.990 | 0.994 | 0.778 | 0.997 | 0.983 | 0.193 | 0.741 |  |
| CS 1.5 cpd | 0.110 | 0.088 | 0.270 | 0.260 | 0.337 | 0.640 | 0.053 | 0.047 |  |
| CS 3 cpd | 0.300 | 0.323 | 0.559 | 0.425 | 0.674 | 0.596 | 0.138 | 0.288 |  |
| CS 6 cpd | 0.262 | 0.250 | 0.508 | 0.319 | 0.629 | 0.618 | 0.029 | 0.170 |  |
| CS 12 cpd | 0.288 | 0.370 | 0.553 | 0.398 | 0.594 | 0.711 | 0.115 | 0.353 |  |
| CS 18 cpd | 0.540 | 0.740 | 0.855 | 0.747 | 0.875 | 0.989 | 0.306 | 0.592 |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Visual <br> Performance | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| DVA | 0.006 | 0.307 | 0.029 | 0.014 | 0.111 | 0.022 | 0.268 | 0.845 |  |
| NVA | 0.097 | 0.454 | 0.313 | 0.046 | 0.560 | 0.367 | 0.150 | 0.967 |  |
| CS 1.5 cpd | 0.013 | 0.889 | 0.182 | 0.213 | 0.091 | 0.242 | 0.416 | 0.360 |  |
| CS 3 cpd | 0.002 | 0.097 | 0.262 | 0.183 | 0.238 | 0.235 | 0.697 | 0.589 |  |
| CS 6 cpd | 0.007 | 0.059 | 0.199 | 0.289 | 0.151 | 0.182 | 0.607 | 0.149 |  |
| CS 12 cpd | 0.077 | 0.155 | 0.494 | 0.938 | 0.200 | 0.642 | 0.432 | 0.342 |  |
| CS 18 cpd | 0.107 | 0.197 | 0.267 | 0.768 | 0.149 | 0.332 | 0.544 | 0.414 |  |

Table 5.29. The probability value derived by ANOVA for the association between the changes in distance visual acuity, near visual acuity and contrast sensitivity for the six spatial frequencies, from the Pre-operative examination to the Second Follow-up examination and the corresponding changes in each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.


Figure 5.24. The change in the Total component of the Total HOA from the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in contrast sensitivity for spatial frequencies of $1.5,3$ and 6 cycles per degree, amongst 40 of the 41 individuals within the case series in whom the measurement was available (Top; Middle and Bottom). Negative contrast sensitivity values refer to a reduced value at the Second Follow up examination and a negative RMS refers to a lower RMS at the Second Follow up examination.


Figure 5.24 Continued. The change in the Total component of the T.Trefoil HOA from the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in contrast sensitivity for a spatial frequency of 18 cycles per degree, amongst 40 of the 41 individuals within the case series in whom the measurement was available. Negative contrast sensitivity values refer to a reduced value at the Second Follow up examination and a negative RMS refers to a lower RMS at the Second Follow up examination. Note the difference in the scaling of the abscissa and the ordinate between the four graphs.


Figure 5.25. The change in the Corneal component of the T.Sph HOA from the Preoperative to the Second Follow-up examinations as a function of the corresponding change in contrast sensitivity for a spatial frequency of 6 cycles per degree, amongst 27 of the 41 individuals within the case series in whom the measurement was available. Negative contrast sensitivity values refer to a reduced value at the Second Follow up examination and a negative RMS refers to a lower RMS at the Second Follow up examination.


Figure 5.25 Continued. The change in the Corneal component of the HiAstig HOA from the Pre-operative to the Second Follow-up examination as a function of the corresponding change in contrast sensitivity for a spatial frequency of 1.5 cycles per degree, amongst 27 of the 41 individuals within the case series in whom the measurement was available. Negative contrast sensitivity values refer to a reduced value at the Second Follow up examination and a negative RMS refers to a lower RMS at the Second Follow up examination. Note the difference in the scaling of the abscissa and the ordinate between the two graphs.


Figure 5.26. The change in the Internal component of the Total HOA from the Preoperative to the Second Follow-up examination as a function of the corresponding change in contrast sensitivity for a spatial frequency of 1.5 cycles per degree, amongst 30 individuals of the 41 individuals within the case series in whom the measurement was available. Negative contrast sensitivity values refer to a reduced value at the Second Follow up examination and a negative RMS refers to a lower RMS at the Second Follow up examination.


Figure 5.26 Continued. The change in the Internal component of the Total HOA from the Pre-operative to the Second Follow-up examination as a function of the corresponding change in contrast sensitivity for spatial frequencies of 3 and 6 cycles per degree, amongst 30 individuals of the 41 individuals within the case series in whom the measurement was available (Top and Bottom). Negative contrast sensitivity values refer to a reduced value at the Second Follow up examination and a negative RMS refers to a lower RMS at the Second Follow up examination. Note the difference in the scaling of the abscissa between the three graphs.

| TOTAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| Pupil | 0.446 | 0.376 | 0.783 | 0.023 | 0.665 | 0.614 | 0.518 | 0.073 |  |  |
| CC Mean | 0.257 | 0.740 | 0.191 | 0.571 | 0.153 | 0.198 | 0.879 | 0.825 |  |  |
| CC Flattest | 0.711 | 0.792 | 0.407 | 0.816 | 0.291 | 0.192 | 0.712 | 0.881 |  |  |
| CECD | 0.386 | 0.707 | 0.936 | 0.456 | 0.936 | 0.890 | 0.916 | 0.796 |  |  |
| Sph Equiv | 0.0006 | 0.466 | 0.504 | 0.112 | 0.487 | 0.629 | 0.287 | 0.823 |  |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| Pupil | 0.311 | 0.324 | 0.361 | 0.284 | 0.426 | 0.327 | 0.188 | 0.259 |  |  |
| CC mean | 0.130 | 0.025 | 0.135 | 0.027 | 0.194 | 0.143 | 0.374 | 0.388 |  |  |
| CC flattest | $<0.001$ | 0.002 | $<0.001$ | $<0.001$ | $<0.001$ | $<0.001$ | 0.133 | 0.103 |  |  |
| CECD | 0.204 | 0.465 | 0.165 | 0.183 | 0.130 | 0.194 | 0.983 | 0.993 |  |  |
| Sph Equiv | 0.068 | 0.175 | 0.104 | 0.109 | 0.109 | 0.083 | 0.180 | 0.474 |  |  |


| INTERNAL |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |  |
| Structural | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |
| Pupil | 0.362 | 0.098 | 0.874 | 0.017 | 0.782 | 0.753 | 0.504 | 0.397 |  |  |
| CC mean | 0.012 | 0.140 | 0.195 | 0.621 | 0.054 | 0.374 | 0.776 | 0.718 |  |  |
| CC flattest | 0.274 | 0.021 | 0.282 | 0.054 | 0.160 | 0.465 | 0.651 | 0.971 |  |  |
| CECD | 0.149 | 0.287 | 0.529 | 0.216 | 0.374 | 0.735 | 0.440 | 0.923 |  |  |
| Sph Equiv | 0.008 | 0.113 | 0.221 | 0.075 | 0.079 | 0.457 | 0.636 | 0.582 |  |  |

Table 5.30. The probability value derived by ANOVA for the association between the change in the magnitude of each of the structural variables pupil size, mean central corneal curvature (CC), flattest central corneal curvature (CC), corneal endothelial cell density (CECD), and spherical equivalent (SE), from the Pre-operative to the Second Follow-up examinations and the corresponding changes in each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 5.5.5.9 Dilated Pupil Diameter

Some association was present between the change from the Pre-operative to the Second Follow-up examinations, in the Total and Internal components of the T.Coma HOA ( $\mathrm{p}=0.023$ and $\mathrm{p}=0.017$, respectively) and the corresponding change in the dilated pupil diameter (Table 5.30 and Figure 5.27).

This apparent inverse association indicates that the magnitude of the T.Coma HOA declines with increase in the dilated pupil diameter, however, the apparent relationship is seemingly influenced by the presence of several prominent outliers particularly for the Internal Component of the T.Coma HOA.


Figure 5.27. The change in the Total and Internal components of the T.Coma HOA from the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in the dilated pupil diameter amongst 39 and 29 of the 41 individuals within the case series, in whom the measurement was available, for the Total and the Internal components, respectively. A negative pupil diameter refers to a smaller pupil at the Second Follow-up examination and a negative RMS refers to a lower RMS at the Second Follow-up examination. Note the difference in the scaling of the ordinate between the two graphs. The circled data points indicate outlying values.

### 5.5.5.10 Mean Corneal Curvature

The magnitude of the change in the Corneal component of the Tilt (S1), T.Coma HOAs and of the Internal component of the T.Coma HOA from the Pre-operative to the Second Follow-up examinations decreased as the corresponding change in the mean corneal curvature increased i.e., flattened ( $\mathrm{p}=0.025, \mathrm{p}=0.027$ and $\mathrm{p}=0.012$, respectively) (Table 5.30 and Figure 5.28). However, these relationships seem to be influenced by outliers.


Figure 5.28. The change in the Corneal component of the Tilt (S1) and the T.Coma HOAs from the the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in the mean corneal curvature amongst 30 of the 41 individuals within the case series in whom the measurement was available (Top and Bottom). A negative mean corneal curvature refers to a steeper cornea at the Second Follow-up examination and a negative RMS refers to a lower RMS at the Second Follow-up examination. The circled data points indicate outlying values.


Figure 5.28 Continued. The change in the Internal component of the Total HOA from the the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in the mean corneal curvature amongst 30 of the 41 individuals within the case series in whom the measurement was available. A negative mean corneal curvature refers to a steeper cornea at the Second Follow-up examination and a negative RMS refers to a lower RMS at the Second Follow-up examination. Note the difference in the scaling of the ordinate between the three graphs. The circled data points indicate outlying values.

### 5.5.5.11 Flattest Corneal Curvature

The magnitude of the change in the flattest corneal curvature from the Pre-operative to the Second Follow-up examinations was associated with the corresponding change in the Corneal component of the Total, Tilt (S1), High, T.Coma, T.Trefoil and T.4Foil HOAs ( $\mathrm{p}<0.0001, \mathrm{p}=0.002, \mathrm{p}<0.0001, \mathrm{p}<0.0001, \mathrm{p}<0.0001, \mathrm{p}<0.0001$, respectively) and with the Internal component of the Tilt ( S 1 ) HOA ( $\mathrm{p}=0.021$ ) (Table 5.30 and Figures 5.29, 5.30 respectively). However, all such associations appear to have resulted from obvious outliers.


Figure 5.29. The change in the Corneal component of the Total, Tilt (S1) and High HOAs from the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 30 of the 41 individuals within the case series in whom the measurement was available (Top; Middle and Bottom). A negative change in flattest corneal curvature indicates a steeper curvature at the Second Follow-up examination and a negative change in HOA refers to a smaller RMS at the Second Follow-up examination. The circled data points indicate outlying values.


Figure 5.29 Continued. The change in the Corneal component of the T.Coma, T.Trefoil and T.4Foil HOAs from the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 30 of the 41 individuals within the case series in whom the measurement was available (Top; Middle and Bottom). A negative change in flattest corneal curvature indicates a steeper curvature at the Second Follow-up examination and a negative change in HOA refers to a smaller RMS at the Second Follow-up examination. Note the difference in the scaling of the ordinate between the six graphs. The circled data points indicate outlying values.


Figure 5.30. The change in the Internal component of the Tilt (S1) HOA from the Preoperative to the Second Follow-up examinations as a function of the corresponding change in the flattest corneal curvature amongst 30 of the 41 individuals within the case series in whom the measurement was available. A negative change in flattest corneal curvature indicates a steeper curvature at the Second Follow-up examination and a negative change in HOA refers to a smaller RMS at the Second Follow-up examination. Note the difference in the scaling of the ordinate between this and the previous graphs. The circled data points indicate outlying values.

### 5.5.5.12 Corneal Endothelial Cell Density

No association was present between the change in the corneal endothelial cell density from the Pre-operative to the Second Follow-up examinations and the corresponding change of any of the three components for each of the eight HOAs (Table 5.30).

### 5.5.5.13 Spherical Equivalent Refraction

An association was present between the change in the Total and Internal components of the Total HOA ( $\mathrm{p}=0.0006$ and $\mathrm{p}=0.008$, respectively) from the Pre-operative to the Second Follow-up examinations and the corresponding change in the spherical equivalent
refraction (Table 5.30 and Figure 5.31). Both components decreased with increase in the magnitude of the reduction in myopia/ increase in hyperopia.


Figure 5.31. The change in the Total and Internal components of the Total HOA from the Pre-operative to the Second Follow-up examinations as a function of the corresponding change in the spherical equivalent refraction amongst 40 and 29 of the 41 individuals within the case series for the Total and the Internal components, respectively in whom the measurement was available (Top and Bottom). A negative change in the spherical equivalent refraction indicates a reduction in myopia/ increase in hyperopia at the Second Follow-up examination and a negative change in HOA refers to a smaller RMS at the Second Follow-up examination. Note the difference in the scaling of the ordinate between the two graphs.

### 5.5.5.14 Cataract Type

Some association was present between nuclear opalescence and the magnitude of the change in the Total component for the High HOA from the Pre-operative to the Second Follow-up examinations and between both nuclear opalescence and nuclear colour and the magnitude of the change in the Total component for the T.4Foil HOA from the Preoperative to the Second Follow-up examinations (Table 5.31). An association was also present between cortical cataract and the magnitude of the change in the Internal component of the Total HOA ( $\mathrm{p}=0.043$ ) and between nuclear colour and the magnitude of the change in the Internal component of the T.4Foil HOA ( $\mathrm{p}=0.025$ ) from the Preoperative to the Second Follow-up examination (Table 5.31).

| TOTAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| NO | 0.671 | 0.379 | 0.035 | 0.230 | 0.290 | 0.010 | 0.273 | 0.311 |  |
| NC | 0.540 | 0.361 | 0.064 | 0.234 | 0.418 | 0.020 | 0.330 | 0.317 |  |
| C | 0.076 | 0.645 | 0.624 | 0.120 | 0.815 | 0.681 | 0.993 | 0.248 |  |
| P | 0.714 | 0.482 | 0.916 | 0.704 | 0.535 | 0.600 | 0.444 | 0.389 |  |


| CORNEAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| NO | 0.309 | 0.227 | 0.304 | 0.253 | 0.350 | 0.365 | 0.167 | 0.168 |  |
| NC | 0.313 | 0.239 | 0.310 | 0.269 | 0.348 | 0.369 | 0.236 | 0.177 |  |
| C | 0.183 | 0.230 | 0.146 | 0.080 | 0.153 | 0.114 | 0.914 | 0.723 |  |
| P | 0.845 | 0.920 | 0.690 | 0.695 | 0.634 | 0.592 | 0.775 | 0.734 |  |

Table 5.31. The probability value derived by ANOVA for the association between the cataract type at the Pre-operative examination (Nuclear Opalescence, NO; Nuclear Colour, NC; Anterior Cortical, C; posterior subcapsular cataract, P) and the change in the Total and Corneal components of each of the eight HOAs from the Pre-operative to the Second Follow-up and the examinations (Top: Total, Bottom: Corneal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

| INTERNAL |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| NO | 0.546 | 0.241 | 0.051 | 0.202 | 0.213 | 0.244 | 0.538 | 0.996 |  |
| NC | 0.476 | 0.227 | 0.054 | 0.175 | 0.230 | 0.025 | 0.501 | 0.995 |  |
| C | 0.043 | 0.195 | 0.278 | 0.900 | 0.193 | 0.497 | 0.838 | 0.536 |  |
| P | 0.985 | 0.713 | 0.628 | 0.596 | 0.814 | 0.564 | 0.901 | 0.922 |  |

Table 5.31 Continued. The probability value derived by ANOVA for the association between the cataract type at the Pre-operative examination (Nuclear Opalescence, NO; Nuclear Colour, NC; Anterior Cortical, C; posterior subcapsular cataract, P) and the change in the Internal component of each of the eight HOAs from the Pre-operative to the Second Follow-up and the examinations. Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 5.6 Discussion

The case series comprised 41 individuals from the original case series of 99 individuals who underwent the Pre-operative examination. It was felt that the retention in the study of such a relatively large number of individuals (42\%) after a period of approximately 80 weeks following surgery (mean 80.19, SD 17.61; median 85.14, IQR 80.00, 89.57) represented an excellent outcome, given that all individuals were volunteers and that no financial inducement was offered for participation in the study.

It was shown in Chapter 4 that, based upon 64 and 45, respectively, of the 67 individuals, both the Total (slope $-0.33 ; \mathrm{R}^{2}=45 \%$ ) and the Internal (slope $-0.39 ; \mathrm{R}^{2}=51 \%$ ) components of the Total HOA declined with reduction in myopia/ increase in hyperopia from the Preoperative examination to the First Follow-up examination. Similar findings were present from the Pre-operative examination to the Second Follow-up examination based upon 40 and 29 individuals, respectively (Total component: slope $-0.29 ; \mathrm{R}^{2}=36 \%$; Internal component: slope $-0.45 ; \mathrm{R}^{2}=54 \%$ ).

The findings also confirm the results from Chapter 3. The results from Chapters 3, 4 and 5 provide compelling evidence for the increase in the Total HOA with increase in myopic spherical equivalent refraction particularly that associated with age-related cataract.

The summary statistics for the corneal endothelial cell density for the 41 individuals at the Second Follow-up examination were mean 1744 cells $/ \mathrm{mm}^{2}$, SD 696.42 and median 1637, IQR 1302, 2293. The summary statistics for the corneal endothelial cell density for the same 41 individuals at the Pre-operative and at the First Follow-up examinations were mean 2157 cells $/ \mathrm{mm}^{2}$, SD 486.87; median 2179, IQR 1903, 2465; and mean 1635 cells $/ \mathrm{mm}^{2}$, SD 573.82; median 1636 , IQR 1277, 2090, respectively. The changes in corneal endothelial cell density from the Pre-operative to the First Follow-up examinations were $21 \%$ (SD 0.28), from the First Follow-up to the Second Follow-up examinations were $12.5 \%$ (SD 0.32) and from the Pre-operative to the Second Follow-up examinations were $18 \%$ (SD 0.29). As discussed in Chapter 4, the reduction in corneal endothelial cell density at the First Follow-up was notably higher than that of the literature. The clinically equivalent reduction in corneal endothelial cell density at the Second Follow-up examination confirms this finding.

It was shown in Chapter 4 that, for the 67 individuals, the magnitude of the difference in the Corneal component of the T.Coma HOA from the Pre-operative examination to the First Follow-up examination increased linearly as the corresponding corneal endothelial cell density decreased $\left(\mathrm{R}^{2}=12 \%\right)$.

A similar outcome was also present when the relationship was recalculated for the 41 of the 67 individuals who attended both the First and the Second Follow-up examinations $\left(\mathrm{R}^{2}=19 \%\right)$. The slope of the latter was steeper than the former by two orders of magnitude.

However, no association was present for the corresponding relationship between the Second Follow-up examination and the Pre-operative examination.

It was hypothesized in Chapter 4 that the magnitude of the change in the Corneal component of the T.Coma HOA from the Pre-operative to the First Follow-up examinations increased as a result of post-operative corneal oedema rather than from a reduction in Corneal endothelial cell density as a consequence of the surgical intervention. The absence of an association for the change in the Corneal component of T.Coma from the Pre-operative to the Second Follow-up examinations suggests that the transient corneal oedema had subsided by the time of the Second Follow-up examination.

It was also shown in Chapter 4 that for the First Follow-up examination, the magnitude of the contrast sensitivity at spatial frequencies of 1.5 and 3 cycles per degree, in particular, improved as the Corneal components of the Total, Tilt (S1), High and T.Trefoil HOAs declined. No such associations were present at the Second Follow-up examination. The absence of such an association at the Second Follow-up examination is compatible with the hypothesis of the existence of post-operative corneal oedema at the First Follow-up examination and which resolved by the Second Follow-up examination.

No association was present between the change in the contrast sensitivity from the Preoperative examination to the Second Follow-up examination and the corresponding change in any of the three components for each of the eight HOAs. Such a finding is compatible with the lack of association from the Pre-operative examination to the First Follow-up examination described in Chapter 4.

It was shown in Chapter 4 that the magnitude of the change in the Corneal component of the Total, High and T.Trefoil HOAs from the Pre-operative to the First Follow-up examinations seemingly increased as the change in the mean corneal curvature flattened.

However, it was suggested that this relationship arose from the presence of two obvious outlying data points.

No association was present at the Second Follow-up examination between either mean or flattest corneal curvature and any of the three components for each of the eight HOAs. However, the magnitude of the change in the Corneal components of the Tilt (S1), T.Coma HOAs and of the Internal component of the Total HOA from the Pre-operative to the Second Follow-up examinations decreased as the corresponding change in the mean corneal curvature increased i.e., flattened. These latter relationships were much less affected by outlying data points and are more likely to be representative of the 'true' situation. It can be speculated that the presence of apparent outliers in the corresponding relationships described in Chapter 4 may have arisen from corneae still compromised at the First Follow-up examination by the surgery. It can be further speculated that such compromise would have declined by the Second examination. The finding of a reduction in HOA with an increase in the flattening of the mean corneal curvature from the Preoperative to the Second Follow-up examination is compatible with the reduction in myopic spherical equivalent refraction form the Pre-operative to each of the two Followup examinations, albeit that such an outcome was largely attributable to the cataract extraction and IOL implantation.

It was shown in Chapter 4 that the magnitude of the change in the Corneal component of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs, increased as the magnitude of the change in the flattest corneal curvature from the Pre-operative to the First Follow-up examinations increased. However, it was noted that all such associations appeared to have resulted from two obvious outlying data points corresponding to individuals with study numbers 6 and 43, respectively.

It was not known whether such data points represented 'true' values and thereby implicated flattest corneal curvature as a generator of HOAs or whether such points were artifactual and that the flattest corneal curvature was not implicated.

In the current study, the magnitude of the change in the Corneal component of the T.4Foil HOA, as well as those of the Total, Tilt (S1), High, T.Coma, T.Trefoil HOAs, also increased as the magnitude of the change in the flattest corneal curvature from the Preoperative to the Second Follow-up examinations increased. However, these relationships for the Second Follow-up examination were also influenced by the presence of outliers, most notably those from individuals with study numbers 6 and 11, respectively. It should be noticed that the NAVEX Station (Version 2.10) software could not determine the Corneal component for any of the HOAs from the individual with a study number 43 at the Second Follow-up examination. It cannot be ruled out that 'spurious but true' changes in the vertical corneal meridian could have occurred as a consequence of the incision and the resultant wound healing process.

An apparent problem with outliers also occurred in terms of the relationship of the change, from the Pre-operative examination to the Second Follow-up examination, of dilated pupil diameter and the given component of the given HOA. Apparent associations were present between the Total and Internal components of the Total and T.Coma HOAs, respectively, and the change in the HOA from the Pre-operative to the Second Follow-up examination. The latter seemed to increase as the change in the diameter of the dilated pupil decreased. Such an outcome is clearly contrary to that of established opinion whereby the magnitude of any given HOA increases with increase in pupil diameter (Liang and Williams 1997; Wang et al 2003; Hu et al 2004; Wu et al 2008; Fritzsch et al 2011).

As occurred with the study described in Chapter 4, a number of individuals were consistently identified as contributors of obvious outliers in the various relationships described in the current study.

Fifteen individuals contributed outliers to the outcomes of the current study of whom 4 (individuals with study numbers $6,14,37$ and 79 ) were common to the outcomes of the study described in Chapter 4. In addition, as was mentioned previously, the individual HOAs at the Second Follow-up examination could not be obtained from the individual with study number 43 who contributed apparent outlying data points in the study described in Chapter 4. No particular feature could again be determined in the characteristics of either the 15 individuals who contributed apparent outlying data points in the current study or in those 4 individuals who also contributed outlying data points in the study described in Chapter 4.

It was shown in Chapter 4 that the magnitude of the dilated pupil diameter was smaller at the First Follow-up examination compared to that at the Pre-operative examination. The summary statistics for the dilated pupil diameter of the 39 individuals who attended for all three examinations are given in Table 5.32. The dilated pupil diameter at the Second Follow-up examination was larger than that at the First Follow-up examination but smaller than that at the Pre-operative examination ( $\mathrm{p}<0.001$ ).

The larger dilated pupil at the Second Follow-up examination compared to the First Follow-up examination indicates some longer term recovery in either the dilatator pupillae muscle function (Komatsu et al 1997; Möller et all 2000) or the corneal metabolic function (Lohmann et al 1996; Hooman et al 2000) or both.

> Dilated Pupil Diameter (mm)

| Examination | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pre-operative | 39 (of 99) | 6.17 | 0.82 | 6.22 | 4.50 | 8.03 | $5.58,6.67$ |
| First Follow-up | 39 (of 67) | 5.72 | 0.87 | 5.78 | 3.72 | 7.46 | $5.17,6.28$ |
| Second Follow-up | 39 (of 41) | 5.90 | 0.78 | 5.90 | 4.24 | 7.45 | $5.30,6.38$ |

Table 5.32. The summary statistics for the distribution of the dilated pupil diameter, amongst 39,39 and 39 of the 99,67 and 41 individuals, respectively, within the case series, as measured by the Nidek Optical Path Difference Scanning System ARK-10000 aberrometer at the three different examinations.

A comparison of the characteristics of each of the three components of each of the eight post-operative HOAs, described in this Chapter and in the previous Chapter, with those occurring in 'less severe' cataract and in individuals with a clear media was beyond the scope of this thesis. Nevertheless, a pilot study using retrospective data was, therefore, undertaken and is described in Chapter 6.

## CHAPTER 6

## COMPARISON OF THE HIGHER ORDER ABERRATIONS, OBTAINED PREAND POST-OPERATIVELY, WITH THOSE IN ‘LESS SEVERE’ CATARACT AND WITH THOSE EXHIBITING CLEAR MEDIA

### 6.1 Introduction

It was shown in Chapter 3 that few studies have investigated the magnitude of the various HOAs in individuals with age-related cataract (Kuroda et al 2002; Sachdev et al 2004; Fujikado et al 2004; Kim et al 2006; Fujikado et al 2006; Rocha et al 2007; Lee et al 2008; Wali et al 2009).

The characteristics, within the case series, of the HOAs present in eyes with age-related cataract, before and after cataract extraction and IOL implantation, were described in Chapters 3, 4 and 5. It was shown that the Total and Internal components of the Total HOA in the pre-operative eye decreased as the spherical equivalent refraction became less myopic/ more hyperopic. Both components declined as the post-operative spherical equivalent refraction tended to Plano. The magnitude of the latter reduction varied between the four types of IOL. The Internal components of the Tilt (S1) HOA increased with increased severity of posterior sub-capsular cataract and that of T.Sph and of HiAstig HOAs increased with severity of cortical cataract and of combined nuclear colour and cortical cataract. However, the magnitudes of these outcomes, in terms of microns, relative to those with clear media and to those associated with 'less severe' cataract, are unknown.

It was shown in Chapter 3 that an extensive literature exists on the magnitudes of the various HOAs in the normal eye (Marcos et al 2000; Porter et al 2001; Castejon-Mochon
et al 2002; Paquin et al 2002; Shah et al 2003; Hu et al 2004; Klyce et al 2004; Zadok et al 2005; Burakgazi et al 2006; Bisneto et al 2007; Goebels et al 2008; Kwan et al 2009; Karimian et al 2010). Although, a number of studies have been undertaken with the NIDEK Optical Path Difference Scanning System ARK-10000 aberrometer (Shah et al 2003; Klyce et al 2004; Zadok et al 2005; Burakgazi et al 2006; Goebels et al 2008), the general literature concerning the magnitude of the various HOAs in the normal eye report values for any given HOA in terms of a Total component rather than for the individual components Total, Corneal and Internal. In addition, those studies undertaken with the OPD aberrometer have determined the HOAs for a 6.0 mm zone diameter rather than for the 4.0 mm zone diameter used in the current study.

Clearly, there is a need to place the outcomes of the various HOAs associated with the pre- and post-operative characteristics of the cataractous eye in the context of the magnitudes present in eyes with 'less severe' cataract. In addition, it would be useful to compare the former to those in the normal eye. The acquisition of such data by means of a cross-sectional controlled study was beyond the scope and timeframe of the thesis (Chapter 2). Nevertheless, the compilation of such data sets, retrospectively, was possible by using the information contained within the medical notes of patients attending the Einaim Refractive Clinic in Beer-Sheva, Israel.

### 6.2 Aim

The purpose of the current study was threefold. Firstly, to compare the characteristics and magnitudes of the distribution of each of the three components for each of the eight HOAs in the pre- and post-operative catactous eye, with those in eyes with 'less severe' cataract referenced to the NIDEK OPD Scanning System ARK-10000 aberrometer for a
4.0 mm zone diameter. Secondly, to compare the same pre- and post-operative outcomes to those with clear media. Thirdly, to explore any association between the structural variables, corneal curvature, spherical equivalent and the primary cataract type and severity; the functional variables, distance and near visual acuity; and the magnitudes of each of the Total, Corneal and Internal components for each of the eight HOAs in the individuals with 'less severe' cataract and in those with a clear media.

### 6.3 Methods

### 6.3.1 Case Series

Three case series were used for the study.

### 6.3.1.1 Pre- and Post-operative Case Series

The case series comprised 36 eyes from the 36 individuals who had attended both the preoperative and the Second post-operative examinations and in whom the NAVEX Station software (Version2.10) had successfully generated all three components for each of the eight HOAs.

### 6.3.1.2 'Less Severe' Cataract Case series

The case series comprised 27 individuals, consecutively identified from the first 100 appropriate medical records, at the Einaim Refractive Clinic, with cataract considered insufficiently severe to warrant surgery.

All individuals in the case series conformed to the inclusion criteria described in Chapter 3, namely, an age greater than 18 years; absence of corneal scarring and/ or pterygium in the eye designated; no ocular trauma in the designated eye; intra-ocular pressure less than 22 mmHg ; no previous or current ocular surgery or co-existing disease in the designated eye including glaucoma, age-related macular degeneration, diabetic retinopathy or any other retinal disease likely to cause a reduction in vision; and a negative history of useage of topical ophthalmic drops.

### 6.3.1.3 Clear Media Case Series

The case series comprised 49 individuals, consecutively identified from a second set of 100 appropriate medical records of those attending the Einaim Refractive Clinic for potential refractive surgery. All individuals in the case series conformed to the same inclusion criteria for the individuals with less severe cataract with the exception that they manifested a normal appearance to the crystalline lens.

### 6.3.2 Experimental Procedures

All individuals had undergone a standard ophthalmic examination undertaken by an optometrist and by an ophthalmologist including subjective refraction (distance and near); visual acuity, obtained with and without correction, using a high contrast Snellen chart; gonioscopy, with a Goldmann two mirror lens; Goldmann applanation tonometry; anterior segment slit-lamp biomicroscopy; and fundus examination using a Volk +90 dioptres lens through a pupil dilated with 1-2 drops of Tropicamide $1 \%$. Aberrometry had been undertaken through the dilated pupil prior to gonioscopy and to applanation
tonometry. The latter had been undertaken following installation of two drops of Oxybuprocaine 0.4\% (Localin 0.4\%).

For those individuals with cataract, the type had been classified by an ophthalmologist as either, or a combination of, Nuclear (N), Anterior sub-capsular (ASC), Posterior subcapsular (PSC) and Cortical (C).

The aberrometry data set for each individual was downloaded and processed, relative to a 4 mm diameter zone, for the Total, Corneal and Internal components for each of the eight HOAs, in an identical manner to that of Chapters 3, 4 and 5. The data from the right eye of each individual in the 'less severe' cataract case series and in the normal eye case series were used for the analysis.

The limited demographical and clinical data were described using measures of central tendency (i.e., mean and standard deviation and median and inter-quartile range) and were tabulated accordingly.

The comparison of the HOAs between case series was undertaken by comparing the ratio of the median for the distribution of the given component of the given HOA in one case series with that of the corresponding median in another case series (Tables 6.21-6.26).

The inferential analysis for the 'less severe' and the clear media case series was separately undertaken using separate analyses of variance (ANOVA) for each component of each HOA whereby the influence of each independent variable on the magnitude of the dependent variable, the given Higher Order Aberration, was determined. As discussed in Chapter 2, no a priori attempt was made to adjust the level of significance to account for the presence of Type I errors arising from the numerous comparisons that were investigated. The equivalent analysis for the post-operative case series had previously
been undertaken in Chapter 5. The equivalent analysis for the pre-operative case series was not undertaken since it had previously been undertaken in Chapter 3 for a larger case series of 99 individuals and had, therefore, manifested greater statistical power.

The study was undertaken in accordance with the ethical requirements of the Soroka University Medical Centre Ethics Committee.

### 6.4 Results

### 6.4.1 Characteristics of Case Series

### 6.4.1.1 Pre- and Post-Operative Case Series

### 6.4.1.1.1 Pre-Operative Eyes

### 6.4.1.1.1.1 Age and Gender

The 36 individuals who attended the Pre-operative examination (13 males and 23 females) stratified by age, gender and operated eye are described in Table 6.1. The mean age was 73.47 , SD 8.63 , median 73.00 , IQR $66.75,81.00$. The case series composed two individuals aged between 51-60 years of age, 14 between 61-70 years of age, 10 between 71-80 years of age and 10 between 81-90 years of age.

| Pre-operative Eyes |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years) | Gender | Operated eye |  | Total |  |
|  |  | R | L | M | F |
| 51-60 | M | - | 1 | 1 | 1 |
|  | F | 1 | - |  |  |
| 61-70 | M | 4 | 3 | 7 | 7 |
|  | F | 2 | 5 |  |  |
| 71-80 | M | 2 | - | 2 | 8 |
|  | F | 5 | 3 |  |  |
| 81-90 | M | 1 | 2 | 3 | 7 |
|  | F | 3 | 4 |  |  |
| Total |  | 18 | 18 | 13 | 23 |
| Total |  | 36 |  | 36 |  |

Table 6.1. The 36 individuals within the pre- and post-operative case series, stratified by age at the pre-operative examination, gender and operated eye.

### 6.4.1.1.1.2 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst the case series is given in
Table 6.2 for the 36 individuals. Thirty-one eyes were myopic; of these, one manifested a spherical equivalent refraction higher than -9.99 dioptres, 19 between -9.99 and -2.00 dioptres and 11 between -1.99 dioptres and Plano. Five eyes were hyperopic; of these, 4 manifested a positive spherical equivalent refraction between +0.01 and +3.99 dioptres and one individual higher than +4.00 dioptres. No data were available for the remaining five individuals.

| Pre-operative Eyes |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |  |
| Less than -9.99 | 1 | -16.00 | - | - | - | - | - |  |
| -8.00 to -9.99 | 3 | -8.00 | - | -8.00 | -8.00 | $8.00-$ | - |  |
| -6.00 to -7.99 | 4 | -6.25 | - | -6.25 | -6.50 | -6.00 | $-6.50,-6.00$ |  |
| -4.00 to -5.99 | 4 | -4.63 | - | -4.50 | -5.50 | -4.00 | $-5.13,-4.00$ |  |
| -2.00 to -3.99 | 8 | -2.25 | 0.35 | -2.00 | -2.75 | -2.00 | $-2.56,-2.00$ |  |
| 0.00 to -1.99 | 11 | -0.68 | 0.66 | -0.75 | -1.75 | 0.00 | $-1.13,0.00$ |  |
| +0.01 to +1.99 | 3 | 0.50 | - | 0.50 | 0.50 | 0.50 | - |  |
| +2.00 to +3.99 | 1 | 2.25 | - | - | - | - | - |  |
| Greater than +3.99 | 1 | 4.00 | - | - | - | - | - |  |
| Group | 36 | -2.81 | 3.70 | -2.00 | -16.00 | 4.00 | $-5.13,-0.19$ |  |

Table 6.2. The summary statistics for the distribution of the spherical equivalent refraction, amongst the 36 individuals at the pre-operative examination.

### 6.4.1.1.1.3 Distance Visual Acuity

The distribution of the distance visual acuity amongst the case series is shown in Figure 6.1. Three individuals exhibited a visual acuity of between $6 / 7.5$ and $6 / 9,15$ of between 6/12 and $6 / 24$, 4 of $6 / 36,11$ of between $6 / 60$ and $6 / 120$, one exhibited Hand Movements and one Count Fingers. No data were available for the remaining five individuals.

### 6.4.1.1.1.4 Near Visual Acuity

The distribution of the near visual acuity amongst the case series is shown in Figure 6.2. Six individuals exhibited a near visual acuity of between Jaeger 1 and Jaeger 2, 19 of between Jaeger 3 and Jaeger 6, 6 of between Jaeger 7 and Jaeger 12 and one of Jaeger 16 .


Figure 6.1. The distribution of the distance visual acuity amongst the 36 individuals at the pre-operative examination.


Figure 6.2. The distribution of the near visual acuity in Jaeger notation amongst the 36 individuals at the pre-operative examination.

### 6.4.1.1.1.5 Mean Corneal Curvature

The distribution of the mean corneal curvature within the case series is shown in Table 6.3. One individual exhibited a mean corneal curvature of $7.18 \mathrm{~mm}, 17$ of between 7.21 and $7.60 \mathrm{~mm}, 15$ of between 7.61 and 8.00 mm and 3 of between 8.01 and 9.00 mm .

| Pre-operative Eyes |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Mean Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| 7.01 to 7.20 | 1 | 7.18 | - | - | - | - | - |
| 7.21 to 7.40 | 8 | 7.30 | 0.06 | 7.28 | 7.22 | 7.37 | $7.26,7.35$ |
| 7.41 to 7.60 | 9 | 7.49 | 0.06 | 7.50 | 7.41 | 7.57 | $7.43,7.55$ |
| 7.61 to 7.80 | 13 | 7.67 | 0.04 | 7.68 | 7.61 | 7.72 | $7.64,7.70$ |
| 7.81 to 8.00 | 2 | 7.95 | - | - | 7.92 | 7.97 | - |
| 8.01 to 9.00 | 3 | 8.08 | - | 8.09 | 8.02 | 8.12 | - |
| Group | 36 | 7.58 | 0.24 | 7.59 | 7.18 | 8.12 | $7.40,7.69$ |

Table 6.3. The summary statistics for the distribution of the mean corneal curvature amongst the 36 individuals at the pre-operative examination.

### 6.4.1.1.1.6 Flattest Corneal Curvature

The distribution of the flattest corneal curvature within the case series is shown in
Table 6.4. Seven individuals exhibited a mean corneal curvature of between 7.21 and $7.40 \mathrm{~mm}, 21$ of between 7.41 and 7.80 mm and 8 of between 7.81 and 9.00 mm .

| Pre-operative Eyes |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Flattest Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |  |
| 7.21 to 7.40 | 7 | 7.31 | 0.04 | 7.30 | 7.25 | 7.39 | $7.30,7.32$ |  |
| 7.41 to 7.60 | 6 | 7.50 | 0.06 | 7.51 | 7.42 | 7.58 | $7.45,7.53$ |  |
| 7.61 to 7.80 | 15 | 7.71 | 0.06 | 7.73 | 7.61 | 7.8 | $7.65,7.75$ |  |
| 7.81 to 8.00 | 3 | 7.91 | - | 7.91 | 7.9 | 7.93 | - |  |
| 8.01 to 9.00 | 5 | 8.15 | 0.12 | 8.10 | 8.02 | 8.35 | $8.10,8.17$ |  |
| Group | 36 | 7.67 | 0.27 | 7.66 | 7.25 | 8.35 | $7.48,7.79$ |  |

Table 6.4. The summary statistics for the distribution of the flat corneal curvature amongst the 36 individuals at the pre-operative examination.

### 6.4.1.1.2 Post-Operative Eyes

### 6.4.1.1.2.1 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst the case series is given in
Table 6.5 for 35 of the 36 individuals. Twenty-six eyes were myopic and 2 were emmetropic and 7 were hyperopic. One individual manifested a negative spherical equivalent refraction higher than -2.99 dioptres, 13 between -2.00 and -1.99 dioptres and 14 between -1.99 and Plano. Four individuals manifested a positive spherical equivalent refraction between +0.01 and +1.00 dioptres and 3 between +1.00 and +2.00 dioptres. No data were available for the remaining individual.

### 6.4.1.1.2.2 Distance Visual Acuity

The distribution of the distance visual acuity amongst the case series is shown in Figure 6.3. Sixteen individuals exhibited a visual acuity of $6 / 6$ and $6 / 9,17$ of between
$6 / 7.5$ and $6 / 9$, one of $6 / 10$ and one of $6 / 15$. No data were available for the remaining individuals.

| Post-operative Eyes |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |  |
| Less than -2.99 | 1 | -3.88 | - | - | - | - | - |  |
| -2.00 to -2.99 | 4 | -2.28 | - | -2.19 | -2.75 | -2.00 | $-2.38,-2.09$ |  |
| -1.00 to -1.99 | 9 | -1.39 | 0.32 | -1.25 | -1.75 | -1.00 | $-1.75,-1.13$ |  |
| 0.00 to -0.99 | 14 | -0.36 | 0.27 | -0.31 | -0.88 | 0.00 | $-0.50,-0.25$ |  |
| 0.01 to +1.00 | 4 | 0.38 | - | 0.25 | 0.25 | 0.75 | $0.25,0.38$ |  |
| +1.01 to +2.00 | 3 | 1.63 | - | 1.75 | 1.13 | 2.00 | - |  |
| group | 35 | -0.69 | 1.21 | -0.50 | -3.88 | 2.00 | $-1.44,-0.01$ |  |

Table 6.5. The summary statistics for the distribution of the spherical equivalent refraction amongst the 35 of the 36 individuals at the post-operative examination. No data were available for the remaining individual.


Figure 6.3. The distribution of the distance visual acuity amongst the 35 of the 36 individuals at the post-operative examination. No data were available for the remaining individual.

### 6.4.1.1.2.3 Near Visual Acuity

The distribution of the near visual acuity amongst the case series is shown in Figure 6.4. Nine individuals exhibited a near visual acuity of Jaeger 1, 20 of Jaeger 2 and 6 of Jaeger 3.


Figure 6.4. The distribution of the near visual acuity in Jaeger notation amongst the 35 of the 36 individuals at the post-operative examination. No data were available for the remaining individual.

### 6.4.1.1.2.4 Mean Corneal Curvature

The distribution of the mean corneal curvature within the case series is shown in Table 6.6. Two individuals exhibited a mean corneal curvature of less than $7.21 \mathrm{~mm}, 17$ of between 7.21 and 7.60 mm , 14 of between 7.61 and 8.00 mm and 3 greater than 8.00 mm .

| Post-operative Eyes |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Mean Corneal <br> Curvature (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| Less than 7.21 | 2 | 7.17 | - | - | 7.16 | 7.17 | - |
| $(7.21)-(7.40)$ | 8 | 7.28 | 0.04 | 7.28 | 7.22 | 7.35 | $7.26,7.31$ |
| $(7.41)-(7.60)$ | 9 | 7.53 | 0.05 | 7.55 | 7.43 | 7.60 | $7.49,7.57$ |
| $(7.61)-(7.80)$ | 11 | 7.68 | 0.06 | 7.68 | 7.61 | 7.79 | $7.63,7.72$ |
| $(7.81)-(8.00)$ | 3 | 7.92 | - | 7.94 | 7.85 | 7.98 | - |
| Greater than 8.00 | 3 | 8.06 | - | 8.06 | 8.01 | 8.10 | - |
| Group | 36 | 7.58 | 0.26 | 7.59 | 7.16 | 8.10 | $7.34,7.72$ |

Table 6.6. The summary statistics for the distribution of the mean corneal curvature amongst the 36 individuals at the post-operative examination.

### 6.4.1.1.2.5 Flattest Corneal Curvature

The distribution of the flattest corneal curvature within the case series is shown in Table
6.7. Seven individuals exhibited a flattest corneal curvature of between 7.21 and
$7.40 \mathrm{~mm}, 23$ of between 7.41 and 8.00 mm and 6 greater than 8.00 mm .

| Post-operative Eyes |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Flattest Corneal <br> Curvature (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| $(7.21)-(7.40)$ | 7 | 7.30 | 0.04 | 7.31 | 7.23 | 7.34 | $7.29,7.33$ |
| $(7.41)-(7.60)$ | 6 | 7.50 | 0.07 | 7.50 | 7.43 | 7.58 | $7.45,7.56$ |
| $(7.61)-(7.80)$ | 11 | 7.69 | 0.07 | 7.69 | 7.61 | 7.79 | $7.64,7.75$ |
| $(7.81)-(8.00)$ | 6 | 7.87 | 0.05 | 7.85 | 7.82 | 7.95 | $7.83,7.90$ |
| Greater than 8.00 | 6 | 8.08 | 8.18 | 8.07 | 8.01 | 8.18 | $8.01,8.13$ |
| Group | 36 | 7.68 | 0.27 | 7.68 | 7.23 | 8.18 | $7.47,7.85$ |

Table 6.7. The summary statistics for the distribution of the flattest corneal curvature amongst the 36 individuals at the post-operative examination.

### 6.4.1.2 'Less Severe' Cataract Case Series

### 6.4.1.2.1 Age and Gender

The 22 individuals ( 6 males and 16 females) stratified by age and by gender are described in Table 6.8. The mean age was 53.0 years, SD 4.99; median 53.5, IQR 48.5, 59.5. The case series comprised 14 individuals aged between 51-60 years of age, one individual older than 60 years of age and 7 individuals less than 50 years of age.

| Less Severe Cataract |  |  |
| :---: | :---: | :---: |
| Age (years) | R eye |  |
|  | M | F |
| $41-50$ | 1 | 6 |
| $51-60$ | 5 | 9 |
| $61-70$ | - | 1 |
| Total | 6 | 16 |
| Total | 22 |  |

Table 6.8. The 22 individuals within the 'less severe' cataract, stratified by age and by gender.

### 6.4.1.2.2 Cataract Type and Severity

The cases series was composed of individuals diagnosed with a cataract insufficiently severe to warrant surgery. The distribution of cataract type amongst the 22 individuals within the case series namely, nuclear, anterior subcapsular, posterior subcapsular and cortical, is given in Table 6.9. For convenience, ASC and PSC have been merged in the table as subcapsular cataract type. The predominant type of cataract in the case series was
nuclear cataract (11 individuals) followed by subcapsular cataract (6 individuals). There were no individuals in the series with 'pure' cortical cataract type. One individual had a combined nuclear and subcapsular cataract, one a combined nuclear and cortical and 3 a combined cortical and subcapsular cataract.

| Less Severe Cataract |  |
| :---: | :---: |
| Cataract type <br> classification | Number of <br> Individuals |
|  | R eye |
| N | 11 |
| SC | 6 |
| C | - |
| $\mathrm{N}+\mathrm{SC}$ | 1 |
| $\mathrm{~N}+\mathrm{C}$ | 1 |
| $\mathrm{~N}+\mathrm{C}+\mathrm{SC}$ | - |
| $\mathrm{C}+\mathrm{SC}$ | 3 |
| Total | 22 |

Table 6.9. The distribution of 'less severe' cataract type amongst the 22 individuals, namely, N (nuclear), ASC (anterior subcapsular), PSC (posterior subcapsular) and C (cortical). ASC and PSC were merged and described as subcapsular (SC) cataract.

### 6.4.1.2.3 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst the case series is given in Table 6.10. Twelve eyes were myopic; of these, 3 manifested a spherical equivalent refraction greater than -9.99 dioptres and 9 between -8.00 and Plano. Ten eyes were hyperopic; of these, 9 manifested a positive spherical equivalent refraction between +0.01 and +3.99 dioptres and one individual greater than +4.00 dioptres.

| Less Severe Cataract |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| Less than -9.99 | 3 | -10.63 | - | -10.63 | -11.25 | -10.00 | - |
| -8.00 to -9.99 | 1 | -6.87 | - | - | - | - | - |
| -6.00 to -7.99 | - | - | - | - | - | - | - |
| -4.00 to -5.99 | - | - | - | - | - | - | - |
| -2.00 to -3.99 | 3 | -2.54 | - | -2.25 | -3.25 | -2.12 | - |
| 0.00 to -1.99 | 5 | -1.10 | 0.70 | -1.25 | -1.75 | -0.25 | $-1.75,-0.50$ |
| +0.01 to +1.99 | 4 | 0.88 | - | 0.81 | 0.12 | 1.75 | $0.50,1.19$ |
| +2.00 to +3.99 | 5 | 2.35 | 0.24 | 2.38 | 2.00 | 2.62 | $2.25,2.50$ |
| Greater than +3.99 | 1 | 6.12 | - | - | - | - | - |
| Group | 22 | -1.39 | 4.59 | -0.37 | -11.25 | 6.12 | $-2.25,1.94$ |

Table 6.10. The summary statistics for the distribution of the spherical equivalent refraction amongst the 22 individuals with 'less severe' cataract.

### 6.4.1.2.4 Distance Visual Acuity

The distribution of the distance visual acuity amongst the case series is shown in Figure 6.5. Six individuals exhibited a visual acuity of $6 / 6,7$ of $6 / 7.5,6$ of between $6 / 9$ and $6 / 12$ and 2 of $6 / 15$. No data were available for one individual.

### 6.4.1.2.5 Near Visual Acuity

The distribution of the near visual acuity was only available for 8 of the 22 individuals in the case series. Of these, 5 exhibited a near visual acuity of Jeager 1, two of Jeager 2 and one of Jeager 16.


Figure 6.5. The distribution of the distance visual acuity amongst the 21 of the 22 individuals with 'less severe' cataract. No data were available for one individual.

### 6.4.1.2.6 Mean Corneal Curvature

The distribution of the mean corneal curvature within the case series is shown in Table 6.11. One individual exhibited a mean corneal curvature of less than 7.01 mm , one of $7.03 \mathrm{~mm}, 10$ of between 7.21 and $7.60 \mathrm{~mm}, 9$ of between 7.61 and 8.00 mm and one greater than 8.00 mm .

| Less Severe Cataract |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Mean Corneal <br> Curvature (mm) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| Less than 7.01 | 1 | 6.97 | - | - | - | - | - |
| 7.01 to 7.20 | 1 | 7.03 | - | - | - | - | - |
| 7.21 to 7.40 | 5 | 7.35 | 0.06 | 7.38 | 7.26 | 7.39 | $7.31,7.39$ |
| 7.41 to 7.60 | 5 | 7.48 | 0.03 | 7.48 | 7.42 | 7.51 | $7.46,7.50$ |
| 7.61 to 7.80 | 1 | 7.65 | - | - | - | - | - |
| 7.81 to 8.00 | 8 | 7.87 | 0.04 | 7.87 | 7.81 | 7.90 | $7.84,7.90$ |
| Greater than 8.00 | 1 | 8.85 | - | - | - | - | - |
| Group | 22 | 7.62 | 0.40 | 7.51 | 6.98 | 8.86 | $7.39,7.86$ |

Table 6.11. The summary statistics for the distribution of the mean corneal curvature amongst the 22 individuals with 'less severe' cataract.

### 6.4.1.2.7 Flattest Corneal Curvature

The distribution of the flattest corneal curvature within the case series is shown in Table 6.12. Two individuals exhibited a mean corneal curvature of between 7.01 and $7.20 \mathrm{~mm}, 9$ of between 7.21 and $7.60 \mathrm{~mm}, 9$ of between 7.61 and 8.00 mm and 2 greater than 8.00 mm .

| Less Severe Cataract |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Flattest Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| Less than 7.01 | - | - | - | - | - | - | - |
| 7.01 to 7.20 | 2 | 7.04 | - | - | 7.02 | 7.05 | - |
| 7.21 to 7.40 | 2 | 7.36 | - | - | 7.35 | 7.36 | - |
| 7.41 to 7.60 | 7 | 7.51 | 0.04 | 7.50 | 7.46 | 7.55 | $7.49,7.54$ |
| 7.61 to 7.80 | 2 | 7.71 | - | - | 7.68 | 7.73 | - |
| 7.81 to 8.00 | 7 | 7.91 | 0.05 | 7.91 | 7.85 | 7.97 | $7.88,7.96$ |
| Greater than 8.00 | 2 | 8.51 | - | - | 8.01 | 9.01 | - |
| Group | 22 | 7.69 | 0.41 | 7.62 | 7.02 | 9.01 | $7.49,7.91$ |

Table 6.12. The summary statistics for the distribution of the flattest corneal curvature amongst the 22 individuals with 'less severe' cataract.

### 6.4.1.3 Clear Media Case Series

### 6.4.1.3.1 Age and Gender

The 49 eyes from the 49 individuals with clear media ( 23 males and 26 females) stratified by age and by gender are described in Table 6.13. The mean age was 44.7, SD 9.15; median 45.0, IQR 38.0, 52.0. The case series composed two individuals aged between 21-30 years of age, 15 between 31-40 years of age, 15 between 41-50 years of age, 15 between 51-60 years of age and one 61 years old.

| Clear Media |  |  |
| :---: | :---: | :---: |
| Age (years) | R eye |  |
|  | $\mathbf{M}$ | $\mathbf{F}$ |
| $21-30$ | 1 | 1 |
| $31-40$ | 7 | 9 |
| $41-50$ | 7 | 8 |
| $51-60$ | 7 | 8 |
| $61-70$ | 1 | - |
| Total | 23 | 26 |
| Total | 49 |  |

Table 6.13. The 49 individuals within the clear media case series, stratified by age and by gender.

### 6.4.1.3.2 Spherical Equivalent Refraction

The distribution of the spherical equivalent refraction amongst the case series is given in Table 6.14 for 46 of the 49 individuals. Thirty-nine eyes were myopic; of these, 25 manifested a spherical equivalent refraction between -8.00 and -2.00 dioptres and 14 between -2.00 and Plano. Seven eyes were hyperopic; of these, 5 manifested a positive spherical equivalent refraction between +0.01 and +3.99 dioptres and 2 individuals greater than +4.00 dioptres. No data were available for the remaining three individuals.

### 6.4.1.3.3 Distance Visual Acuity

The distribution of the distance visual acuity amongst the case series is shown in Figure 6.6. Thirty-four individuals exhibited a visual acuity of $6 / 6,7$ of $6 / 7.5,4$ of between $6 / 9$ and $6 / 12$ and one of $6 / 40$. No data were available for the remaining three individuals.

## Clear Media

| Spherical Equivalent <br> (Dioptres) | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Less than -9.99 | - | - | - | - | - | - | - |
| -8.00 to -9.99 | 3 | -8.54 | - | -8.38 | -9.25 | -8.00 | - |
| -6.00 to -7.99 | 5 | -7.15 | 0.31 | -7.38 | -7.38 | -6.75 | $-7.38,-6.88$ |
| -4.00 to -5.99 | 6 | -4.54 | 0.44 | -4.44 | -5.13 | -4.00 | $-4.88,-4.28$ |
| -2.00 to -3.99 | 11 | -2.67 | 0.49 | -2.50 | -3.75 | -2.13 | $-2.81,-2.31$ |
| 0.00 to -1.99 | 14 | -0.85 | 0.55 | -1.00 | -1.50 | 0.00 | $-1.25,-0.37$ |
| +0.01 to +1.99 | 3 | 0.75 | - | 0.88 | 0.38 | 1.00 | - |
| +2.00 to +3.99 | 2 | 2.69 | - | - | 2.13 | 3.25 | - |
| Greater than +3.99 | 2 | 5.13 | - | - | 4.75 | 5.50 | - |
| Group | 46 | -2.43 | 3.31 | -2.25 | -9.25 | 5.50 | $-4.34,-0.47$ |

Table 6.14. The summary statistics for the distribution of the spherical equivalent refraction, amongst the 46 of the 49 individuals with clear media. No data were available for the remaining three individuals.


Figure 6.6. The distribution of the distance visual acuity amongst the 46 of the 49 individuals with clear media. No data were available for the remaining three individuals.

### 6.4.1.3.4 Near Visual Acuity

The distribution of corrected near visual acuity was only available for 14 of the 49 individuals in the case series. Of these, 11 exhibited a corrected near visual acuity of Jeager 1 and 3 of Jeager 2.

### 6.4.1.3.5 Mean Corneal Curvature

The distribution of the mean corneal curvature within the case series is shown in Table 6.15. One individual exhibited a mean corneal curvature of between 7.01 and $7.20 \mathrm{~mm}, 4$ of between 7.21 and $7.40 \mathrm{~mm}, 24$ of between 7.41 and $7.80 \mathrm{~mm}, 11$ of between 7.81 and 8.00 mm and 9 of between 8.01 and 9.00 mm .

| Clear Media |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Mean Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| 7.01 to 7.20 | 1 | 7.12 | - | - | - | - | - |
| 7.21 to 7.40 | 4 | 7.37 | - | 7.40 | 7.28 | 7.40 | $7.37,7.40$ |
| 7.41 to 7.60 | 12 | 7.47 | 0.04 | 7.46 | 7.42 | 7.58 | $7.44,7.48$ |
| 7.61 to 7.80 | 12 | 7.72 | 0.06 | 7.73 | 7.62 | 7.80 | $7.67,7.76$ |
| 7.81 to 8.00 | 11 | 7.79 | 0.22 | 7.85 | 7.81 | 8.00 | $7.82,7.87$ |
| 8.01 to 9.00 | 9 | 8.18 | 0.14 | 8.17 | 8.01 | 8.47 | $8.06,8.25$ |
| Group | 49 | 7.73 | 0.29 | 7.74 | 7.12 | 7.12 | $7.47,7.88$ |

Table 6.15. The summary statistics for the distribution of the mean corneal curvature amongst the 49 individuals with clear media.

### 6.4.1.3.6 Flattest Corneal Curvature

The distribution of the flattest corneal curvature within the case series is shown in Table 6.16. One individual exhibited a mean corneal curvature of $7.26 \mathrm{~mm}, 24$ of between 7.41 and $7.80 \mathrm{~mm}, 24$ of between 7.81 and 9.00 mm .

| Clear Media |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Flattest Corneal <br> Curvature $(\mathrm{mm})$ | Number of <br> Individuals | Mean | SD | Median | Min | Max | IQR |
| 7.21 to 7.40 | 1 | 7.26 | - | - | - | - | - |
| 7.41 to 7.60 | 12 | 7.49 | 0.05 | 7.49 | 7.41 | 7.58 | $7.46,7.52$ |
| 7.61 to 7.80 | 12 | 7.72 | 0.06 | 7.73 | 7.63 | 7.8 | $7.67,7.77$ |
| 7.81 to 8.00 | 12 | 7.89 | 0.06 | 7.90 | 7.81 | 7.98 | $7.85,7.93$ |
| 8.01 to 9.00 | 12 | 8.21 | 0.20 | 8.13 | 8.02 | 8.58 | $8.07,8.33$ |
| Group | 49 | 7.82 | 0.30 | 7.80 | 7.26 | 8.58 | $7.58,7.98$ |

Table 6.16. The summary statistics for the distribution of the mean corneal curvature amongst the 49 individuals with clear media.

### 6.4.2 Higher Order Aberrations

The summary statistics of the distributions of each of the three components Total, Corneal and Internal, for each of the eight HOAs, amongst each of the three case series, are given in Tables 6.17-6.20 and are illustrated in terms of Box and Whisker plots in Figures 6.7-6.14.

| Pre-operative Eyes |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |  |
| Component |  | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | Mean | 3.251 | 0.759 | 1.191 | 0.25 | 0.75 | 0.68 | 0.145 | 0.355 |
|  | SD | 4.18 | 0.87 | 2.16 | 0.28 | 1.18 | 1.40 | 0.19 | 0.73 |
|  | Median | 2.231 | 0.605 | 0.686 | 0.169 | 0.464 | 0.294 | 0.097 | 0.059 |
|  | Min | 0.841 | 0.033 | 0.205 | 0.048 | 0.083 | 0.032 | 0.012 | 0.014 |
|  | Max | 9.553 | 1.804 | 5.306 | 0.598 | 2.867 | 3.455 | 0.448 | 1.736 |
|  | Min IQR | 1.524 | 0.312 | 0.516 | 0.109 | 0.232 | 0.121 | 0.048 | 0.039 |
|  | Max IQR | 2.958 | 0.893 | 0.865 | 0.316 | 0.697 | 0.435 | 0.163 | 0.086 |
| Corneal | Mean | 0.885 | 0.617 | 0.536 | 0.183 | 0.717 | 0.283 | 0.072 | 0.070 |
|  | SD | 0.93 | 1.14 | 1.18 | 0.31 | 1.14 | 0.66 | 0.08 | 0.12 |
|  | Median | 0.597 | 0.231 | 0.149 | 0.073 | 0.421 | 0.038 | 0.058 | 0.029 |
|  | Min | 0.206 | 0.023 | 0.093 | 0.019 | 0.012 | 0.007 | 0.014 | 0.010 |
|  | Max | 5.311 | 2.765 | 2.905 | 0.714 | 2.867 | 1.621 | 0.162 | 0.295 |
|  | Min IQR | 1.482 | 0.709 | 0.796 | 0.190 | 0.725 | 0.411 | 0.051 | 0.081 |
|  | Max IQR | 4.034 | 2.08 | 2.202 | 0.533 | 2.153 | 1.217 | 0.125 | 0.224 |
| Internal | Mean | 3.337 | 0.975 | 1.290 | 0.335 | 0.811 | 0.715 | 0.179 | 0.390 |
|  | SD | 1.42 | 0.79 | 0.96 | 0.46 | 0.75 | 0.77 | 0.34 | 0.60 |
|  | Median | 1.960 | 0.539 | 0.982 | 0.179 | 0.411 | 0.287 | 0.115 | 0.053 |
|  | Min | 0.626 | 0.103 | 0.156 | 0.043 | 0.054 | 0.039 | 0.019 | 0.020 |
|  | Max | 9.918 | 2.965 | 5.402 | 0.974 | 2.779 | 3.50 | 0.559 | 1.838 |
|  | Min IQR | 2.949 | 0.819 | 1.467 | 0.275 | 0.735 | 0.919 | 0.154 | 0.475 |
|  | Max IQR | 7.595 | 2.250 | 4.090 | 0.741 | 2.098 | 2.680 | 0.424 | 1.383 |

Table 6.17. The summary statistics of the distributions of each of the three components Total, Corneal and Internal, for each of the eight HOAs, amongst the 36 individuals within the pre-operative case series.

| Post-operative Individuals |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |  |
| Component |  | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | Mean | 1.596 | 0.497 | 0.751 | 0.179 | 0.473 | 0.386 | 0.116 | 0.243 |
|  | SD | 1.64 | 0.72 | 1.14 | 0.29 | 0.67 | 0.65 | 0.15 | 0.46 |
|  | Median | 1.197 | 0.339 | 0.323 | 0.092 | 0.195 | 0.111 | 0.061 | 0.052 |
|  | Min | 0.530 | 0.042 | 0.129 | 0.031 | 0.036 | 0.015 | 0.006 | 0.009 |
|  | Max | 3.336 | 1.701 | 2.581 | 0.636 | 1.392 | 1.470 | 0.289 | 1.071 |
|  | Min IQR | 1.010 | 0.236 | 0.224 | 0.071 | 0.132 | 0.053 | 0.028 | 0.036 |
|  | Max IQR | 1.661 | 0.467 | 0.561 | 0.135 | 0.389 | 0.200 | 0.113 | 0.077 |
| Corneal | Mean | 0.962 | 0.433 | 0.286 | 0.122 | 0.484 | 0.111 | 0.071 | 0.114 |
|  | SD | 1.40 | 0.73 | 0.48 | 0.14 | 0.66 | 0.23 | 0.10 | 0.24 |
|  | Median | 0.598 | 0.206 | 0.180 | 0.083 | 0.218 | 0.049 | 0.045 | 0.030 |
|  | Min | 0.299 | 0.057 | 0.065 | 0.023 | 0.036 | 0.009 | 0.019 | 0.010 |
|  | Max | 3.409 | 1.785 | 1.187 | 0.280 | 1.392 | 0.551 | 0.231 | 0.579 |
|  | Min IQR | 0.439 | 0.140 | 0.131 | 0.058 | 0.136 | 0.035 | 0.028 | 0.022 |
|  | Max IQR | 0.889 | 0.339 | 0.260 | 0.120 | 0.397 | 0.073 | 0.068 | 0.062 |
| Internal | Mean | 1.705 | 0.689 | 0.806 | 0.194 | 0.476 | 0.434 | 0.156 | 0.312 |
|  | SD | 0.94 | 0.67 | 0.75 | 0.37 | 0.57 | 0.59 | 0.32 | 0.52 |
|  | Median | 1.196 | 0.322 | 0.396 | 0.101 | 0.204 | 0.127 | 0.174 | 0.040 |
|  | Min | 0.413 | 0.117 | 0.138 | 0.040 | 0.045 | 0.026 | 0.010 | 0.014 |
|  | Max | 3.881 | 2.035 | 2.580 | 0.638 | 1.358 | 1.498 | 0.379 | 1.185 |
|  | Min IQR | 0.878 | 0.200 | 0.242 | 0.076 | 0.129 | 0.073 | 0.040 | 0.026 |
|  | Max IQR | 1.620 | 0.526 | 0.574 | 0.142 | 0.393 | 0.280 | 0.205 | 0.083 |

Table 6.18. The summary statistics of the distributions of each of the three components Total, Corneal and Internal, for each of the eight HOAs, amongst the 35 of the 36 individuals within the post-operative case series.

| Less Severe Cataract |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |  |
| Component |  | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | Mean | 3.156 | 1.025 | 0.788 | 0.245 | 0.453 | 0.373 | 0.097 | 0.283 |
|  | SD | 3.08 | 1.78 | 1.27 | 0.40 | 0.770 | 0.74 | 0.16 | 0.51 |
|  | Median | 2.33 | 0.278 | 0.246 | 0.095 | 0.196 | 0.058 | 0.035 | 0.037 |
|  | Min | 0.832 | 0.048 | 0.09 | 0.037 | 0.019 | 0.005 | 0.006 | 0.007 |
|  | Max | 5.325 | 3.953 | 2.743 | 0.876 | 1.482 | 1.645 | 0.26 | 1.079 |
|  | Min IQR | 1.479 | 0.184 | 0.173 | 0.064 | 0.105 | 0.036 | 0.017 | 0.026 |
|  | Max IQR | 3.979 | 0.466 | 0.446 | 0.184 | 0.343 | 0.396 | 0.09 | 0.065 |
| Corneal | Mean | 0.710 | 0.390 | 0.219 | 0.128 | 0.583 | 0.064 | 0.059 | 0.058 |
|  | SD | 0.64 | 0.45 | 0.25 | 0.16 | 0.89 | 0.07 | 0.06 | 0.07 |
|  | Median | 0.617 | 0.262 | 0.163 | 0.099 | 0.198 | 0.038 | 0.047 | 0.03 |
|  | Min | 0.258 | 0.091 | 0.092 | 0.019 | 0.012 | 0.013 | 0.011 | 0.005 |
|  | Max | 1.154 | 0.942 | 0.495 | 0.346 | 1.860 | 0.125 | 0.117 | 0.135 |
|  | Min IQR | 0.422 | 0.138 | 0.112 | 0.065 | 0.098 | 0.026 | 0.034 | 0.013 |
|  | Max IQR | 0.800 | 0.446 | 0.213 | 0.142 | 0.386 | 0.065 | 0.072 | 0.065 |
| Internal | Mean | 3.178 | 1.117 | 0.835 | 0.245 | 0.495 | 0.391 | 0.132 | 0.311 |
|  | SD | 1.28 | 0.98 | 0.83 | 0.44 | 0.64 | 0.60 | 0.29 | 0.54 |
|  | Median | 2.144 | 0.316 | 0.231 | 0.090 | 0.131 | 0.078 | 0.075 | 0.048 |
|  | Min | 0.949 | 0.043 | 0.124 | 0.039 | 0.014 | 0.032 | 0.011 | 0.009 |
|  | Max | 5.638 | 4.613 | 2.864 | 0.972 | 0.154 | 1.706 | 0.354 | 1.182 |
|  | Min IQR | 1.371 | 0.193 | 0.183 | 0.066 | 0.059 | 0.053 | 0.045 | 0.023 |
|  | Max IQR | 4.189 | 0.581 | 0.394 | 0.150 | 0.287 | 0.096 | 0.121 | 0.084 |

Table 6.19. The summary statistics of the distributions of each of the three components Total, Corneal and Internal, for each of the eight HOAs, amongst the 22 individuals within the case series of 'less severe' cataract.

| Clear Media |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |  |
| Component |  | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | Mean | 2.585 | 0.832 | 0.661 | 0.226 | 0.441 | 0.335 | 0.088 | 0.175 |
|  | SD | 2.98 | 1.94 | 1.21 | 0.50 | 0.89 | 0.74 | 0.15 | 0.44 |
|  | Median | 1.464 | 0.222 | 0.17 | 0.072 | 0.123 | 0.056 | 0.035 | 0.028 |
|  | Min | 0.381 | 0.043 | 0.065 | 0.02 | 0.007 | 0.011 | 0.004 | 0.005 |
|  | Max | 6.594 | 5.141 | 2.77 | 1.329 | 2.335 | 1.927 | 0.339 | 1.155 |
|  | Min IQR | 1.090 | 0.135 | 0.148 | 0.049 | 0.074 | 0.034 | 0.014 | 0.019 |
|  | Max IQR | 2.746 | 0.357 | 0.329 | 0.104 | 0.246 | 0.104 | 0.065 | 0.058 |
| Corneal | Mean | 0.691 | 0.338 | 0.161 | 0.097 | 0.095 | 0.045 | 0.062 | 0.041 |
|  | SD | 0.65 | 0.45 | 0.16 | 0.12 | 0.11 | 0.05 | 0.07 | 0.04 |
|  | Median | 0.595 | 0.075 | 0.143 | 0.067 | 0.068 | 0.034 | 0.05 | 0.032 |
|  | Min | 0.204 | 0.001 | 0.069 | 0.009 | 0.014 | 0.009 | 0.009 | 0.005 |
|  | Max | 1.482 | 1.159 | 0.370 | 0.291 | 0.262 | 0.108 | 0.17 | 0.092 |
|  | Min IQR | 0.475 | 0.108 | 0.105 | 0.049 | 0.044 | 0.023 | 0.035 | 0.021 |
|  | Max IQR | 0.785 | 0.327 | 0.177 | 0.091 | 0.108 | 0.049 | 0.067 | 0.050 |
| Internal | Mean | 2.525 | 0.806 | 0.661 | 0.253 | 0.427 | 0.33 | 0.126 | 0.156 |
|  | SD | 1.20 | 0.82 | 0.74 | 0.47 | 0.60 | 0.54 | 0.30 | 0.38 |
|  | Median | 1.486 | 0.294 | 0.212 | 0.082 | 0.12 | 0.07 | 0.068 | 0.031 |
|  | Min | 0.344 | 0.09 | 0.11 | 0.024 | 0.015 | 0.018 | 0.015 | 0.012 |
|  | Max | 6.153 | 4.542 | 0.818 | 1.519 | 2.244 | 1.85 | 0.573 | 1.03 |
|  | Min IQR | 1.051 | 0.164 | 0.157 | 0.061 | 0.077 | 0.047 | 0.051 | 0.022 |
|  | Max IQR | 0.283 | 0.508 | 0.289 | 0.110 | 0.209 | 0.107 | 0.113 | 0.044 |

Table 6.20. The summary statistics of the distributions of each of the three components Total, Corneal and Internal, for each of the eight HOAs, amongst the 49 individuals within the case series of eyes with a clear media.


Figure 6.7. The summary statistics of the distributions of the Total, Corneal and Internal components of the Total HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the Total HOA and the remaining 7 HOAs.




Figure 6.8. The summary statistics of the distributions of the Total, Corneal and Internal components of the Tilt (S1) HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the Tilt (S1) HOA and the remaining 7 HOAs.


Figure 6.9. The summary statistics of the distributions of the Total, Corneal and Internal components of the High HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the High HOA and the remaining 7 HOAs.


Figure 6.10. The summary statistics of the distributions of the Total, Corneal and Internal components of the T.Coma HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the T.Coma HOA and the remaining 7 HOAs.


Figure 6.11. The summary statistics of the distributions of the Total, Corneal and Internal components of the T.Trefoil HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the T.Trefoil HOA and the remaining 7 HOAs.


Figure 6.12. The summary statistics of the distributions of the Total, Corneal and Internal components of the T.4Foil HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the T.4Foil HOA and the remaining 7 HOAs.


Figure 6.13. The summary statistics of the distributions of the Total, Corneal and Internal components of the T.Sph HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the T.Sph HOA and the remaining 7 HOAs.


Figure 6.14. The summary statistics of the distributions of the Total, Corneal and Internal components of the HiAstig HOA, amongst each of the four case series illustrated in terms of Box and Whisker plots. Note the difference in scaling of the ordinate of the HiAstig HOA and the remaining 7 HOAs.

### 6.4.3 Comparison of the HOAs between Case Series

The outcome of the comparison of the HOAs between the three case series is given in Tables 6.21-6.26.

### 6.4.3.1 Pre- and Post-operative Case Series

The ratio of the median of the pre-operative distribution to the median of the postoperative distribution for the 36 individuals with age-related cataract was appreciably greater than 1.0 for the Total component in 7 of the 8 HOAs and ranged from 1.59 for the T.Sph HOA to 2.68 for the T.4Foil HOA indicating that, as would be expected, the 7 HOAs were greater in the pre-operative eye. The remaining HOA, HiAstig approximated to unity (1.13), suggesting that this HOA was less influenced by cataract. As would be expected, the higher pre-operative values for these 7 HOAs arose from the Internal component which ranged from 1.55 for the T.Sph HOA to 2.27 for the T.4Foil HOA (median 1.76). The ratio for the Internal component of the HiAstig HOA was 1.33 suggesting that this HOA was, indeed, influenced by age-related cataract. The ratios for the Corneal component of the 7 HOAs ranged from 0.77 for the T.Trefoil and T.4Foil HOAs to 1.28 for T.Sph HOA (median 0.88 ). The ratio was 0.96 for the Corneal component of HiAstig HOA.

### 6.4.3.2 Pre-operative and 'Less Severe' Cataract Case Series

The ratio of the median for the pre-operative distribution for the 36 individuals with agerelated cataract compared to that for the 22 individuals with 'less severe' cataract approximated to unity for all 3 components of the Total HOA (Total 0.96, Corneal 0.97
and Internal 0.91). However, the Total component of the remaining 7 HOAs ranged from 1.59 for the HiAstig HOA to 5.07 for the T.4Foil HOA (median 2.37) indicating that these HOAs were materially higher in the individuals with cataract sufficiently severe to have warranted extraction compared to those with 'less severe' cataract. As would be expected, the difference in the ratios between the two case series for the seven HOAs arose from the magnitudes of the Internal component which ranged from 1.54 for the T.Sph HOA to 3.67 for the T.4Foil HOA (median 2.47).

| Pre-operative and Post-operative |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |
| Component | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | 1.86 | 1.78 | 2.12 | 1.84 | 2.38 | 2.68 | 1.59 | 1.13 |
| Corneal | 1.00 | 1.12 | 0.83 | 0.88 | 0.77 | 0.77 | 1.28 | 0.96 |
| Internal | 1.64 | 1.67 | 1.72 | 1.78 | 2.02 | 2.27 | 1.55 | 1.33 |

Table 6.21. The comparison of the HOAs between the pre- and post-operative case series, expressed as the ratio of the median for the pre-operative distribution to the median for the post-operative distribution, for the given component of the given HOA.

| Pre-operative and Less Severe Cataract |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |
| Component | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | 0.96 | 2.18 | 2.79 | 1.78 | 2.37 | 5.07 | 2.77 | 1.59 |
| Corneal | 0.97 | 0.88 | 0.91 | 0.91 | 1.08 | 0.99 | 1.24 | 0.94 |
| Internal | 0.91 | 1.71 | 2.95 | 2.95 | 3.14 | 3.67 | 1.54 | 1.11 |

Table 6.22. The comparison of the HOAs between the pre-operative case series and the 'less severe' cataract case series expressed as the ratio of the median for the pre-operative distribution to the median for the 'less severe' distribution, for the given component of the given HOA.

### 6.4.3.3 Post-operative and Clear Media Case Series

The ratio of the post-operative median to that of the median for the 49 individuals with clear media was appreciably greater than 1.0 for the Total component in only 7 of the 8 HOAs and ranged from 1.28 for the T.Coma HOA to 1.90 for the High HOA indicating that these 7 HOAs were better in the the eye containing an IOL than in the eyes with clear media. The ratio for the Total component of the Total, Tilt (S1) and T.Coma HOAs was appreciably less than 1.0 indicating that these HOAs were greater in the eyes containing an IOL than in the eyes with clear media. Of these 7 HOAs, only three HOAs (High, T.Trefoil and T.4Foil) exhibited a ratio for the Internal component which was notably greater than 1.0. Interestingly, two HOAs (T.Trefoil and T.4Foil) exhibited a ratio for the Corneal component which was notably greater of that in the normal eye. This would imply that the post-operative cornea had been compromised by the surgery.

| Post-operative and Clear Media |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |
| Component | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | 0.82 | 1.53 | 1.90 | 1.28 | 1.59 | 1.98 | 1.74 | 1.86 |
| Corneal | 1.01 | 0.96 | 1.26 | 1.24 | 1.92 | 1.45 | 0.92 | 0.93 |
| Internal | 0.80 | 1.10 | 1.87 | 1.22 | 1.70 | 1.82 | 1.09 | 1.29 |

Table 6.23. The comparison of the HOAs between the post-operative case series and the clear media case series expressed as the ratio of the median for the post-operative distribution to the median for the clear media distribution, for the given component of the given HOA .

### 6.4.3.4 Post-operative and 'Less Severe' Cataract Case Series

The ratio of the post-operative median for the 22 individuals to that of the median for the 35 individuals with 'less severe' cataract was appreciably greater than 1.0 for the Total component in 4 of the 8 HOAs and ranged from 1.22 for the Tilt (S1) HOA to 1.91 for the T.4Foil HOA indicating that these 4 HOAs were greater in the the eye containing an IOL than in the eyes with 'less severe' cataract. The ratios of the Total component for T.Coma and T.Trefoil HOAs approximated to unity whilst that for the Total HOA was notably greater in 'less severe' cataract. It is notable that the ratios for the Corneal and Internal components of the T.Trefoil and the T.4Foil HOAs were notably greater than 1.0 indicating that these aberrations were higher in the post-operative eye than in the 'less severe' cataract eye. This finding is compatible with the larger post-operative outcome for these HOAs compared to the clear media case series (Table 6.23). These two findings suggest that surgery lessens the magnitude of the Internal component but increases the magnitude of the Corneal component for both the T.Trefoil and T.4Foil HOAs.

| Post-operative and Less Severe Cataract |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |
| Component | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | 0.51 | 1.22 | 1.31 | 0.97 | 0.99 | 1.91 | 1.74 | 1.41 |
| Corneal | 0.97 | 0.78 | 1.10 | 0.84 | 1.39 | 1.30 | 0.96 | 0.98 |
| Internal | 0.56 | 1.02 | 1.72 | 1.12 | 1.55 | 1.62 | 0.99 | 0.83 |

Table 6.24. The comparison of the HOAs between the post-operative case series and the 'less severe' case series expressed as the ratio of the median for the post-operative distribution to the median for the 'less severe' distribution, for the given component of the given HOA.

### 6.4.3.5 Pre-operative and Clear Media Case Series

The outcomes for the ratios of the pre-operative and clear media comparison represent a control evaluation, the magnitudes of which should validate the more salient comparisons. As would be expected, the Total and Internal components of all the HOAs were markedly greater for the pre-operative case series compared to the clear media case series. In addition, as would also be expected, the ratios for the Corneal component of all the HOAsapproximated to unity, with the exception of T.Trefoil HOA.

| Pre-operative and Clear Media |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |
| Component | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | 1.52 | 2.73 | 4.04 | 2.35 | 3.77 | 5.25 | 2.77 | 2.11 |
| Corneal | 1.00 | 1.08 | 1.04 | 1.10 | 1.48 | 1.11 | 1.18 | 0.89 |
| Internal | 1.32 | 1.83 | 3.21 | 2.18 | 3.43 | 4.12 | 1.69 | 1.71 |

Table 6.25. The comparison of the HOAs between the pre-operative case series and the clear media case series expressed as the ratio of the median for the pre-operative distribution to the median for the clear media distribution, for the given component of the given HOA.

### 6.4.3.6 'Less Severe' Cataract and Clear Media Case Series

The outcomes for the ratios of the 'less severe' cataract and clear media comparison also represents a control evaluation. Although, the Total component of six HOAs for the 'less severe' cataract case series was greater than that for the clear media case series, the Internal component for six of the eight HOAs approached unity. The remaining two HOAs, Total and HiAstig HOAs exhibited a notably greater Internal component.

| Less Severe Cataract and Clear Media |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of HOA |  |  |  |  |  |  |  |  |
| Component | Total | Tilt (S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |
| Total | 1.59 | 1.25 | 1.45 | 1.32 | 1.59 | 1.04 | 1.00 | 1.32 |
| Corneal | 1.04 | 1.23 | 1.14 | 1.48 | 1.38 | 1.12 | 0.95 | 0.95 |
| Internal | 1.44 | 1.07 | 1.09 | 1.09 | 1.09 | 1.12 | 1.09 | 1.55 |

Table 6.26. The comparison of the HOAs between the 'less severe' case series and the clear media case series expressed as the ratio of the median for 'less severe' distribution to the median for the clear media distribution, for the given component of the given HOA. and the Clear Media Case Series

### 6.4.4.1 'Less Severe' Cataract Case Series

The results of the explanatory analysis for the 'less severe' cataract case series are given in Table 6.27.

### 6.4.4.1.1 Distance Visual Acuity

Distance visual acuity was adversely influenced by the Total component of the Tilt (S1) $\left(\mathrm{R}^{2}=40.7 \% ; \mathrm{p}<0.001\right)$, High $\left(\mathrm{R}^{2}=16.2 \% ; \mathrm{p}=0.042\right)$, T.Coma $\left(\mathrm{R}^{2}=34.7 \% ; \mathrm{p}=0.001\right)$, T.Trefoil $\left(\mathrm{R}^{2}=16.2 \% ; \mathrm{p}=0.042\right)$, $\mathrm{T} . \mathrm{Sph}\left(\mathrm{R}^{2}=41.1 \% ; \mathrm{p}=<0.001\right)$ HOAs (Table 6.27).

However, any association with the corresponding Corneal and Internal components failed to reach statistical significance.

### 6.4.4.1.2 Near Visual Acuity

No association was present between the near visual acuity and any of the three components for each of the eight HOAs (Table 6.27).

### 6.4.4.1.3 Mean and Flattest Corneal Curvature

Although associations were seemingly present between either the mean or the flattest corneal curvature, or both, and a given component of the various HOAs, the strength and direction of the association were almost always influenced by an outlying value of either the given corneal curvature or the given component of the given HOA (Table 6.27).

### 6.4.4.1.4 Spherical Equivalent Refraction

No association was present between the spherical equivalent refraction and any of the three components for each of the eight HOAs (Table 6.27).

### 6.4. 1.1.5 Cataract Type

No association was present between cataract type and the Total and Internal components of each of the eight HOAs (Table 6.28).

| Less severe cataract - Right Eye |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| TOTAL |  |  |  |  |  |  |  |  |  |  |
| Variable |  | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Performance | DVA | 0.188 | $<0.001$ | 0.042 | 0.002 | 0.012 | 0.420 | $<0.001$ | 0.579 |  |
|  | NVA | 0.387 | 0.370 | 0.616 | 0.539 | 0.776 | 0.776 | 0.520 | 0.405 |  |
|  | CC mean | 0.090 | 0.002 | 0.122 | 0.0002 | 0.149 | 0.094 | 0.035 | 0.004 |  |
|  | CC flattest | 0.062 | $<0.001$ | 0.007 | $<0.001$ | 0.093 | 0.080 | 0.013 | 0.003 |  |
|  | SE | 0.157 | 0.837 | 0.906 | 0.742 | 0.914 | 0.983 | 0.661 | 0.587 |  |


| Less severe cataract - Right Eye |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CORNEAL |  |  |  |  |  |  |  |  |  |
| Variable |  | HOA |  |  |  |  |  |  |  |
|  |  | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |
| Performance | DVA | 0.648 | 0.691 | 0.707 | 0.537 | 0.196 | 0.448 | 0.793 | 0.730 |
|  | NVA | 0.905 | 0.420 | 0.699 | 0.815 | 0.750 | 0.971 | 0.393 | 0.476 |
| Structural | CC mean | 0.149 | 0.034 | 0.009 | 0.074 | 0.832 | 0.004 | 0.196 | 0.886 |
|  | CC flattest | 0.100 | 0.041 | 0.009 | 0.087 | 0.004 | 0.168 | 0.854 | 0.042 |
|  | SE | 0.843 | 0.843 | 0.690 | 0.810 | 0.829 | 0.292 | 0.964 | 0.336 |


| Less severe cataract - Right Eye |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Variable |  | INTERNAL |  |  |  |  |  |  |  |  |  |
|  | Total | Tilt(S1) | High | T.Coma | H. Trefoil | T.4Foil | T.Sph | HiAstig |  |  |  |
| Performance | DVA | 0.384 | 0.135 | 0.575 | 0.430 | 0.623 | 0.739 | 0.349 | 0.545 |  |  |
|  | NVA | 0.436 | 0.438 | 0.743 | 0.330 | 0.825 | 0.204 | 0.509 | 0.334 |  |  |
|  | CC mean | 0.067 | $<0.0001$ | 0.012 | $<0.0001$ | 0.018 | 0.237 | 0.0003 | 0.0007 |  |  |
|  | CC flattest | 0.062 | $<0.0001$ | 0.012 | $<0.0001$ | 0.017 | 0.233 | $<0.0002$ | 0.0005 |  |  |
|  | SE | 0.258 | 0.723 | 0.642 | 0.658 | 0.518 | 0.718 | 0.771 | 0.587 |  |  |

Table 6.27. The probability value derived by ANOVA for the association between the performance variables (DVA and NVA); the structural variables (mean central corneal curvature, flattest central corneal curvature, and spherical equivalent) and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

| Less severe cataract - Right Eye |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| TOTAL |  |  |  |  |  |  |  |  |  |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |  |
| N | 0.968 | 0.392 | 0.175 | 0.307 | 0.209 | 0.186 | 0.464 | 0.356 |  |
| ASC | 0.653 | 0.545 | 0.369 | 0.466 | 0.487 | 0.383 | 0.323 | 0.533 |  |
| PSC | 0.710 | 0.501 | 0.638 | 0.338 | 0.546 | 0.969 | 0.857 | 0.551 |  |
| C | 0.266 | 0.574 | 0.288 | 0.501 | 0.311 | 0.315 | 0.589 | 0.478 |  |


| Less severe cataract - Right Eye |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CORNEAL |  |  |  |  |  |  |  |  |  |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |  |
| N | 0.701 | 0.244 | 0.104 | 0.096 | 0.236 | 0.466 | 0.011 | 0.557 |  |
| ASC | 0.605 | 0.547 | 0.235 | 0.198 | 0.298 | 0.947 | 0.021 | 0.388 |  |
| PSC | 0.435 | 0.676 | 0.205 | 0.315 | 0.403 | 0.176 | 0.830 | 0.063 |  |
| C | 0.042 | 0.069 | 0.299 | 0.309 | 0.482 | 0.691 | 0.308 | 0.174 |  |


| Less severe cataract - Right Eye |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| INTERNAL |  |  |  |  |  |  |  |  |  |
|  | HOA |  |  |  |  |  |  |  |  |
| Cataract Type | Total | Tilt(S1) | High | T.Coma | T.Trefoil | T.4Foil | T.Sph | HiAstig |  |
| N | 0.607 | 0.810 | 0.366 | 0.815 | 0.362 | 0.349 | 0.980 | 0.287 |  |
| ASC | 0.531 | 0.735 | 0.516 | 0.770 | 0.710 | 0.529 | 0.334 | 0.404 |  |
| PSC | 0.285 | 0.954 | 0.419 | 0.789 | 0.267 | 0.471 | 0.634 | 0.452 |  |
| C | 0.632 | 0.944 | 0.521 | 0.733 | 0.522 | 0.466 | 0.939 | 0.503 |  |

Table 6.28. The probability value derived by ANOVA for the association between the cataract type ( N (nuclear), ASC (anterior subcapsular), PSC (posterior subcapsular) and C (cortical), and each of the three components of each of the eight (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 6.4.4.2 Clear Media Case Series

The results of the explanatory analysis for the case series for the normal individuals are given in Table 6.29.

### 6.4.4.2.1 Distance Visual Acuity

Distance visual acuity was adversely influenced by the Total component of the Tilt (S1) $\left(R^{2}=40.7 \% ; p<0.001\right)$, High $\left(R^{2}=16.2 \% ; p=0.042\right)$, T.Coma $\left(R^{2}=34.7 \% ; p=0.001\right)$, T.Trefoil $\left(\mathrm{R}^{2}=16.2 \% ; \mathrm{p}=0.042\right)$, $\mathrm{T} . \mathrm{Sph}\left(\mathrm{R}^{2}=41.1 \% ; \mathrm{p}=<0.001\right)$ HOAs (Table 6.29). However, any association with the corresponding Corneal and Internal components failed to reach atatistical significance.

### 6.4.4.2.2 Near Visual Acuity

No association was present between the near visual acuity and any of the three components for each of the eight HOAs (Table 6.29).

### 6.4.4.2.3 Mean and Flattest Corneal Curvature

No associations were present between either the mean or the flattest corneal curvature and any of the three components for each of the eight HOAs (Table 6.29).

### 6.4.4.2.4 Spherical Equivalent Refraction

No association was present between the spherical equivalent refraction and any of the three components for each of the eight HOAs with the exception of the Corneal component of the T.Sph HOA ( $\mathrm{p}=0.015$ ) (Table 6.29).

| Clear Media - Right Eye |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| TOTAL |  |  |  |  |  |  |  |  |  |
| Variable |  | HOA |  |  |  |  |  |  |  |
|  |  | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |
| Perform | DVA | <0.001 | $<0.001$ | 0.001 | <0.001 | 0.722 | <0.001 | 0.001 | $<0.001$ |
|  | NVA | 0.325 | 0.890 | 0.600 | 0.356 | 0.612 | 0.651 | 0.578 | 0.813 |
| Structur | CC mean | 0.878 | 0.100 | 0.165 | 0.083 | 0.306 | 0.289 | 0.169 | 0.284 |
|  | CC flattest | 0.996 | 0.162 | 0.332 | 0.159 | 0.487 | 0.505 | 0.243 | 0.406 |
|  | SE | 0.162 | 0.550 | 0.173 | 0.315 | 0.220 | 0.288 | 0.212 | 0.592 |


| Clear Media - Right Eye |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CORNEAL |  |  |  |  |  |  |  |  |  |
| Variable |  | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |
| Perform | DVA | 0.216 | 0.492 | 0.001 | 0.008 | 0.009 | 0.031 | 0.704 | 0.097 |
|  | NVA | 0.647 | 0.191 | 0.197 | 0.182 | 0.661 | 0.042 | 0.645 | 0.624 |
|  | CC mean | 0.878 | 0.461 | 0.973 | 0.926 | 0.832 | 0.118 | 0.105 | 0.898 |
|  | CC flattest | 0.397 | 0.515 | 0.899 | 0.912 | 0.596 | 0.131 | 0.073 | 0.723 |
|  | SE | 0.614 | 0.830 | 0.372 | 0.704 | 0.449 | 0.437 | 0.015 | 0.861 |


| Clear Media - Right Eye |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| INTERNAL |  |  |  |  |  |  |  |  |  |  |
| Variable |  | Total | Tilt(S1) | High | T.Coma | T. Trefoil | T.4Foil | T.Sph | HiAstig |  |
| Perform | DVA | 0.003 | $<0.001$ | $<0.001$ | $<0.001$ | 0.839 | $<0.001$ | $<0.001$ | $<0.001$ |  |
|  | NVA | 0.312 | 0.231 | 0.638 | 0.343 | 0.765 | 0.579 | 0.576 | 0.323 |  |
|  | CC mean | 0.720 | 0.144 | 0.187 | 0.181 | 0.350 | 0.233 | 0.077 | 0.269 |  |
|  | CC flattest | 0.873 | 0.186 | 0.334 | 0.275 | 0.510 | 0.406 | 0.094 | 0.433 |  |
|  | SE | 0.128 | 0.520 | 0.121 | 0.355 | 0.185 | 0.130 | 0.244 | 0.485 |  |

Table 6.29. The probability value derived by ANOVA for the association between mean central corneal curvature, flattest central corneal curvature, and spherical equivalent, and each of the three components of each of the eight HOAs (Top: Total; Middle: Corneal and Bottom: Internal). Probability values at $\mathrm{p} \leq 0.025$ are shaded in light grey and those $>0.025 \leq 0.05$ in dark grey.

### 6.5 Discussion

The findings from this pilot study indicate that cataract extraction, by phacoemmulsification and IOL implantation results in a dramatic reduction (upto 2.7 fold) in the magnitudes of the post-operative HOAs. However, the ratio of the pre-
operative median to the post-operative median for the Corneal component of the T.Trefoil and T.4Foil HOAs, suggests an increase in these HOAs post-operatively. The latter may have arisen from the incision and the ensuing post-operative recovery.

The conclusions from the remaining comparisons must be treated with caution in that the data for the 'less severe' cataract and the clear media case series were acquired retrospectively. The summary statistics for the Total component of the Total, T.Coma, T.Trefoil and T.Sph HOAs for the 4.0 mm zone diameter in the individuals exhibiting a clear media were mean 2.585 microns, SD (2.98); median 1.464 microns, (IQR) (1.090, 2.746), mean 0.226 microns, $\mathrm{SD}(0.50)$; median 0.072 microns, (IQR) $(0.049,0.104)$, mean 0.441 microns, $\mathrm{SD}(0.89)$; median 0.123 microns, (IQR) $(0.074,0.246)$ and mean 0.088 microns, $\mathrm{SD}(0.15)$; median 0.035 microns, (IQR) ( $0.014,0.065$ ), respectively. These values bear little resemblance to those obtained with the OPD for a 6.0 mm zone diameter in 61 myopic eyes (mean 0.347 microns, SD ( 0.25 ); mean 0.165 microns, SD (0.11); mean 0.252, SD (0.16) and mean 0.120, SD (0.17) microns, respectively) (Zadok et al 2005). Clearly, these latter values were obtained with a previous, but unspecified, version of the OPD aberrometer software. No study has yet been published on the magnitudes of the various components of the eight HOAs in the normal eye with the (current) NAVEX Station software version 2.10 used in this thesis.

The age profile of the case series of the clear media case series was younger than that of the individuals with 'less severe' cataract which, in turn, was younger than that of the pre- and post-operative case series. The influence of age on the optical/ neural component of the given HOAs has not been studied using the OPD aberrometer, irrespective of software version. The Total component of the Total HOA in the normal eye declines (Fujikado et al 2004; Berrio et al 2010) and the Total components of the T.Coma and
T.Sph HOAs increase (Fujikado et al 2004; Wei et al 2006; Jahnke et al 2006; Radhakrishnan and Charman 2007; Cermáková et al 2010) with age when the given HOA is derived by a Hartmann-Shack type aberrometer. However, no age-related relationship was found for any of the components of any of the eight HOAs amongst the individuals exhibiting a clear media within the case series. The latter comprised a median age of 45 years (IQR 38, 52; range). It is possible, therefore that an age-related relationship might exist for some, or more, components over a wider age range.

It will be recalled from Chapter 3 that the Total and Internal components of the preoperative Total HOA declined with decrease in the myopic spherical equivalent refraction for the 99 individuals enrolled in the study. Indeed, this relationship was maintained for the 36 of the 99 individuals who attended the Second Follow-up examination $\left(\mathrm{R}^{2}=0.532\right)$. However, there was no equivalent association for the case series with 'less severe' cataract and for the case series of clear media. It is possible that the difference in the distributions of spherical equivalent refraction between the post operative, 'less severe' cataract and clear media case series (Tables 6.5, 6.10 and 6.14, respectively) (mean -0.69 dioptres, SD 1.21 ; median -0.50 dioptres, $\mathrm{IQR}-1.44,-0.01$; mean -1.39 dioptres, SD 4.59; median -0.37, IQR -2.25, 1.94; mean -2.43 dioptres, SD 3.31; median -2.25, IQR 4.34, - 0.47 , respectively) could account for the lack of association in the two retrospective case series.

It was not possible to match the three case series in terms of age and spherical equivalent. The two case series were derived from patients attending a refractive surgery clinic and from patients attending the same clinic for ophthalmological follow-up of cataract. By definition, both types of patients are younger and exhibit different distributions of myopic refractive error compared to the prospective case series.

It was not possible within the time constraints of the thesis to recruit age- and spherical equivalent-matched individuals from other sources and to arrange the logistics necessary for their attendance at the Enaim Refractive Clinic.

Notwithstanding, the above limitations, the remaining comparisons suggest, at least qualitatively, that the post-operative Total and Internal components of the High, T.Trefoil, T.4Foil and HiAstig (i.e., with the IOL in situ) are greater than for the clear media case series and are likely to have arisen from the IOL. The increased postoperative Corneal components of the T.Trefoil and T.4Foil HOAs are likely to have arisen from the incision and the post-operative sequelae. It can be speculated that such aberrations may be overcome either with the the continuing development of laser induced incisions (Moshirfar et al 2011; Yu and Yao 2012) or with the advent of IOLs designed to reduce such HOAs, or both.

Distance visual acuity in the clear media case series declined as the Total and Internal components of the Total, Tilt (S1), High, T.Coma, T.Sph, T.4Foil and HiAstig HOAs increased. These strong associations ( $\mathrm{R}^{2} \leq 67.6 \%$ and $\mathrm{R}^{2} \leq 63.9 \%$, respectively) can be attributed to the presence of three individuals with acuities of $6 / 10,6 / 15$ and $6 / 40$ diagnosed with stabismic and anysometropic abmlyopia, respectively. Nevertheless, the reduction in acuity with increase in magnitude for the two components of the 7 HOAs is highly compatible with that for the pre-operative case series described in Chapter 3. It is also compatible, to some extent, with the outcome for the 'less severe' cataract case series; however, the Internal component, surprisingly, was not associated with the attenuation in acuity.

The severity of the cataract in the case series with 'less severe' cataract was not available within the medical notes. The reason for the apparent similarity in the ratios for the

Internal components of the various HOAs between the 'less severe' cataract case series and that of the clear media case series may, therefore, have arisen from a 'mild' range of severity within the case series of the 'less severe' cataract. Such a hypothesis is consistent with the predominantly larger values for the Internal components of the post-operative case series compared to the case series of 'less severe' cataract.

Anecdotal inspection of the retrospective data sets suggests that these data were more variable than those acquired in the prospective series.

Despite the limitations of this pilot study, the outcomes were considered to be such as to warrant a well controlled cross-sectional study based upon the types of case series described here.

## CHAPTER 7

## CONCLUSIONS AND FUTURE WORK

To date, the study described in Chapters 3, 4 and 5 represents the largest and the longest prospective case series observational study of pre- and post-operative HOAs in agerelated cataract.

The results from Chapter 3 provided the baseline characteristics of the 99 individuals with age-related cataract. As would be expected, such individuals exhibited reduced distance visual acuity and contrast sensitivity. The distribution of distance visual acuity was bi-modal with peaks at $6 / 15$ and $6 / 60$, respectively, and was independent of age. As would also be expected, a majority of individuals exhibited poor contrast sensitivity for each of the five spatial frequencies, with the number of individuals experiencing difficulty increasing with each successive increase in spatial frequency.

Slight associations were present between age and the Total components of the Total ( $\mathrm{p}=0.018$ ) and of the T.Coma ( $\mathrm{p}=0.011$ ) HOAs. The former declined with age by 0.0360 microns per year $\left(\mathrm{R}^{2}=5.7 \%\right)$ and the latter by 0.0047 microns per year $\left(\mathrm{R}^{2}=6.6 \%\right)$.

Weak inverse associations were present for the Total and Internal components of all the HOAs ( $\mathrm{R}^{2} \leq 11.4 \%$ ) and distance visual acuity with the exception of the T.Trefoil and Hi Astig HOAs.

Weak inverse associations were also present for the Total and Internal components of the Total HOA and the Internal component of the Tilt (S1) HOA and contrast sensitivity at 1.5 and 3 cycles per degree.

The lack of any association for the higher spatial frequencies was considered to have arisen as a result of the floor effect of $100 \%$ contrast.

The spherical equivalent refraction was highly associated both with the Total ( $\mathrm{p}<0.001$ ) and the Internal ( $\mathrm{p}<0.001$ ) components of the Total HOA. Both components decreased with decrease in myopia/ increase in hyperopia $\left(\mathrm{R}^{2}=56.2 \%\right.$ and $\mathrm{R}^{2}=53.0 \%$, respectively).

The axial length was associated with both the Total and the Internal components of the Total HOA (both $\mathrm{p}<0.001$ ). Both components increased with increase in the axial length $\left(\mathrm{R}^{2}=29.3 \%\right.$ and $\mathrm{R}^{2}=27.4 \%$, respectively). The Corneal component of the Total HOA was independent of axial length ( $\mathrm{p}=0.157, \mathrm{R}^{2}=0.9 \%$ ). It was also less strongly associated with the Total and the Internal components of the High, T.Trefoil HOAs.

As might be expected, the spherical equivalent refraction co-varied with the axial length $\left(\mathrm{R}^{2}=0.245\right)$ : myopia increased with increase in axial length.

Weak associations were present between increase in cortical cataract and increase in the Total and Internal components of the T.Sph and HiAstig HOAs, particularly in the presence of nuclear colour cataract. Increasing severity of cortical cataract was also weakly associated with an increase in the Total component of the Tilt (S1) HOA. Weak associations were also present between increase in posterior subcapsular cataract and increase in the Total $(\mathrm{p}=0.003)$ and Internal $(\mathrm{p}=0.018)$ components of the Tilt (S1) HOA.

The results from Chapter 4 were based upon the 67 individuals attending the First Follow-up examination from the original 99 individuals recruited for the study. The design of the study was such that the data set derived at the follow-up examination could be analysed both in terms of the absolute outcomes and also of the change in the outcomes relative to baseline. The former permitted an identical explanatory analysis of
the HOAs to that in Chapter 3 except that it enabled such an analysis to be undertaken over a potentially larger (and improved) range of magnitude for the given HOA. The latter permitted the explanatory analysis of associations between the change in magnitude of a given variable and that of a given HOA.

At the First Follow-up examination, the Post-operative visual acuity was inversely associated with the Corneal component of all the HOAs with the exeption of the T.Sph and the HiAstig HOAs. In addition, an increase in the magnitude of the Corneal component, only, of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs was weakly associated with a decline in contrast sensitivity for 1.5 and 3.0 cycles per degree. A similar finding was present for the Corneal component of the Tilt (S1) HOA and contrast sensitivity for 6.0 and 12.0 cycles per degree. The lack of an association with contrast sensitivity for 18.0 cycles per degree was attributed to the lack of individuals manifesting such vision.

A weak association, at the First Follow-up examination, was present between the increase in the Corneal component, only, of each of these four HOAs and a reduction in endothelial cell density. It is also possible that the Corneal component of the Total, Tilt (S1), High and T.Trefoil HOAs, but not T.Coma HOA, decreased with increase in flattest corneal radius. However, the latter associations may have arisen from what may have been outlier values of the flattest corneal curvature.

The association of the cornea with the Corneal component of the various HOAs, and the inverse association of the latter with distance visual acuity, at the First Follow-up examination, was attributed to the surgery and the post-operative healing.

No association was present between the post-operative spherical equivalent refraction and any of the three components for each of the eight HOAs.

The post-operative Total and Internal components of all HOAs were smaller than the preoperative value with the possible exception of HiAstig HOA. The magnitudes of these reductions, between 1.4 fold and 2.7 fold, were similar for 5 of the 7 HOAs and were slightly lower for the Tilt (S1) and T.Sph HOAs. However, no associations were present between pre-operative cataract type and severity and the change in any of these components. The improvement in the HOAs was independent of the type of IOL with the exception of the Total HOA.

The reduction in endothelial cell density was only associated with an increase in the Corneal component of the T.Coma HOA. The reason for a lack of an association between the reduction in endothelial cell density and the change in each Corneal component of the Total, Tilt (S1), High, and T.Trefoil HOAs is unknown. The apparent association between the reduction in corneal curvature, principally that of the flatter meridian, and the increase in the Corneal component of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs, was likely to be arisen from apparent outlying values for changing corneal curvature.

As would be expected, the post-operative reduction in myopic/ increase in hyperopic spherical equivalent refraction was strongly associated with the reduction in the Total and Internal components of the Total HOA $\left(\mathrm{R}^{2}=45.3 \%\right.$ and $51.1 \%$, respectively $)$.

The results from Chapter 5 were based upon the 41 of the 67 individuals attending the First Follow-up examination, who had attended the Second Follow-up examination. The analysis of the results was undertaken in a similar manner to that for Chapter 4 with the change in results being referenced to the baseline rather than to the First Follow-up.

The outcome of the analysis benefitted from more stable ocular parameters resulting from the longer post-operative recovery time but suffered from a loss of statistical power compared to the analysis undertaken in Chapter 4. Nevertheless, the outcomes both in terms of the ratios of the pre- to post-operative medians of the distributions of the given component of the given HOA, and in terms of the explanatory analysis were, in essence, identical to those of the First Follow-up examination.

The results from the pilot study described in Chapter 6 suggest that the post-operative HOAs are higher than those present in younger eyes with clear media. However, there is some suggestion that, although there is a post-operative reduction in the Total and Internal components of the T.Trefoil and T.4Foil HOAs, there is an associated increase in the Corneal component of the Total HOA, which increased with increase in age at the Second Follow-up examination and of the T.Coma HOA, which increased at the First Follow-up examination as the corresponding corneal endothelial cell density decreased. The increase in the Corneal component of the Total, Tilt (S1), High, T.Coma and T.Trefoil HOAs, was also associated with an increased in the magnitude of the change in the flattest corneal curvature from the Pre-operative to the First- and to the Second Follow up examinations. However, such associations appeared to have arisen from two obvious outlying data points.

The results from the various studies confirm that most Total and Internal components of the HOAs were larger pre-operatively than post-operatively and thereby implicate the role of age-related cataract in their aetiology/ progressive increase. However, no one particular cataract type could be unequivocally identified with any one particular HOA. Nevertheless, an association was found, in Chapter 3, between the Total component of the Tilt (S1) HOA which increased with increase in both cortical and posterior subcapsular cataract. These associations are a novel finding. The association with the

Internal component of the Tilt (S1) HOA was maintained for posterior subcapsular cataract only. The Total and Internal components of both the T.Sph and the HiAstig HOAs increased with increase in severity of cortical cataract. These latter findings are in agreement with Kuroda et al (2002), Sachdev et al (2004), Rocha et al (2007) and Lee et al (2008). The associations were particularly apparent in the presence of increasing nuclear colour cataract. The Total Component of the T.Coma HOA increased with increase in severity of the posterior subcapsular cataract. The association between T.coma HOA and cortical cataract (Lee et al 2008; Rocha et al 2007; Sachdev et al 2004; Kuroda et al 2002) was not present in the current study. A different study suggests that nuclear and cortical cataract produce a higher amount of tetrafoil (Sachdev et al 2004). In the current study, a weak association was found between the Internal component of the T.4Foil HOA and nuclear opalescence ( $\mathrm{p}=0.046$ ).

The studies described in Chapters 3, 4 and 5 were well controlled and involved the investigation of associations between a wide range of functional and structural variables, obtained using a variety of different equipment. In addition, the HOA data set from each of these Chapters was analyzed in terms of the latest NAVEX Station software (Version 2.10 of the Nidek OPD Scanning System ARK-10000 aberrometer, which enables the partition of the given HOA into three components, Total, Corneal and Internal.

Although no power calculations could be undertaken, confidence can be placed in the results described in Chapter 3, given that the outcome was derived from a case series of 99 individuals.

However, the logistical and time constraints necessary for data acquisition and analysis of the data and compilation of the thesis prevented the enrolment of an age-matched normal control group and thus the utilization of a case-control study. However, given that the
development of cataract is a natural consequence of aging, a 'normal' control group would inevitably have contained individuals with (less severe) age-related cataract.

All, but one, of the age-related cataracts present in the case series of the 99 individuals contained more than one type of cataract. The absence of 'pure' cataract (i.e., of one particular type) in those listed for surgery prevents a clear understanding of the relationship between cataract type and HOAs.

Although there was no statistical significant difference on the post-operative outcomes between the four surgeons, the study would have been more robust had the post-operative case series emanated from a single surgeon. The post-operative outcomes in terms of the magnitudes of the various HOAs varied between the four types of IOL used in the case series. The study would, again, have been more robust if a single type of IOL had been used. However, the logistical and time constraints, discussed earlier, precluded such a design.

The algorithm which enables the partition of the given HOA into the three components has not been described in detail in the literature and, as such, the OPD aberrometer must be treated as a 'black box' in terms of the absolute value of the given component of the given HOA. Commercial availability does not guaranty validity (Pesudovs and Applegate 2009). The 'black box' nature of the OPD aberrometer was exemplified by the lack of resemblance, for the case series, of the magnitudes of the Total component of the various HOAs derived for a 6.0 mm zone diameter by the 'partitioning' software compared with that output directly from the aberrometer, itself, (i.e., without partition) and also with that published in the literature for an earlier version of the software (Zadok et al 2005).

The HOAs were described for the 4.0 mm zone diameter rather than for the 'gold' standard 6.0 mm zone diameter to maximize the number of individuals within the case
series; despite pupil dilatation, many elderly individuals could not achieve a pupil diameter greater than 6.0 mm necessary for the 6.0 mm zone diameter measurement.

A comparative study of six different commercially available aberrometers undertaken on normal individuals found that the Nidek aberrometer (albeit not with the NAVEX Station version 2.10 software) underestimated the magnitudes of polynomials describing 4- and 5 -fold symmetries (i.e., $4^{\text {th }}$ order vertical and oblique cuadrifoil HOAs, and $5^{\text {th }}$ order oblique pentafiol HOA) and overestimated vertical and oblique trefoil HOAs ( $3^{\text {rd }}$ order), vertical ( $4^{\text {th }}$ order) and oblique ( $5{ }^{\text {th }}$ order) secondary astigmatism HOAs relative to the other aberrometers (Rozema et al 2006). The NAVEX software has yet to be validated against other types of aberrometers. A similar study to the one described in this thesis, and undertaken in the future, could benefit from the use of more than one type of aberrometer. The ensuing comparison of the absolute values for any given component of any given HOA derived by each different types of aberrometer could result in a more robust study in that the outcome for any one type of aberrometer might be more representative of the 'true' value than any other type and thus provide a stronger association with potential structural correlates.

The OPD aberrometer has the option for an assessment of corneal topography. Such an option was not considered in the current study and, with hindsight, the study would perhaps have been more robust if such data had been recorded and included in the explanatory analysis. This approach would have been particularly useful given the implication of the immediate post-operative cornea in the generation of the Corneal components of some HOAs and the presence of possible outliers in the post-operative mean and flattest central corneal curvatures.

The OPD aberrometer also has the option to provide the MTF. The use of such an option was not considered possible within the time constraints of the thesis. Such data is stored electronically and an analysis could be undertaken in a future project.

Clearly, wavefront aberrometry has the potential to perform a useful role in the understanding of cataract formation and its consequences on vision. It would appear to have value in the identification of (currently) sub-clinical changes in the crystalline lens; for example, those associated with diabetes (Shahidi et al 2004) with Retinitis Pigmentosa (Rajagopalan et al 2005) with systemic steroids (Liu and Manche 2011) and with other drug-induced cataract, such as that arising from the anti-psychotic Quetiapine, with radiation cataract (Milacic 2009) and with traumatic cataract. It could also be used for the early detection of other lenticular-related events such as posterior capsular thickening and a potentially subluxating lens.

Equally, wavefront aberrometry could also be used for the early detection of corneal dystrophies, for example Fuchs' endothelial dystrophy (Patel et al 2012). In this context, an important systemic condition, with both corneal and crystalline lens manifestations, which would benefit from investigation with wavefront aberrometry is that of Still's disease. Aberrometry should enable the earlier detection of the band keratopathy and of the cataract associated with this condition.

Aberrometry also has the potential to provide useful information not only on the visual outcomes of presbyopia but also on the mechanism(s) for the condition, and on the surgical correction whether of corneal (Pinelli et al 2008; Telandro 2009; Uy and Go 2009; Holzer et al 2012; Bouzoukis et al 2012) or IOL (Olson et al 2006; MontésMicó et al 2008; Alfonso et al 2008; Klaproth et al 2011) origin.

A further useful study would be a comparison of the outcome of aberrometry with that of densitomerty in advanced nuclear cataract.

The current study was undertaken without knowledge of the test-retest variability, over a given time period, of the given HOAs with the OPD aberrometer, particularly in individuals with cataract. Indeed, no such information is available in the literature. Perhaps, in hind-site, such an investigation would have resulted in a more robust study. Some indication can be gained from a study of the comparative performance of three aberrometers in a case series of 19 ocularly normal individuals. The $95 \%$ confidence interval for repeated measurements with the OPD aberrometer, using an early version of the software, was 0.12 for Total, 0.03 for T.Sph, 0.10 for Coma and 0.14 for Trefoil HOAs (Burakgazi et al 2006). In the current study, the difference between the given HOA at the First Follow-up compare to that at the Pre-operative examination was -2.284 , $-0.137,0.166$ and -0.570 microns, respectively, for these four HOAs. Thus, the postoperative difference for each HOA lay outside the $95 \%$ confidence interval for repeated measurements published by Burakgazi et al (2006) albeit with the NAVEX Station software.

The explanatory analysis did not incorporate intraocular pressure as an independent variable since the techniques had been undertaken by numerous different ophthalmologists and not by the Author. In addition, incorporation of any further variables into the explanatory modeling would have reduced the variance available for the modeling of the selected independent variables. The IOP lay within the normal range (i.e., $\leq 21 \mathrm{mmHg}$ ) at all examination visits for all individuals and the literature suggests that the influence of IOP on the HOAs is equivocal (minimal).

The study did not incorporate an assessment of ocular surface integrity at any of the three examinations.

A decision to omit such an assessment largely resulted from the time constraints imposed by the other examination procedures used in the study and by the need to incorporate these procedures within the scheduled time for the normal clinical visits and alongside other patients attending for routine medical care. More importantly, the decision was made at the outset of the study, when the partitioning software had not been released and it was considered that the influence of any induced HOAs arising from ocular surface abnormality would be minimal relative to those arising from age-related cataract and the associated surgical sequelae. Any future study could benefit from the inclusion of an assessment of ocular surface characteristics.

The explanatory analysis involved an in-depth investigation of potential univariate linear associations with HOAs. The logical next-step would be to develop a multivariate model for the description of HOAs such as principal components analysis.

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