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# The Effects of Surgical Factors on Post-Operative Astigmatism in Patients Enrolled in the Infant Aphakia Treatment Study (IATS)

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University of Florida

2011

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An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

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in Biostatistics

2013

#### Abstract

## The Effects of Surgical Factors on Post-Operative Astigmatism in Patients Enrolled in the Infant Aphakia Treatment Study (IATS)

## By Jason Lee

Cataract surgery in infants is a very complicated process, with no clear answers on the proper treatment and rehabilitation. While contact lenses are the traditional optical correction after lens removal, physicians have advocated using an intra-ocular lens (IOL) to achieve better visual outcomes. This thesis focuses on one such outcome, astigmatism. We examine whether different demographic factors or factors within the surgical technique affect severity of post-operative astigmatism levels. Many of these factors are unexplored as they relate to aphakic infants. Data were obtained from 114 patients enrolled in the Infant Aphakia Treatment Study (IATS) at baseline (date of cataract removal surgery) and 1 year of age. Outcome measurements included keratometric astigmatism levels at baseline, 1 year, and the difference between the two time points. 1 and 2-sample t tests were used to assess the bivariate relationships between factors and astigmatism. Additionally, two regression models were fit, using surgical factors: a stepwise model, using p = 0.10 as stay criterion, and a mixed model with age as a random effect. While keratometric astigmatism in fellow eyes significantly decreased at 1 year of age (p = 0.0003), levels in treated eyes did not significantly change (p = 0.362). The contact lens group had significantly less astigmatism at 1 year than the IOL group, a difference of 0.47 D (p = 0.023). All other comparisons were insignificant at  $\alpha = 0.05$ . However, the significant differences in bivariate comparisons are less than 0.5 diopters, a clinically insignificant value. The stepwise regression model for surgical factors included incision location and the number of sutures. The small sample size of reviewed surgeries, and the lopsided divide of some factors within the surgical technique, means that some results should be viewed with caution.

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## **Acknowledgements**

My extreme gratitude goes to my faculty advisor, thesis advisor, and mentor, Mike Lynn, for guiding me through this thesis and this degree program. I would also like to thank Dr. Lance Waller for his continued support as well as our always-entertaining conversations about music and statistics. Thanks go to Azhar Nizam and Andy Lee for reviewing this thesis. Finally, I wish to give heartfelt thanks to two groups of colleagues: my fellow students in the Biostatistics and Bioinformatics Department, and my fellow co-workers on the IATS team.

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#### Chapter 1: INTRODUCTION

## **1.1 Cataracts and Cataract Surgery**

Cataracts are fairly rare in the general population (about 1 in 15), but fairly common in more elderly patients: more than half of people aged 80 or over have had cataracts (Wilmer Eye Institute). An infant born with cataracts is a very rare occurrence: approximately 3 of every 10,000 births have at least one eye that is cataractous (AAPOS, 2011). Cataract surgery among the elderly is fairly straightforward: an incision is made in the eye, and the lens removed and an artificial lens implanted (Wilmer Eye Institute). However, surgery in infants is a much more complicated process, with no clear answers on the proper treatment and rehabilitation. While contact lenses are the traditional optical correction after removal of the lens, some physicians have advocated using an intra-ocular lens (IOL) to achieve better visual outcomes. However, doing so may result in more ocular complications.

## 1.2 The Infant Aphakia Treatment Study (IATS)

The Infant Aphakia Treatment Study was designed to determine which treatment option (contact lenses or IOL) was the better choice for treating aphakia, the condition in which the eye does not have its natural lens. The study entered 114 patients over 14 sites over the course of five years (2005-2009). Entrance criteria for the study consisted of having a unilateral congenital cataract at birth in one eye. Patients were scheduled for cataract removal between 30 and 210 days from birth, and randomly placed into a treatment group: either use of a removable contact lens or an IOL placed inside the eye.

## **1.3 What Is Astigmatism?**

There are four different types of refractive error found in eyes. Astigmatism is one of these types of errors, in which irregular curvature of the cornea and lens results in a non-focused image on the retina. It is a fairly common type of refractive error in the general population. Astigmatism is measured in diopters, a unit of measurement related to focal length of the eye, with larger numbers corresponding to more correction.

Keratometry measures the corneal radius of curvature on the eye (SPIE). When astigmatism is present, the eye becomes elliptical, rather than spherical, in shape. The axes of the ellipse help to measure the amount of astigmatism (Schwiegerling). Focal lengths are taken, in diopters, along the steepest and flattest meridians of the eye. The difference in focal length between these two meridians is what is referred to as keratometric astigmatism (Schwiegerling).

## **1.4 Research Question**

During the process of removing the cataract, the amount of trauma inflicted on the eye can depend on various surgical techniques that are used. If such options produce more trauma on the eye, more refractive error may be expected, due to the malleability of the eye at such a young age (Wilson and Travedi, 2005; AAPOS, 2011).

This thesis focuses on the prevalence and severity of astigmatism in infant aphakic patients, and the differences in levels of this astigmatism that may arise from different demographic and surgical factors. Specifically, we answer the question of whether choice of an intra-ocular lens versus a replaceable contact lens has any long term effect on astigmatism. We also investigate whether factors such as age at surgery or gender have an effect on the astigmatism levels. Finally, we will discuss whether various surgical factors over the course of surgery to remove the cataract and insert the IOL had any significant effect on post-operative astigmatism levels.

#### Chapter 2: LITERATURE REVIEW

## 2.1 The Importance of IATS

Literature in the ophthalmology circles has looked at pediatric cataract surgery and the best way to go about treating this rare but serious condition. Unfortunately, while the debate continues about the best way to treat it, not much research has been done in the area of comparing surgical techniques or different treatments with respect to clinical outcomes like astigmatism or visual acuity. Much of the research in the literature is fairly recent, coming out of the Infant Aphakia Treatment Study (IATS), where the data for this project originated. The research being done in this rare field is incredibly important in a number of different ways. The results of IATS could aide in determining the appropriate rehabilitation method for infant aphakia (Biglan, 2011). Some other ways in which IATS is shaping the debate among pediatric ophthalmologists include monitoring for adverse events in specific cataract types (specifically persistent fetal vascaliture, or PFV, cataracts) and, perhaps most importantly, comparing treatments to determine differences in visual acuity in both the short and long term (Biglan, 2011).

#### **2.2 Surgical Factors of Interest**

Surgical factors used when removing the cataract have not been explicitly researched in the case of infants. However, in the cases of incision type and location, some research has been done on comparing astigmatism values in the population at large. The incision type can have one of two options: a clear corneal incision (also referred to as a corneal tunnel incision) or a scleral tunnel incision. The clear cornea incision is the preferred method (Wilson and Travedi) for intraocular lens treatment. This is typically a smaller incision than that of the scleral tunnel, and is typically used when the replacement lens is foldable. However, in rare cases where the intra ocular lens is rigid, a scleral tunnel incision is typically used. The incision is extended as far and deep as it needs to be to place the new lens into the eye. Scleral tunnel surgeries appear to be more common in adults than children, as there is less risk of hemorrhage (Cehang and Beglan, 2002; Karimian et al, 2007). The astigmatism levels in clear corneal incision types appeared to be statistically significantly lower than those with scleral tunnel incisions (Gupta, 2012; Lam and Yen, 2008). However, the difference is not clinically significant, as it is less than one half of one diopter's difference between the incision types (Gupta, 2012). Further, this is apparently only common immediately after surgery: due to low corneal and scleral rigidity, infant eyes tend to return to preoperative levels of astigmatism within 1 to 2 months after surgery (Wilson and Travedi; Lam and Yen, 2008).

Whether astigmatism values can be altered by the incision location has not been studied well in children (Wilson and Travedi). This is in part due to the fact that locating the site of the incision according to the pre-existing astigmatism has not been done very often, as most of the patients will end up wearing glasses after surgery regardless (Wilson and Travedi).

## **2.3 Demographic Factors of Interest**

Demographic links to astigmatism have been studied in the general population, but no such research exists in aphakic infants. Even in the population of non-aphakic infants, the literature includes very few articles on demographic factors and astigmatism. What does exist tends to show little to no significance within demographic factors. The link between gender and astigmatism is not clear or perhaps even non-existent in children (Montes-Mico, 2000; Atkinson, et al, 2000). With age, it is determined that infants aged 0 to 6 months seem to have more

astigmatism than children up to six years of age (Gwiazda, 1984; Mohindra, 1978), as the incidence of clinically significant astigmatism (i.e., greater than 1.0 D) decreased over time. This includes incidence of "severe astigmatism," classified as greater than 3.0 diopters. Much of the early astigmatism may be resolved between 1 and 6 years because the eye is not as malleable as during the first year of life.

#### **Chapter 3: METHODS**

## 3.1 Data Collection

Patients were given an exam under anesthesia (EUA) immediately prior to cataract removal, where measurements, including keratometric astigmatism, were performed on both the cataractous and fellow eyes. The cataract was then removed, and either a contact lens or an IOL placed into the eye.

All surgeries were videotaped. Dr. Elias Traboulsi of Cleveland Clinic reviewed 40 of the 57 surgeries in the IOL treatment group. Patients were then followed up, and the same measurements taken again in an EUA, at 1 year of age. Dr. Traboulsi's reviews of the surgeries, as well as astigmatism values from both time points, were uploaded into multiple SAS datasets from iDataFax 4.0, the database management system used in IATS. Datasets were saved on a Linux server. Datasets from different forms were then merged and saved in SAS 9.3 for Linux, and transferred from the Linux server to Windows for use in SAS 9.3, Minitab 16.0, and R 2.15.1.

#### **3.2 The Dataset**

Data from all 114 patients was used in tests between demographic factors, treatment groups, and treated versus fellow eyes. Of the 114, 8 patients had EUA's at the 1 year of age follow up visit where keratometry measurements were not made. Additionally, 1 patient did not have an EUA at the 1 year visit. This left 105 patients with keratometry measurements at 1 year of age. All comparisons and tests for demographic factors, treatment groups, and treated versus fellow eyes at 1 year of age, and the change between baseline and 1 year of age, were based on these 105 patients. Of those 40 patients who had surgeries reviewed by Dr. Traboulsi, 4 did not

have keratometry measurements at 1 year of age; the comparisons and the change variables for all surgical factors excepting treatment were thus among 36 patients.

#### **3.3 Bivariate Associations**

This project examined the relationship between keratometric astigmatism (in diopters, D) and various demographic and surgical factors. Factors examined included: the treatment applied (contact lens vs. IOL); age at surgery; gender; incision type (clear cornea vs. scleral tunnel); the location of the incision on the eye, given as a "clock hours" location; presence or absence of an extended keratome; the number of sutures needed to close the incision; and suture type (interrupted vs. running). Finally, the differences in keratometric astigmatism between cataractous and fellow eyes was examined.

Two sample t tests were performed to compare mean keratometric astigmatism values between various binary factor groups. Means of these factors were compared at both baseline, defined as date of surgery for cataract removal, and the visit at 1 year of age. The relationship between the change in mean keratometric astigmatism between these two time points, defined as the 1 year value minus the baseline value for each individual patient, and various factors was also examined. Some factors were considered as binary for the purposes of this analysis: number of sutures (1-2 sutures vs. 3-4 sutures), and age at surgery (less than 49 days vs. at least 49 days). The cutoff of 49 days was used since this was the age range defined for the stratification of the randomization of treatment. In comparing keratometric astigmatism in treated versus fellow eyes, a paired t-test was used.

To further investigate the effects of incision location, a non-binary surgical factor, an analysis of variance with Tukey's multiple comparisons testing was used. While possible values were given in "clock hours," giving possible values {1, 1.5, 2, ..., 12.5}, only six values were used: 10; 10.5; 11; 11.5; 12; and 12.5. 21 comparisons were therefore made, with an alpha in an omnibus test of  $\alpha = 0.05$ . These comparisons were done at baseline, 1 year, and the change between the two time points.

## 3.4 Regression and Mixed Modeling

In addition to performing bivariate analyses, two linear regressions were performed using the keratometric astigmatism value at 1 year of age and the change of astigmatism between baseline and 1 year as the dependent variables. Backward elimination was used with a significance level of 0.10 to identify surgical factors that were significant predictors of keratometric astigmatism.

A mixed model analysis was also performed, using subject-specific intercepts and slopes along with surgical factors and a variable for a patient's age at each visit. Each subject had two time points: one at the baseline visit, and the other at the 1 year of age visit, using 365 days as the time point (exact ages at the 1 year visit were not available for this analysis). The mixed model takes the form:  $\hat{Y}_{ij} = \alpha_i + b_{ij} t_{ij} + \beta_1 X_1 + ... + \beta_k X_k + \beta_t t_{ij}$ , where  $\hat{Y}_{ij} = \text{keratometric astigmatism in patient } i$  at visit j;  $\alpha_i = \text{Subject specific random effect on$ the intercept for subject <math>i;  $b_{ij} = \text{Subject specific random effect on the slope; t_{ij} = Age of patient <math>i$ at visit j, given in months;  $\beta_t$  is the population effect for age  $t_{ij}$ , and  $\beta_1, ..., \beta_k$  are fixed effects for predictors  $X_1, ..., X_k$ .

#### Chapter 4: RESULTS

#### **4.1 Astigmatism in Treated vs. Fellow Eyes**

Information on astigmatism values in treated and fellow eyes is presented in Table 1. In both treated and fellow eyes, mean baseline astigmatism values were both slightly less than 2 diopters (1.99 for treated eyes, SD = 1.31 D; 1.93 for fellow eyes, SD = 1.08 D). Medians for these values were very similar to the means (1.755 for treated eyes; 1.90 for fellow eyes). The histograms for the baseline astigmatism values of the treated and fellow eyes are shown in Figures 1(a) and 1(d). These histograms show similar distributions of keratometric astigmatism values among treated and fellow eyes at baseline. The paired t-test between treated and fellow eyes indeed confirms that the average astigmatism for the two eyes was similar at baseline: the mean difference (treated eyes minus fellow eyes) is 0.06, with p = 0.632 (Table 1).

Figures 1(b) and (e) show histograms for astigmatism values in treated and fellow eyes, respectively, at 1 year of age. Treated eyes have a mean keratometric astigmatism of 1.86 (median of 1.75) and standard deviation of 1.06, as seen in Table 1. Fellow eyes have a similar standard deviation as treated eyes, 0.95; however, the mean keratometric astigmatism of 1.42 and median of 1.25 are approximately 0.5 diopters less than that of treated eyes. There is a statistically significant difference in mean keratometric astigmatism values between treated and fellow eyes at 1 year of age (paired difference = 0.44; p-value = 0.0003).

The distribution of the change between baseline and 1 year for aphakic and fellow eyes is shown by histograms in Figures 1(c) and (f), respectively. Scatter plots of individual baseline versus 1 year of age values are shown in Figures 2(a) and (b), for fellow and treated eyes, while values and 95% confidence intervals are found in Table 1. Treated eyes had a mean difference of -0.14 diopters (1 year minus baseline); the change was not significantly different from 0 (p = 0.362). Fellow eyes showed a difference of -0.49 diopters, however, a statistically significant departure from 0 (p = 0.0003). The paired difference between treated and fellow eyes is not significant when  $\alpha = 0.05$  (mean paired difference = 0.34, p-value = 0.062).

## 4.2 Comparisons of Demographic Factors and Treatment

Table 2 gives results for mean keratometric astigmatism values when compared among levels of the demographic factors. There is almost no difference in mean keratometric astigmatism between treatment groups at baseline (CL: 1.98 D; IOL: 2.00 D; Diff: -0.02 D, p = 0.94); this should be expected, though, since patients were randomly assigned to treatment groups. However, the difference between treatment groups at 1 year of age is -0.47 D (CL: 1.62 D; IOL: 2.09 D), a statistically significant difference (p = 0.023). Despite the significant difference at 1 year of age, the difference in treatment groups in the mean change from baseline to 1 year is -0.30 D (CL: -0.29 D; IOL: 0.01 D), not a significant difference (p = 0.343). Figure 3(a) shows boxplots of keratometric astigmatism at baseline, 1 year, and the change, according to treatment group.

Figure 3(b) displays boxplots of keratometric astigmatism at the two time points, and the change between them, according to age group. Fifty-two of the 114 patients had surgery at less than 49 days from birth, while 62 patients had surgery at 49 days or greater. Keratometric astigmatism levels at baseline in these two groups differed by -0.40 D, not a statistically significant difference (< 49 Days: 1.77 D;  $\geq$  49 Days: 2.17 D; p = 0.104). The difference between the two groups remained approximately the same at 1 year of age (Diff: -0.30 D; p = 0.110);

change from baseline to 1 year of age was nearly identical in the two age groups (Diff: 0.005; p = 0.988); these results can be seen in Table 2.

Boxplots showing keratometric astigmatism versus gender can be found in Figure 3(c). Males, comprising 54 of the 114 patients, had a mean 2.19 diopters of astigmatism at baseline, while the 60 females had a mean of 1.81 diopters. This was not a statistically significant difference (0.38 D; p = 0.118). At 1 year of age, males and females had a decreased difference of only 0.06 D (Males: 1.89 D; Females: 1.83 D; p = 0.761). The mean change in keratometric astigmatism between baseline and 1 year in males and females was not significant (Diff: -0.22 D; p = 0.482); however, the variances in the two groups were significantly different. Thus, the Satterthwaite approximation for the 95% confidence interval shown in Table 2 was used.

## **4.3 Comparisons of Surgical Factors**

A comparison of mean keratometric astigmatism values stratified by the surgical factors is found in Table 3. When number of sutures is classified as a binary variable, the difference in keratometric astigmatism between 1 or 2 sutures and 3 or 4 sutures is -0.39 D (p = 0.364). The difference is slightly more pronounced at 1 year of age (Diff: -0.43 D; p = 0.307), but neither are significant. The change in the two groups between baseline and 1 year is also non-significant (Diff: -0.08 D; p = 0.895). Boxplots showing the distribution of keratometric astigmatism when stratified by the number of sutures as a binary variable are shown in Figure 4(a).

In Figure 4(b) boxplots of keratometric astigmatism versus the presence of extended keratome at both time points and the change between them are presented. Only 6 of 39 surgeries reviewed had keratome extension; the mean keratometric astigmatism at baseline was 1.88 D. The five subjects that were followed up at 1 year of age had an increase in keratometric

astigmatism to 2.27 diopters; however, the change between baseline and 1 year was only 0.02 diopters. Meanwhile, those that did not have a keratome extension had a mean baseline astigmatism value of 1.97 diopters, a value that increased to a mean of 2.17 D at 1 year of age. The mean change, as seen in Table 3, between baseline and 1 year in non-extended keratome patients was 0.11 diopters, for a difference between the two groups of -0.08 D (p = 0.909).

Of the two incision types, clear cornea and scleral tunnel, 20 of each type were reported in the reviewed surgeries. Boxplots for incision types in keratometric astigmatism can be found in Figure 4(c). At baseline, there was a difference of -0.54 diopters between the two incision types (CC: 1.78 D; ST: 2.32 D; p = 0.169); at 1 year of age, both mean keratometric astigmatism values in the two groups increased slightly (CC: 1.89 D; ST: 2.37 D) for a mean difference of -0.48 diopters (p = 0.214). The mean changes from baseline to 1 year go in opposite directions, as the average change in the clear cornea group was -0.19 D, while the scleral tunnel incision group had a slight increase in astigmatism, of 0.09 diopters. This difference is not statistically significant, however, as seen in Table 3 (Diff: 0.28 D; p = 0.590).

Figure 4(d) shows boxplots for suture type and keratometric astigmatism values at baseline, 1 year of age, and the difference between the two values. 37 surgeries have clear suture types, and of these, 32 are interrupted sutures. Those with running sutures had average baseline astigmatism of 2.25 D, while those with interrupted sutures were slightly less, at 1.91 D. At 1 year of age, interrupted sutures had average keratometric astigmatism readings of 2.33 D, while those with running sutures had an average of 1.57 diopters of astigmatism. The difference of 0.76 D between the two groups was not statistically significant (p = 0.186) (Table 3). The group of interrupted sutures patients on average gained 0.26 diopters of astigmatism between baseline measurements and 1 year follow-up measurements. Meanwhile, those with running sutures lost

an average of 0.68 diopters of astigmatism. The change of 0.94 D between the two groups was not statistically significant (p = 0.215).

A comparison of keratometric astigmatism and incision location is performed in Table 4. The incision location is given in clock hours, and only locations in the upper left quadrant were given in the 40 surgeries reviewed. 18 surgeries had incision locations of "12 o' clock"; 10 had "11 o'clock" incisions, and the other 4 locations in the upper left quadrant had 3 surgeries each. Baseline mean astigmatism levels stratified this way varied from 1.08 to 2.75 diopters; no two comparisons were significant, and the overall p = 0.582. At 1 year of age, mean astigmatisms ranged from 1.00 D in "11:30" incisions to 3.17 D in "10:30" incisions. All comparisons were not deemed statistically significant either (overall p = 0.310). The change between baseline and 1 year keratometric astigmatism values gave the largest difference between the "11:30" and "10:30" incisions (-1.75 D and 1.68 D, respectively). However, all comparisons of the change were also not significant (overall p = 0.111).

## 4.4 Model Selection

Using backwards elimination with a significance level of 0.10, the linear regression model for keratometric astigmatism at 1 year of age did not give any significant variables among surgical factors. Using the change variables, two surgical factors were given in the stepwise regression model: individual number of sutures (p = 0.061) and incision location (p = 0.071). The model is then:  $\Delta$  K-Ast = 11.971 – 0.818 (Incision Loc.) – 0.830 (# Sutures).

A mixed model with subject-specific intercepts containing all potential surgical factors of interest gave no significant results. The mixed model was given as:  $\hat{Y}_{ij} = \alpha_i + b_{ij} t_{ij} + 0.213 X_1 - 0.014 X_2 + 0.061 X_3 + 0.20 X_4 - 0.14 X_5 + 0.010 t_{ij}$ 

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where:  $\hat{Y}_{ij}$  = Keratometric astigmatism in patient *i* at visit *j*;  $\alpha_i$  = Subject specific random effect on the intercept for subject *i*;  $b_{ij}$  = Subject specific random effect on the slope;  $X_1$  = Incision Type: 1 for Scleral Tunnel, 0 for Clear Corneal;  $X_2$  = Incision Location;  $X_3$  = Extended Keratome: 1 for Yes, 0 for No;  $X_4$  = Number of Sutures;  $X_5$  = Suture Type: 1 for Running, 0 for Interrupted;  $t_{ij}$  = Age of patient *i* at visit *j*, given in months. The lowest p-value of these variables was number of sutures (p = 0.190). The age variable in this model was also non-significant (p = 0.574). In the context of the model, all surgical factors are considered fixed effects, while age at surgery is treated as both a fixed and a random (subject-specific) effect.

#### Chapter 5: DISCUSSION

## **5.1 Significant Results**

The two significant results when comparing means are by treatment group and treated vs. fellow eyes, both at 1 year. The first of these results suggests that the contact lens treatment decreases astigmatism (Table 3), whereas the IOL treatment does not. A similar result can be seen in the comparison between treated and fellow eyes at 1 year: the fellow eyes decreased in astigmatism between baseline and 1 year, while the treated eyes had only a very slight decrease. In both cases, however, our results are less than clinically significant. The difference of 0.47 diopters between the two treatment groups at 1 year of age is statistically significant; however, less than one half of one diopter of astigmatism is only moderately significant in the clinical setting. The same can be said for treated and fellow eyes. Here the difference between the two groups at 1 year is even less than the other significant result. No other demographic factors or elements of the surgical technique significantly increase astigmatism at 1 year of age, or the change in keratometric astigmatism from baseline measurements, in IATS patients.

One possible cause for decreased astigmatism in one treatment group may be due to the fact that wearing a contact lens can reshape the cornea. A practice, called orthokeratology, is sometimes used to correct other refractive errors like myopia. However, orthokeratology, according to contact lens manufacturers, can also correct small amounts of astigmatism: amounts between 0.75 and 1.50 diopters are considered correctable. However, in a new case report (Baertschi and Wyss, 2010), it is reported that new orthokeratology designs in contact lenses may correct more severe levels of astigmatism, as high as 7.0 D. It is therefore possible that some contact lens wearers, especially those with smaller baseline astigmatism values in the contact lens arm of treatment, may unknowingly be receiving orthokeratology treatment by

attempting to correct for myopia. This may explain small changes in the mean values at 1 year and, especially, the change values between baseline and 1 year of age.

## **5.2 Cautions**

Despite some significant results, some cautions should be taken when we examine these results further. For surgical factors, among the 114 patients in the study, only 40 videos among the 57 patients randomized to IOL treatment were reviewed. Further, since surgeons had the freedom to use their own surgical techniques, some counts of variables within the surgical factors are very small. For instance, for suture type and keratome extension, there were categories with 5 and 6 observations at baseline and 1 year. With sample sizes for some groups being so small, the statistical power of the performed comparison tests is quite limited. Thus, considering the small amount of data, the conclusions stated here need to be viewed with caution.

One way to remedy the problem of small data within the surgical factor data analyses is to bootstrap the data. This would involve taking a random or weighted sample of observations given in each group (Shao and Tu, 1995). While this may be helpful in giving larger sample sizes, thus allowing us to perform more powerful tests, with the data given, conducting a simulation with such a small amount of possible values would likely give inaccurate or highly biased results for means and standard deviations.

## **5.3 Conclusion**

In summary, an apahkic eye treated with a contact lens as opposed to an IOL significantly reduces astigmatism and the change of astigmatism from baseline, at 1 year of age. Further, eyes treated for infant aphakia have significantly more astigmatism at 1 year of age than do fellow

eyes of the same patient. While all of these comparisons are significant, differences are less than 0.5 diopters, a clinically insignificant value. These are the only statistically significant results. All other comparison tests for other demographic and surgical factors came up as not significant, indicating that surgeons do not place an amount of trauma on the eye that is clinically or statistically significant within their individual surgical technique. However, the small sample size of reviewed surgeries, and the lopsided divide of some factors within the surgical technique, means that these non-significant results should be viewed with caution. Future studies may wish to randomize surgical factors, as well as increase the number of follow up time points, to potentially have more accurate comparisons and models.

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# **APPENDIX A: Tables**

Eye	N	Baseline Mean (SD)	N	1 Year Mean (SD)	N	Change (1Y – BL) Est, p (95% CI)
Treated	114	1.99 (1.31)	105	1.86 (1.06)	105	-0.14, 0.361 (-0.45, 0.17)
Fellow	114	1.93 (1.08)	106	1.42 (0.95)	106	-0.48, <b>0.0003</b> * (-0.74, -0.23)
Paired Diff (Treated – Fellow): Est, p (95% CI)	114	0.06, 0.632 (-0.18, 0.30)	105	0.44, <b>0.0003</b> * (0.20, 0.67)	105	0.34, <b>0.062</b> (-0.02, 0.70)

TABLE 1. Keratometric astigmatism in Treated and Fellow Eyes, at Baseline and 1 Year.

Bold, \*: Significant difference ( $p \le 0.05$ )

Bold: Marginally significant difference (0.05

<sup>+</sup>: Satterthwaite approximation used (Variances in comparison groups are not equal)

Factor		N (%)	Baseline	N	Age = 1 Y	N	Change (1Y – BL): Est (95% CI)
Treatment (Cataractous Eye)	CL: Mean (SD)	57 (50.0)	1.98 (1.37)	52	1.62 (0.98)	52	-0.29 (-0.76, 0.17)
	IOL: Mean (SD)	57 (50.0)	2.00 (1.25)	53	2.09 (1.09)	53	0.01 (-0.42, 0.42)
	Diff: Estimate, p (95% CI)	114	-0.02, 0.944 (-0.50, 0.47)	105	-0.47, <b>0.023*</b> (-0.87, -0.07)	105	-0.30, 0.343 (-0.92, 0.32)
Age at Surgery	Less Than 49 Days	52 (45.6)	1.77 (1.24)	47	1.68 (1.16)	47	-0.14 (-0.58, 0.30)
	At Least 49 Days	62 (54.4)	2.17 (1.35)	58	2.01 (0.96)	58	-0.15 (-0.59, 0.30)
	Difference	114	-0.40, 0.104 (-0.88, 0.08)	105	-0.33, 0.110 (-0.74, 0.08)	105	0.005, 0.988 (-0.62, 0.63)
Gender	Male	54 (47.4)	2.19 (1.23)	52	1.89 (1.01)	52	-0.25 (-0.64, 0.13)
	Female	60 (52.6)	1.81 (1.36)	53	1.83 (1.12)	53	-0.03 (-0.53, 0.46)
	Difference	114	0.38, 0.118 (-0.10, 0.87)	105	0.06, 0.761 (-0.35, 0.48)	105	-0.22, 0.482 $(-0.84, 0.40)^+$

TABLE 2. Keratometric Astigmatism vs. Demographic Factors, Glaucoma; Treated vs. Fellow Eyes.

\*: Significant difference (p  $\leq$  0.05)  $^+$  : Satterthwaite approximation used (Variances in comparison groups are not equal)

F	actor	N (%)	Baseline	N	Age = 1 Y	N	Change (1Y – BL) Est (95% CI)
	1-2 Sutures: Mean (SD)	12 (30.0)	1.77 (1.10)	11	1.88 (1.13)	11	-0.05 (-0.84, 0.74)
# Sutures	3-4 Sutures: Mean (SD)	28 (70.0)	2.16 (1.27)	25	2.31 (1.16)	25	0.03 (-0.67, 0.72)
	Diff: Estimate, p (95% CI)	40	-0.39, 0.364 (-1.24, 0.47)	36	-0.43, 0.307 (-1.28, 0.41)	36	-0.08, 0.895 (-1.22, 1.07)
	Yes	6 (15.4)	1.88 (1.79)	5	2.27 (0.77)	5	0.02 (-2.51, 2.56)
Keratome Extension	No	33 (84.6)	1.97 (1.06)	30	2.17 (1.23)	30	0.11 (-0.42, 0.64)
	Difference (Yes – No)	39	-0.09, 0.860 (-1.16, 0.97)	35	0.11, 0.850 (-1.05, 1.27)	35	-0.08, 0.909 (-1.57, 1.40)
	Clear Cornea	20 (50.0)	1.78 (1.31)	17	1.89 (0.99)	17	-0.19 (-0.92, 0.55)
Incision Type	Scleral Tunnel	20 (50.0)	2.32 (1.10)	19	2.37 (1.25)	19	0.09 (-0.69, 0.87)
	Difference (CC – ST)	40	-0.54, 0.169 (-1.31, 0.24)	36	-0.48, 0.214 (-1.25, 0.29)	36	-0.28, 0.590 (-1.32, 0.76)
	Interrupted	32 (86.5)	1.91 (1.20)	28	2.33 (1.22)	28	0.26 (-0.33, 0.85)
Suture Type	Running	5 (13.5)	2.25 (1.56)	5	1.57 (0.54)	5	-0.68 (-2.54, 1.19)
	Difference (Int – Run)	37	-0.34, 0.576 (-1.55, 0.88)	33	$0.\overline{76}, 0.186$ (-0.39, 1.90)	33	$0.\overline{94}, 0.215$ (-0.57, 2.45)

TABLE 3. Keratometric Astigmatism vs. Surgical Factors.

\*: Significant difference ( $p \le 0.05$ ) +: Satterthwaite approximation used (Variances in comparison groups are not equal)

Incision Location	Ν	Baseline	Ν	Age = 1 Y	Ν	Change
10: Mean (SE)	3	2.42 (0.36)	3	2.32 (0.56)	3	-0.10 (0.89)
10.5	3	1.48 (0.48)	3	3.17 (0.79)	3	1.68 (0.47)
11	10	2.01 (0.24)	10	2.37 (0.40)	10	0.36 (0.57)
11.5	3	2.75 (0.80)	3	1.00 (0.25)	3	-1.75 (0.58)
12	18	2.16 (0.34)	16	2.16 (0.26)	16	-0.08 (0.31)
12.5	3	1.08 (0.96)	1	2.00	1	-1.00
Overall p		0.582		0.310		0.111

**TABLE 4.** Comparing Keratometric Astigmatism vs. Incision Location.

# **APPENDIX B: Relevant Figures**



FIGURE 1(a). Histogram of Keratometric astigmatism in Treated Eyes at Baseline.



FIGURE 1(b). Histogram of Keratometric astigmatism in Treated Eyes at 1 Year.



FIGURE 1(c). Histogram of Change in Astigmatism, Treated Eyes.



FIGURE 1(d). Histogram of Keratometric astigmatism in Fellow Eyes at Baseline.



FIGURE 1(e). Histogram of Keratometric astigmatism in Fellow Eyes at 1 Year.



FIGURE 1(f). Histogram of Change in Astigmatism, Fellow Eyes.



FIGURE 2(a). Scatterplot of Keratometric astigmatism, Baseline vs. 1 Year, Treated Eyes.



FIGURE 2(b). Scatterplot of Keratometric astigmatism, Baseline vs. 1 Year, Fellow Eyes.



FIGURE 3(a), i. Boxplot of Keratometric Astigmatism vs. Treatment, at Baseline.



FIGURE 3(a), ii. Boxplot of Keratometric Astigmatism vs. Treatment, at 1 Year.



FIGURE 3(a), iii. Boxplot of Change in Keratometric Astigmatism vs. Treatment.



FIGURE 3(b), i. Boxplot of Keratometric Astigmatism vs. Age at Surgery, at Baseline.



FIGURE 3(b), ii. Boxplot of Keratometric Astigmatism vs. Age at Surgery, at 1 Year.



FIGURE 3(b), iii. Boxplot of Change in Keratometric Astigmatism vs. Treatment.



FIGURE 3(c), i. Boxplot of Keratometric Astigmatism vs. Gender, at Baseline.



FIGURE 3(c), ii. Boxplot of Keratometric Astigmatism vs. Gender, at 1 Year.



FIGURE 3(c), iii. Boxplot of Change in Keratometric Astigmatism vs. Gender.



FIGURE 4(a), i. Keratometric Astigmatism vs. Number of Sutures, Baseline.



FIGURE 4(a), ii. Keratometric Astigmatism vs. Number of Sutures, 1 Year.



FIGURE 4(a), iii. Boxplot of Change in Keratometric Astigmatism vs. Number of Sutures.



FIGURE 4(b), i. Keratometric Astigmatism vs. Presence of Extended Keratome, Baseline.



FIGURE 4(b), ii. Keratometric Astigmatism vs. Presence of Extended Keratome, 1 Year.



FIGURE 4(b), iii. Boxplot of Change in Keratometric Astigmatism vs. Extended Keratome.



FIGURE 4(c), i. Keratometric Astigmatism vs. Incision Type, Baseline.



FIGURE 4(c), ii. Keratometric Astigmatism vs. Incision Type, 1 Year.



FIGURE 4(c), iii. Boxplot of Change in Keratometric Astigmatism vs. Incision Type.



FIGURE 4(d), i. Keratometric Astigmatism vs. Suture Type, Baseline.



FIGURE 4(d), ii. Keratometric Astigmatism vs. Suture Type, 1 Year.



FIGURE 4(d), iii. Boxplot of Change in Keratometric Astigmatism vs. Suture Type.

#### APPENDIX C: SAS Code

From SAS for Linux:

\*\*\*\*\*\* data baseline; set iats.baseline; run; proc contents data=baseline; run; data bl; set iats.eua; keep id trt kread\_cat kread\_ncat kast\_cat kast\_ncat; run; data oneyear; set iats.eua\_va; refract\_cyl\_cat\_one = refract\_cyl\_cat; kread\_cat\_one = kread\_cat; kread\_ncat\_one = kread\_ncat; kast\_cat\_one = kast\_cat; kast\_ncat\_one = kast\_ncat; keep id trt kread\_cat\_one kread\_ncat\_one kast\_cat\_one kast\_ncat\_one; run; data surg; set iats.plate311; keep id comments incision\_type incision\_loc\_hr incision\_loc\_min keratome\_ext suture\_no sutures\_type para\_closed; run; \*\*\*Data for Patients for which we have video\*\*\*; data iats.allone; merge surg bl oneyear; by id; if trt='CL' then delete; if comments=' ' then delete; \*\*\*Creating Change in Astigmatism Variables\*\*\*; deltast\_cat = kast\_cat\_one - kast\_cat; deltacat = 0; if deltast\_cat lt 0 then deltacat = -1 \* deltast\_cat; else if deltast\_cat ge 0 then deltacat = deltast\_cat; \*\*\*Creating Incision Location Variables\*\*\*; incisionloc = (incision\_loc\_hr) + (incision\_loc\_min / 60);

run;

```
***Data for all patients (for general comparisons)***;
data iats.alltwo;
        merge surg bl oneyear;
                by id;
        keep id trt kread_cat kread_ncat kast_cat kast_ncat kread_cat_one
kread ncat one kast cat one kast ncat one;
run;
data iats.allthr;
set alltwo;
        ***Creating Change in Astigmatism Variables***;
        deltast_cat = kast_cat_one - kast_cat;
        deltacat = 0;
                if deltast_cat lt 0 then deltacat = -1 * deltast_cat;
                else if deltast_cat ge 0 then deltacat = deltast_cat;
        deltast_ncat = kast_ncat_one - kast_ncat;
        deltancat = 0;
                if deltast_ncat lt 0 then deltancat = -1 * deltast_ncat;
                else if deltast_ncat ge 0 then deltancat = deltast_ncat;
run;
```

## From SAS for Windows:

```
/*JASON LEE
**THESIS
**"The Effects of Surgical Factors on Postoperative Astigmatism in Patients
**Enrolled in the Infant Aphakia Treatment Study (IATS)"
*/
libname jl 'H:/My Documents/THESIS/';
/*Imports AllOne Dataset from XLS format into SAS.*/
PROC IMPORT OUT= JL.ALLONE
            DATAFILE= "H:\My Documents\THESIS\allone.xls"
            DBMS=EXCEL REPLACE;
     RANGE="ALLONE";
     GETNAMES=YES;
     MIXED=NO;
     SCANTEXT=YES;
     USEDATE=YES;
     SCANTIME=YES;
RUN;
/*Imports AllThr Dataset from XLS format into SAS.*/
PROC IMPORT OUT= JL.allthr
            DATAFILE= "\\dataserver.sph.emory.edu\JLEE923\My
Documents\THESIS\allthr.xls"
           DBMS=EXCEL REPLACE;
     RANGE = "ALLTHR";
     GETNAMES=YES;
     MIXED=NO;
     SCANTEXT=YES;
     USEDATE=YES;
```

```
SCANTIME=YES;
RUN;
/*Formats for the baseline dataset.*/
proc format;
 value yn
                 99 = "Blank"
                 0 = "No"
                 1 = "Yes" ;
 value sex
                 99 = "Blank"
                 1 = "Male"
                 2 = "Female" ;
  value race
                 99 = "Blank"
                 1 = "American Indian/Alaskan"
                 2 = "Asian"
                 3 = "Black or African American"
                 4 = "Native Hawaiian or Pacific Islan"
                 5 = "White"
                 6 = "More than one race"
                 7 = "Other" ;
 value odos
                 99 = "Blank"
                 1 = "OD"
                 2 = "OS";
                 99 = "Blank"
 value tcat
                 1 = "Nuclear"
                 2 = "Posterior Lentiglobus"
                 3 = "Total"
                 4 = "PFV"
                 5 = "Other" ;
 value trt
                99 = "Blank"
                 1 = "Contact Lens"
                 2 = "Intraocular Lens" ;
 value iage
                 1='28-48 days'
                2='49-210 days';
 value age_cat 1 = '28-48 days'
                2 = '49 days - 3.0 mo'
                3 = '3.1 - 5.0 \text{ mo'}
                4 = '5.1 - 7.0 \text{ mo'}
                5 = '< 28 days'
                6 = '> 7.0 mo';
  value acat
               2='Light Perception'
                4='Fixes Well, Some Follow'
                6='Fix & Follow (Degree NS)';
 value ancat 2='Light Perception'
              4='Fixes Well, Some Follow'
              5='Fixes Well, Robust Follow'
              6='Fix & Follow (Degree NS)';
 value refer 99 = "Blank"
```

```
1 = "Pediatrician"
                2 = "Pediatric Ophthalmologist"
                3 = "Non-pediatric Ophthalmologist"
                4 = "Self"
                5 = "Other" ;
  value tropia
               99 = "Blank"
                1 = "Intermittent"
                2 = "Constant" ;
  value normal
                99 = "Blank"
                1 = "Normal"
                2 = "Abnormal" ;
 value calc
                99 = "Blank"
                1 = "IOL calculator on U/S machine"
                2 = "Look-up tables" ;
run;
data sum_stats;
set jl.allthr;
run;
/*PROGRAM I. K-ASTIGMATISM AT BASELINE, 1 YEAR, AND CHANGE. SUMMARY
STATISTICS AND COMPARISONS.
* *
**Program gives summary statistics found in Table 1. Program also compares
**astigmatism at baseline, 1 year, and change in astigmatism for treated
**versus fellow eyes. Histograms, tables, and scatter plots were all created,
**using the dataset below, in Minitab.
*/
/*Gives means for astigmatism variables.*/
proc univariate data=sum_stats;
var kast_cat kast_ncat kast_cat_one kast_ncat_one deltast_cat deltast_ncat;
run;
proc ttest data=sum stats;
var deltast_cat deltast_ncat;
run;
/*T-Tests for comparing treatment to baseline, 1-yr astigmatism and change in
astigmatism level.*/
proc ttest data=sum_stats;
class trt;
var kast_cat kast_ncat kast_cat_one kast_ncat_one deltast_cat deltast_ncat;
run;
/*Paired T-Tests for comparing treated eyes to fellow eyes, at baseline, 1
year, and change.*/
proc ttest data=sum_stats;
paired kast_cat*kast_ncat kast_cat_one*kast_ncat_one
deltast cat*deltast ncat;
run;
```

```
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```

/\*PROGRAM II. BASELINE ASTIGMATISM BY CATARACT TYPE. \* \* \*\*Program wishes to compare percentage of patients with greater than 3 \*\*diopters of astigmatism, in treated eyes, grouping by cataract type. \*/ data cat\_type; set jl.baseline; keep id trt kast\_cat type\_cataract; if type\_cataract=3 then type\_cataract=5; run; data cat\_type1; set cat\_type; if kast\_cat ge 3.00 then ast3 = 1; else ast3 = 0; nucl=0; plent=0; total=0; pfv=0; other=0; if type\_cataract=1 then nucl=1; else if type\_cataract=2 then plent=1; else if type cataract=4 then pfv=1; else if type\_cataract=5 then other=1; format ast3 nucl plent pfv other yn.; run; proc freq data=cat\_type1; tables type cataract\*ast3 nucl\*ast3 plent\*ast3 pfv\*ast3 other\*ast3 / fisher; run; /\*Pairwise comparisons using Tukey's HSD\*/ proc glm data=cat\_type1; class type\_cataract; model ast3=type\_cataract; means type\_cataract / tukey; run; /\*PROGRAM III. AGE AT SURGERY AND GENDER VERSUS ASTIGMATISM AT BASELINE, 1 YEAR, AND CHANGE. \* \* \*\*Program compares age at surgery to the three astigmatism measures. \*\*Age is measured in days and months. It is also stratified into 4 groups \*\*using the "age\_cat" variable. \*\*There is also the variable IAGE that stratifies age into 2 groups, at 49 \*\*days. \*\*Analyses using age in months and stratified age groups are performed in \*\*this program. \*/ data age; set jl.baseline; keep id sex age days age age cat iage; run;

data astvsage;

merge sum\_stats age; by id; run; /\*T-Tests for comparing stratification @ 49 days in baseline, 1-yr \*\*astigmatism, and change in astigmatism variable.\*/ proc ttest data=astvsage; class iage; var kast\_cat kast\_ncat kast\_cat\_one kast\_ncat\_one deltast\_cat deltast\_ncat; run; \*\*T-Tests for comparing age category stratifciation in baseline, 1-yr astigmatism, and change variable.\*\*; proc ttest data=astvsage; by age\_cat; var kast\_cat kast\_ncat kast\_cat\_one kast\_ncat\_one deltast\_cat deltast\_ncat; run; /\*T-Tests for comparing gender in baseline, 1-yr astigmatism, and change variable.\*/ proc ttest data=astvsage; class sex; var kast\_cat kast\_ncat kast\_cat\_one kast\_ncat\_one deltast\_cat deltast\_ncat; run; /\*PROGRAM IV. SURGICAL FACTORS VERSUS ASTIGMATISM AT BASELINE, 1 YEAR, AND CHANGE. \* \* \*\*Program uses "ALLONE" dataset to compare surgical factors in 43 patients to \*\*the three astigmatism measures. \*\*Number of sutures is compared both individually and by stratification. \*\*Two multivariate analyses are performed using linear regression with \*\*backwards elimination: one using 1 year astigmatism values and the other \*\*using change in astigmatism. Potential variables for these analyses include \*\*all surgical factors given in the "ALLONE," and age at surgery. \*/ data surgfact; set jl.allone; if suture\_no = . then suture\_class=.; else if suture\_no le 2 then suture\_class=0; else if suture\_no gt 2 then suture\_class=1; trt\_ = trt; drop trt; run; data surg\_age; merge surgfact age; by id; if comments=' ' then delete; run; \*\*Comparing number of sutures individually.\*\*; proc means data=surgfact stderr;

```
var kast_cat kast_cat_one deltast_cat;
class suture_no;
run;
/*Comparing number of sutures (1-2 vs. 3-4).*/
proc ttest data=surgfact;
class suture_class;
var kast_cat kast_cat_one deltast_cat;
run;
/*Comparing incision location individually.*/
proc means data=surgfact stderr;
var kast_cat kast_cat_one deltast_cat;
class incisionloc;
run;
/*Comparing incision location and number of sutures together.*/
proc glm data=surgfact;
class incisionloc suture_no;
model kast_cat = suture_no*incisionloc;
means suture_no*incisionloc / tukey;
run;
proc glm data=surgfact;
class incisionloc suture_no;
model kast_cat_one = suture_no*incisionloc;
means suture no*incisionloc / tukey;
run;
proc glm data=surgfact;
class incisionloc suture_no;
model deltast_cat = suture_no*incisionloc;
means suture_no*incisionloc / tukey;
run;
proc ttest data=surgfact;
class incision type;
var kast_cat kast_cat_one deltast_cat;
run;
proc ttest data=surgfact;
class keratome_ext;
var kast_cat kast_cat_one deltast_cat;
run;
proc ttest data=surgfact;
class para_closed;
var kast_cat kast_cat_one deltast_cat;
run;
proc ttest data=surgfact;
class sutures_type;
var kast_cat kast_cat_one deltast_cat;
run;
/*Linear regression using backwards elimination for 1 year astigmatism with
**surgical factors and age at surgery.*/
```

```
proc reg data=surg_age;
model kast_cat_one = incisionloc incision_type keratome_ext para_closed
suture_no sutures_type age / selection=backward slstay=0.10 stb details;
run;
/*Linear regression using backwards elimination for change in astigmatism
**with surgical factors and age at surgery.*/
proc reg data=surg_age;
model deltast_cat = incisionloc incision_type keratome_ext para_closed
suture_no sutures_type age / selection=backward slstay=0.10 stb details;
run;
/*PROGRAM V. VISUAL ACUITY AND GLAUCOMA VERSUS ASTIGMATISM AT BASELINE, 1
**YEAR, AND SURGICAL FACTORS.
* *
**Program relates visual acuity at 1 year of age to astigmatism at baseline,
**1 year, and change value.
**Program also relates glaucoma prevalence (defined as glaucoma or glaucoma
**suspect) to baseline astigmatism and surgical factors.
**All 114 participants in the study are used for these comparisons. For
**comparisons using surgical factors, only those 43 with surgical factors
**given are considered.
*/
data glaucoma;
merge jl.glaucoma jl.allone sum_stats;
     glaucoma=0;
     if glauc=1 then glaucoma=1;
     else if gl_sus=1 then glaucoma=1;
     else glaucoma=0;
format glaucoma yn.;
run;
data va;
merge jl.visacu jl.allone sum stats;
run;
/*Comparing 1-yr visual acuity to astigmatism values.*/
proc reg data=va;
model affected_logmar = kast_cat kast_cat_one;
run;
proc reg data=va;
model affected_logmar = deltast_cat;
run;
proc reg data=va;
model fellow_logmar = kast_ncat kast_ncat_one;
run;
proc reg data=va;
model fellow logmar = deltast ncat;
run;
```

```
/*Comparing visual acuity to surgical factors.*/
proc reg data=va;
model affected_logmar = incision_type incisionloc keratome_ext suture_no
sutures_type para_closed / selection=backward slstay=0.10 stb details;
run;
proc reg data=va;
model fellow_logmar = incision_type incisionloc keratome_ext suture_no
sutures_type para_closed / selection=backward slstay=0.10 stb details;
run;
/*Comparing glaucoma prevalence to astigmatism values.*/
proc ttest data=glaucoma;
class glaucoma;
var kast_cat kast_cat_one deltast_cat;
proc mixed data=glaucoma;
model kast_cat = glauc gl_sus;
run;
proc mixed data=glaucoma;
model kast_cat_one = glauc gl_sus;
run;
proc mixed data=glaucoma;
model deltast_cat = glauc gl_sus;
run;
/*Comparing glaucoma prevalence to surgical factors.*/
proc reg data=glaucoma;
model glaucoma = incision_type incisionloc keratome_ext suture_no
sutures_type para_closed / selection=backward slstay=0.10 stb details;
run;
proc reg data=glaucoma;
model glaucoma = incision_type incisionloc keratome_ext suture_no
```

sutures\_type para\_closed / selection=backward slstay=0.10 stb details;
run;