Eye Size in Threshold Retinopathy of Prematurity, Based on a Danish Preterm Infant Series: Early Axial Eye Growth, Pre- and Postnatal Aspects

Hans Callo Fledelius¹ and Christian Fledelius²

PURPOSE. To validate a hypothesis of restricted postnatal ocular growth associated with advanced retinopathy of prematurity (ROP), with a view also to preceding intrauterine growth retardation.

METHODS. A clinically uniform sample of 28 preterm neonates was examined under general anesthesia from 1997 to 2002 for threshold retinopathy of prematurity (T-ROP). Axial ultrasound oculometry being part of the evaluation (valid data in 53 eyes). Median values for gestational age at delivery (GA) and birth weight (BW) 27 weeks and 855 g, respectively, ranges 24.7–30.9 weeks and 480–1594 g. Median postconceptional age (PCA) at exam was 36.2 weeks (32.2–41.4 weeks) and median postnatal age was 9 weeks (5.8–14 weeks). “Small for gestational age” (SGA) at delivery was given by an individual birth weight standard deviation score.

RESULTS. Compared with a previous Danish preterm series with less ROP age-adjusted axial lengths (AL) in the T-ROP eyes were roughly 1 mm shorter and anterior chambers shallower. A higher GA was found to coincide with lower AL values; this appeared due to a subpopulation of infants loaded by SGA. The literature has no other uniform oculometry series of preterms of a similar advanced ROP degree. The present Danish results add to the composite picture drawn by neonatal reports from other investigators.

CONCLUSIONS. There is evidence of postnatal ocular growth restriction in preterms associated with severe ROP. Some kind of latency is probable, from the immediate delivery-related biological effects until the appearance of macroscopic evidence. Statistics further suggested SGA as an apparently independent prenatal predictor of subsequent ocular growth restriction. (Invest Ophthalmol Vis Sci. 2012;53:4177–4184) DOI:10.1167/iovs.12-9516

In a cross-sectional study 40 years ago children born prematurely (PT) had shorter eyes than full-term (FT) children when examined around the age of 10 years.¹² Mean keratometry values further indicated a more peaked contour of the cornea, the anterior chamber depth was shallower, and lenses were thicker. Body height and cranial circumference completed the picture of a general deficit in growth for this group of natural history ex-prematures born 1959 to 1961, then part of a large-scale pediatric Copenhagen University prospective study.

Ultrasonic biometry studies worldwide (Table 1) eventually generated data about the early growth pattern of the eye, full-term or preterm.¹⁻¹⁸ In a Danish study of eye size around term (week 40) we found no significant difference between PT and FT groups, but within the PT group there was a trend of shorter axial length (AL) for those of a very low gestational age (GA) at delivery.¹⁷,¹⁸

With the introduction of the retinopathy of prematurity (ROP) classification in 1984,¹⁹ subsequent clinical and biometric studies subdivided PT findings according to the presence and severity of the retinal disorder (Table 1). Changes in the ROP profile over time have been marked by the immense progress of care and therapy within neonatology, and also by the expanding ophthalmic experience gained from the routine surveillance for ROP in infants at risk. With many ROP cases included in their series of neonates, Laws and colleagues¹¹ reported “the higher the maximum stage of ROP reached, the shorter the axial length.” Otherwise, the trend is that visual parameters and biometry findings in mild regressed ROP (up to stages 1–2) generally compare with what is found in preterms without ROP.²⁰⁻²²

For the present study we analyzed eye size based on ultrasonic measurement data from 53 eyes of 28 infants with threshold ROP (T-ROP), as defined by the Cryo-ROP study of 1988.²³ They were all referred (1997–2002) to the vitreoretinal service of the Copenhagen University eye department of Rigshospitalet, where retinal ablation therapy for threshold ROP (T-ROP) has been centralized on a national basis.

Prompted by axial length trends according to low GA at delivery, the issue of small for gestational age (SGA) was further analyzed.

MATERIALS AND METHODS

The 28 ROP infants under study in a cross-sectional setup (20 males, 8 females) during 1997–2002 were either in-patients in Rigshospitalet’s tertiary level neonatal intensive care unit, or referrals from other neonatology services throughout the country. Progression to classical TROP²⁴ released the factual evaluation under general anesthesia, and 26 had retinal cryotherapy, usually in both eyes. The remaining subgroup of 6 untreated eyes was considered too small for separate analysis.

At delivery gestational age (GA) and birth weight (BW) values had ranged from 24.7 to 30.9 weeks and from 480 to 1594 g, respectively, and median values were 27 weeks and 855 g. Age of the infants was given in weeks, as postnatal age (PNA), and as postconceptional age (PCA = GA + PNA).

The issue of intrauterine growth retardation, here used synonymously with SGA, was approached by calculating a standard deviation score (SDS) for the BW of each subject, as relative to expected weight.
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>GA</th>
<th>ACD (mm)</th>
<th>LT (mm)</th>
<th>AL (mm)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gernet(^3) n = 80 term</td>
<td></td>
<td></td>
<td>2.9</td>
<td>3.4</td>
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<tr>
<td>Luyckx(^4) n = 52 term</td>
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<td>2.55</td>
<td>3.65</td>
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<tr>
<td>Grignolo(^5) n = 19 FT/PT</td>
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<td></td>
<td>2.38</td>
<td>3.96</td>
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<tr>
<td>Larsen(^6) n = 80 term</td>
<td></td>
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<td>2.6</td>
<td>3.6</td>
<td>16.6</td>
<td>7.0</td>
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<td>Blomdahl(^7) n = 28 term</td>
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<td>2.65</td>
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<td>17.29</td>
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<tr>
<td>Gordon(^8,9) n = 23 PT + FT</td>
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<td></td>
<td>2.33</td>
<td>4.04</td>
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<tr>
<td>Fledelius(^10) n = 25 FT</td>
<td>25w</td>
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<td>2.65</td>
<td>3.76</td>
<td>17.29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37w</td>
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<td>2.38</td>
<td>3.99</td>
<td>17.0</td>
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<tr>
<td>Laws(^11) n = 171</td>
<td>PCA 32w</td>
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<td>2.5</td>
<td>3.96</td>
<td>16.6</td>
<td>6.78</td>
</tr>
<tr>
<td></td>
<td>PCA 40w</td>
<td></td>
<td>2.44</td>
<td>3.95</td>
<td>17.16</td>
<td></td>
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<tr>
<td>O'Brien(^12) n = 100 PT</td>
<td>w35</td>
<td></td>
<td>2.33</td>
<td>4.04</td>
<td>16.95</td>
<td></td>
</tr>
<tr>
<td></td>
<td>w37</td>
<td></td>
<td>2.38</td>
<td>3.99</td>
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</tr>
<tr>
<td></td>
<td>PCA 32w</td>
<td></td>
<td>2.5</td>
<td>3.96</td>
<td>16.6</td>
<td>6.78</td>
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<tr>
<td></td>
<td>PCA 40w</td>
<td></td>
<td>2.44</td>
<td>3.95</td>
<td>17.16</td>
<td></td>
</tr>
<tr>
<td>Tucker(^13) n = 70 PT</td>
<td>25w</td>
<td></td>
<td>12.6</td>
<td>37w</td>
<td>16.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCA 32w</td>
<td></td>
<td>15.4</td>
<td>PCA 40w</td>
<td>16.6</td>
<td></td>
</tr>
<tr>
<td>O'Brien(^13) n = 100 PT</td>
<td>w35</td>
<td>15.38</td>
<td>15.38</td>
<td>15.98</td>
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<td>w52</td>
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<td>18.23</td>
<td>18.23</td>
<td>18.23</td>
<td>18.23</td>
</tr>
<tr>
<td>Isenberg(^13)</td>
<td></td>
<td></td>
<td>2.2</td>
<td>16.6</td>
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<tr>
<td>Cook(^14) n = 68 PT</td>
<td>w32.9</td>
<td>1.98</td>
<td>15.44</td>
<td>6.10</td>
<td>Longitudinal data</td>
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<td></td>
<td>w36.1</td>
<td>2.11</td>
<td>15.44</td>
<td>6.45</td>
<td>Weekly elong. 0.16 mm over full PCA range, no ROP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>w40</td>
<td>2.25</td>
<td>3.98</td>
<td>16.84</td>
<td>6.94</td>
<td></td>
</tr>
<tr>
<td></td>
<td>w44.7</td>
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<td>17.43</td>
<td>7.21</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>w52.9</td>
<td>2.80</td>
<td>18.58</td>
<td>7.55</td>
<td></td>
<td></td>
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<tr>
<td>Axer-Siegel(^15) n = 133 PT</td>
<td>PCA w31</td>
<td>2.15</td>
<td>15.6</td>
<td></td>
<td>Treated ROP excluded</td>
<td></td>
</tr>
<tr>
<td></td>
<td>w35</td>
<td>2.17</td>
<td>16.0</td>
<td>71 in vitro fertl., 62 no IVF; Weekly elong. 0.13 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>w39-43</td>
<td>2.25</td>
<td>3.89</td>
<td>16.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azad(^16) n = 25</td>
<td>No or low ROP</td>
<td>2.49</td>
<td>17.0</td>
<td></td>
<td>Weekly elong. 0.14 mm; past w40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cryo-treated</td>
<td>16.20</td>
<td></td>
<td></td>
<td>Pre T-ROP, when treated</td>
<td></td>
</tr>
</tbody>
</table>

Estimated weekly growth rates under Remarks, mainly as extrapolations from the published data. PT, preterm; FT, full-term; ACD, anterior chamber depth; LT, lens thickness; AL, axial length; Crad, corneal curvature radius.
according to normative intrauterine ultrasonic parameters expressing infant size during pregnancy.24

Axial A-scan ultrasound biometry was performed when “allowed by conditions”; otherwise, the series was considered random. An ultrasound scanner (Sonometrics DBR 400; Sonometrics Corp., London, Ontario, Canada) was used and a handheld solid-tip 12.5-MHz transducer, with a concavity to match the corneal curvature (to minimize shortening by contact and flattening). Axial echograms with acceptable lens and fundus peaks were frozen and calibrated from the screen according to Jansson,25 usually with at least three readings in fair agreement per eye. Satisfactory axial length data were obtained from 39 male and 14 female eyes, although with anterior chamber depth (ACD) and lens thickness (LT) missing in 18 eyes presenting from 39 male and 14 female eyes, although with anterior chamber depths and lens thicknesses were approximately 2.1 and 3.9 mm, respectively (Table 4).

An infant lid speculum was used; otherwise, a handheld applana tion tonometer (Perkins Mk2 Tonometer; Veatch Instruments, Tempe, AZ; to exclude buphthalmic states and blowing up eye size) was the only contact procedure carried out prior to the ultrasonography. Three funduscopy techniques were used, in a team including at least two senior specialists: indirect ophthalmoscopy, direct ophthalmoscopy (the Richardson contact lens method; Richardson Contact Lenses, Houston, TX), and by wide-field digital retinal photography (RetCam 120 fundus camera; Clarity Medical Systems, Pleasanton, CA). Scleral depressors were used only for the final full clock-hour staging of the ROP.

RESULTS

Median and Range, Mean Values, and Standard Deviation

Table 2 presents the demography and the oculometry findings in the T-ROP study group. The median PCA was 36.2 weeks (range 32.2–41.4 weeks), and postnatal age averaged 9 weeks (PNA range 5.8–14 weeks) (cf. the scattergrams of Fig. 1).

Table 3 shows mean axial length measurements and BW standard deviation scores, an individual measure of “weight for GA”; with focus on the role of intrauterine growth retardation this was labeled SGA SDS. The series was subdivided by GA values at delivery, of 26 and 28 weeks, respectively. Findings indicated that the least SGA load was found when GA was low, the median SD score here coming out as zero, compared with more than two negative SDS steps for the higher GA subgroups.

Distribution of SGA scores showed no influence by sex. Here only two significant differences occurred: boys qualified for examination earlier (PCA 35.9 vs. 37.7 weeks, $P < 0.05$ by Student’s t-test, 0.057 by Mann–Whitney), and AL adjusted to GA week 36 was longer in boys (15.68 vs. 15.09 mm, $P < 0.02$, $P < 0.057$ by Mann–Whitney).

Scatterplots and Regression Statistics

Selected results are shown in Figures 1–3, and the regression statistics specified in Table 4. Omitted are differences possibly associated with chronology, referring to the current progress in neonatal intensive care unit handling over the 6 years of sampling. Here only the BW parameter came close to significance. A $P$ value for the negative slope was 0.08, with an on-regression line value of 999 g for birth year 1997 and of 788 g for endpoint year 2002. Compared with the stable GA findings this suggests an increasing share of infants (relatively) small for gestational age (SGA) over time.
With gestational age at delivery on x-axis significant associations were first achieved with the following parameters:

1. **BW (r = 0.51; slope value 67.45, different from zero, P = 0.0001),** that is, higher GA generally = higher BW (Fig. 1A).

2. **Age at examination (r = 0.34, slope 0.40; different from zero, P = 0.012),** that is, higher GA at delivery also means later appearance of T-ROP, given by the PCA when examined (Fig. 1B).

3. With a negative slope, and a correlation coefficient of $r = -0.42$, the postnatal age at examination also had a significant correlation. The regression line is given by $y = 20.71 - 0.43X$ ($P = 0.002$ for slope, different from zero). The lower the GA at delivery, the longer thus the latency to observed T-ROP, and the subsequent examination under general anesthesia (Fig. 1C).

4. It appeared that adjusted ALw36 had a negative slope of $-0.135$ (significantly differing from zero, $P = 0.007$). Mathematically this implies that eyes of the most immature infants, usually considered at highest risk for pathology, had grown more as judged from adjusted ALw36 value (Fig. 2B). A less steep regression line for the actually measured AL at the given age of the infant emerged as $y = 17.65 - 0.0775X$, $r = -0.25$; the $P$ value for the slightly negative slope was 0.07 (Fig. 2A).

5. Given the results under (4), the SGA standard deviation score was further included, as y-value. A negative slope of $-0.424$ ($P = 0.0002$) indicated that intrauterine growth retardation, here expressed by the relative indication of SGA, increased in prevalence the higher the GA at delivery (Fig. 5A).

6. With **BW (g) on the x-axis**, the association to both axial length parameters (adjusted ALw36, $r = 0.14$, and real AL, $r = 0.24$) showed a positive slope for the regression line. This also held for age at examination (PCA), but only the association with AL came close to significance ($P = 0.089$). The trend suggested, accordingly: the higher the BW (possibly as a marker of good health, in contrast to SGA), the longer the AL when measured during the T-ROP initiated examination, which, however, would also be (a little) later on the PCA time axis.

7. Age at examination (PCA) further correlated with postnatal age (Fig. 1D) and with anterior chamber depth.

8. Finally, with the SGA standard deviation score on x-axis significant $P$ values for slopes different from zero indicated that shorter axial lengths were associated with higher degrees of intrauterine growth retardation (Figs. 3C, 3D).

**DISCUSSION**

**Axial Eye Dimensions in Preterms**

With progression to T-ROP confirmed, our main oculometry finding was a smaller eye, given by a shorter axial length and a more shallow anterior chamber, when compared with data from a previous, less immaturity-loaded Danish PT sample. It is interpreted as early evidence of reduced general eye growth for the present group of highly selected PT neonates.
The Early Growth Pattern of the Eye

Table 3. Birthweight, Axial Length, Age Parameters, and Birth Weight Small for Gestational Age (SGA) Standard Deviation Score

<table>
<thead>
<tr>
<th>Birthweight Parameter</th>
<th>PCA at Exam (wk)</th>
<th>PNA at Exam (wk)</th>
<th>AL Measured (mm)</th>
<th>ALw36 (mm)</th>
<th>SGA (SD Score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW (g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GA ≤26 w (n = 19)</td>
<td>784 (1.45)</td>
<td>36.1 (2.82)</td>
<td>10.2 (2.48)</td>
<td>15.79 (0.47)</td>
<td>15.79 (0.65)</td>
</tr>
<tr>
<td>26.1–28 w (n = 20)</td>
<td>852 (246)</td>
<td>35.5 (1.18)</td>
<td>8.3 (1.44)</td>
<td>15.53 (0.50)</td>
<td>15.69 (0.53)</td>
</tr>
<tr>
<td>&gt;28 w (n = 14)</td>
<td>1121 (285)</td>
<td>38.3 (1.51)</td>
<td>8.3 (1.25)</td>
<td>15.24 (0.78)</td>
<td>14.95 (0.76)</td>
</tr>
</tbody>
</table>

Values are all given as means (SD), in the full TROP series (53 eyes), subdivided by gestational age 26 and 28 weeks.

For comparison, relevant reports from the literature are collected in Table 1. For the present sample of TROP eyes. As primary reference, we use Danish preterm findings from approximately one decade earlier that were achieved by the same experienced ultrasound scanner and expert reading of the ocular ultrasonograms. The consecutive sample was from a regional center, and the expert reading of the ocular ultrasonograms was less premature. The mean axial length around term was 17.06 mm. Boys presented larger ocular dimensions than girls, but with an equal boy:girl ratio the two sexes were pooled, as applied also to the various ultrasonic measuring data selected for Table 1.

By contrast, the present TROP sample is a clinically homogeneous highly selected national sample of even smaller preterm infants, in whom advanced ROP after a postnatal latency was documented as rapidly progressing over weeks, eventually to include vascular insufficiency of retina and usually also iris. Adjusted to the actual median age of 36.2 weeks at exam (see Materials and Methods), the mean AL measured in the full recent TROP series came out as 15.53 mm (SD 0.72), with a 16.2-mm value when further adjusted to week 40. This is significantly lower than that in the regional preterm reference group, with which it shared the oculometry setting, although differing by chronology.

Birth Weight versus Gestational Age

The trend among the TROP infants was slight eye elongation by increasing BW (although statistically only close to significance; Table 4). Those heavier at delivery had marginally longer axial lengths when eventually measured.

Here gestational age certainly differs from its main covariable, the BW. Regression calculations with GA on the x-axis thus present the opposite trend, whatever considering actually measured AL or the value adjusted for age to PCA week 36. Both had negative slopes significantly different from zero. The lower the initial GA values, the higher thus the eventual AL value, if on the regression line. Paradoxically, those of lowest GA appeared least growth restricted.

In the UK in a large-scale study of neonates, eyes were generally shorter, the more advanced the ROP; further, treated stage 3 ROP had a lower AL score than untreated stage 3, a trend that could be noted also prior to the advanced ROP stage 3. Both had negative slopes significantly different from zero. The lower the initial GA values, the higher thus the eventual AL value, if on the regression line. Paradoxically, those of lowest GA appeared least growth restricted.

Table 4. Linear Regression Statistics, with Gestational Age at Delivery (weeks), Birth Weight (g), Age When Examined (PCA, weeks), and SGA Standard Deviation Score as Independent Variable, against the Parameters under Study

<table>
<thead>
<tr>
<th>On x-Axis</th>
<th>Cf. Figure</th>
<th>Dependent Variable</th>
<th>r</th>
<th>Calculated Regression Line</th>
<th>P Value for Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA (w)</td>
<td>1B</td>
<td>PCA at exam (w)</td>
<td>0.34</td>
<td>y = 25.44 + 0.402 X</td>
<td>0.013</td>
</tr>
<tr>
<td>GA (w)</td>
<td>2A</td>
<td>AL (mm)</td>
<td>-0.25*</td>
<td>y = 17.65 - 0.0775 X</td>
<td>0.07*</td>
</tr>
<tr>
<td>GA (w)</td>
<td>2B</td>
<td>ALw36 (mm)</td>
<td>-0.37</td>
<td>y = 19.20 - 0.135 X</td>
<td>0.007</td>
</tr>
<tr>
<td>GA (w)</td>
<td>1A</td>
<td>BW (g)</td>
<td>0.51</td>
<td>y = 934 + 67.45 X</td>
<td>0.0001</td>
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<tr>
<td>GA (w)</td>
<td>1C</td>
<td>PNA (w)</td>
<td>0.42</td>
<td>y = 20.71 - 0.433 X</td>
<td>0.0021</td>
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<tr>
<td>GA (w)</td>
<td>3A</td>
<td>SGA (SDscore)</td>
<td>0.50</td>
<td>y = 0.104 - 0.424 X</td>
<td>0.0002</td>
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<tr>
<td>BW (g)</td>
<td>1D</td>
<td>PCA at exam (w)</td>
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<td>y = 35.54 + 0.00091 X</td>
<td>0.46</td>
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<tr>
<td>BW (g)</td>
<td>2C</td>
<td>AL (mm)</td>
<td>0.44*</td>
<td>y = 15.06 + 0.00055 X</td>
<td>0.089*</td>
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<tr>
<td>BW (g)</td>
<td>2D</td>
<td>ALw36 (mm)</td>
<td>0.14</td>
<td>y = 15.17 + 0.00039 X</td>
<td>0.31</td>
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<tr>
<td>PCA (w)</td>
<td>3B</td>
<td>PNA (w)</td>
<td>0.56</td>
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<td>&lt;0.0001</td>
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<tr>
<td>PCA (w)</td>
<td>3D</td>
<td>IT (mm)</td>
<td>0.49</td>
<td>y = 15.84 + 0.178 X</td>
<td>0.0002</td>
</tr>
<tr>
<td>SGA SDscore</td>
<td>3C</td>
<td>AL (mm)</td>
<td>0.48</td>
<td>y = 15.87 + 0.208 X</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

* Italics mark correlation coefficients and slopes significantly different from zero (P < 0.05), and close to significance (P < 0.10) by *. Reference to Figures 1–3.
of the chosen factors, however, would not affect the main

trends.

On the Time Sequence

ROP is not observed until weeks 31–32, a PCA apparently to be

tained before the retinal physiology can manifest as the

observed abnormal vessel morphology of ROP.\textsuperscript{17,18,26–30} For

those of lowest GA at delivery this implies an interval of at least

up to 6–8 weeks until ROP is first recorded.

Evidently, the ultrasonographic indication of “lowest GA,

least growth arrest” does not immediately fit with the

theoretical model of a general restraining effect of immaturity,

in particular if active from PT day one. By analogy with the

delayed retinal findings, tentatively we could hypothesize that

the balance between the early effects on eye growth might

include a hardly affected postnatal axial elongation initially, and

a latency until restrained growth is manifested.\textsuperscript{31,32} Our present

SGA analysis further supports prenatal growth retardation as a

much stronger factor than hitherto perceived, a finding not

reported in ROP literature so far.

In accordance with the literature, it was further confirmed

that the smallest GA infants (<26 weeks at delivery, Table 2;

regression line Table 4, also cf. Fig. 1) required more time until

manifest T-ROP.\textsuperscript{28–30} Their T-ROP–related examinations were

performed on average in week 10.2 (PNA, in weeks, SD 2.48)

versus a PNA mean age of 8.3 weeks (SD 1.38; \(P < 0.01\)) for

those above week 26. The trend is similar with a binary cutoff

at GA week 28. The smallest infants thus take longer before (1)

they show first evidence of ROP, if any, and (2) before

established ROP progresses to T-ROP.

As for the course after successful cryotherapy, we can

hypothesize that the retinal ablation therapy not only saves

retinal anatomy and function, but also brings the globe as a

whole into a state from which reduced growth can be restarted

and go on in a more natural gear, although from a new starting

point. This would explain the so-called more fetal anterior and

posterior eye segment proportions as met for instance in

children and adolescents with myopia of prematurity (eyes

shorter for myopia degree, lenses thicker, and located more

anteriorly).\textsuperscript{1,2,9,20,22,33–42}

Small for Gestational Age (SGA)

The issue of retarded intrauterine growth, here manifesting as

less retardation the more immature the infant, was addressed

by way of an SD score that indicated how much an individual

BW deviated from expectedly normal for gestational age.\textsuperscript{24} A

larger share of those with higher GA values at delivery

presented evidence of intrauterine growth retardation, as a

prenatal marker that, as generally valid for preterm series, also

affected our PT group as a whole. Weighting the two

parameters, with AL as yardstick, the effects of SGA could at

least match that of gestational age.

Summing Up the Various Studies on Eye Growth in

Preterms

There is fair agreement between most results presented in

Table 1, a harmony that is impressive, considering the

complicated measuring situation in a tiny infant, the method-
ological error of the various A-scan techniques used, and also the variation in clinical profile of the included preterm samples. The mean axial length in an FT infant at term (week 40) is approximately 16.6–17 mm, and anterior chamber depth and AL values increase over time, in contrast to the more constant early childhood figures reported for lens thickness.

Regarding weekly axial elongation prior to term, linear values from the oculometry studies of prematures range from 0.13 to 0.23 mm per week, with an outlier value of 0.30 mm given in a single study. We regard exponential growth as likely also during this early phase of life, but the various scattergrams in the literature support that linear regression mathematics can be applied when only narrow age spans are under study, as actually done in the reports quoted in the table. Linear regression has even been reported as best fit, also when tested against quadratic models.

**Conclusions**

To conclude, our main result is that premature eyes when progressing to advanced retinopathy of prematurity (T-ROP) are generally small(er) eyes, apparently restrained in growth.

In accord with previous studies we further suggested that at a given low GA a very low BW (SGA) might be a (prenatal) marker of added risk regarding ophthalmic sequels, and that the role of BW as an immaturity parameter is not merely parallel or subordinate to GA. A more substantial support is given by the SGA analyses that were added in the present study. The lower the birth weight for gestational age at delivery, the shorter also the eye near term.

An early biological delay or latency soon after the untimely delivery is cautiously hypothesized, of significance not only for the observed manifestations of ROP, but also for the intricate patterns pertaining to the growth of the eye. Here, the present data support a preexisting intrauterine growth retardation as a significant prenatal cofactor.

Clearly our data call for further investigations with similar aims.

**References**