Higher order monochromatic aberrations of the human infant eye

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The monochromatic optical aberrations of the eye degrade retinal image quality. Any significant aberrations during postnatal development could contribute to infants’ immature visual performance and provide signals for the control of eye growth. Aberrations of human infant eyes from 5 to 7 weeks old were compared with those of adult subjects using a model of an adult-like infant eye that accounted for differences in both eye and pupil size. Data were collected using the COAS Shack-Hartmann wavefront sensor. The results demonstrate that the higher order aberrations of the 5-to-7-week-old eye are less than a factor of 2 greater than predicted for an adult-like infant eye of this age. The data are discussed in the context of infants’ visual performance and the signals available for controlling growth of the eye.

Keywords: visual development, optical aberrations, human infant

Introduction

The visual performance of human infants improves dramatically after birth. The spatial contrast sensitivity function matures over a number of months so that both the resolution limit and peak sensitivity to contrast increase by approximately a factor of 10 during the first postnatal year (reviewed by Teller, 1997).

A number of studies have sought to determine the structural immaturities that limit performance in the neonatal visual system (in humans, see Brown, Dobson, & Maier, 1987; Banks & Bennett, 1988; Wilson, 1988; Candy, Crowell, & Banks, 1998; in macaque, see Boothe, 1982; Jacobs & Blakemore, 1988; Kiorpes, Tang, Hawken, & Movshon, 2003). These analyses incorporated immaturities in dimensions of the eye, the photoreceptors, and the receptive field properties of neurons. The studies of human development were unable to fully address the role of the eye’s optical quality because the available data were limited to the lower order aberrations of defocus and astigmatism (reviewed by Saunders, 1995). One previous study had noted the presence of spherical aberration in human infant eyes but had not measured it (Molteno & Sanderson, 1984). The studies of infant macaques, however, were able to incorporate data from a study conducted by Williams and Boothe (1981). They used a double-pass technique to measure the optical transfer function (OTF) of the infant monkey eye. These data demonstrated a small maturation of the OTF over the first 13 weeks after birth, but clearly showed that the optical quality of the newborn monkey eye was superior to the resolution of their visual system as a whole. In those experimental viewing conditions, the macaque OTF extended out to 32 cpd at an age when visual acuity is only 1-2 cpd (Teller, Regal, Videen, & Pulos, 1978).

The higher order optical aberrations, beyond defocus and astigmatism, are unlikely to dramatically limit human infants’ visual performance. Fundus details are easily resolved during an infant eye examination (Cook & Glasscock, 1951) and a recent study demonstrated almost adult-like resolution of stages of the infant visual system preceding the first major nonlinearity (Candy & Banks, 1999). However, given the structural differences between infant and adult eyes, optical quality of the infant eye may differ significantly from that of the adult. The length of the human newborn eye is approximately two-thirds of the adult length (e.g., Larsen, 1971; Fledelius, 1992; Denis et al., 1993), the cornea has greater curvature than in the adult (Mandell, 1967; Inagaki, 1986; Insler, Cooper, May, & Donzis, 1987), and the lens undergoes significant postnatal reconfiguration (Gordon & Donzis, 1985; Wood, Mutti, & Zadnik, 1996). In fact, coordinated growth of the eye over the first two postnatal years leads to a loss of 20-30 D of total optical power while approximate emmetropia is maintained (Bennett & Francis, 1962).

At a more detailed level, the distribution of individual higher order aberrations in the infant eye is of particular interest (e.g., coma or spherical aberration). In the presence of defocus alone, the retinal image is the same for equal amounts of myopic and hyperopic defocus. The visual system therefore requires an additional signal to determine the sign or direction of any defocus. Higher order monochromatic aberrations have been proposed to provide retinal image cues that guide the control of defocus through accommodation and emmetropization (Wilson, Decker, & Roorda, 2002; Wallman & Winawer, 2004). The types and amount of aberrations present in the infant eye need to be...
understood to assess their potential role in these processes. The growth of the cornea and lens has also been proposed to be coordinated with each other, so that their combined aberrations become lower than those of either the cornea or the lens alone (Kelly, Mihashi, & Howland, 2004; Artal, Giurao, Berrio, & Williams, 2001). What is the pattern of the combined aberrations at birth? Does this pattern change with further growth of the cornea and lens?

The goal of this study was to measure the higher order monochromatic aberrations of the human infant eye and to compare them with those of the adult. The impact of these aberrations on retinal image quality was assessed, as was their potential for signaling defocus to the developing visual system.

**Methods**

**Aberrometer**

Monochromatic aberrations were measured using a Complete Ophthalamic Analysis System Aberrometer (COAS) manufactured in 2000 (Wavefront Sciences Inc., Albuquerque, NM). The COAS incorporates a Shack-Hartmann wavefront sensor that samples the wavefront emanating from a point object generated on the retina. The sensor takes up to 44 x 33 simultaneous, evenly distributed samples of the local slope of the wavefront using a lenslet array. The lenslets have a separation of 288 μm in the entrance pupil plane. The shape of the wavefront leaving the eye can then be interpolated, reconstructed, and described using Zernike polynomials. The design, validation, and reliability of the COAS aberrometer at Indiana University have been described previously (Cheng, Himebaugh, Kollbaum, Thibos, & Bradley, 2003, 2004).

**Subjects**

Twenty-two full-term infants from 5-to-7-weeks old and one parent of each infant were recruited from the public birth records and the local community. None of the subjects had any clinically significant ocular abnormalities. The parents provided informed consent after the study had been fully explained to them. The protocol had been reviewed and approved by the local Indiana University Institutional Review Board (See Appendix A for a discussion of retinal light exposure).

**Procedure**

One Shack-Hartmann image was collected from the right eye of each subject in dim room illumination. The luminance of the instrument case around the viewing aperture was 20 cd/m². The illumination was made bright enough to provide a clear image of the eye for alignment purposes, but kept at the minimum usable value to maximize the subject’s pupil size. The subjects wore no optical correction.

**Alignment**

The adult subjects were asked to fixate the center of the instrument’s fixation target while their head was placed in the chin-rest. The instrument was then aligned with their entrance pupil such that the exiting beam from the pupil was centered on the instrument’s measurement axis and lenslet array.

The infants could not be asked to fixate the fixation target in the instrument and therefore their alignment had to be performed objectively. The chin-rest was removed and the infant’s chin gently rested in an experimenter’s hand while the experimenter aligned the infant using real-time video. The video contained an image of the eye and a series of 1st Purkinje images generated by LEDs adjacent to the instrument’s viewing aperture (see Figure B1). Aberration data were collected only when the experimenter holding the infant and another observer operating the COAS were in agreement that the image of the eye was in focus and all Purkinje images fell within the infant’s entrance pupil (as demonstrated in Figure B1). This criterion led to an estimate of the deviation between the measurement and pupillary axes of less than 10 deg (see Appendix B). Assuming that the neonatal line of sight sits an average of 8 deg nasally from the pupillary axis, this limit would define an extreme range for the measurement axis from 2 deg nasally to 18 deg temporally from the line of sight (Slater & Findlay, 1972; Riddell, Hainline, & Abramov, 1994; Wick & London, 1980).

**Data analysis**

Aberration estimates and image quality both vary with pupil size, so comparisons of optical quality between eyes are typically made after equating pupil size (e.g., Thibos, Hong, Bradley, & Cheng, 2002). This is appropriate for comparing eyes of the same axial length but will result in unequal numerical apertures in eyes of different sizes, such as infant and adult eyes.

We therefore developed predictions for an adultlike eye scaled to the size of an infant eye (see Appendix C). The adultlike eye was a three-dimensionally (3D) scaled version of the adult eye with adultlike refractive indices. This adultlike eye therefore included a pupil size scaled down by the ratio of eye sizes. With such a model, the wavefront root mean square (RMS) error of the scaled adultlike eye will differ from that of the adult eye by the scaling factor (see also Howland, 2005), whereas the adult and adultlike point spread functions (PSFs) will be approximately matched in angular units (although the effect of diffraction on the PSFs will scale with pupil size).

The axial length of the human newborn eye is approximately two-thirds of the adult axial length (e.g., Larsen, 1971; newborn mean axial length of 16.6 mm and adult mean axial length of 24.0 mm). This scaling factor was used to estimate the difference in eye size between adults and infants and to generate the scaled adultlike predictions. The pupil sizes used for the aberrometry analysis...
were scaled by this ratio (pupil diameters of 3 mm were used for infants and 4.5 mm for adults). Zernike coefficients up to the 6th order and the combined RMS wavefront error were then calculated for each individual subject according to the Optical Society of America (OSA) recommended standards (Thibos, Applegate, Schwiegerling, & Webb, 2002). Thus the infant RMS data would be considered adultlike if they equaled two-thirds of the real adult values, and the infant PSFs would be considered adultlike if they had approximately the same angular size as the real adult data.

**Results**

Data were successfully collected from all of the adults and 17 of the 22 infant subjects. The remaining five infants were either too sleepy or fussy.

**Shack-Hartmann images**

Shack-Hartmann images from infant subjects were included in the analysis if the natural pupil size was greater than 3 mm, and there were no missing centroids in the analyzed pupil area. These criteria permitted inclusion of data from 12 of the infant subjects, whose pupil sizes ranged from 3.06 mm to 4.65 mm. Data from these infants’ parents were used for the adult analysis. In this adult group, the pupil size ranged from 4.52 mm to 6.58 mm (all 12 adults therefore had pupil sizes greater than the required 4.5 mm). The Shack-Hartmann images from the 12 included infant eyes are shown in *Figure 1*, panel A, and from the adults in *Figure 1*, panel B. The adult images include a bright spot caused by the reflection of the collimated super-luminescent diode beam. The infant images typically do not include this spot, indicating that the subjects were displaced laterally from exact alignment with the instrument (this has been shown to have little impact on the measurements; Cheng, Himebaugh et al., 2003).

The data in Table 1 illustrate that, in the viewing conditions used, the ratio of actual infant to adult pupil sizes closely approximated the 2:3 ratio used in the analysis. Therefore, the theoretically motivated use of a common numerical aperture actually closely reflects the physiological pupil size ratio for these subjects.

<table>
<thead>
<tr>
<th>Pupil diameter (mm)</th>
<th>Infant</th>
<th>Adult</th>
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<tbody>
<tr>
<td>Minimum</td>
<td>3.06</td>
<td>4.52</td>
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<tr>
<td>Maximum</td>
<td>4.65</td>
<td>6.58</td>
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<tr>
<td>Mean</td>
<td>3.89</td>
<td>5.65</td>
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Table 1. Infant and adult measured pupil sizes.

**2nd-order aberrations**

The distribution of 2nd-order Zernike coefficients for individual infant and adult subjects is shown in *Figure 2*. t tests indicated that there were no significant differences in the adult $Z_2^0$ data occurred because some of the subjects are myopic (positive coefficients correspond to myopic focus).
between the infant and adult means for either of the astigmatic terms ($Z_1^2$: $p = .429$; $Z_3^2$: $p = .718$). Overall, there was also no significant difference in the defocus term at this sample size ($Z_1^0$: $p = .152$), even though some of the adults were myopic and we could not instruct the infants to accommodate accurately to the target. Infants in this age range are typically hyperopic (Cook & Glasscock, 1951; Mayer, Hansen, Moore, Kim, & Fulton, 2001), but overaccommodate for distant targets such as the one presented in the COAS (Banks, 1980). The $Z_0^0$ coefficients were converted to equivalent diop ters giving a mean absolute magnitude of defocus of 1.79 D, SD ± 2.35, for the adults, and 1.62D, SD ± 0.71, for the infants (see Appendix C, Equation 2).

3rd-, 4th-, and 5th-order aberrations

The distribution of 3rd-to-5th-order Zernike coefficient values is shown for the infant and adult groups in Figure 3, panel A. The mean values are all comparable and close to zero in the two groups. A Hotelling $T^2$ test suggested that the vector of mean coefficients was not significantly different between groups, $F = 0.699$, df1 = 22, df2 = 1, $p = .756$. The difference between the groups for each individual Zernike component was also analyzed in a two-sample $t$ test (with no correction for multiple tests). The only component to reach a $t$ test $p$ value of < .05 for the difference between the groups was $Z_4^1$ ($p = .014$). This was not considered highly significant given the large number of $t$ tests being performed. The $Z_4^0$ spherical aberration term had a $p$ value of .091. One-sample $t$ tests were also performed to determine whether the individual 3rd-to-5th-order components differed significantly from a mean of zero. In the infant data, the components that reached a $t$ test $p$ value of < .05 were $Z_2^1$ ($p = .015$) and $Z_3^1$ ($p = .031$). The $Z_4^1$ term had a $p$ value of .051. In the infant data, the components that reached a $t$ test $p$ value of < .05 were $Z_4^2$ ($p = .019$) and $Z_4^4$ ($p = .026$). The $Z_4^0$ term for that group had a $p$ value of .93. These values < .05, again, were not considered highly significant due to the large number of tests being performed, although the adult data are consistent with the literature finding positive values of $Z_4^0$ (e.g., Thibos, Hong et al., 2002). Overall, these data suggest that there is no consistent trend in the sign of the coefficients within the populations, and that the infant distribution is not dramatically different from that of the adult.

The distributions of absolute magnitude of each Zernike coefficient are shown in Figure 3, panel B. Both the adult and infant data in this figure are consistent with the previous adult literature in that they show a decrease in the mean magnitude with increasing order (Liang & Williams, 1997; Porter, Guirao, Cox, & Williams, 2001; Thibos, Hong et al., 2002; Castejon-Mochon, Lopez-Gil, Benito, & Artal, 2002). A Hotelling $T^2$ test suggested no significant difference between the distribution of infant and adult absolute coefficient values, $F = 1.720$, df1 = 22, df2 = 1, $p = .546$, and the components that reached a $p$ value of < .05 in $t$ tests of the difference between groups for individual components were $Z_4^1$ ($p = .014$), $Z_3^1$ ($p = .047$), and $Z_4^4$ ($p = .021$).

**RMS wavefront error**

The Zernike coefficients from the 3rd to 6th order were combined to form RMS errors in Figure 4. The RMS wavefront error is shown for each subject and individual order, and then for each subject for the combined 3rd to 6th orders. The lowest $p$ value resulting from $t$ tests of the difference between infants and adults for each of these variables was $p = .337$, which was considered insignificant.

**Figure 4.** RMS wavefront error for individual subjects. The data are presented for each of the 3rd to 6th orders separately and then as a combined higher order value.

The model of an adult-like infant eye developed in Appendix C predicts that the real infant RMS values should equal two-thirds of the real adult values. To test this prediction, two-sample $t$ tests were performed as a function of scale factor applied to the adult data. The results indicated that the infant and adult combined RMS (3rd to 6th order) were most similar when the adult data...
were scaled by 0.87 (the $p$ value for the adult data scaled by the adultlike model of 0.67 was 0.076, for the adult data scaled by 0.8 was 0.580, scaled by 0.87 was 0.977, and scaled by 0.9 was 0.793). That is, when employing the same numerical aperture, infant eyes have an RMS that is 0.87 that of adult eyes, not the 0.67 predicted by the simple scaled eye model. Thus, the data suggest that the mean higher order aberrations of the infant eye are somewhat larger (by 20% of the mean adult value) than predicted by the adultlike model. This mean difference is small when compared with immaturities in infants’ visual performance at this age and the range of higher order aberrations seen in both adult and infant eyes.

**Radial modulation transfer functions**

Adult and infant mean optical modulation transfer functions (MTFs) are shown in Figure 5. These functions were calculated from the wavefront error maps. Each MTF function is averaged over meridia and includes the effects of aberrations from the 3rd to 6th order. These data again suggest that the infants’ higher order optical quality is slightly worse than that of adults at 5 to 7 weeks after birth. For example, at 10 c/deg, the infant optics transfer a mean of 20% of the object contrast to the image, whereas adult optics transfer a mean of 33%. Interestingly, if we compare the contrast transferred at spatial frequencies scaled to the acuity limit, we find the reverse is true. For example, at 50% of the adult resolution limit (~25 c/deg), only 11% is transferred, but at 50% of the infant resolution limit (~1 c/deg), 93% is transferred. Thus, although the infant optics are inferior to those in the adult eye, they are more efficient at transferring a neurally detectable signal to the retinal image.

The PSFs for the 3rd to 6th-order aberrations were calculated from the wavefront error maps. Each MTF was calculated using Fourier optics. PSF width was quantified using the equivalent width metric (Thibos, Hong, Bradley, & Applegate, 2004), which gives the width of a uniform circular PSF with the same intensity as the peak of the actual PSF. The mean adult value was 1.57 arcmin (SD ± 0.49) and the mean infant value was 2.07 arcmin (SD ± 0.48). These distributions were significantly different ($p = .016$), implying again that the effect of higher order aberrations is somewhat more disruptive to retinal image quality in infants than in adults. An adultlike infant eye was predicted to have the same angular PSF width as the real adults (Appendix C).

**Point spread functions**

The PSFs for the 3rd to 6th-order aberrations were calculated using Fourier optics. PSF width was quantified using the equivalent width metric (Thibos, Hong, Bradley, & Applegate, 2004), which gives the width of a uniform circular PSF with the same intensity as the peak of the actual PSF. The mean adult value was 1.57 arcmin (SD ± 0.49) and the mean infant value was 2.07 arcmin (SD ± 0.48). These distributions were significantly different ($p = .016$), implying again that the effect of higher order aberrations is somewhat more disruptive to retinal image quality in infants than in adults. An adultlike infant eye was predicted to have the same angular PSF width as the real adults (Appendix C).

**Correlation between infants and parents**

The fact that the adult data were collected from the infants’ parents (9 mothers and 3 fathers) allowed us to determine whether an infant’s higher order aberrations were more correlated with their parent than any of the other adult subjects. The first analysis is shown in Figure 6, panel A. The $x$axis represents infant subject number, and the $y$-axis represents the correlation between that infant’s set of 3rd-to-6th-order coefficients and an adult’s. The black symbols show each infant’s correlation with their own parent, and the small gray symbols show the correlation with each of the other adults. The horizontal line shows the level at which the correlation becomes significant at the .01 level (one-tailed test, alpha level = 0.01, df = 10, $r = 0.658$, with a null hypothesis of zero correlation and an alternative hypothesis that the correlation is positive, with no compensation for multiple tests). The graph demonstrates that the correlation between individual infants and their parents is inconsistent across infants, and also that the range of correlations with parents across the group approximates the range of correlations between each infant and any other adult. These correlations are typically insignificant, with only 4 (2 with parent and 2 with another adult) of the total 144 correlations reaching significance at the 0.01 level.

An alternative analysis is shown in Figure 6, panel B. In this graph the $x$-axis represents individual Zernike coefficients, and the $y$-axis represents the correlation of that coefficient in the infant group with the adult group. The black symbols show the correlations when the infants are all aligned with their parents, and the small gray symbols show the correlations when the infants are compared with the other possible arrangements of the adult group (each infant matched with each adult only once). The horizontal line again shows the level at which the correlation becomes significant (one-tailed test, alpha level = 0.01, df = 20, $r = 0.492$, with a null hypothesis of zero correlation and an alternative hypothesis that the correlation is positive, with no compensation for multiple tests). The aligned infant and parent correlations are very variable. The cases where the parent correlation is clearly greater than the correlation with other adults are $Z_3^1$, $Z_4^2$, and $Z_4^0$. The parent correlations for $Z_3^1$ and $Z_4^0$ are also greater than the 0.01 significance level for the one-tailed test, although given the num-

**Figure 5.** Mean and standard deviation of the infant and adult radial-average MTF data. Aberrations from 3rd to 6th order were included. Pupil sizes were set to 3 mm and 4.5 mm for infants and adults, respectively.
Figure 6. A. Correlation between infant and adult 3rd-to-6th-order Zernike coefficient values. Black symbols represent the correlation between an infant and their parent across the set of coefficients. Gray symbols represent the correlation between the infant and the other adults. The line represents threshold for a significant positive correlation at the 0.01 level. B. Correlation between infant and adult distributions of each Zernike coefficient. Black symbols represent the correlation between infants aligned with their parents. Gray symbols represent the correlation between the infants and adults in a different alignment. The line represents threshold for a significant positive correlation at the 0.01 level.

Discussion

Higher order monochromatic aberrations were measured in human infant and adult eyes. The wavefront errors (defined as individual Zernike coefficients or overall wavefront RMS) of 5-to-7-week-old eyes differed little from adult eyes when the pupil size was scaled to maintain a constant numerical aperture. The ratio of infant to adult natural pupil sizes in these experimental conditions was consistent with the constant numerical aperture scaling, and therefore suggests that the adult and infant wavefront errors were also comparable in natural viewing.

The RMS data are not consistent with a hypothesis that the infant eye is a 3D-scaled version of the adult eye with adultlike refractive indices. That model predicts smaller RMS in the infant eyes than the adult eyes by a factor of two-thirds (see Appendix C). Howland (2005) has recently developed the same prediction for equivalent optical quality in eyes of different sizes, and extended the analysis to include relative pupil size changes in the eyes being compared.

The infant and adult RMS data were most similar when the adult data were scaled by a factor of 0.87, suggesting that the infant aberrations are somewhat greater than the adultlike prediction. There are a number of possible explanations for this result.

We were unable to direct the infants’ accommodative response to the instrument’s fogged distant target. Infants aged 5-7 weeks tend to be hyperopic and to overaccommodate to distant targets (Banks, 1980). Thus the infants are likely to have been exerting accommodative effort when the...
measurements were made. The adults could be instructed to fixate the target and had a range of refractive errors. The adults were therefore unlikely to be matched with the infants for accommodative effort during data collection. He, Burns, and Marcos (2000) (first 35 terms with defocus excluded) and Cheng, Barnett et al. (2004) (2nd to 6th order excluding defocus) have both noted minimal change in adult higher order RMS for accommodative efforts from 0-3 D, but an increase in RMS of almost a factor of 2 between 3 D and 6 D of effort. If the infant eyes also exhibit this behavior, the relatively greater RMS in the infant eyes could result from their increased accommodative effort. If this were the case, the infant RMS may actually be closer to the adult prediction for a matched accommodative response (although any increase in aberrations associated with the myopic refractive errors of the adults could negate the increase due to the accommodation in the infants (Collins, Wilsoet, & Atchison, 1995; Carkeet, Luo, Tong, Saw, & Tan, 2002; Llorente, Barbero, Cano, Dorrorsoro, & Marcos, 2004; but see Cheng, Bradley, Hong, & Thibos, 2003).

The studies of aberrations as a function of accommodation in adults have also demonstrated that spherical aberration ($Z_4^1$) becomes less positive with increasing accommodation (He et al., 2000; Cheng, Barnett et al., 2004). If this is also true in infants, the spherical aberration data (Figure 3) are also consistent with the infants exerting a greater accommodative effort than the adults. The mean $Z_4^1$ coefficient is less positive in the infants than in the adults. An alternative interpretation of these data is that the positive increase in mean $Z_4^1$ with age is consistent with the same trend seen across the adult age range (McLellan, Marcos, & Burns, 2001; Glasser & Campbell, 1998).

Poor fixation control in the infant group might provide another explanation for the relatively larger RMS aberrations in the infant eyes. The adult aberrations were measured along the line of sight, but this may not be the case for the infant eyes. Our observation of pupil and Purkinje images indicates that the infant data were collected within ±10 deg of the pupillary axis. Optical aberrations tend to increase with increasing eccentricity in adults (Jennings & Charman, 1981; Navarro, Moreno, & Dorrorsoro, 1998; Cheng, Himebaugh et al., 2004), and if infant eyes demonstrate the same characteristic, it is possible that the infant aberrations would have been slightly lower if we were able to measure them closer to the line of sight. If correct, this explanation also implies that foveal retinal image quality in the infant eye may actually be even more similar to that of adults than we have observed.

Alternatively, if the relative increase in infant RMS is a true indication that the infant aberrations are greater than in the adult eye, this increase may result from the immature steeper and more powerful dimensions of the ocular structures (e.g., Mandell, 1967; Inagaki, 1986; Inslter et al., 1987) or the infant eye having a higher refractive index than found in adults (the adultlike prediction generated in Appendix C was based on adultlike refractive indices) (Wood et al., 1996).

**Effect of higher order monochromatic aberrations on visual performance**

The poorer MTFs (Figure 5) and larger equivalent width of the 5-to-7-week-old higher order PSFs both suggest a slightly inferior image quality relative to adults. This difference may be due to the accommodative or fixation factors mentioned above or be fully attributable to fundamental differences in optical quality. This likely upper bound estimate of the difference between infants and adults can be approximated in diopters of defocus using the concept of “equivalent defocus” (Thibos, Hong et al., 2002; see Equation 2 in Appendix C). This conversion provides the dioptrical defocus necessary to generate the same level of wavefront RMS. The 3rd-to-6th order RMS of adult and infant eyes are equivalent to 0.22 D (SD ± 0.09) and 0.43 D (SD ± 0.13), respectively, and thus the difference between them is equivalent to 0.21 D of defocus.

The cutoff of the preferential-looking contrast sensitivity function at 5-7 weeks old is approximately 2 cycles/deg (Atkinson, Bradick, & Moar, 1977; Banks & Salapatek, 1978). A visual system with this acuity is not sensitive to subtle changes in focus, as quantified by Green, Powers, and Banks (1980), who predicted a depth of focus of approximately ±1 D at this age (based on infants’ acuity and pupil size). Thus the 0.43 D of absolute equivalent defocus is unlikely to have a large impact on infants’ visual performance, and the 0.21 D increase relative to adults would have even less effect.

It is also interesting to note that the Nyquist limit of the foveal infant photoreceptor array falls well within the bandwidth of their OTF. Based on inner segment spacing, Candy et al. (1998) calculated a newborn foveal Nyquist limit of approximately 15 cpd. Based on the MTF data in Figure 5, the 5-to-7-week-old infant eye would pass more than 10% of the contrast in a stimulus at that spatial frequency. These data support the potential for aliasing of periodic patterns in the young infant eye, although the effect of any aliasing on perception will depend on the spatial frequency and contrast of the alias itself, plus the amounts of lower order aberrations—defocus and astigmatism—in the image. Foveal vision in the adult eye is protected from aliasing because the optics of the eye do not transmit sufficient contrast at spatial frequencies higher than the Nyquist limit of the photoreceptor sampling array (Campbell & Green, 1965; Williams, 1985).

**The role of monochromatic aberrations in the development of the visual system**

It has been shown that adult observers can distinguish hyperopic from myopic defocus using higher order monochromatic aberrations in defocused PSFs (Wilson et al., 2002). It has also been suggested that these differences in
the PSFs may play a role in the control of both infant accommodation and emmetropization processes (reviewed by Wallman & Winawer, 2004). We have examined the nature of this cue derived from our aberration data. Using Fourier optics, we computed PSFs for three representative infant eyes for a range of defocus levels (a through-focus analysis of the PSF). These PSFs are shown in Figure 7. It is clear that positive and negative defocus generate discriminable PSFs in two of the three infants (A and C) and thus that the cue could be used to control the direction of accommodation and emmetropization in these individuals. However, for this cue to be employed, it must be detectable. Its visibility will therefore once more depend on photoreceptor sampling and neural processing of the image, as in the case of spatial aliases.

The variability of the Zernike coefficients across individuals also implies that the PSF can be dramatically different for any two infants (as shown in Figure 7). This variability suggests that any mechanism responsible for interpreting defocus in the PSF using higher order aberrations would need to be calibrated for the individual’s optics. The accuracy of the interpretation might also be strongly influenced by changes in an individual’s ocular aberrations with growth of the eye (Kelly et al., 2004; Artal et al., 2001).

Given the hereditary component of myopia development in humans (Hammond, Snieder, Gilbert, & Spector, 2001; Rose, Morgan, Smith, & Mitchell, 2002; Mutti, Mitchell, Moeeschberger, Jones, & Zadnik, 2002), one might ask whether there is a correlation between the optics of the eyes of infants and their parents. For this sample size, there was no consistent correlation between the set of coefficients in an infant and their parent, and the range of correlations for related individuals approximated that between infants and unrelated adults. It is possible, however, that the correlations would have been higher if the parent and infant aberrations could be compared at the same age. The parent’s aberrations may have more closely correlated with their infant’s during their own infancy, but then have changed as their eye grew or their refractive error changed (Artal et al., 2001).

The coefficient showing the most significant positive correlation between infants and their parents was $Z_{4}^{0}$ spherical aberration (even though it had one of the larger differences between adult and infant mean amplitudes in Figure 3). There is some evidence of a correlation between the amount of spherical aberration and refractive error in adults (Collins et al., 1995; Carkeet et al., 2002; Llorente et al., 2004; but see Cheng, Bradley et al., 2003), and so it could be interesting to explore more closely this coefficient and its relationship with current and future refractive error in infants. Overall, these correlations might obviously be increased if the infant alignment were controlled.

The low levels of monochromatic aberrations and the population means of approximately zero for almost every aberration in adults (Liang & Williams, 1997; Porter et al., 2001; Thibos, Hong et al., 2002; Castejon-Mochon et al., 2002) combined with the elegant compensatory relationship between the corneal and lenticular aberrations (Artal...
et al., 2001; Kelly et al., 2004) are possibly indicative of a postnatal emmetropization-like process that refines higher order aberrations (Kelly et al., 2004). However, the observations from our infant eyes, that they also have low levels of aberrations and that their population means are also almost zero, seem to suggest that if present any active feedback process does not change the overall aberrations of the eye dramatically.

**Appendix A**

After performing routine calculations to confirm that the retinal exposure generated by the COAS falls within ANSI standards established for adult eyes (ANSI Z136.1, 2000), the question that remains is whether the biological tissue in the developing infant eye is more susceptible to damage than in the adult eye. Is the human threshold for light damage lower in the developing eye than in the mature eye? This question cannot be answered definitively in animal models because of potential species differences. A theoretical analysis of relevant immaturities in the human infant eye was therefore undertaken before conducting this study.

The super-luminescent diode in the COAS system generates an image of a point source on the retina at a wavelength of 850 nm. This wavelength presents a potential photothermal hazard to the posterior segment of the eye, through heat generation and temperature elevation in structures containing pigments that absorb near infrared (IR) (Slney & Wolbarsht, 1980, p. 126).

The risk to photoreceptors in adults is small because the photopigments absorb very little at this wavelength. Human infants have immature photoreceptors with even less photopigment than those of the adult. Yuodelis and Hendrickson (1986) found neonatal human outer segments to be shorter than those of an adult by a factor of approximately 10. Thus, infant photoreceptors would absorb even fewer photons than adult photoreceptors.

After passing through the photoreceptor layer, near IR will be absorbed by the melanin pigment in the retinal pigment epithelium (RPE) or by hemoglobin in the choroid. The chief concern is absorption in the RPE (see Slney & Wolbarsht, 1980, Figure 4.16). The proportion of photons absorbed by the RPE depends on the density of melanin granules in its cells, and unfortunately there is little developmental human data available on this topic. Studies have noted that the RPE has become an adultlike single layer of cells with some pigment by 2 months of gestation (Mund, Rodrigues, & Fine, 1972; Hollenberg & Spira, 1973), and that pigment melanosomes are formed from the 7th to 27th week of gestation (Mund et al, 1972), but the absolute density of pigment has not been plotted as a function of age. However, of relevance to the current study, Friedman and Ts’o’s (1968) study of donor tissue notes that the gradient of pigment density typically found in adults (greatest density in the macula region and least in the periphery) was reversed in their fetal and neonatal eyes. Streten (1969, p. 393) also notes a delay in RPE pigmentation in the macula until well into infancy. Her data document a reduced RPE cell density in the posterior pole in the neonatal period with a later cell migration into the macular area. An adultlike or higher RPE cell density was found in the neonate only at eccentricities in the mid-periphery or beyond. Robb (1985) also notes a postnatal migration of RPE cells toward the macular area during the first 6 postnatal months. These data suggest that the infant RPE in the posterior pole does not contain a higher pigment density than found at the same location in the adult.

If anything, these lines of evidence suggest that the 850-nm image formed on the retina in the posterior pole should result in less temperature elevation in the infant eye than in the adult.

**Appendix B**

The optical quality of the adult eye varies as a function of retinal eccentricity (e.g., Navarro, Artal, & Williams, 1993). It is likely that this is also the case for the infant eye. We, therefore, wanted to estimate the eccentricity at which the aberration measurements were recorded from infants to help determine how closely the data represented foveal optical quality. The data were collected only when the 1st Purkinje images generated by the LEDs around the instrument’s viewing aperture all fell within the entrance pupil (a typical situation is shown in Figure B1). This inclusion criterion limited the angular deviation of the pupillary axis.

![Figure B1](http://jov.arvojournals.org/pdfaccess.ashx?url=/data/journals/jov/933512/ on 06/18/2017)
from the instrument axis, and thus the deviation of the line of sight from the instrument axis. For example, if the Purkinje image ring had the same radius as the pupil, this criterion would force the data to be collected on the pupillary axis. The radii of the pupil and the Purkinje image ring (which depends on the individual's corneal curvature) were not equal, however, and were not constant across observers. The fixation error tolerance therefore varied across observers.

The range of pupil diameters recorded from the included infants was 3.06–4.65 mm and the Purkinje image ring, which was smaller than the pupil, was noted to have a radius greater than one-third of the pupil radius. The most extreme deviation possible, therefore, where the Purkinje image ring would be decentered the most from the pupil center, would be when the Purkinje image ring is abutting the pupil margin and has a radius of one-third of the pupil radius. In this case the ring would have a center 1–1.5 mm from the center of the pupil for this range of pupil sizes. Using a standard Hirschberg ratio of 12 deg/mm (Wick & London, 1980; Riddell et al., 1994), we therefore estimate that aberration data could be collected no more than 12–18 deg from the pupillary axis.

As previously stated, however, the Purkinje image ring radius was noted to be more than one-third the pupil radius, and the ring was generally well centered on the pupil when data were collected. For the mean infant pupil size of 3.8 mm and a more typical case such as shown in Figure B1, where the ring might be decentered from the pupillary axis by one quarter of the pupil radius, the deviation would equate to 0.5 mm or 6 deg. We therefore consider it is reasonable to estimate that our infant aberration data were collected within 10 deg of the pupillary axis.

Appendix C

Zernike coefficients are a representation of the summed wavefront modulation across the pupil area. Changing pupil size will therefore change the Zernike coefficients that describe an otherwise identical eye (e.g., Thibos, Hong et al., 2002). It might be logical to compare adult and infant eyes for a matched pupil size to control for this effect. However, the infant eye is considerably smaller than the adult eye and so a matched pupil size corresponds to a relatively larger aperture in the infant eye (Figure C1A). To determine whether the higher order aberrations of the infant eye are adultlike, it was necessary to generate a prediction for an adultlike infant eye that addressed the fundamental difference in both eye and pupil size between infant and adult eyes.

The simplest model to test is to propose that the infant eye is merely a compressed version of the adult eye— it is smaller in all three dimensions by a constant factor (with adultlike refractive indices). Compressing the adult pupil and wavefront by the constant factor across the 2D pupil plane has no effect on the RMS wavefront error, but compression in the axial 3rd dimension will reduce the amplitude of the optical path difference (OPD) by the scaling factor at all points (Figure C1B). Thus a 3D-scaled version of the adult eye is predicted to have a total RMS that is reduced from the true adult value by the scaling factor. Beyond its simplicity, this compression model is attractive in that it results in the same numerical aperture for the adult and scaled eyes and therefore light being collected over the same angle at the retina (Figure C1C).

What would the prediction be for the point spread function of the adultlike scaled eye? The size of the blur circle on the retina in radians subtended at the exit pupil, \( b \), can be approximated using the following equation:

\[
b = P \times D
\]

(1)

where \( P \) is the pupil diameter in meters, and \( D \) is defocus in diopters (Smith, 1982).

Using Equation 1, the smaller pupil size in the scaled eye, with no change in defocus, would result in a reduction...
in the angular size of the blur circle. Does defocus remain constant with scaling of eye size? As described above, the RMS of the aberrations is predicted to be smaller in the scaled eye. The change in RMS can be converted into an equivalent defocus, \( D \), using the following equation:

\[
D = k \times \frac{\text{RMS}}{r^2}
\]

(2)

where \( r \) is the pupil radius in mm, \( \text{RMS} \) is the root mean square wavefront error in microns and \( k \) is a constant (Thibos, Hong et al., 2002).

With reference to Equation 2, the pupil radius and RMS are both predicted to decrease by the scaling factor in the scaled eye. The equivalent dioptric defocus, \( D \), will therefore increase by the scaling factor, as a result of the \( r^2 \) term in the denominator.

If the equivalent defocus increases and the pupil size decreases by the scaling factor, Equation 1 predicts that the angular size of the blur circle will be the same for the scaled model and the true adult eye.

Thus to a first approximation, the scaled eye size model, including scaling of pupil size, would predict an RMS that is reduced by the scaling factor from the true adult value, and an angular blur circle size that is equal to the true adult value (also see Howland, 2005).

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