Predictability of Intraocular Lens Calculation and Early Refractive Status

The Infant Aphakia Treatment Study

Deborah K. VanderVeen, MD; Azhar Nizam, MS; Michael J. Lynn, MS; Erick D. Bothun, MD; Scott K. McClatchey, MD; David R. Weakley, MD; Lindreth G. DuBois, MEd, MMSc; Scott R. Lambert, MD; for the Infant Aphakia Treatment Study Group

Objective: To report the accuracy of intraocular lens (IOL) power calculations and the early refractive status in pseudophakic eyes of infants in the Infant Aphakia Treatment Study.

Methods: Eyes randomized to receive primary IOL implantation were targeted for a postoperative refraction of +8.0 diopters (D) for infants 28 to 48 days old at surgery and +6.0 D for those 49 days or older to younger than 7 months at surgery using the Holladay 1 formula. Refraction 1 month after surgery was converted to spherical equivalent, and prediction error (PE; defined as the calculated refraction minus the actual refraction) and absolute PE were calculated. Baseline eye and surgery characteristics and A-scan quality were analyzed to compare their effect on PE.

Main Outcome Measures: Prediction error.

Results: Fifty-six eyes underwent primary IOL implantation; 7 were excluded for lack of postoperative refraction (n=5) or incorrect technique in refraction (n=1) or biometry (n=1). Overall mean (SD) absolute PE was 1.8 (1.3) D and mean (SD) PE was +1.0 (2.0) D. Absolute PE was less than 1 D in 41% of eyes but greater than 2 D in 41% of eyes. Mean IOL power implanted was 29.9 D (range, 11.5-40.0 D); most eyes (88%) implanted with an IOL of 30.0 D or greater had less postoperative hyperopia than planned. Multivariate analysis revealed that only short axial length (<18 mm) was significant for higher PE.

Conclusions: Short axial length correlates with higher PE after IOL placement in infants. Less hyperopia than anticipated occurs with axial lengths of less than 18 mm or high-power IOLs.

Application to Clinical Practice: Quality A-scans are essential and higher PE is common, with a tendency for less hyperopia than expected.

Trial Registration: clinicaltrials.gov Identifier: NCT00212134

Arch Ophthalmol. 2012;130(3):293-299

ELECTION OF AN INTRAOCULAR lens (IOL) with appropriate power for implantation in pediatric eyes can be difficult. Obtaining accurate and reproducible biometry measures in children, particularly infants, is challenging because of the lack of patient cooperation and limitations in equipment. Technical difficulty with IOL placement during surgery may result in ciliary sulcus instead of capsular bag placement, adding additional error in achieving the target refraction. Inaccuracies in formulas for giving the lowest prediction error (PE), particularly for eyes with shorter axial length. Even when using these formulas, the PE in pediatric eyes remains higher than that achieved in adult populations.

See also page 300

IOL power calculation for small eyes may be exaggerated in the infantile eye. Previous studies have evaluated the accuracy of formulas for use in pediatric eyes, with the Holladay and Hoffer Q formulas giving the lowest prediction error (PE), particularly for eyes with shorter axial length. Even when using these formulas, the PE in pediatric eyes remains higher than that achieved in adult populations.

The Infant Aphakia Treatment Study (IATS) is a multicenter, randomized, controlled clinical trial sponsored by the National Eye Institute undertaken to determine whether primary IOL implantation in infants between 1 and 6 months of age with unilateral cataract would result in improved visual outcomes over contact lens correction of aphakia. Half of the 114 infants enrolled in this multicenter study were randomized to receive an IOL and then receive spectacle correction for residual refractive error. In the IATS, IOL
power was chosen based on the Holladay 1 calculation. The purposes of this report are to review the PE of refraction for infant eyes undergoing primary IOL implantation in the IATS and to look for ocular characteristics or biometry techniques that may be associated with higher error rates.

### METHODS

The study design, surgical techniques, patching and optical correction regimens, follow-up schedule, examination methods, and baseline characteristics of patients enrolled in this study have been reported previously, and therefore are only briefly summarized in this report. The study was approved by the institutional review boards of all participating centers and was in compliance with the Health Insurance Portability and Accountability Act. The off-label research use of the AcrySof SN60AT and MA60AC IOLs (Alcon Laboratories) was covered by US Food and Drug Administration investigational device exemption G020021.

### STUDY DESIGN

Infants with a unilateral, visually significant cataract (>3-mm central opacity) and an age of 28 to 209 days at the time of cataract surgery were eligible for enrollment in the study. The main exclusion criteria were persistent fetal vasculature associated with stretching of ciliary processes or involvement of the optic nerve or retina, corneal diameter less than 9 mm, premature birth (<36 weeks' gestational age), presence of a medical condition that might interfere with later visual acuity testing, or acquired cataract. Patients were randomized either to have an IOL placed at the time of the initial surgery (with spectacle correction) or to be left aphakic (with contact lens correction).

### SCREENING EXAMINATION

Before randomization, each infant underwent examination while under anesthesia to confirm study eligibility and so that biometry could be performed on both eyes. Keratometry was performed with a handheld keratometer, with a mean of at least 2 readings that varied by less than 1 diopter (D). A-scan ultrasonography of both eyes was performed, using immersion whenever possible. Measures were taken from the scan with the best waveforms (ie, highest peaks with a perpendicular retinal spike) using the phakic setting. If an A-scan ultrasonography was performed, the A-scan with the greatest anterior chamber depth was used.

### SURGICAL TECHNIQUE AND IOL POWER DETERMINATION

Infants randomized to the IOL group had the lens aspired followed by the implantation of an AcrySof SN60AT IOL into the capsular bag. If both haptics could not be implanted into the capsular bag, an AcrySof MA60AC IOL was implanted into the ciliary sulcus. After IOL placement, a posterior capsulectomy and an anterior vitrectomy were performed for all eyes.

The IOL power was determined in the operating room based on A-scan ultrasonography and keratometry readings using the Holladay 1 formula. An IOL power was chosen that was closest to the power predicted to produce a +8.0 postoperative refraction for infants 4 to 6 weeks of age and a +6.0-D postoperative refraction for infants 7 weeks and older. If the IOL was implanted into the ciliary sulcus, then 1.0 D was subtracted from the calculated IOL power (http://www.doctor-hill.com).

### FOLLOW-UP REFRATION AND PE

Follow-up examinations were performed 1 day, 1 week, and 1 month after surgery. Retinoscopy was performed under cycloplegia to determine residual refractive error at the 1-month postoperative examination. This measure was converted to spherical equivalent and compared with the predicted refraction. The predicted refraction was calculated from the Holladay 1 formula using the IOL power implanted and the patient’s axial length and mean keratometry reading recorded at the time of surgery. The PE and absolute PE were calculated as follows:

$$\text{PE} = \text{Predicted Refraction} - \text{Actual Refraction}$$

$$\text{Absolute PE} = |\text{Predicted Refraction} - \text{Actual Refraction}|$$

### ASSESSMENT OF THE QUALITY OF A-SCAN ULTRASONOGRAPHY

All available A-scans were reviewed by a certified echographer. A-scans were graded as good quality if the gates and mode were set correctly and corneal, lens, and retinal spikes were visible and of sufficient gain to be measurable, with a perpendicular leading edge for the retinal spike. Whether A-scan ultrasonography was performed using a contact or immersion technique was also determined. A-scans were judged as unreadable if the quality of the printout was sufficiently degraded such that the scan could not be adequately assessed. If an error was detected that could cause the axial length measurement to be inaccurate by more than 0.2 mm (such as inappropriate mode, improper gate or caliper placement, or poor spike quality), then the scan was classified as poor quality.

### STATISTICAL ANALYSIS

Descriptive analyses were performed for baseline and surgery characteristics (age, axial length, mean keratometry reading, corneal diameter, A-scan quality, IOL power, and site of IOL placement) and for the 1-month refraction and the PE. Two-sample t tests and, for nonnormal factors, Wilcoxon rank sum tests for differences between younger patients (28-48 days old) and older patients (49-209 days old) were performed.

Bivariate associations between PE and absolute PE and the baseline and surgery characteristics were examined using the 2-sample t test for means, the Wilcoxon rank sum test for medians, and the chi² test for percentages. Groups were compared based on age at surgery (<49 vs ≥49 days), keratometry readings (<46.5 vs ≥46.5 D), axial length (<18.0 vs ≥18.0 mm), corneal diameter (<10.5 vs ≥10.5 mm), IOL power (<30.0 vs ≥30.0 D), A-scan rating (good quality vs unreadable, unavailable, or poor quality), A-scan method (immersion vs contact), and site of IOL placement (capsular bag vs ciliary sulcus).

The relationship between PE and baseline and surgery characteristics (age category, axial length, mean keratometry reading, corneal diameter, A-scan quality, and IOL placement) was examined using multiple linear regression; backward elimination was used to remove factors that were insignificant at the .05 level of significance. In this analysis, axial length, mean keratometry reading, and corneal diameter were included as continuous variables. Results are reported as mean (SD).

### RESULTS

### STUDY PATIENTS AND BASELINE CHARACTERISTICS

Fifty-seven of the 114 patients in the IATS were randomized to receive an IOL, and IOL implantation was com-
The mean refraction was PE of actual refractions at the 1-month visit showed less re-
formed for 1 patient in the younger age group and 2 pa-
capsular bag. Ciliary sulcus IOL placement was per-
greater.
were implanted with an IOL with a power of 35.0 D or
28.7[6.0] D for the older age group); IOL power range
overall (31.5[5.0] D for the younger age group and
length (linear regression coefficient, −0.8; SE, 0.2;
A negative trend for PE was seen with increasing axial
PE in relation to axial length is shown in Figure 2. A negative trend for PE was seen with increasing axial
length (linear regression coefficient, −0.8; SE, 0.2; \(R^2=0.3; P <.001\)); that is, an increase in axial length of 1 mm was
associated with a 0.8-D decrease in mean PE in this co-
hort. When an IOL with a power greater than 30 D was
implanted, 88% of patients had less residual hyperopia
when refracted at 1 month after surgery than intended.
Of the 20 eyes with an absolute PE greater than 2.0 D, 14 (70%)
had axial lengths of less than 18 mm compared with 13
correlated to the IATS target. At the 1-month postopera-
target. A patient was deemed to be of poor quality.
Baseline A-scan ultrasonographic reports of the pseudo-
kterior of the target refraction of 6.0 D out-
other patient was excluded because an incorrect ultra-
specific postoperative refraction of +16.5 D instead of the +8.0 D targeted. The remaining 49 eyes were included for analysis. The baseline and IOL
characteristics of these 49 pseudophakic eyes are re-
Table 1. Baseline Characteristics of Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Patients</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery, mo</td>
<td>49</td>
<td>2.5 (1.5)</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>49</td>
<td>18.1 (1.4)</td>
</tr>
<tr>
<td>28-48 days old</td>
<td>22</td>
<td>17.3 (0.9)</td>
</tr>
<tr>
<td>&gt;48 days old</td>
<td>27</td>
<td>18.7 (1.4)</td>
</tr>
<tr>
<td>Keratometry reading, D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>49</td>
<td>46.2 (2.4)</td>
</tr>
<tr>
<td>28-48 days old</td>
<td>22</td>
<td>47.1 (1.8)</td>
</tr>
<tr>
<td>&gt;48 days old</td>
<td>27</td>
<td>45.5 (2.6)</td>
</tr>
<tr>
<td>Corneal diameter, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>49</td>
<td>10.5 (0.8)</td>
</tr>
<tr>
<td>28-48 days old</td>
<td>22</td>
<td>10.0 (0.6)</td>
</tr>
<tr>
<td>&gt;48 days old</td>
<td>27</td>
<td>10.9 (0.8)</td>
</tr>
<tr>
<td>Intraocular pressure, mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>49</td>
<td>11.5 (4.6)</td>
</tr>
<tr>
<td>28-48 days old</td>
<td>22</td>
<td>10.6 (4.0)</td>
</tr>
<tr>
<td>&gt;48 days old</td>
<td>27</td>
<td>12.3 (4.9)</td>
</tr>
</tbody>
</table>

Abbreviation: D, diopters.

\(^{a}\) Difference between the age group means is significant at the .001 significance level.

\(^{b}\) Difference between the age group means is significant at the .05 significance level.

**Figure 2** shows the distribution of PEs. Only 6 of the 49 eyes (12%) had an absolute PE of less than 0.5 D, 20 (41%) had an absolute PE of less than 1.0 D, and 29 (59%) had an absolute PE of less than 2.0 D (Figure 2). Of the 20 eyes with an absolute PE greater than 2.0 D, 14 (70%) had axial lengths of less than 18 mm compared with 13 of 29 eyes (45%) with an absolute PE of 2.0 D or greater (\(P = .08\); 95% CI for difference in percentages \([\text{PE} > 2.0 \text{ D} \text{ minus } \text{PE} \leq 2.0 \text{ D}], −3\% \text{ to } 54\%\)).

**Figure 3** shows the distribution of axial length. Infants in the IATS underwent surgery using standard-
ized techniques and IOL selection criteria, using the Hol-
laday 1 formula for a specified postoperative refractive
target. At the 1-month postoperative visit, only 41% of
eyes were within 1 D of the refractive target, and PE greater than 2 D was seen in another 41% of eyes. Higher PE in
IOL calculation is not surprising in this population of in-
fantile eyes, where extremely short axial length and steep keratometry readings are common. In a multivariable

**COMMENT**
analysis, axial length was the only factor found to be independently associated with PE, with shorter eyes having greater PE. In addition, of the 20 eyes with an absolute PE greater than 2 D, most (80%) were overcorrected, leaving less residual hyperopia than expected.

Errors in IOL calculation often come from measurement error during biometry, instrumentation error, or formula error.9,10 An improper A-scan ultrasonographic technique was used in 1 patient, resulting in a large error in globe axial length assessment. This eye was excluded from the overall analysis because such an error would outweigh any eye or surgery characteristics that could affect postoperative refraction targeting. Because keratometry and A-scans for infants are usually performed with the patients under anesthesia, lack of fixation may also induce measurement error. Instruments are calibrated for adult eyes, and the proportional differences in the infant globe may cause errors in measure-

![Figure 1. Distribution of refractive error at 1 month, overall and stratified by age group (28-48 vs 49-209 days). The overall mean (SD) refractive error was 5.1 (2.0) diopters (D). The mean (SD) refractive error was 6.6 (1.9) D in the younger age group and 5.7 (1.9) D in the older age group.](image)

### Table 2. Bivariate Associations Between PE and Baseline and Surgery Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
<th>PE, D</th>
<th>Absolute PE, D</th>
<th>P Valuea</th>
<th>Mean (SD)</th>
<th>P Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediction error</td>
<td>49</td>
<td>1.0 (2.0)</td>
<td>1.8 (1.3)</td>
<td>.10</td>
<td>.04</td>
<td>.01</td>
</tr>
<tr>
<td>Age at surgery, d</td>
<td>22/27</td>
<td>1.6 (2.0)</td>
<td>2.0 (1.6)</td>
<td>.047</td>
<td>2.2 (1.5)</td>
<td>.01</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>27/22</td>
<td>0.5 (1.9)</td>
<td>1.6 (1.1)</td>
<td>.01</td>
<td>.32</td>
<td>.90</td>
</tr>
<tr>
<td>Keratometry reading, D</td>
<td>27/22</td>
<td>1.8 (2.0)</td>
<td>2.2 (1.5)</td>
<td>.01</td>
<td>.10</td>
<td>.01</td>
</tr>
<tr>
<td>Corneal diameter, mm</td>
<td>28/23</td>
<td>1.0 (2.0)</td>
<td>1.8 (1.4)</td>
<td>.04</td>
<td>1.8 (1.3)</td>
<td>.90</td>
</tr>
<tr>
<td>A-scan rating</td>
<td>21/28</td>
<td>1.8 (2.0)</td>
<td>2.3 (1.5)</td>
<td>.01</td>
<td>1.5 (1.1)</td>
<td>.01</td>
</tr>
<tr>
<td>A-scan method</td>
<td>4/4</td>
<td>1.1 (2.0)</td>
<td>1.8 (1.4)</td>
<td>.10</td>
<td>1.8 (0.9)</td>
<td>.99</td>
</tr>
<tr>
<td>IOL power, D</td>
<td>32/14</td>
<td>1.0 (2.0)</td>
<td>1.7 (1.3)</td>
<td>.90</td>
<td>1.8 (1.3)</td>
<td>.91</td>
</tr>
<tr>
<td>IOL placement</td>
<td>24/25</td>
<td>0.9 (2.0)</td>
<td>1.8 (1.3)</td>
<td>.90</td>
<td>2.3 (1.5)</td>
<td>.004</td>
</tr>
<tr>
<td>Capsular bag</td>
<td>46/3</td>
<td>1.1 (2.0)</td>
<td>1.8 (1.3)</td>
<td>.34</td>
<td>2.1 (1.7)</td>
<td>.89</td>
</tr>
</tbody>
</table>

Abbreviations: D, diopters; IOL, intraocular lens; PE, prediction error.

a P values are for 2-sample t tests except for baseline A-scan rating and IOL placement (Wilcoxon rank sum test).
b Poor quality, unreadable, or missing A-scans.
ment. Ultrasonography uses a mean velocity of 1550 m/s, but the infant eye with a proportionally larger lens would have a faster velocity. We did not find a significant difference in mean PE based on method of ultrasonography, although there is concern that contact biometry may underestimate axial length due to compression forces.11-13 However, others have shown no significant difference in axial length measurements using contact vs immersion ultrasonographic methods,14 including a pediatric series comparing PE in eyes that had immersion vs contact ultrasonographic measurements with the patient under general anesthesia.15 Axial length measurement errors in children have been shown to result in larger errors in IOL power selection, such that a 4- to 14-D/mm error in axial length may occur in pediatric eyes compared with a 3- to 4-D/mm error in axial length in adults.9 The IOL power calculation difference with a keratometry error of 0.8 to 1.3 D/D was noted to be similar between children and adults.9 Formulaic errors may occur based on assumptions about IOL position within the eye and anterior chamber depth and are magnified with placement of higher-powered IOLs.16 Half of the eyes in this cohort had an IOL power greater than 30.0 D. Although a higher mean PE was demonstrated with an IOL power greater than 30.0 D and even higher for the 10 eyes that received an IOL with a power of 35.0 D or greater, these were typically implanted in shorter eyes, so analyses of the effect of IOL power on PE are confounded by axial length.

The IATS used the Holladay 1 formula for IOL calculation. In adult populations, the Holladay, Hoffer Q, and Haigis formulas have been used for eyes with axial lengths of less than 22 mm.17-19 Pediatric studies2,5 have failed to show a significant difference in mean absolute PE among formulas overall, and in a mathematical analysis of IOL power prediction in the pediatric range of keratometry and axial length values, it appears unclear which formula may give the best prediction for an individual patient.20 Postoperative refraction was determined by retinoscopy. The inability of an infant to cooperate may lead to off-axis retinoscopy or variations in the vertex distance during retinoscopy. Errors are also magnified with high refractive errors. Eye growth occurs rapidly in the first 6 months of life so that increases in axial length during the first month after surgery could result in a reduction in the amount of hyperopia measured. On the basis of a hybrid logarithmic model of typical refractive growth,21 a typical eye made pseudophakic at the age of 1 month with a postoperative refraction of +8.0 D will have a myopic shift of 0.7 D by the age of 2 months, and a typical eye made pseudophakic at the age of 5 months with a postoperative refraction of +6.0 D will have a myopic shift of 0.4 D by the age of 6 months. Refraction was deferred until the 1-month visit to allow for resolution of the potentially large astigmatic error that can be induced by sutures in infant eyes or changes induced by inflammation or corneal edema.

The overall mean absolute PE was 1.8 (1.3) D. Previous reports6,13,15,22 have shown mean absolute PEs ranging from 0.7 to 1.5 D for pediatric eyes undergoing primary IOL implantation. Mean absolute PE is often higher and less predictable for eyes with axial lengths of less than 22 mm, even when using formulas designed for short
eyes, and in this cohort, 48 of 49 eyes had axial lengths of less than 22 mm. Most eyes with absolute PEs greater than 2D in this cohort had axial lengths of less than 18 mm. Because axial length measurements greater than 20 mm were uncommon in this population (only 4 eyes), axial length measurements that are substantially longer than this should be carefully reviewed for accuracy.

Mean PE was calculated to assess the direction of miscalculation, with an undercorrection (more residual hyperopia than expected) represented by a negative value and an overcorrection (less residual hyperopia than expected) represented by a positive value. The mean PE for eyes with axial lengths greater than 18 mm was −0.1 (1.6) D, reflecting an almost equal number of overcorrections and undercorrections postoperatively, but eyes with axial lengths of less than 18 mm were often overcorrected, with less residual hyperopia than anticipated. Similarly, when eyes were compared by age group at surgery, less overcorrection was seen in the older group compared with the younger group. However, this may be explained by the expectation of more rapid ocular growth in the shorter, younger eyes in the early postoperative period. Elevated intraocular pressure can cause axial elongation and myopic shift in the infant eye, although none of the eyes were diagnosed as having glaucoma by the 1-month visit.

Gale et al. have suggested that after uncomplicated adult cataract surgery, 35% of eyes should have a PE of ±0.5 D and 85% should have a PE of ±1.0 D. In pediatric populations, however, the number of eyes with a PE of ±1.0 D is lower. In one series, 43% of pediatric eyes had a PE of ±0.5 D and 74.5% had a PE of ±1.0 D using Holladay 1, but in the subset of eyes with axial lengths of less than 22 mm, only 20% had a PE of ±0.5 D and 45% had a PE of ±1.0 D. Not surprisingly, in the IATS, a similarly low percentage of infant eyes achieved a PE of ±0.5 D (12%) or ±1.0 D (41%).

In conclusion, a relatively large PE is common when performing IOL implantation in infant eyes, especially with the shortest axial lengths (<18 mm), even when using a formula designed for short eyes. In addition, implantation of an IOL with a power of 30.0 D or greater usually resulted in less residual hyperopia than expected. In these growing eyes, with less baseline hyperopia than planned and expected axial elongation, significant myopia may result in the long term. Refractive status of these children as they become older will be the subject of a future report.

Submitted for Publication: March 13, 2011; final revision received May 27, 2011; accepted May 31, 2011.

Author Affiliations: Department of Ophthalmology, Children’s Hospital Boston, Harvard Medical School, Boston, Massachusetts (Dr VanderVeen); Departments of Biostatistics and Bioinformatics (Messrs Nizam and Lynn) and Ophthalmology (Mr DuBois and Dr Lambert), School of Public Health, Emory University, Atlanta, Georgia; Departments of Ophthalmology and Pediatrics, University of Minnesota, Minneapolis (Dr Bothun); Naval Medical Center San Diego, San Diego, California (Dr McClatchey); Uniformed Services University of Health Sciences, Bethesda, Maryland (Dr McClatchey); Loma Linda University Medical Center, Loma Linda, California (Dr McClatchey); and Department of Ophthalmology, University of Texas Southwestern Medical Center, Dallas (Dr Weakley).

Correspondence: Deborah K. VanderVeen, MD, Department of Ophthalmology, Children’s Hospital Boston, 300 Longwood Ave, Fegan 4, Boston, MA 02115 (deborah.vanderveen@childrens.harvard.edu).

Group Information: The following is a list of the members of the IATS group. Administrative Units and Participating Clinical Centers: Clinical Coordinating Center (Emory University): Scott R. Lambert, MD (study chair), Lindreth G. DuBois, ME, MMSc (national coordinator); Data Coordinating Center (Emory University): Michael J. Lynn, MS (director), Betsy Bridgman, BS, Marianne Celano, PhD, Julia Cleveland, MSPH, George Cotsonis, MS, Carey Drews-Botsch, PhD, Nana Freret, MSN, Lu Lu, MS, Azhar Nizam, MS, Seegar Swanson, Thandeka Tutu-Gxashe, MPH; Visual Acuity Testing Center (University of Alabama, Birmingham): E. Eugenie Hartmann, PhD (director), Clara Edwards, Claudio Busettini, PhD, Samuel Hayley; Steering Committee: Scott R. Lambert, MD, Edward G. Buckley, MD, David A. Plager, MD, M. Edward Wilson, MD, Michael J. Lynn, MS, Lindreth G. DuBois, ME, MMSc, Carolyn Drews-Botsch, PhD, E. Eugenie Hartmann, PhD, Donald F. Everett, MA; Contact Lens Committee: Buddy Russell, COMT, Michael Ward, MMSc. Participating Clinical Centers (in order by the number of patients enrolled): Medical University of South Carolina, Charleston, South Carolina (14): M. Edward Wilson, MD, Margaret Bozic CCRC, COA; Harvard University, Boston, Massachusetts (14): Deborah K. VanderVeen, MD, Theresa A. Mansfield, RN, Kathryn Biscigella Miller, OD; University of Minnesota, Minneapolis, Minnesota (13): Stephen P. Christiansen, MD, Erick D. Bothun, MD, Ann Holleschau, Jason Jedlicka, OD, Patricia Winters, OD, Jacob Lang, OD; Cleveland Clinic, Cleveland, Ohio (10): Elias I. Traboulsi, MD, Susan Crowe, BS, COT, Heather Haley Cinimo, OD; Baylor College of Medicine, Houston, Texas (10): Kimberly G. Yen, MD, Maria Castanes, MPH, Alma Sanchez, COA, Shirley York; Oregon Health and Science University, Portland, Oregon (9): David T. Wheeler, MD, Ann U. Stout, MD, Paula Rauch, OT, CRC, Kimberly Beaudet, CO, COMT, Pam Berg, CO, COMT; Emory University, Atlanta, Georgia (9): Scott R. Lambert, MD, Amy K. Hutchinson, MD, Lindreth G. DuBois, ME, MMSc, Rachel Robb, MMSc, Marla J. Shainberg, CO; Duke University, Durham, North Carolina (8): Edward G. Buckley, MD, Sharon F. Freedman, MD, Lois Duncan, BS, B.W. Phillips, FCLSA, John T. Petrovski, OD; Vanderbilt University, Nashville, Tennessee (8): David Morrison MD, Sandy Owings COA, CCRP, Ron Biernacki COA; University of Miami Children’s Hospital Birmingham: Stacey Kruger, MD, Charlotte Tibi, CO, Susan Vegra, University of Texas Southwestern, Dallas, Texas (6): David R. Weakley, MD, David R. Stager Jr, Joost Felius, PhD, Clare Dias, CO, Debra L. Sager, Todd Brantley, OD; Data and Safety Monitoring Committee: Robert Hardy, PhD (chair), Eileen Birch, PhD, Ken Cheng, MD, Richard Hertle, MD, Craig Kollman, PhD, Marsha-
REFERENCES


