Ocular Biometry in Preterm Infants: Implications for Estimation of Retinal Illuminance

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PURPOSE. Retinal illumination varies with stimulus luminance, pupil size, eye size, and transmissivity of the ocular media. There are few published data to inform estimates of retinal illumination in early infancy, and no concurrent studies of pupil size and ocular length have been described. The goals were to document simultaneously the measured ocular parameters in growing preterm infants and to estimate the potential errors associated with using either stimulus luminance or troland value as a proxy for retinal illumination in this population.

METHODS. Ocular biometry including diameters of the eye, vitreous chamber depth (VCD) and dilated pupil diameter was performed on 111 occasions in 33 preterm infants aged between 30 and 55 weeks’ postmenstrual age.

RESULTS. Eye size increased rapidly between 30 and 55 postmenstrual weeks and was comparable to that of term-born infants. The ratio of dilated pupil area to VCD² was highly variable. Retinal illumination of the infant eye compared with adult eyes was underestimated by both stimulus luminance and troland values.

CONCLUSIONS. Stimulus luminance and troland values cannot be used to infer retinal illumination when comparing eyes of markedly differing sizes or transmittivities. Error in estimating retinal illumination in prematurely born infants is inevitable because of uncertainty regarding media transmissivity, but this discrepancy can be minimized by using directly measured pupil diameter and data presented herein for eye size in this population. (Invest Ophthalmol Vis Sci. 2008;49:453–457) DOI:10.1167/iovs.07-0540

Retinal illumination is defined as the incident luminous flux per unit of retinal surface area (luminance per square meter). Knowledge of retinal illumination is an essential requirement for electrophysiological and psychophysical studies of infant vision. It varies with stimulus luminance, pupil size, eye size, and transmissivity of the ocular media. For brief flash stimuli, retinal illumination is given by

\[ E_r = \frac{A_p}{d^2} \tau_{lp} \lambda_{lp} \]  

where \( E_r \) is retinal illumination (lumens seconds per square meter), \( A_p \) is pupil area (in square millimeters), \( d \) is posterior nodal distance (PND) of the eye (in millimeters), \( \tau_{lp} \) is media transmissivity at wavelength \( \lambda \) (dimensionless), and \( \lambda_{lp} \) is stimulus luminance (in candela-seconds per square meter). In our laboratory, to study rod function in the newborn, short-wavelength flashes (\( \lambda \approx 450 \text{ nm} \)) are most commonly used.

It has been assumed that the infant and adult ratios of dark-adapted pupil area \( (A_p) \) to PND squared \( (d^2) \) are approximately equal,\(^6\) implying that a given stimulus luminance will deliver similar levels of retinal illumination to the dark-adapted infant and adult eye\(^5,7\) (also assuming intraocular light losses to be the same for the infant and adult eye). If these are reasonable assumptions, it would mean that stimulus luminance at the cornea could be used as a proxy for retinal illumination, removing the need to account for either eye or pupil size. However, the constancy of the ratio \( A_p/d^2 \) across individual subjects of differing ages and for pharmacologically dilated (rather than dark-adapted) pupils has not been confirmed.

Many infant rod photoreceptor imaging studies (Fulton AB, et al. IOVS 2004;45:ARVO E-Abstract 1355)\(^{6–8}\) have used the troland as a proxy measure of retinal illumination:

\[ T = A_p L \]  

where \( T \) is troland value (candela-seconds per square meter per square millimeter), \( A_p \) is pupil area (in square millimeters), and \( L \) is stimulus luminance (candela-seconds per square meter).\(^9\) Intraocular losses are not accounted for. The troland does not account for eye size and therefore may be an inaccurate proxy for retinal illumination if eye size varies within the population studied—particularly relevant in a population in which the eye is growing rapidly, as in preterm infants.

We report the results of ocular biometry performed on preterm infants between 30 and 55 weeks’ postmenstrual age. Measurements included diameters of the eye, VCD, and dilated pupil diameter. VCD was taken to represent PND, since the nodal point used to define PND does not equate to any physical landmarks that could be imaged with ultrasound. It is likely that VCD and PND coincide within a fraction of a millimeter: according to eye models, although adult PND is 0.15 mm longer than the VCD,\(^10\) the infant PND is 0.5 mm shorter than the VCD.\(^11\) Because the resolution of an ultrasound scanner is ~0.2 mm (Siemens Medical Solutions USA, personal communication, December 1998) and repeatability of ultrasonic ocular measures is ~0.5 mm,\(^12\) VCD is likely to be a very reasonable approximation of PND.

The purposes of the study were to compare ocular length with dilated pupil measurements in individual infants and to estimate the errors associated with using either stimulus luminance or trolands as a proxy for retinal illumination in this population. Since study of rod function in the newborn in our laboratory is mostly achieved with short-wavelength flashes, media transmissivity has been specified at 430 nm throughout.

MATERIALS AND METHODS

Patients

Eligible infants were those who fulfilled locally agreed criteria for ROP screening (i.e., <31 completed weeks’ gestation and/or <1251 g...
birth weight). The infants ranged in maturity from 30 to 55 postmenstral weeks and ranged in weight from 1080 to 6800 g. Postnatal ages ranged from 9 to 194 days.

Procedure
Biometry was performed to coincide with ROP screening examinations. For the purposes of the study, screening examinations began as soon as the infant was self-ventilating and clinically stable and were repeated at the discretion of the attending ophthalmologist (usually at 2-week intervals), until the retinas were fully vascularized. Further measurements were made at ~50 postmenstrual weeks. For each examination, the infant’s pupils were dilated with 1 drop each of 0.5% cyclopentolate and 2.5% phenylephrine, repeated after 30 minutes. The study was approved by the local research ethics committee and informed, written consent was obtained from the parents. The study conformed to the tenets of the Declaration of Helsinki.

Ultrasonic Measurement of Eye Size
Ultrasound recordings were made (Acuson 128 XP; Siemens Medical Solutions USA., Inc., Malvern, PA; or an ATL 5000 HDI system, Philips Medical Systems, Bothell, WA) with a 7-MHz linear probe held over the eyelid. Measurements were made of the diameters of the eyeball in both longitudinal and transverse planes with VCD defined as the distance between the posterior surface of the lens capsule and the posterior pole (Fig. 1). The average of the two VCD measurements made in each of the longitudinal and transverse planes was used. Most of the measurements were made by one radiologist (SM), who also reviewed the few measurements made in his absence.

An estimate of retinal surface area (RSA) was derived using the formula

$$A = 2\pi R d,$$

where $A$ is RSA (in square millimeters), $R$ is the mean of the superior-inferior and axial globe radii, and $d$ is the mean VCD from longitudinal and transverse planes (in millimeters).13

Direct Measurement of Pupil Diameter
Pupil diameters were measured approximately 60 minutes after completion of the dilation protocol by using a half-moon ruler divided into 0.5-mm increments. The measurements were made under bright light and were repeated until two researchers independently agreed on their value.

Estimation of Error Propagation
Relative contributions of eye size and pupil size variability to uncertainty in retinal illuminance estimates were derived by calculating standard deviations and means of $A_p$ and VCD$^2$ from 26 measurements from 26 infants aged around 50 postmenstral weeks. This age was chosen, as media transmissivity data for similarly aged term-born infants are available to provide an estimate of the relative contribution of media transmissivity to the uncertainty in retinal illuminance.14

RESULTS
Because of the potentially confounding effects of laser photoocoagulation on retinal and/or ocular growth,15,16 only data from infants who did not require treatment for ROP are considered in this article. We included 111 ultrasound measurements made from 33 infants. Linear regression analysis showed that no individual subject significantly influenced results and therefore repeated measures could remain within the data set. Superior-inferior and transverse diameters increased with maturity, with transverse diameters being slightly larger than superior-inferior diameters. Mean transverse diameter increased from 13 mm at 30 postmenstrual weeks to 18 mm at 50 postmenstrual weeks, and superior-inferior diameter increased from 12.5 mm at 30 postmenstrual weeks to 17.5 mm at 50 postmenstrual weeks (Fig. 2).

Mean VCD increased from 8.5 to 11 mm between 30 and 55 postmenstrual weeks. During this time, VCD ($d$) can be estimated from the sigmoidal regression equation as follows:

$$d = \frac{1}{2} \left( 25 - 50 \left(1 + e^{-0.02(x-55)}ight) \right),$$

where $x$ is postmenstrual age (in weeks). Regression lines enclose 95% of data points. Filled symbols: data from full-term infants and adults.17
where \( d \) is VCD (in millimeters) and age is in postmenstrual weeks. The accuracy of this estimate is \( \pm 1.2 \) mm.

As a result of increasing eye size, calculated RSA (equation 3) almost doubled between 30 and 55 postmenstrual weeks: from \( -350 \) to \( 650 \) mm\(^2\) (Fig. 3).

Dilated pupil diameter showed wide variability. The mean diameter increased with increasing maturity from 5 to 8 mm between 30 and 55 postmenstrual weeks (Fig. 4). Average dilated pupil diameter was within adult limits at \( \sim 50 \) postmenstrual weeks. Infants who developed threshold ROP showed no difference in dilated pupil diameter compared with unaffected or prethreshold infants.

**Ratio of Pupil Area to VCD\(^2\)**

This ratio was highly variable, ranging from 0.15 to 0.53 during the preterm period and from 0.27 to 0.60 at 50 postmenstrual weeks (Fig. 5). The mean ratio increased from 0.30 to 0.41 between 30 and 55 postmenstrual weeks. By comparison, reported data from term-born neonates and from adults show a more stable ratio of less than 0.2.\(^{18}\)

**Implications for Estimates of Retinal Illumination**

Typical values for VCD, pupil diameter, and media transmissivity at 430 nm are documented in Table 1. Based on these values, the likely retinal illuminance ranges achieved at 40 weeks' postmenstrual age (typical term age), 50 weeks' postmenstrual age (10 weeks postterm) and adult eyes by an arbitrary 1-cd \( \cdot \) s \( \cdot \) m\(^{-2}\) stimulus are presented in Figure 6, as well as the relative trolands delivered by the same arbitrary stimulus.

This fixed-luminance stimulus is likely to deliver 0.48 log units more retinal illuminance to a newborn eye and 0.45 log units more retinal illuminance to a 10 weeks postterm eye than it will to an adult eye (dilated pupils), meaning that stimulus illuminance is not a good proxy for retinal illuminance when comparing eyes differing greatly in size or in media transmissivity (Fig. 6). If eyes are more similar in size and transmissivity, the discrepancy is less (e.g., this fixed luminance stimulus is likely to deliver only 0.03 log units more retinal illuminance to the newborn eye than to the 10-week postterm eye). Stimulus illuminance is therefore a reasonable proxy for retinal illuminance when comparing eyes of similar size and media transmissivity.

Conversely, expressing outcomes in trolands implies that the fixed luminance stimulus delivers 0.18 log units less “retinal illuminance” to the newborn eye and 0.05 log units less to the 10-week old eye than to the adult eye (dilated pupils)—in fact a reversal of the actual retinal illuminance delivered.

**DISCUSSION**

In this study, eye growth was documented between 30 and 55 postmenstrual weeks in direct conjunction with measurements of dilated pupil diameter.

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**Figure 3.** Changes in retinal surface area with maturity. Regression lines enclose 95% of data points. *Filled symbols:* data from full-term infants and adults.\(^{17}\)

**Figure 4.** Changes in dilated pupil diameter with maturation. Regression lines enclose 95% of data points. *Square:* mean (errors: 95% reference values) adult values.

**Figure 5.** Changes in ratio of pupil area to VCD\(^2\) with maturation. *Dashed regression line:* indicates trend toward higher ratios with age. *Open square data points and shaded gray area:* normal range (95% reference values) for term-born neonates and adult values.\(^{18}\) *Filled squares:* data from adult and infants based on estimated infant eye size.\(^{6}\)
Our eye growth data agree closely with previous studies including data collected in utero, ex utero, and postmortem, with our 95% prediction intervals enclosing all values from other studies.3,15–17 At term-corrected age, our prematurely born infants have eye measurements exactly matching published data from term-born infants,20 suggesting that preterm birth per se does not significantly affect eye growth.

Dilated pupil diameters in this study tended to be larger than reported elsewhere, and were also larger than pupil diameters reported in dark-adapted conditions.25 The combination of anticholinergic (0.5% cyclopentolate) and sympathomimetic (2.5% phenylephrine) drops used in this study is more effective in preterm infants than anticholinergic drops alone.24 Other dilating protocols achieve less dilation, ie around 5 mm in term-born infants.18,19

The second purpose of the study was to estimate the errors associated with using either stimulus luminance or troland value as a proxy for retinal illuminance in this preterm infant population. The uncertainty of a function (e.g., retinal illuminance as expressed in equation 1) is a result of the uncertainties of its variables (e.g., the measured variability of \( VCD \), \( A_p \), and \( \lambda \)). Assuming a nominal stimulus, uncertainty in media transmissivity,14 pupil area, and \( VCD \)2 account for 34%, 46%, and 20% of variability in estimated retinal illuminance, respectively, in these infants.

Our findings have implications for the estimation of retinal illuminance. If the retinal illuminances received by eyes of differing sizes or (particularly) differing media transmissivities are to be compared, only units of retinal illuminance (equation 1) will be accurate. In the more extreme case of comparing a newborn eye with an adult eye, using stimulus luminance or troland value as a proxy for retinal illuminance will underestimate true retinal illuminance by ~0.48 or 0.65 log units, respectively, in the newborn eye relative to the adult eye. The effect is less when comparing eyes of more similar sizes, such as during the first 10 weeks of life, or when pupils are less aggressively dilated. Stimulus luminance and troland value underestimate retinal illuminance by 0.03 and 0.14 log units, respectively, in newborn eyes relative to 10-week postterm eyes. The effect would also be less for longer wavelengths of light where transmissivity of the infant and adult eye are similar. For example, stimulus luminance and troland value underestimate retinal illuminance by 0.30 and 0.47 log units, respectively, in newborn eyes relative to adult eyes for light of wavelength 550 nm, 0.18 log units less of an underestimate than with 430 nm light.

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It has been assumed here that PND is approximately equal to VCD. If, as in adults,10 PND is shorter than VCD, then the underestimate of retinal illuminance resulting from using luminance or troland units will be slightly less than just stated.

No data currently exist regarding optical media density in infants, particularly during the preterm weeks, would also be of great use.

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References