




# Biometry and corneal aberrations after cataract surgery in childhood

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## Abstract

**Background:** To report long-term biometric and refractive outcomes in a group of Danish children after surgery for childhood cataract.

**Methods:** Children between 7 and 18 years who had undergone uni- or bilateral cataract surgery at the Department of Ophthalmology, Rigshospitalet, Denmark, were examined in this cross-sectional study. Swept source optical coherence tomography (OCT) based optical biometry (IOLmaster 700) and anterior tomography (Pentacam) was performed. Healthy fellow eyes from those with unilateral cataract were used as controls.

**Results:** We included 56 children in the study with a median age at surgery of 43.8 months (1.6–137.6). The amount of higher order aberrations was significantly increased in operated eyes (median root mean square 0.461  $\mu\text{m}$  [range 0.264–1.484]) compared with non-operated eyes (median root mean square 0.337  $\mu\text{m}$  [range 0.162–0.498],  $p < 0.001$ ). Younger age at surgery was positively associated with more higher order aberrations at follow-up ( $p < 0.001$ ), but we found no significant associations between the amount of higher order aberrations and visual acuity or contrast vision. Longer axial length was associated to glaucoma while shorter axial length was associated to strabismus ( $p < 0.001$ ).

**Conclusions:** Eyes operated for childhood cataract have higher order aberrations compared with non-operated eyes. Higher order aberrations are complex refractive errors that cannot be corrected by normal lenses and may contribute to poor visual outcomes for the children. We found an association between young age at surgery and higher order aberrations.

## KEYWORDS

axial length, central corneal thickness, congenital cataract, developmental cataract, higher order aberrations

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## 1 | INTRODUCTION

Children with cataract require frequent monitoring to adjust for changes in refraction as the eye grows and to diagnose potential long-term complications such as amblyopia, glaucoma and visual axis opacification.<sup>1</sup> Axial elongation continues throughout childhood and it is recommended to aim for hyperopia in smaller children when intraocular lenses (IOLs) are implanted to obtain emmetropia in adulthood.<sup>2,3</sup> The factors influencing normal eye growth and emmetropization are not fully understood but genetic and environmental factors such as visual input play important roles.<sup>4</sup> Childhood cataract is often associated with shorter axial length.<sup>5,6</sup> The growth rate after surgery did not differ from healthy fellow eyes in the Infant Aphakia trial, but growth might accelerate due to secondary glaucoma<sup>5</sup> and it may be different in eyes with bilateral cataract as they often have a shorter axial length.

The associations between eye growth and complications after cataract surgery in childhood, for example, amblyopia and strabismus, are unknown but they may influence eye development due to disturbances in visual stimulation.<sup>6–10</sup> Moreover, the literature regarding long-term effect of cataract surgery in childhood on corneal astigmatism is sparse<sup>11,12</sup> and we have not been able to find any long-term studies of the presence or visual effects of higher order aberrations in cataract operated children.

This study describes long-term refractive and biometric outcomes and their relation to visual outcomes in a group of children operated for cataract and followed at the Department of Ophthalmology, Rigshospitalet, Denmark. The results are compared with the fellow healthy eyes of children with unilateral cataracts.

## 2 | METHODS

### 2.1 | Study design

This is a cross sectional study of the refractive and biometric outcomes in 56 children between the age of 7 and 18 years previously operated for uni- or bilateral congenital or developmental cataract. In general, children operated <6 months of age were aphakic and children operated >6 months of age received an IOL at the time of cataract surgery. It was not possible to include a control group of age matched children with no eye abnormalities, why we used the second best—the fellow-eye of unilateral cases. One eye of a participant with bilateral Peters anomaly and unilateral cataract surgery was excluded from the control group. Cases of nystagmus were

included as they often present with the worse visual outcomes why other complications such as increased amounts of higher order aberrations could be more prevalent in this group. Invitations and study information were sent by mail that was followed by a telephone call if the parents did not respond to the initial invitation letter. Children who were deemed not able to comply with the examination due to severe intellectual disabilities were not invited. The study was approved by The Committee on Health Research Ethics for the Capital Region (j.nr.: H170370337) and the Danish Data Protection Agency (RH-2018-47, I-Suite no. 6244). The study followed the tenets of the Helsinki declaration. For a child to participate, parents or legal custody holders had to provide written informed consent and children provided oral consent.

### 2.2 | Eye examination

Corrected distance visual acuity was measured using the HOTV 3 Meter visual chart (HOTV3M, Precision Vision, Inc., Woodstock, IL). Contrast vision was measured in a dark room using Freiburg Visual Acuity Contrast Test (FrACT v. 3.3.9a, Michael Bach). The power and type of refractive correction used was noted, for example, mono- or bifocal glasses, contact lenses or a combination thereof. Subjective refraction was done before testing the visual acuity. Subjective refraction was guided by the child's own refractive prescription. Automated cycloplegic refractive measurements were then obtained after administration of one drop 10 mg/ml cyclopentolate-hydrochloride (Alcon, Fort Worth, TX) administered twice with 5 min interval using the Retinomax K plus three autorefractor (Righton, Tokyo, Japan).

Intraocular pressure was measured using a handheld tonometer (TA01, Icare, Vantaa, Finland). If eye pressure exceeded 21 mmHg, applanation tonometry was performed if possible. Glaucoma was defined according to a classification system for paediatric glaucoma<sup>13</sup> as two or more of the following criteria fulfilled: intraocular pressure > 21 mmHg, visual field defects, glaucoma suspicious corneal finding (e.g., corneal diameter > 13 mm), glaucoma suspicious optic nerve finding (e.g., focal rim thinning) or increased ocular dimensions that outpace normal growth. If the patient only fulfilled one of the abovementioned criteria the patient was categorised as glaucoma suspect. All eyes that had undergone glaucoma surgery were also classified as having glaucoma. Amblyopia was defined as eyes that were or had been under amblyopia therapy. Strabismus was defined as manifest exo-, eso, hyper- or hypotropia during a corneal light reflex test.

Information about previous medical history including information on date of cataract surgery and subsequent surgeries, for example, for visual axis opacifications or glaucoma, was retrieved from medical files.

### 2.3 | Optical biometry

Swept source optical coherence tomography (OCT) based optical biometry was performed using the IOLmaster 700 (Carl Zeiss Meditec, Inc, Dublin, CA) providing information about the axial length, axial length, white-to-white, spherical equivalent, lens thickness and keratometry (K) readings.

### 2.4 | Anterior eye segment tomography

Anterior eye segment tomography was performed using the Pentacam (OCULUS Optikerg r te, GmbH, Wetzlar, Germany) providing data of the anterior chamber, and the anterior and posterior corneal surfaces. The asphericity, the axis of the flattest meridian, radius and power of the flattest and steepest curvatures, and the absolute power of the corneal astigmatism were measured. Corneal Thickness (CT) was evaluated at the pupil centre (central CT), apical CT and as thinnest location CT. The corneal wavefront aberrations were measured using Zernike Analysis as the root mean square of first and second order aberrations and the root mean square of third and higher aberrations. The corneal volume, anterior chamber volume, anterior chamber depth and the anterior chamber angle were noted. Only anterior segment tomographies graded as 'OK' by the in-built Pentacam quality software were included in our analysis.

### 2.5 | Statistical analysis

The operated eyes of unilateral cases and right eyes in bilateral cases were included in the analysis. Healthy fellow eyes of the unilateral group were used as controls. The median and range was used to describe our results as most of our data did not follow normal distribution judged by Shapiro-Wilks test of normality  $p < 0.05$ . When data followed a normal distribution, unpaired- or paired t-test was performed as appropriate and Wilcoxon rank-sum test or Wilcoxon signed-rank test when not. Associations in our data were investigated by stepwise regression analysis. Data were collected and stored using REDCap (v. 10.6.18, REDCap electronic data capture tools), and all statistical analysis was performed in Rstudio for Windows (v. 3.6.1, RStudio, Inc.).

## 3 | RESULTS

We included 56 children (30 males and 26 females) between the age of 7.5 and 18.1 years; 28 children had been operated for bilateral cataract and 28 for unilateral cataract in the period 2000–2018 with a median age at surgery of 43.8 (1.6–137.6) months. Axial length measurements were attainable in 55 children and anterior segment tomography could be performed in 45 children. Presence of nystagmus limited the number of acceptable quality tomographies to 5 out of 10 children and 4 of 10 were acceptable for the Zernike Analysis. Baseline demographics of the study population is shown in Table 1.

### 3.1 | Axial length

Glaucoma and unilateral surgery were associated to a significantly longer axial length and strabismus to a shorter axial length ( $p < 0.001$ , stepwise regression analysis). Age at examination, age at surgery, pseudophakia versus aphakia and previous treatments for visual axis opacification were not significant predictors of axial length. Eyes with secondary glaucoma had a median axial length of 25.49 mm (range, 21.50–31.06) versus axial length 22.32 mm (range 20.05–27.36) in operated eyes without glaucoma. Operated eyes with strabismus had a median axial length of 21.89 mm (range 20.15–25.49) and operated eyes without strabismus had a median axial length 22.76 mm (range 20.05–31.06) (Figure 1).

### 3.2 | Cornea and anterior chamber depth

No significant difference in central corneal thickness between operated and unoperated eyes was found with a median of 565  $\mu\text{m}$  (range 504–773) in operated eyes and 570  $\mu\text{m}$  (range 494–605) in unoperated eyes, ( $p = 0.47$ ). Central corneal thickness was increased in operated eyes with secondary glaucoma, in glaucoma suspect eyes and in unilateral eyes ( $p < 0.001$ ). Age at examination, age at surgery, aphakia versus pseudophakia, unilateral versus bilateral surgery and contact lens use versus no contact lens use were not significant predictors. Operated eyes had a smaller (white to white) corneal diameter (median 11.75 mm [range 9.70–14.50]) compared with controls (median 12.00 mm [range 11.30–13.90],  $p = 0.004$ ). In operated eyes glaucoma, older age at the examination and unilateral surgery were associated to a wider white to white ( $p < 0.001$ ). There was no significant effect of aphakia or pseudophakia, age at surgery or axial length. The anterior chamber was deeper in operated eyes

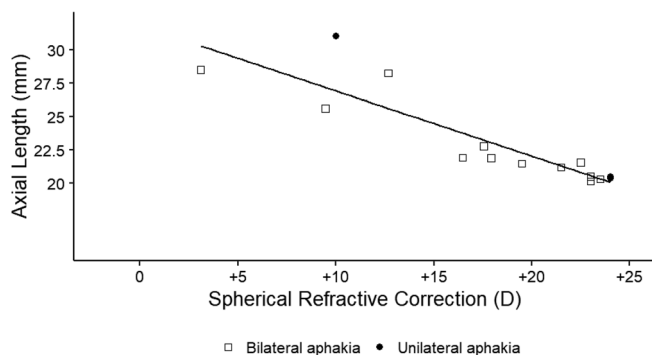


TABLE 1 Baseline demographics, ocular biometry and anterior segment tomographies

	Bilateral surgery		Unilateral surgery		All operated eyes	Controls
	Aphakia	Pseudophakia	Aphakia	Pseudophakia		
Male/Female	8/4	7/9	1/4	14/9	30/26	15/12
CDVA (logMAR)	0.64 (0.02 to 1.06)	0.1 (-0.1 to 0.98)	1.1 (0.6 to 1.1)	0.8 (0.06 to 1.1)	0.62 (-0.1 to 1.1)	-0.06 (-0.3 to 0.2)
Glaucoma	4 (33.3%)	0 (0.0%)	3 (60.0%)	1 (4.3%)	8 (14.3%)	0 (0.0%)
Glaucoma suspects	2 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)
Visual axis opacification	3 (25%)	6 (37.5%)	0 (0.0%)	5 (21.7%)	13 (23.2%)	0 (0.0%)
Amblyopia	2 (16.7%)	1 (6.3%)	2 (40.0%)	22 (95.7%)	27 (48.2%)	-
Age at examination (years)	11.1 (7.6-18.1)	12.6 (8.6-18.0)	9.0 (8.0-15.3)	10.6 (7.5-16.1)	11.15 (7.5-18.1)	10.4 (7.5-16.1)
Age at surgery (months)	3.8 (1.8-36.0)	63.1 (5.0-137.6)	2.8 (1.6-48.4)	50.4 (12.8-127.4)	43.8 (1.6-137.6)	-
Axial Length (mm)	21.74 (20.15-28.52)	22.73 (20.05-24.89)	22.36 (20.39-31.06)	22.76 (20.77-27.36)	22.49 (20.05-31.06)	22.92 (21.60-24.63)
White to white (mm)	11.1 (10.6-12.7)	11.65 (11.1-12.5)	11.6 (9.7-14.5)	11.8 (11.0-12.3)	11.7 (9.7-14.5)	12.0 (11.3-13.9)
Sphere (D)	14.75 (8.25-22.00)	-2.50 (-9.25-1.00)	9.13 (0.00-18.25)	-2.13 (-10.50-2.50)	-0.50 (-10.50-22.00)	1.00 (-1.25-7.93)
Spherical equivalent (D)	17.5 (8.7-22.5)	-1.1 (-7.9-2.6)	9.7 (1.1-18.4)	-0.5 (-9.7-3.4)	0.10 (-9.7-22.5)	1.4 (-0.6-3.1)
Pentacam cylinder (D)	1.6 (0.3-5.0)	2.8 (1.2-5.3)	1.8 (0.2-2.3)	1.8 (0.9-4.9)	2.2 (0.2-5.3)	0.6 (0.0-2.0)
Children with "OK" Pentacam scans	7 (58.3%)	16 (100.0%)	4 (80.0%)	18 (78.3%)	45 (80.4%)	25 (92.6%)
Higher order aberrations (RMS) (µm)	0.549 (0.420-1.099)	0.412 (0.338-0.778)	0.539 (0.420-0.573)	0.455 (0.264-1.031)	0.455 (0.264-1.099)	0.337 (0.162-0.498)
Pentacam K1 (D)	43.6 (41.6-44.5)	42.0 (38.6-45.9)	40.70 (36.1-42.2)	42.6 (38.6-44.9)	42.3 (36.1-45.9)	43.0 (39.3-46.3)
Pentacam K2 (D)	44.9 (43.9-48.7)	44.9 (41.2-48.4)	41.9 (37.4-44.5)	44.3 (42.1-47.3)	44.6 (37.4-48.7)	43.7 (40.2-46.6)
With the rule astigmatism	4 (57.2%)	15 (93.8%)	2 (50.0%)	15 (83.3.2%)	36 (80.0%)	23 (92.0%)
Against the rule astigmatism	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	2 (4.4%)	0 (0.0%)
Central CT (µm)	565 (504-645)	557 (519-660)	657 (595-773)	585 (513-620)	565 (504-773)	570 (494-605)
Apical CT (µm)	568 (507-638)	557 (523-662)	657 (595-774)	585 (427-649)	568 (527-774)	572 (496-608)
Thinnest Location CT (µm)	561 (501-625)	550 (513-656)	652 (595-761)	580 (509-612)	562 (501-761)	566 (486-603)
AC Depth (mm)	3.68 (2.73-5.63)	4.18 (3.52-4.99)	3.95 (3.51-5.25)	4.26 (3.36-5.33)	4.14 (2.73-5.63)	3.15 (2.62-3.48)
AC angle (°)	45.40 (36.30-50.60)	40.70 (20.20-56.80)	42.3 (37.3-54.1)	38.75 (17.70-54.30)	40.40 (17.70-56.80)	33.60 (15.90-54.80)

Note: Table values are presented as median (range) except when numbers (percentage) are given. For the bilateral group, data from the right eye was used. In the bilateral pseudophakic group 5 left eyes had been under amblyopia treatment. Visual axis opacification depicts if the eye previously had been treated for visual axis opacification.

Abbreviations: AC, anterior chamber; CT, corneal thickness; K1, flat corneal meridian; K2, steep corneal meridian; mm, millimetre, µm, micrometre, RMS, root means square.



**FIGURE 1** Relationship between axial length in millimetre (mm) and the spherical correction currently used in children with aphakia in diopters (D). Only data from right eyes in the bilateral aphakic children and operated eyes in the unilateral aphakic children are displayed,  $R^2 = 0.890$ ,  $p < 0.001$ . Contact lens prescriptions were used, and if not available the spectacle prescription was converted using the formula: estimated contact lens sphere = spectacle sphere / (1 - 0.012 spectacle sphere)

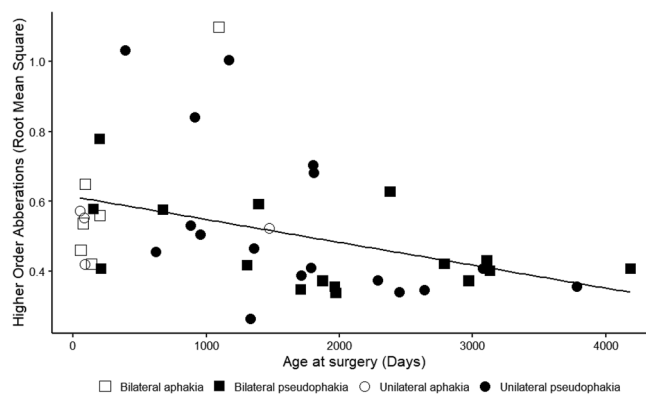
(anterior chamber depth median 4.14 mm [range 2.73–5.63] versus 3.15 mm [range 2.62–3.48] in control eyes,  $p < 0.001$ ). There was no significant effect of age at the examination, age at surgery, pseudophakia, unilateral versus bilateral surgery, or glaucoma on the anterior chamber depth in our study population in a stepwise regression analysis.

### 3.3 | Astigmatism

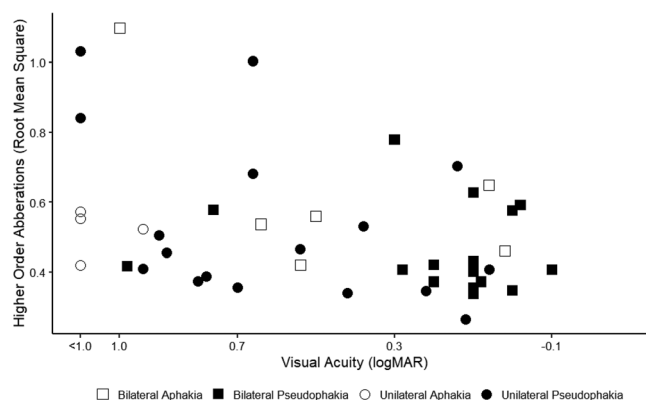
Operated eyes had median total frontal corneal astigmatism of 2.20 D (range, 0.20–5.30) versus 0.60 D (range, 0.00–2.00) in the control group ( $p < 0.001$ ). No significant effect of aphakia/pseudophakia, bilateral or unilateral surgery, age at the examination, age at surgery or glaucoma on frontal corneal astigmatism could be shown in a stepwise regression analysis. Operated eyes also had higher total astigmatism of the back of the cornea (median 0.50 D, range: 0.10–1.10, vs. 0.30 D, range, 0.10–0.60,  $p = 0.001$ ) and it was higher in pseudophakic than aphakic eyes. Pseudophakia was a significant predictor of increased total astigmatism of the back of the cornea ( $p < 0.001$ ) in a stepwise regression analysis, but there were no effect of bilateral or unilateral surgery, age at the examination, age at surgery or glaucoma.

### 3.4 | Higher order aberrations

Higher order aberrations were significantly higher in operated eyes (median root mean square 0.455 [range 0.264–1.099] vs. 0.337  $\mu\text{m}$  [range 0.162–0.498],  $p < 0.001$ ).



**FIGURE 2** Scatterplot presenting the relationship between surgery age and the amount of root mean square higher order aberrations at the examination date. Only data from right eyes in the bilateral group and operated eyes in the unilateral group are displayed



**FIGURE 3** Scatterplot presenting the relationship between visual acuity (logMAR) and the amount of higher order aberrations at the examination date. Only data from right eyes in the bilateral group and operated eyes of the unilateral group are displayed

When contact lens users were excluded from the analysis, higher order aberrations remained significantly higher in operated eyes (median root mean square 0.425 [range 0.338–1.099],  $p < 0.001$ ). Younger age at surgery was associated to increased amounts of higher order aberrations in a stepwise regression analysis ( $p < 0.001$ ) and continued to be so when only including children who did not use contact lenses in the analysis, ( $p = 0.006$ , Figure 2). There were no associations between higher order aberrations and aphakia or pseudophakia, glaucoma, the use of contact lenses, the presence of amblyopia or the presence of nystagmus using stepwise regression. The amount of higher order aberrations did not influence visual acuity or contrast vision in a stepwise regression analysis accounting for aphakia/pseudophakia, bilateral/unilateral surgery, age at surgery and age at the time of examination, Figure 3, neither when excluding children



using contact lenses. The amount of lower order aberrations was also significantly higher in operated eyes (median root mean square  $2.444\ \mu\text{m}$  [range 0.902–5.473] vs.  $1.033\ \mu\text{m}$  [range 0.395–4.492] in control eyes,  $p < 0.001$ ). There was no association between age at surgery, aphakia/pseudophakia, bilateral or unilateral surgery, age at the examination, use of contact lenses or the presence of amblyopia, glaucoma or nystagmus on the amount of lower order aberrations measured at the examination,  $p = 0.87$ .

## 4 | DISCUSSION

This study investigated long-term biometric and refractive outcomes after cataract surgery in childhood. Eyes in the operated group had significantly higher number of higher order aberrations and greater amount of astigmatism than control eyes. There was an association between young age at surgery and increase in higher order aberrations. Higher order aberrations are complex refractive errors that cannot be corrected by normal lenses. In theory higher order aberrations could be a contributing factor to poor visual outcomes and may increase the risk of amblyopia after surgery for childhood cataract but there were no associations between the amount of higher order aberrations and visual function measured as visual acuity or contrast vision but to rule out an effect of higher order aberrations on visual function larger studies are needed. The increased amount of higher order aberrations in eyes with younger age at surgery could be induced by surgical incisions in a softer more malleable cornea in younger eyes.

Contact lens wear is known to increase higher order aberrations in healthy eyes<sup>14</sup> and as participants was not instructed to avoid contact lens use this could be a confounding factor, however, contact lenses were only used in 8 out of the 45 eyes with anterior segment tomographies with a quality that allowed interpretation and use in the models. No association between higher order aberrations and the presence of nystagmus was found but only 4 out of 10 children with nystagmus had tomographies of acceptable quality for analysis.

Some studies of postoperative corneal astigmatism suggest the astigmatism regress in the first months following cataract surgery.<sup>15–19</sup> However these studies are of older date when large corneal incisions were used. A more recent study in children undergoing unilateral surgery at age 28 days to <7 months and evaluated at 1 year of age found that corneal astigmatism regressed in aphakic children but remain unchanged in pseudophakic children.<sup>20</sup> Interestingly, a long-term study of 12 pseudophakic eyes from nine children showed an increase in corneal astigmatism over

time.<sup>11</sup> Stepwise regression analysis did show a higher level of astigmatism on the back of the cornea associated to pseudophakia but no association between pseudophakia and the level of astigmatism on the front of the cornea was found.

The presence of secondary glaucoma, glaucoma suspicion and unilateral surgery were significant predictors of increased central corneal thickness. The association between secondary glaucoma and increased central corneal thickness have already been described in other studies.<sup>21,22</sup> Several studies have also described increased central corneal thickness in aphakic and pseudophakic eyes of children without secondary glaucoma when compared with healthy fellow eyes.<sup>21–24</sup> One theory is that the increased central corneal thickness is induced by cataract surgery,<sup>22</sup> however central corneal thickness in operated non-glaucoma eyes was not increased in this study when compared with control eyes. Others have ascribed the thicker cornea after childhood cataract surgery to contact lens wear.<sup>24</sup> No such an association was found either but as only 8 of the 45 operated eyes in our study with good quality anterior segment tomographies were contact lens users this might have limited our potential to measure the effect of contact lens use on the central corneal thickness. A thick and rigid cornea increase the risk of measuring a falsely elevated intraocular eye pressure. This emphasises the importance of defining glaucoma using glaucoma specific changes in eye anatomy or visual field defects and not only relying on increased intraocular pressure.

Cataract operated eyes were shorter and had wider ranges in axial length when compared with control eyes which corresponds to previous findings.<sup>6</sup> Glaucoma was associated to a longer axial length as was expected<sup>5,6,25</sup> due to stretching of the young eye by the increased intraocular pressure. Of the 56 operated eyes 27 were amblyopic of which 17 were strabismic. Strabismic eyes had shorter axial length. This could possibly be because the defocusing of the strabismic eye inhibits eye emmetropization.<sup>26</sup> It could also be that the refractive error of a short eye contributes to the development of deprivational amblyopia leading to deep amblyopia and strabismus, or that short and maybe underdeveloped cataract eyes have lesser visual potential ultimately resulting in deprivational amblyopia also leading to deep strabismic amblyopia. Studies in animals have shown that visual deprivation can result in an increased axial length growth.<sup>9,27</sup> However, this is not as predictable in human eyes.<sup>10</sup> The rate of axial length elongation is at its fastest in early life especially during the first 10 months of life.<sup>28</sup> Therefore, for potential visually depriving factors like astigmatism, visual axis opacification or higher order

aberrations to affect eye growth they may have to occur early in life. Amblyopia were particularly prevalent in the unilateral pseudophakic group were 95.7% of eyes were amblyopic.

No significant associations between the amount of astigmatism or higher order aberrations and axial length was found when including these parameters in our analysis. When including astigmatism and higher order aberrations in the analysis eyes with anterior segment tomographies with too poor quality were discarded, thus eyes that were unable to fixate or had severe nystagmus were not included in the analysis. However, the axial length of discarded eyes did not differ significantly from included eyes.

To summarise glaucoma eyes had increased axial length and strabismic eyes had shorter axial length. Glaucoma, glaucoma suspicion and unilateral surgery were significant predictors of increased central corneal thickness. In addition, pseudophakia was associated to increased total astigmatism of the back of the cornea. Eyes operated for congenital and developmental cataract had significantly higher order aberrations compared with healthy fellow eyes, and eyes of children operated at a young age had higher order aberrations. However, the amount of higher order aberrations was not a significant predictor of poor visual outcomes, the presence of amblyopia or nystagmus.

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## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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