

Globe Axial Length Growth at Age 10.5 Years in the Infant Aphakia Treatment Study



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- **PURPOSE:** To report the change in globe axial length (AL) from the time of unilateral cataract surgery at age 1-7 months to age 10.5 years for infants enrolled in the Infant Aphakia Treatment Study, and to compare AL growth of operated eyes with that of fellow unoperated eyes.
- **DESIGN:** Comparative case series.
- **METHODS:** AL growth was analyzed relative to treated vs fellow eye, contact lens (CL) vs intraocular lens (IOL), visual acuity (VA) outcome, and the need for surgery for visual axis opacification. Eyes with glaucoma or glaucoma suspect were excluded from the primary analysis but reported separately.
- **RESULTS:** Fifty-seven patients have reliable AL data available at both visits. AL was shorter in treated eyes preoperatively ($P < .0001$) and at 10.5 years of age ($P = .021$) but AL growth was not different (4.7 mm, $P = .99$). The growth (70.2% up to age 5 and 29.8% from age 5 to 10.5) was similar in the CL and the IOL group ($P = .79$). Eyes grew 4.4 mm when visual acuity (VA) was better than 20/200, and 5.2 mm when VA was 20/200 or worse ($P = .076$). Eyes receiving additional surgery grew more than eyes not receiving additional surgery ($P = .052$). Patients with glaucoma showed significantly more eye growth (7.3 mm) than those without glaucoma (4.7 mm) and glaucoma suspects (5.1 mm) ($P < .05$).
- **CONCLUSIONS:** Eyes with glaucoma or poor VA often grew longer than the fellow eye. Overall, treated eyes grew similarly in the IOL and CL groups and also kept pace with the growth of the fellow eyes. (Am J Ophthalmol 2020;216:147-155. © 2020 Elsevier Inc. All rights reserved.)

AXIAL ELONGATION AFTER CATARACT SURGERY can be difficult to predict. If more axial growth occurs than anticipated, an intraocular lens (IOL) implanted early in life may need to be exchanged when the child is older. Alternatively, if less axial elongation than anticipated occurs, the child may need to wear spectacles or contact lenses (CLs) for hyperopic correction on a long-term basis.¹ A child's eye continues to grow until adulthood is reached. Understanding globe axial length (AL) growth and predicting some of the variability in growth will help to determine IOL power to be implanted and improve the achievement of the desired refractive error when the eye is fully grown. Various factors influence the growth of an eye after cataract surgery, including but not limited to microphthalmia, form vision deprivation, age at cataract development and cataract surgery, and glaucoma during the infant and toddler years.¹

The Infant Aphakia Treatment Study (IATS) is a randomized clinical trial comparing the effect of primary IOL implantation vs aphakia corrected with a CL in infants 1-7 months of age after unilateral cataract surgery. Axial elongation during the first year of life and at 5 years of age in the IATS have been reported.^{2,3} The primary aim of our current study is to report globe AL growth from surgery to 10.5 years in the IATS, and compare AL growth of operated eyes with that of fellow unoperated eyes. In addition, we are also reporting AL and AL growth of both eyes from surgery to 10.5 years of age and from 5 to 10.5 years of age and factors that may have influenced AL growth.

METHODS

THE STUDY FOLLOWED THE TENETS OF THE DECLARATION of Helsinki, was approved by the institutional review boards of the participating institutions, and was in compliance with the Health Insurance Portability and Accountability Act. The main inclusion criteria for IATS were a visually significant congenital cataract (3 mm central opacity) in 1 eye, a normal fellow eye, and an age of 28 days to <210 days at the time of cataract surgery. Patients were randomized to have an IOL placed at the time of the initial surgery or to be left aphakic and optically corrected with a CL. Details of the study design, definitions used for glaucoma and glaucoma suspect, patient characteristics at baseline, and the method to define reliable A-scan ultrasound



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TABLE 1. Axial Length (mm) Measurements for Treated and Fellow Eyes at Baseline, Age 5 Years, and Age 10.5 Years

Visit	Treated Eye		Fellow Eye		Difference (Fellow – Treated)		
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	P Value ^a
Baseline	57	18.0 ± 1.2	53	18.6 ± 0.8	53	0.7 ± 0.7	<.0001
Age 5 years	53	21.2 ± 1.5	53	22.1 ± 0.8	51	0.9 ± 1.4	<.0001
Age 10.5 years	57	22.8 ± 2.1	57	23.4 ± 1.0	57	0.6 ± 2.0	.021

SD = standard deviation.
^aP value (2-sided) for the paired *t* test comparing the axial length or the change in axial length between the treated and fellow eyes.

TABLE 2. Axial Length Growth (mm) in Treated and Fellow Eyes at Baseline, Age 5 Years, and Age 10.5 Years

Axial Length Growth	Treated Eye		Fellow Eye		Difference (Fellow – Treated)		
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	P Value ^a
From baseline to age 5 years	53	3.3 ± 1.3	49	3.5 ± 0.9	47	0.3 ± 1.3	.16
From age 5 to age 10.5 years	53	1.4 ± 0.8	53	1.2 ± 0.5	51	–0.1 ± 0.9	.32
From baseline to age 10.5 years	57	4.7 ± 1.8	53	4.7 ± 1.0	53	0.0 ± 1.8	.99

SD = standard deviation.
^aP value (2-sided) for the paired *t* test comparing the axial length or the change in axial length between the treated and fellow eyes.

TABLE 3. Axial Length (mm) in Treated Eyes at Baseline, Age 5 Years, and Age 10.5 Years, by Treatment

Visit	Treatment				Difference (CL – IOL)	
	CL		IOL			
	N	Mean ± SD	N	Mean ± SD	Mean (95% CI)	<i>P</i> Value ^a
Baseline	26	18.0 ± 1.4	31	18.1 ± 1.0	–0.0 (–0.7 to 0.6)	.90
Age 5 years	22	20.9 ± 1.5	31	21.4 ± 1.4	–0.5 (–1.3 to 0.3)	.19
Age 10.5 years	26	22.8 ± 2.3	31	22.7 ± 1.9	–0.1 (–1.0 to 1.2)	.87

CI = confidence interval; CL = contact lens; IOL = intraocular lens; SD = standard deviation.

^a*P* value for the independent group *t* test comparing the means of CL and IOL treatment groups.

tracings have been reported.^{2,4} Biometry at age 10-11 to determine globe AL was performed on both eyes using either the IOL Master (Carl Zeiss Meditec, Dublin, California, USA) or the Lenstar (Haag-Streit USA, Mason, Ohio, USA). At least 3 measurements were obtained for each eye and then averaged to hundredths of a millimeter. Both the raw data/scan and the summary page were printed and faxed to the Data Coordinating Center.

Patients with glaucoma or glaucoma suspects were excluded from the primary analysis because of the excessive axial elongation that can occur in infantile eyes with glaucoma. This group was analyzed separately. For primary analysis, we included eyes with reliable AL data both before

surgery and at age 10.5 years. We analyzed AL at baseline, at age 5 years, and at age 10.5 years. We calculated the change in AL and analyzed that change relative to treated vs fellow eyes, treatment modality (CL vs IOL), the presence or absence of additional intraocular surgery to clear the visual axis, and visual outcome. For visual outcome, eyes were divided into 2 categories based on visual acuity at age 10.5 years: better than 20/200, and 20/200 or worse.

The AL of operated eyes was compared with that of fellow eyes using a paired *t* test. Independent group *t* test was used to compare data from the CL and IOL groups and to compare eyes according to visual outcome. For all analyses, a *P* value < .05 was deemed statistically

TABLE 4. Axial Length Growth (mm) in Treated Eyes at Baseline, Age 5 Years, and Age 10.5 Years, by Treatment

Axial Length Growth	Treatment				Difference (CL – IOL)	
	CL		IOL			
	N	Mean ± SD	N	Mean ± SD	Mean (95% CI)	P Value ^a
From baseline to age 5 years	22	3.1 ± 1.2	31	3.4 ± 1.4	−0.3 (−1.0 to 0.4)	.42
From age 5 to age 10.5 years	22	1.5 ± 0.8	31	1.3 ± 0.8	0.2 (−0.3 to 0.6)	.45
From baseline to age 10.5 years	26	4.8 ± 1.7	31	4.7 ± 2.0	0.1 (−0.9 to 1.1)	.79

CI = confidence interval; CL = contact lens; IOL = intraocular lens; SD = standard deviation.

^aP value for the independent group *t* test comparing the means of CL and IOL treatment groups.

TABLE 5. Axial Length (mm) in Fellow Eyes at Baseline, Age 5 Years, and Age 10.5 Years, by Treatment

Visit	Treatment				Difference (CL – IOL)	
	CL		IOL			
	N	Mean ± SD	N	Mean ± SD	Mean (95% CI)	<i>P</i> Value ^a
Baseline	24	18.5 ± 0.7	29	18.8 ± 0.8	–0.3 (–0.7 to 0.1)	.16
Age 5 years	23	22.1 ± 0.7	30	22.1 ± 0.8	–0.0 (–0.5 to 0.4)	.86
Age 10.5 years	26	23.6 ± 0.9	31	23.2 ± 1.0	0.4 (–0.1 to 0.9)	.16

CI = confidence interval; CL = contact lens; IOL = intraocular lens; SD = standard deviation.

^a*P* value for the independent group *t* test comparing the means of CL and IOL treatment groups.

TABLE 6. Axial Length Growth (mm) in Fellow Eyes at Baseline, Age 5 Years, and Age 10.5 Years, by Treatment

Axial Length Growth	Treatment				Difference (CL – IOL)	
	CL		IOL			
	N	Mean ± SD	N	Mean ± SD	Mean (95% CI)	P Value ^a
From baseline to age 5 years	21	3.8 ± 0.6	28	3.3 ± 1.0	0.5 (–0.0 to 1.0)	.064
From age 5 to age 10.5 years	23	1.5 ± 0.6	30	1.1 ± 0.4	0.4 (0.1 to 0.7)	.005
From baseline to age 10.5 years	24	5.1 ± 0.9	29	4.4 ± 1.1	0.7 (0.1 to 1.2)	.018

CI = confidence interval; CL = contact lens; IOL = intraocular lens; SD = standard deviation.

^aP value for the independent group *t* test comparing the means of CL and IOL treatment groups.

significant. All statistical analyses were done with SAS 9.4 (SAS Institute Inc, Cary, North Carolina, USA).

RESULTS

OF THE 114 PATIENTS ENROLLED IN IATS, 109 PATIENTS HAD A clinical examination at age 10.5 years (mean, 10.6 years; range, 9.8–11.6 years) with an average length of follow-up of 10.4 years (range, 9.3–11.5 years) after surgery. Twenty-

four patients with glaucoma and 20 glaucoma suspects were excluded from primary analyses. From the remaining 65 patients, valid AL data of treated eyes at both baseline and 10.5 years of age were available for 57 patients. Table 1 illustrates AL in treated and fellow eyes at baseline, age 5 years, and age 10.5 years. There was no significant difference between the AL growth of treated eyes and fellow eyes (Table 2). Tables 3–6 illustrate AL and AL growth of eyes receiving a CL or IOL and untreated fellow eyes. The means of AL growth of the CL and IOL groups were

TABLE 7. Axial Length in the Treated Eye for Intraocular Lens Patients at Baseline, Age 5 Years, and Age 10.5 Years, According to Whether Surgery to Clear the Visual Axis Was Done

Visit	Surgery to Clear Visual Axis				Difference (No – Yes)	
	No		Yes		Mean (95% CI)	P Value ^a
Baseline	11	18.1 ± 1.1	20	18.0 ± 1.0	0.1 (–0.7 to 0.9)	.76
Age 5 years	11	20.8 ± 1.2	20	21.8 ± 1.4	–0.9 (–2.0 to 0.1)	.080
Age 10.5 years	11	21.9 ± 1.2	20	23.2 ± 2.1	–1.3 (–2.8 to 0.1)	.070

CI = confidence interval.

^aP value for the independent groups *t* test comparing the means of the 2 surgery groups.**TABLE 8.** Axial Length Growth (mm) in the Treated Eye for Intraocular Lens Patients at Baseline, Age 5 Years, and Age 10.5 Years, According to Whether Surgery to Clear the Visual Axis Was Done

Visit	Surgery to Clear Visual Axis				Difference (No – Yes)	
	No		Yes		Mean (95% CI)	P Value ^a
From baseline to age 5 years	11	2.7 ± 0.8	20	3.8 ± 1.6	–1.0 (–2.1 to –0.01)	.048
From age 5 to age 10.5 years	11	1.0 ± 0.5	20	1.4 ± 0.9	–0.4 (–1.0 to 0.2)	.19
From baseline to age 10.5 years	11	3.7 ± 0.8	20	5.2 ± 2.3	–1.4 (–2.9 to 0.01)	.052

CI = confidence interval.

^aP value for the independent groups *t* test comparing the means of the 2 surgery groups.**TABLE 9.** Axial Length (mm) of Treated Eye at Baseline, Age 5 Years, and Age 10.5 Years, According to Visual Acuity at 10.5 Years of Age

Visit	Better Than 20/200		20/200 or Worse		P Value ^a
	N	Mean ± SD	N	Mean ± SD	
Baseline	32	18.0 ± 1.2	25	18.0 ± 1.2	.99
Age 5 years	31	21.1 ± 1.5	22	21.4 ± 1.4	.43
Age 10.5 years	32	22.4 ± 1.7	25	23.3 ± 2.5	.12

SD = standard deviation.

^aP value for the independent groups *t* test comparing the means of the 2 visual acuity categories.**TABLE 10.** Axial Length Growth (mm) of Treated Eye at Baseline, Age 5 Years, and Age 10.5 Years, According to Visual Acuity at 10.5 Years of Age

Visit	Better Than 20/200		20/200 or Worse		P Value ^a
	N	Mean ± SD	N	Mean ± SD	
From baseline to age 5 years	31	3.0 ± 0.9	22	3.6 ± 1.7	.14
From age 5 to age 10.5 years	31	1.3 ± 0.7	22	1.4 ± 1.0	.52
From baseline to age 10.5 years	32	4.4 ± 1.2	25	5.2 ± 2.4	.076

SD = standard deviation.

^aP value for the independent groups *t* test comparing the means of the 2 visual acuity categories.

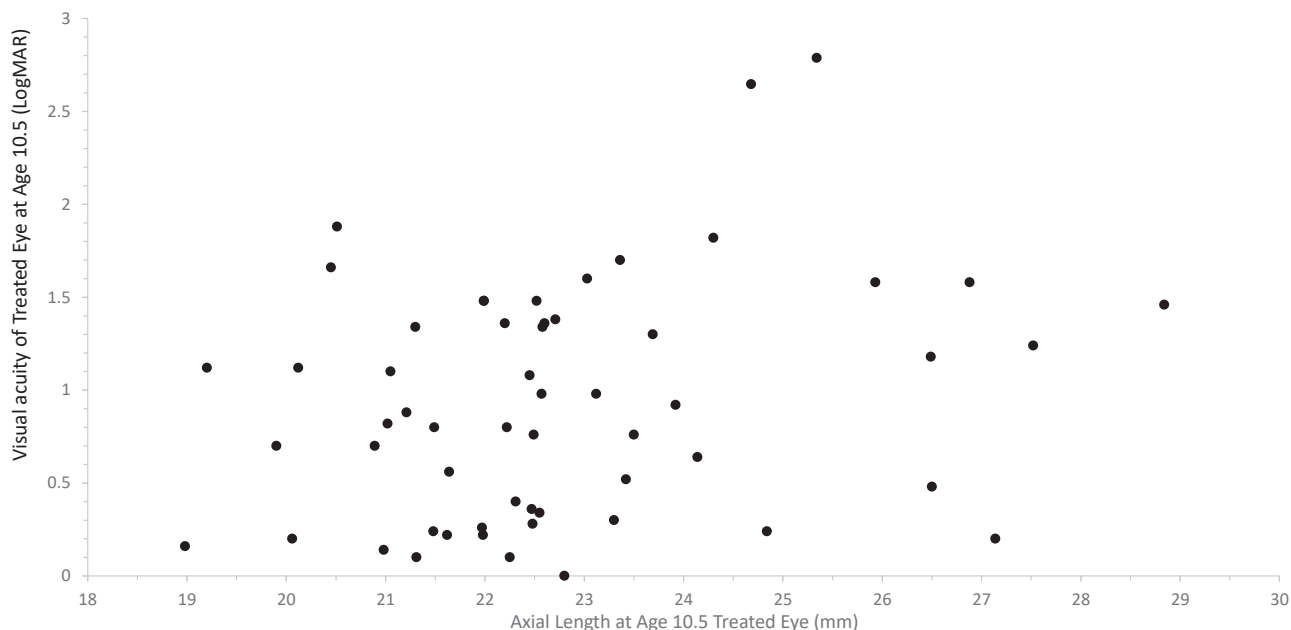


FIGURE 1. Correlation of logMAR visual acuity and axial length at 10.5 years of age.

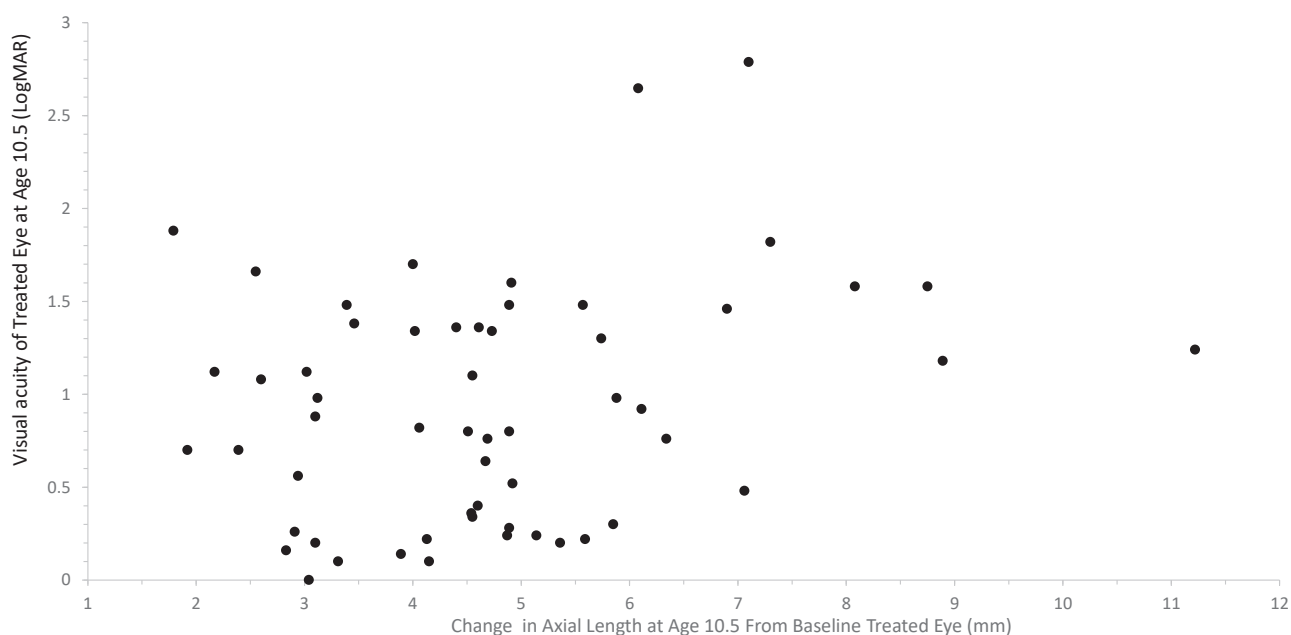


FIGURE 2. Correlation of logMAR visual acuity and axial length growth from preoperative visit to age 10.5 years.

not significantly different (0.1 mm, $P = .79$). Twelve of 26 eyes received secondary IOL implantation before age 10.5 in the primary aphakic group. Table 7 illustrate AL in the treated eyes for those with IOLs who underwent additional intraocular surgery to clear the visual axis. The mean AL growth of eyes receiving surgery to clear the visual axis was 1.4 mm more than eyes not receiving surgery for visual axis opacification ($P = .052$) (Table 8). Table 9 illustrates

AL in the treated eye at baseline, age 5 years, and age 10.5 years, according to visual acuity at 10.5 years of age. The AL growth at age 10.5 years was 5.2 mm in eyes with 20/200 or worse visual acuity, while it was 4.4 mm in eyes with visual acuity better than 20/200 ($P = .076$) (Table 10). Correlation of logMAR visual acuity and AL at 10.5 years of age is shown in Figure 1 (Spearman rank correlation coefficient = 0.254, $P = .0563$). Figure 2 illustrates

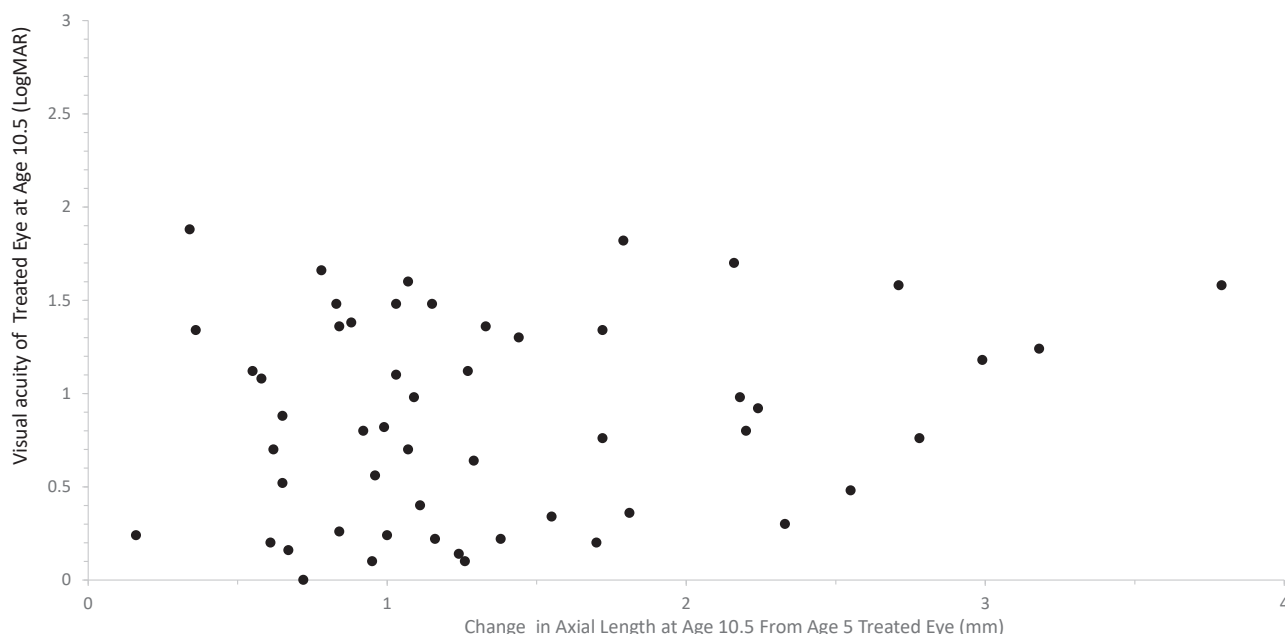


FIGURE 3. Correlation of logMAR visual acuity and axial length growth from 5 to 10.5 years of age.

correlation of AL growth from preoperative visit to age 10.5 years and visual outcome (Spearman rank correlation coefficient = 0.227, $P = .0901$). Figure 3 illustrates AL growth from 5 to 10.5 years of age (Spearman rank correlation coefficient = 0.103, $P = .463$). Figure 4A illustrates the correlation of AL growth from baseline to 10.5 years of age to that of baseline AL in treated eyes (Spearman rank correlation coefficient = -0.106, $P = .4317$). Figure 4B illustrates the correlation of AL growth from baseline to 10.5 years of age to that of baseline AL in fellow eyes (Spearman rank correlation coefficient = -0.450, $P = .0007$).

Supplemental Tables 1-12 (Supplemental Material available at AJO.com) show reports for the entire cohort (including glaucoma and glaucoma suspect, which were excluded from primary analysis). Twenty patients with glaucoma and 18 glaucoma suspects have AL data in the treated eye available at baseline, and at 10.5 years of age. As a group, patients with glaucoma showed significantly more eye growth (7.3 mm) than those without glaucoma (4.7 mm) and glaucoma suspects (5.1 mm) ($P < .05$).

DISCUSSION

NO DATA ARE AVAILABLE DOCUMENTING AXIAL GROWTH after cataract surgery, especially over an entire decade and in a prospective manner. Fellow unoperated eyes represent an important, and rarely documented, normal comparator group. Before cataract surgery, the mean AL was shorter in eyes with cataract compared with fellow eyes (18.0 ± 1.2 vs 18.6 ± 0.8 mm, $P < .0001$). Similar findings have been reported by other investigators.⁵⁻⁸ At age 1 and

5 years, in the IATS cohort, the mean AL remained shorter in eyes operated for cataract compared with fellow unoperated eyes (21.4 ± 1.7 mm vs 22.1 ± 0.7 mm, $P = .0009$). Herein, at age 10.5 years, we observed a similar trend (22.8 ± 2.1 mm vs 23.4 ± 1.0 mm, $P = .021$). In contrast, Vasavada and associates⁷ reported that mean postoperative AL was longer in eyes with unilateral IOL implantation compared with fellow unoperated eyes. The discrepancy in the results may be explained by the fact that in contrast to the series from Vasavada and associates,⁷ our current study excluded eyes that developed postoperative glaucoma. Glaucoma during early childhood can result in excessive elongation. When we analyzed the excluded eyes separately, the glaucoma eyes grew significantly more as compared to glaucoma suspect or nonglaucoma eyes (7.3, 5.1, and 4.7 mm, respectively, $P < .05$).

The AL growth of operative eyes and fellow unoperated eyes was not significantly different from baseline to age 5 years, from age 5 to 10.5 years, and from baseline to age 10.5 years. This trend also was observed at 1 year of age.² As anticipated, AL growth from baseline to age 5 years was more as compared to the interval from 5 to 10.5 years of age (treated eyes: 3.3 mm or 70.2% and 1.4 mm or 29.8% from baseline to age 5 and from age 5 to 10.5, respectively). This was true for fellow eyes as well (3.5 and 1.2 mm from baseline to age 5 and from age 5 to age 10.5, respectively). Several other studies reported that differences in AL growth between operated and fellow eyes were not significantly different.⁸⁻¹¹ In contrast, Griener and associates¹² reported less AL growth in eyes implanted with an IOL compared with fellow unoperated eyes. A few other studies reported greater axial elongation in pseudophakic eyes.^{13,14}

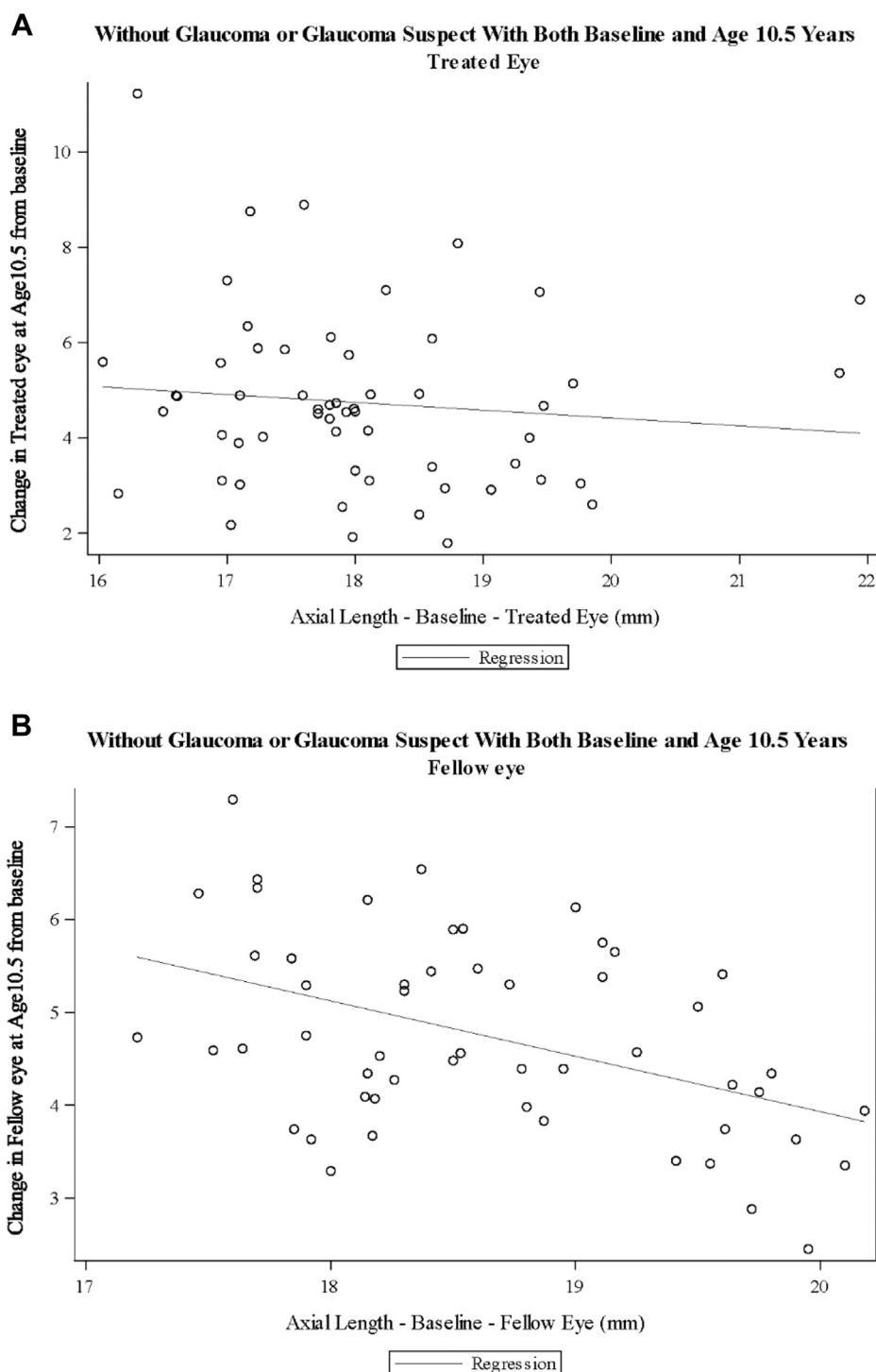


FIGURE 4. A. Correlation of baseline axial length and axial length growth from baseline to 10.5 years of age in the treated eye. B. Correlation of baseline axial length and axial length growth from baseline to 10.5 years of age in the fellow eye.

Eyes with cataract were not only shorter compared with fellow eyes without cataract but also had more variation, as reflected by a higher standard deviation (SD) (baseline SD, 1.2 vs 0.8 in operated eye vs fellow eyes; age 10.5 years SD, 2.1 vs 1.0). More variation in eyes undergoing cataract sur-

gery also was observed in AL growth (SD, 1.8 vs 1.0) from baseline to age 10.5 years.

At 10.5 years of age, the mean AL of the IOL group was 0.1 mm longer than that of the contact lens group ($P = .90$). The mean AL for the cataractous eyes was 0.1 mm

shorter before cataract surgery in the IOL group ($P = .87$). The mean AL of the pseudophakic eyes was 0.6 mm longer than the mean AL of the aphakic eyes at 1 year of age and 0.5 mm at 5 years of age.¹ AL growth was not significantly different between the 2 treatment groups in the treated eye at any visit. For fellow unoperated eyes, at 10.5 years of age, mean AL of the IOL group was 0.4 mm shorter than that of the contact lens group. Fellow eyes had nearly the same axial elongation in the 2 treatment groups at 1 year after surgery. At 5 years of age, the fellow eyes had nonsignificant differences in growth in the 2 treatment groups. AL growth of the fellow eye was significantly different in the 2 treatment groups from age 5 to 10.5 years ($P = .005$) and from baseline to age 10.5 years ($P = .018$). This significant difference may be owing to chance.

Eyes requiring surgery to clear the visual axis grew 1.4 mm more as compared to eyes not requiring surgery to clear the visual axis ($P = .052$). Before cataract surgery, the mean AL was similar for eyes requiring a second surgery later on to clear the visual axis. At 5 years of age, eyes requiring surgery to clear the visual axis grew 0.9 mm more on average than eyes without the need for reoperation ($P = .08$). Visual axis opacification during infancy can lead to excessive axial elongation if left untreated. Perhaps the duration between the onset of visual axis opacification and the surgery to clear the visual axis was sufficient to cause axial elongation from vision deprivation. In the IATS, patients were examined every 3 months. Therefore, it is unlikely that deprivation from visual axis opacification extended beyond 3 months in duration. Reoperation typically was scheduled within a few weeks of the recognition

of the opacity. Eyes requiring reoperation for visual axis opacification may be associated with other ocular anomalies and, despite timely surgery, may have poorer visual acuity, which may have contributed more growth in this group. It is important to note that this excessive growth from baseline to age 5 slowed down from age 5 to age 10.5 years (1 mm vs 0.4 mm).

The AL or AL growth was not significantly different between visual acuity outcome categories. Eyes grew 4.4 mm when visual acuity was better than 20/200, and 5.2 mm when visual acuity was 20/200 or worse ($P = .076$). However, AL at 10.5 years had mild correlation with logMAR visual acuity (Spearman rank correlation coefficient = 0.254, $P = .0563$). Axial elongation has been known to occur in eyes with poor visual acuity. Our study was not powered to evaluate a difference in visual acuity and AL growth. Smaller sample size may have attributed to borderline significance results.

Limitations of our study include AL measurement by different techniques at baseline and at age 10.5 years. However, as any error induced by this factor is likely to be the same in all eyes, it is likely to have had a minimum effect. In addition, since this is a secondary analysis, we did not plan on testing adjustments. With small sample size, there would be no power to detect meaningful associations.

In conclusion, our study showed that eyes undergoing operation for monocular cataract in the first 7 months of life with or without primary IOL implantation had similar axial growth from surgery to age 10.5 years compared to that of fellow unoperated eyes despite having shorter AL at the time of surgery.

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A full listing of members of the Infant Aphakia Treatment Study Group is provided in the Appendix (Supplemental Material available at AJO.com).

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