The influence of retinopathy of prematurity on ocular growth

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CLINICAL STUDY

Abstract

Purpose **Retinopathy of prematurity (ROP) stage 3 eyes that require treatment have a greater tendency to myopia compared with eyes with mild ROP. As the mechanisms controlling this myopia are as yet ill understood, we undertook this study to investigate what effect the initial stage of ROP and modality of treatment had on ocular growth.**

Methods **Eighty-five children were assessed. All children were refracted and underwent 'through-the-lid' biometry using the Zeiss Humphrey biometer 820. The printout obtained was then recorded on video so that the scan could be captured on computer for formal calibration and measurement by a masked observer. Differences in the distribution of variables between the stages of ROP were analysed by one-way analysis of variance, non-parametric Kruskal–Wallis one-way analysis of variance or Mann–Whitney *U*-test as appropriate.**

Results **A difference between the stages of ROP was apparent only for posterior segment length (PSL) (R: $p = 0.03$; L: $p = 0.05$) and a borderline difference for anterior chamber depth (ACD) (R: $p = 0.06$; L: $p = 0.06$). However, if stage 3 was divided into categories of treated and untreated, axial length (AL) achieved borderline significance (R: $p = 0.07$; L: $p = 0.05$) but with no difference between laser-treated and the other stages for AL. Lens thickness (LT) also appears to be influenced by type of treatment (R: $p = 0.06$; L: $p = 0.13$). Myopia was associated with stage 3 (R + L: $p = 0.0001$) and if stage 3 was subdivided the significance was maintained only for the laser- and cryotherapy-treated eyes.**

Conclusions **Laser-treated eyes were less myopic than those treated with cryotherapy. AL does not explain all the myopia found in stage 3 treated eyes. The study confirms the tendency towards anterior segment arrest in stage 3 ROP.**

Key words Anterior chamber depth, Axial length, Biometry, Lens thickness, Posterior segment length, Refractive errors, Retinopathy of prematurity

The recognised association between prematurity and myopia may be exacerbated by retinopathy of prematurity (ROP).[1–8] High myopia is associated with both stage 3 and cicatricial ROP.[9] The latter is found in stages 3, 4 and 5 but not stage 2. Recently several studies have shown that myopia is less severe in laser-treated eyes compared with those treated with cryotherapy.[10–12] However, information in the literature is scant as to the mechanism or mechanisms underlying this induced refractive error. We have previously reported that children with ROP had smaller eyes at 33 weeks compared with premature children without ROP and that this difference had increased by 41 weeks.[13] Furthermore it was found that increasing stage of ROP was inversely related to axial length. Previous studies have also indicated that axial length does not explain all the myopia found in ROP.[1,14–16] The present study was undertaken to analyse what influence, if any, prematurity, ROP and its treatment might have had on subsequent ocular growth and refraction in a group of children born prematurely.

Patients and methods

Ethics approval was granted to perform biometry on subjects from an earlier study whose initial biometry had been performed at 40 weeks. The patients and methods for the initial ocular measurements are detailed elsewhere.[13,17] The stage of acute ROP was documented by one observer (D.C.) in accordance with the guidelines of the Committee for the Classification of Retinopathy of Prematurity.[18]

Children from the original cohort were recruited into this study at a mean age of 40.2 months. Most children of this age are intolerant of direct application of the biometry probe on to the cornea so an alternative method was developed. This involved the use of a 'through-the-lid' technique as previously described using the Zeiss–Humphrey biometer 820, revision G software.[19] Verification and correlation of this method with the original corneal touch technique was confirmed and deemed acceptable, together with inter-observer and inter-session variability.[20] The gain was set to 80% for these through-the-lid measurements.

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Table 1. *Mean (SD) gestational age, birth weight and follow-up according to stage of ROP*

Maximum stage of ROP	*n*	Gestation (weeks)	Birth weight (g)	Age at follow-up (months)
0	13	28.39 (1.45)	1325.08 (262.30)	40.77 (7.98)
1	10	28.90 (1.45)	1117.00 (283.58)	39.20 (7.54)
2	16	26.31 (1.70)	960.63 (193.99)	37.19 (10.00)
3	46	25.61 (1.60)	814.61 (169.40)	43.63 (9.82)

Following cycloplegia with 1% cyclopentolate, the child was encouraged to look at a straight-ahead target with the contralateral eye while the examiner gently closed the ipsilateral upper eyelid. The pattern of lens and retinal spikes was used as the main indicator of axial alignment as judged by a colleague. Readings were accepted only when anterior and posterior lens reflections were present and a sharp retinal spike was visible. Three scans were obtained for each child. The printouts of each scan together with their calibration scale were then video recorded and, from this video, the one deemed to be most accurate for calculating ocular dimensions was transferred to a computer. Using software from the National Institutes of Health, USA, the following measurements were automatically calculated in millimetres: axial length, 'anterior chamber' depth, lens thickness and posterior segment length. Axial length was measured from the longest vertical spike, representing the posterior corneal surface to the retinal spike, i.e. axial length did not include corneal thickness. Anterior chamber depth was calculated from the posterior corneal spike to the anterior lens surface spike, lens thickness from those spikes representing anterior and posterior lens reflections, and posterior segment length from the posterior lens spike to the retinal spike. All measurements were carried out with reference to the calibration scale on each printout and computer recalibration of this scale was performed after each new scan was captured by the computer from the video image. All scans were analysed and measurements performed by the same observer who was masked to the stage of ROP. Following biometry the child underwent cycloplegic refraction. The sphere, positive cylinder and axis were recorded and the mean spherical equivalent was calculated from the formula: spherical equivalent (SE) = (± sphere) + 0.5 (cylinder).[21]

Gestational age, birth weight and age post-term are summarised by their means and standard deviations, the remaining measurements by their medians and range. Differences in the distribution of these variables between the stages of ROP were analysed by one-way ANOVA (*F* statistic), non-parametric Kruskal–Wallis one-way ANOVA (chi-square, χ^2) or Mann–Whitney *U*-test as appropriate. The relationship between stage of ROP and the biometric and refractive data is displayed graphically using boxplots (a 5-measure summary of the variables: median, upper and lower quartiles, minimum and maximum values). All statistical analysis was performed using SPSS version 6.1 for Windows.

Results

Eighty-five children, consisting of 48 males and 37 females, were enrolled into the study. There were 13 children who had no ROP, 10 who were originally stage 1, 16 who were stage 2 and 46 who were stage 3. Recruitment of children who had initial stage 3 disease was greater as they still attended the outpatient clinic. Of these 46 children with stage 3 disease, 21 were originally treated with laser and 17 with cryotherapy. The mean gestational ages, birth weights and age at follow-up for all children according to the stage of ROP are shown in Table 1. The one-way analysis of variance showed that the mean gestational ages and birth weights varied significantly ($F = 18.76$, $p < 0.0001$; $F = 23.40$, $p < 0.0001$, respectively) between stages of ROP. Mean age at follow-up, corrected for term, was 40.2 months. There was no significant difference ($F = 1.84$, $p = 0.15$) for age at follow-up between the different groups.

Median ocular biometric dimensions for all stages of ROP are given in Table 2. No significant difference was found between the stages of ROP in terms of axial length

Table 2. *Median (range) biometric dimensions in millimetres for right (R) and left (L) eyes for all stages of ROP*

Maximum stage of ROP	Eye	Anterior chamber depth (ACD)	Lens thickness (LT)	Posterior segment length (PSL)	Axial length (AL)
0	R	2.26 (1.64–2.80)	3.69 (3.4 –4.09)	13.96 (12.77–15.46)	19.76 (18.55–21.24)
	L	2.42 (1.45–3.06)	3.65 (3.10–4.15)	14.14 (12.58–14.84)	20.19 (18.24–21.66)
1	R	2.13 (1.43–2.64)	3.64 (3.21–3.91)	14.18 (12.88–15.95)	19.88 (18.31–21.35)
	L	2.07 (1.62–2.75)	3.75 (3.35–4.28)	13.70 (12.75–15.34)	19.40 (18.51–21.32)
2	R	2.40 (1.13–3.17)	3.75 (2.62–4.50)	14.29 (12.80–16.12)	20.56 (18.06–21.64)
	L	2.33 (1.49–3.13)	3.57 (3.23–4.25)	14.28 (13.25–15.49)	20.38 (18.82–21.34)
3 – All	R	2.01 (1.38–2.62)	3.68 (2.50–4.35)	14.87 (13.22–20.00)	20.44 (19.08–25.82)
	L	2.03 (1.20–3.01)	3.66 (2.16–4.50)	14.62 (12.39–20.67)	20.32 (18.72–26.06)
3 – Untreated	R	2.49 (1.56–2.54)	3.39 (2.50–3.65)	14.57 (14.06–17.06)	20.50 (19.63–21.13)
	L	2.43 (2.07–2.60)	3.36 (3.23–3.66)	14.51 (13.60–14.97)	20.29 (19.31–20.50)
3 – Laser	R	2.07 (1.42–2.62)	3.65 (3.21–4.35)	14.75 (13.22–16.14)	20.17 (19.08–21.93)
	L	2.03 (1.45–3.01)	3.73 (3.40–4.50)	14.06 (12.39–16.13)	19.67 (18.79–21.79)
3 – Cryotherapy	R	1.87 (1.38–2.27)	3.86 (3.44–4.28)	16.92 (13.85–20.00)	22.32 (19.55–25.82)
	L	1.72 (1.20–2.84)	3.67 (2.16–4.43)	15.57 (13.33–20.67)	21.37 (18.72–26.06)

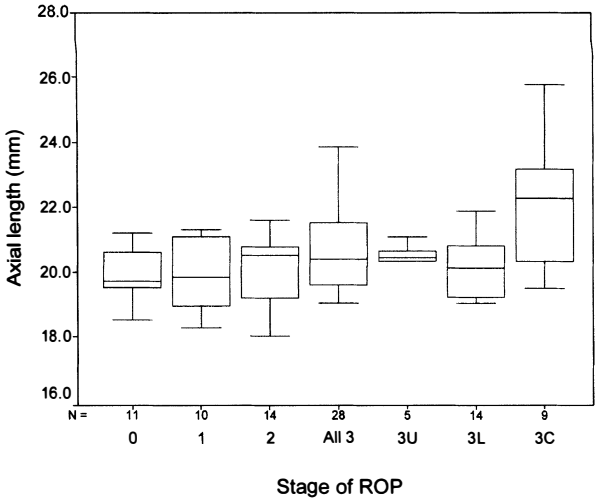

Fig. 1. *Relationship between axial length (AL) (mm) and acute stage of ROP with stage 3 divided into untreated (3U), laser-treated (3L) and cryotherapy-treated (3C). The trend towards longer median AL in stage 3 is due to the influence of the cryotherapy-treated eyes. Values are for right eyes.*

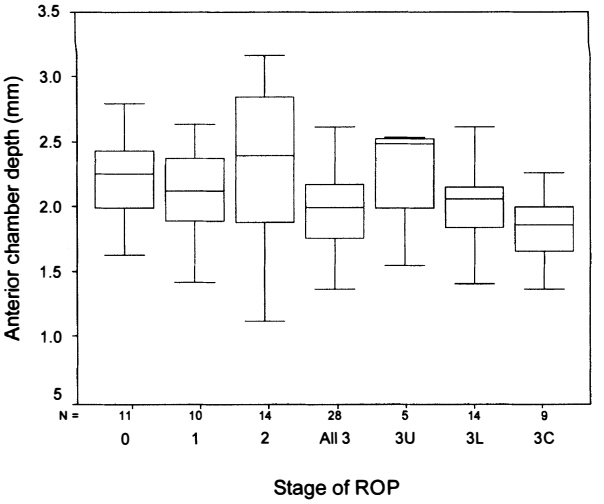

Fig. 3. *Relationship between anterior chamber depth (ACD) (mm) and acute stage of ROP with stage 3 divided into untreated (3U), laser-treated (3L) and cryotherapy-treated (3C). ACD decreases in stage 3 treated eyes. Values are for right eyes.*

(AL), (right eye (RE): $\chi_3^2 = 3.46$, $p = 0.33$; left eye (LE): $\chi_3^2 = 5.11$, $p = 0.16$). Lens thickness (LT) was also similar for all stages (RE: $\chi_3^2 = 1.09$, $p = 0.78$; LE: $\chi_3^2 = 1.09$, $p = 0.78$). However, a significant difference was found between the stages for posterior segment length (PSL) (RE: $\chi_3^2 = 8.93$, $p = 0.03$; LE: $\chi_3^2 = 7.79$, $p = 0.05$). The median values in Table 2 suggest that stage 3 subjects have longer PSLs. Although not of statistical significance for right or left eyes with respect to anterior chamber depth (ACD) (RE: $\chi_3^2 = 7.13$, $p = 0.06$; LE: $\chi_3^2 = 7.28$, $p = 0.06$), from a clinical perspective a trend towards a shallower anterior chamber was observed for the stage 3 eyes.

If stage 3 was subdivided into categories of treated (laser and cryotherapy) and untreated and the analysis repeated then the differences between not only the different stages of ROP but within stage 3 itself with respect to ocular dimensions were far more striking (Table 2). It can be seen in Fig. 1 that the longer median axial length suggested in stage 3 eyes was due to the influence of the stage 3 crotherapy-treated group. Borderline significance was achieved when comparing all stages: 0, 1, 2, 3 – untreated, 3 – laser and 3 – cryotherapy (RE : $\chi_5^2 = 9.90$, $p = 0.07$; LE: $\chi_5^2 = 11.10$, $p = 0.05$). It is of note that AL in stages 0, 1, 2, 3 – untreated and 3 – laser-treated eyes did not differ significantly when the cryotherapy-treated group was removed from the analysis (RE: $\chi_4^2 = 1.44$, $p = 0.84$; LE: $\chi_4^2 = 4.75$, $p = 0.31$). A similar trend emerged for PSL, with significant values for right and left eyes (RE: $\chi_5^2 = 12.56$, $p = 0.03$; LE: $\chi_5^2 = 14.67$, $p = 0.01$). Fig. 2 shows that it was stage 3 eyes requiring cryotherapy which had the longest PSL while Fig. 3 suggests that ACD decreased in stage 3 eyes requiring treatment, the

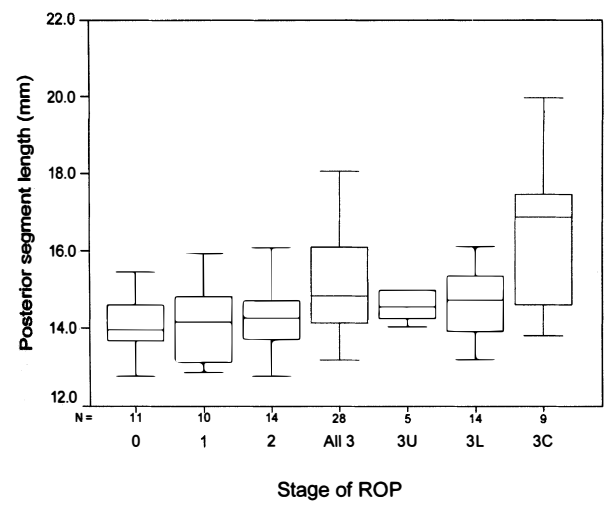

Fig. 2. *Relationship between posterior segment length (PSL) (mm) and acute stage of ROP with stage 3 divided into untreated (3U), laser-treated (3L) and cryotherapy-treated (3C). PSL in stage 3 was significantly different from the other stages, with the longest PSL in the cryotherapy-treated eyes. Values are for right eyes.*

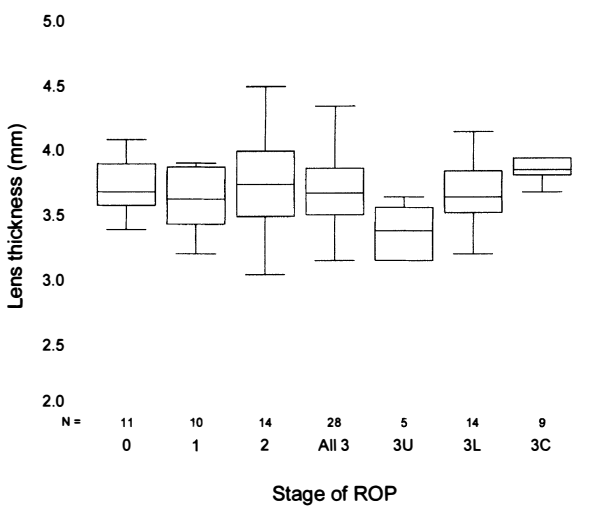

Fig. 4. *Relationship between lens thickness (LT) (mm) and acute stage of ROP with stage 3 divided into untreated (3U), laser-treated (3L) and cryotherapy-treated (3C). A trend towards a thicker lens is seen in stage 3 treated eyes. Values are for right eyes.*

Table 3. *Median (range) refractive data in dioptres for right (R) and left (L) eyes for all stages of ROP*

Maximum stage of ROP	Right	Left
0	MSE: +1.13 (0.00 to +5.75) +Cyl: +0.25 (0.00 to 0.50)	MSE: +1.75 (−2.50 to 7.75) +Cyl: 0.00 (0.00 to 1.00)
1	MSE: +1.63 (+0.38 to +4.50) +Cyl: 0.50 (0.00 to 1.25)	MSE: +1.75 (+0.38 to +5.50) +Cyl: 0.63 (0.00 to 1.00)
2	MSE: +0.88 (0.00 to +4.25) +Cyl: 0.50 (0.00 to 2.50)	MSE: +0.44 (0.00 to +4.75) +Cyl: 0.50 (0.00 to 2.50)
3 – All	MSE: −2.00 (−21.75 to +2.75) +Cyl: 1.00 (0.00 to 3.25)	MSE: −1.69 (−18.25 to +2.00) +Cyl: 1.00 (0.00 to 5.00)
3 – Untreated	MSE: +0.88 (+0.63 to +2.13) +Cyl: 0.25 (0.00 to 0.75)	MSE: +1.13 (+0.50 to +1.63) +Cyl: 0.75 (0.50 to 0.75)
3 – Laser	MSE: −1.00 (−10.50 to +2.75) +Cyl: 1.13 (0.00 to 3.25)	MSE: −1.69 (−11.25 to +2.00) +Cyl: 1.50 (0.00 to 5.00)
3 – Cryotherapy	MSE: −8.00 (−21.75 to 0.00) +Cyl: 0.75 (0.50 to 1.75)	MSE: −7.25 (−18.25 to +1.25) +Cyl: 1.00 (.050 to 3.00)

MSE, mean spherical equivalent.

effect again being greater in the cryotherapy-treated group. Analysis showed that borderline significant differences did exist between the stages of ROP for ACD (RE: $\chi_5^2 = 10.02$, $p = 0.07$; LE: $\chi_5^2 = 13.56$, $p = 0.02$). LT was greater in stage 3 eyes requiring treatment as there was some evidence of a significant difference (RE: $\chi_5^2 = 10.40$, $p = 0.06$; LE: $\chi_5^2 = 8.51$, $p = 0.13$) (Fig. 4).

Table 3 shows the refractive data of the entire cohort. When stage 3 subgroups are taken together then the median mean spherical equivalent (MSE) for the right eye was −2.00 dioptres (D) and −1.69 D for the left eye and the stages differed significantly (RE: $\chi_3^2 = 23.59$, $p < 0.0001$; LE: χ_3^2 21.78, $p < 0.001$). Once again if stage 3 was divided into its subcategories of treated and untreated, we see that the higher degrees of myopia were seen in those requiring treatment, with the cryotherapy-treated group having the highest myopia (RE: $\chi_5^2 = 33.72$, $p < 0.001$; LE: χ_5^2 29.96, $p < 0.001$) (Fig. 5). Comparison of refractive error between stage 0 and stage 3 untreated showed no difference (RE: $U = 55.0$, $p = 0.99$; LE: $U = 55.0$, $p = 0.53$) while there was a marked difference between stage 0 and stage 3 laser-treated (RE: $U = 41.0$, $p = 0.0002$; LE: $U = 44.0$, $p = 0.0003$) and stage 3 cryotherapy-treated (RE: $U = 1.0$, $p < 0.0001$; LE: $U = 15.0$, $p < 0.0001$).

The degree of astigmatism also increased as the stage of ROP increased. If stage 3 subgroups are categorised as one then the median positive cylinder was +1.00 D for both right and left eyes, with stage 3 differing significantly from the other stages (RE: $\chi_3^2 = 12.94$, $p = 0.0048$; LE: $\chi_3^2 = 23.66$, $p < 0.0001$). When stage 3 was subdivided there was no statistical difference between stage 3 untreated and stages 0, 1 and 2 (RE: $\chi_3^2 = 4.9$, $p = 0.18$; LE: $\chi_3^2 = 3.37$, $p = 0.34$). The highest degrees of astigmatism were seen in those requiring treatment (RE: $\chi_5^2 = 17.39$, $p = 0.0038$; LE: $\chi_5^2 = 25.84$, $p = 0.0001$), with the astigmatism being greatest in the laser-treated group (Fig. 6). Axis of astigmatism did not vary significantly between the stages (RE: $\chi_3^2 = 5.03$, $p = 0.17$, LE: $\chi_3^2 = 5.27$, $p = 0.15$) even when stage 3 was subcategorised (RE: $\chi_5^2 = 7.19$, $p = 0.21$, LE: $\chi_5^2 = 7.02$, $p = 0.22$).

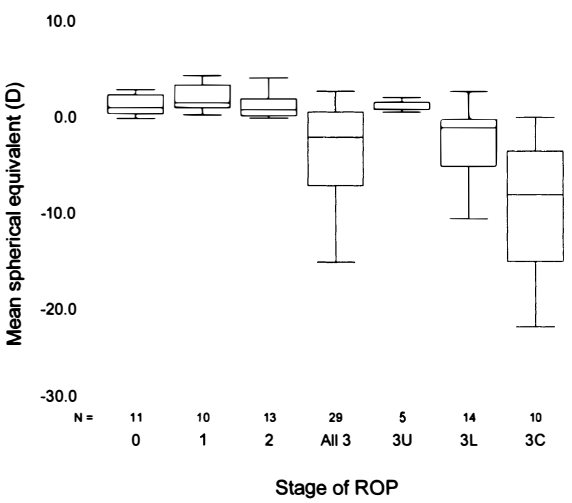

Fig. 5. *Relationship between mean spherical equivalent (MSE) (D) and acute stage of ROP with stage 3 divided into untreated (3U), laser-treated (3L) and cryotherapy-treated (3C). Higher degrees of myopia are seen in stage 3 treated eyes. Values are for right eyes.*

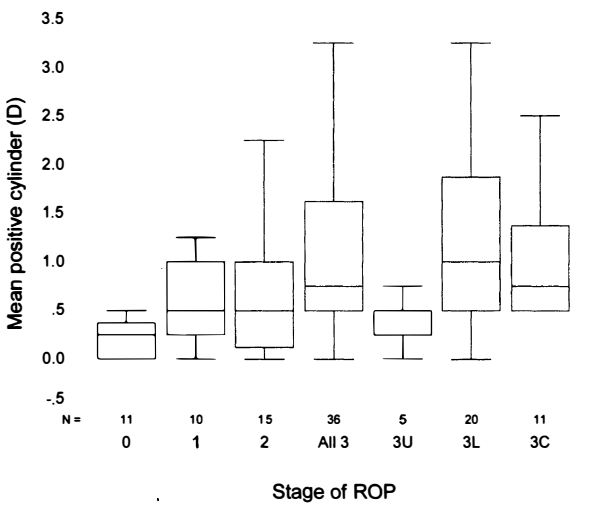

Fig. 6. *Relationship between mean positive cylinder (D) and acute stage of ROP with stage 3 divided into untreated (3U), laser-treated (3L) and cryotherapy-treated (3C). Higher degrees of astigmatism are seen in treated eyes. Values are for right eyes.*

Discussion

This study reports the refractive and ocular biometric outcomes in a cohort of children with a mean age, corrected for term, of 40.2 months who were born prematurely. In particular it analyses what effect, if any, the presence of ROP and its treatment may have had on subsequent ocular growth and how these effects may have contributed to the refractive error seen in these children.

The refractive data obtained confirm previous findings that low-birth-weight infants requiring treatment for ROP are at a high risk of developing myopia, with significantly greater myopia occurring in those who undergo cryotherapy.[10–12] In addition we found that the degree of astigmatism increased with increasing stage of ROP. Laws *et al.*[10] found that there was a significant difference between the laser- and cryotherapy-treated groups even as early as 3 months, and that the actual degree of myopia increased even further in the cryotherapy group for the subsequent duration of the study. The present study reporting at around 40 months agrees with these findings. We found that the degree of myopia in both laser- and cryotherapy-treated groups was greater than that observed within the first year of the above study, while the refractive disparity between the treatments had increased even further. With respect to astigmatism Laws *et al.*[4] found that increasing degrees of astigmatism were associated with increasing stage of ROP. In their cohort no infant reached threshold disease but a significant difference existed between stages 2 and 3. In the present study significance existed only between threshold stage 3 and the other stages. In the treated groups we found that the laser subgroup had the higher degrees of astigmatism. This is in contrast to the findings of Laws *et al.*[10] though the difference between laser and cryotherapy was not significant in their study.

White and Repka[22] found only a minimal advantage of laser ablation over cryotherapy with respect to the amount of induced myopia at 3 years in their prospective trial comparing the two treatment modalities. However, because their numbers were small they were reluctant to draw any definite conclusions regarding any potential advantage of laser over cryotherapy. Although non-randomised, our findings in relation to the degree of induced myopia support a definite advantage of laser treatment over cryotherapy at a follow-up of 40.2 months (mean refractive error RE: laser −2.35 D, cryo −9.34 D; LE: laser −3.08 D, cryo −7.78 D). We must await further analysis on this cohort to see whether these refractive differences will be maintained in the future. It may be that the perceived advantage of laser over cryotherapy in relation to induced refractive error may be an epiphenomenon rather than a true manifestation of laser treatment. Most workers would acknowledge that the standard of neonatal care has improved dramatically in recent years as evidenced by improved survival rates of the very premature. One could similarly deduce that the reduced myopia observed in the laser-treated eyes may be due to the overall improvement in neonatal care. However, cryotherapy was mainly performed on this cohort in 1990–1 and laser intervention was undertaken in 1991–2. We feel that these recognised improved benefits observed in neonatal care are unlikely to have had such a dramatic influence on disease severity in such a short interval and that the perceived beneficial affect of laser is therefore a real one.

The association between myopia and ROP is well documented[1–8] and this study supports these findings. We found a significant difference in the amount of myopia present in stage 3 compared with the other stages. However, when we subcategorised stage 3 into threshold and subthreshold, then significance was maintained only for the treated groups, with no difference being observed for stages 0, 1, 2 and 3 subthreshold. Both Laws *et al.*[4] and Schaffer *et al.*[23] also noted similar findings for stage 3 while Kushner[24] noted a significant trend between all stages.

The biometry results obtained support previous studies in finding an association between ROP and anterior segment abnormalities.[2,13,15,16] When compared with the other stages, stage 3 eyes had shallower ACDs in addition to the posterior findings of longer PSLs and longer ALs. Although statistically of only borderline significance, the trend was towards a definite inverse relationship between ACD and increasing stage of ROP with direct relationships existing for both AL (borderline significance only) and PSL. Both Fledelius[16] and Hittner *et al.*[14] showed similar findings for ACD in their studies while Gordon and Donzis[1] and Teller *et al.*[25] found no such correlation. When stage 3 was subdivided into threshold and subthreshold, it was mainly the influence of the cryotherapy-treated group and to a lesser extent the laser-treated group that caused these trends, while subthreshold ROP stage 3 children had similar ocular dimensions when compared with stages 0, 1 and 2. In addition laser-treated eyes, despite being myopic, had similar ALs to the other stages. They also had shallower ACDs and longer PSLs, whilst those treated with cryotherapy had the most extreme ocular dimensions, i.e. longer ALs, longer PSLs and shallower ACDs. In his work, Fledelius[16] found that in addition to shallow anterior chambers, children with ROP had thicker lenses, which contributed to their myopia. We also found an emerging trend between lens thickness, degree of myopia and increasing severity of stage 3. It has been reported previously[13] that in the neonatal period AL is inversely related to increasing stage of ROP. In the present group this trend has reversed, with longer axial lengths seen in stage 3 children. Perhaps an explanation for this may be that anterior segment maturation may lead to a shorter eye initially but loss of regulation of posterior segment growth later.

Axial length cannot explain all the myopia seen in ROP. A 1 mm difference in AL length would account for just over 3 D of myopia. Yet stage 3 cryotherapy-treated eyes had a MSE of −8.00 D in the right eye and −7.25 D in the left eye. ROP may therefore exert other influences on ocular growth. We found a shallow anterior chamber

to be a feature of all stage 3 eyes but more so in the treated groups. Shallowing of the anterior chamber would give rise to a more anteriorly placed lens that in turn will give rise to increased myopia. Furthermore we found a trend towards a thicker lens, which would also contribute to the overall myopia. Gordon and Donzis,[1] while not finding shallow anterior chambers in their study, actually measured lens power and concluded that lenticular myopia was a significant contributor in all their cases. In an effort to explain this they proposed that ROP may interfere with the normal reduction in lens power that occurs after birth.[26] We also found that PSL was increased in the stage 3 group. Therefore we can deduce that it is anterior segment arrest causing anterior displacement of the crystalline lens, together with increased LT and PSL, that were causative factors in the development of myopia in this cohort.

Whatever the precise mechanism we can conclude that increasing severity of stage 3 ROP is probably a significant contributor to the development of high myopia. Fielder and Quinn[27] have suggested that the ROP insult retards that part of the globe which is undergoing maximal growth, and this effect will in turn mechanically inhibit anterior segment development, as evidenced by shallowing of the anterior chamber and smaller corneal radii. Though we did not perform keratometry in this present study we did find that astigmatism increased with increasing stage of ROP and was highest in those patients who underwent treatment. However, axis of astigmatism did not vary significantly between the stages. Although there was no statistical difference between stage 3 untreated and stage 3 cryotherapy-treated eyes, as evidenced from the boxplot, a trend towards greater astigmatism is seen in the latter group. With greater numbers we feel that this trend may have become significant. Exact cylinder determination is also more difficult in high myopia and this too may have biased the final analysis of astigmatic outcome. If we add to this the destructive effect of treatment to an already underdeveloped anterior segment, it is perhaps not surprising that the greater refractive anomalies occur in stage 3 treated patients. It has been shown that laser treatment[28] (transpupillary) is less tissue destructive than cryotherapy (transscleral).[29] Laser treatment may therefore be less likely to interfere with ocular growth. An alternative explanation might be that both ROP and its treatment might interfere with neuroretinal growth factors which are thought to regulate anterior segment maturation while at the same causing an increase in PSL. As we strive to gain a better understanding of anterior segment arrest in ROP, we hope to report on both corneal and anterior lenticular curvature in the near future.

References

1. Gordon RA, Donzis PA. Myopia associated with retinopathy of prematurity. Ophthalmology 1986;93:1593–8.
2. Hungerford J, Stewart A, Hope P. Ocular sequelae of preterm birth and their relation to ultrasound evidence of cerebral damage. Br J Ophthalmol 1986;70:463–8.
3. Keith CG, Kitchen WH. Ocular morbidity in infants of very low birthweight. Br J Ophthalmol 1983;67:302–5.
4. Laws D, Shaw DE, Robinson J, Jones HS, Ng YK, Fielder AR. Retinopathy of prematurity: a prospective study. Review at six months. Eye 1992;6:477–83.
5. Nissenkorn I, Yassur Y, Mashkowski I, Sherf I, Ben-Sira I. Myopia in premature babies with and without retinopathy of prematurity. Br J Ophthalmol 1983;67:170–3.
6. Robinson R, O'Keefe M. Follow-up study on premature infants with and without retinopathy of prematurity. Br J Ophthalmol 1993;77:91–4.
7. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicentre trial of cryotherapy for retinopathy of prematurity. One year outcome: structure and function. Arch Ophthalmol 1990;108:1408–16.
8. Page JM, Schneeweiss S, Whyte HEA, Harvey P. Ocular sequelae in premature infants. Pediatrics 1993;92:6.
9. Quinn GE, Dobson V, Repka MX, Reynolds J, Kivlin J, Davis B, *et al.*, on behalf of the Cryotherapy for Retinopathy of Prematurity Cooperative Group. Development of myopia in infants with birth weights less than 1251 grams. Ophthalmology 1992;99:329–40.
10. Laws F, Laws D, Clark D. Cryotherapy and laser treatment for acute retinopathy of prematurity: refractive outcomes, a longitudinal study. Br J Ophthalmol 1997;81:12–5.
11. Algawi K, Goggin M, O'Keefe M. Refractive outcome following diode laser versus cryotherapy for eyes with retinopathy of prematurity. Br J Ophthalmol 1994;78:612–4.
12. Connolly BP, McNamara JA, Sharma S, Regillo CD, Tasman W. A comparison of laser photocoagulation with trans-scleral cryotherapy in the treatment of threshold retinopathy of prematurity. Ophthalmology 1998;105:1628–31.
13. Laws DE, Haslett R, Ashby D, O'Brien C, Clark D. Axial length biometry in infants with retinopathy of prematurity. Eye 1994;8:427–30.
14. Hittner MH, Rhodes LM, McPherson AR. Anterior segment abnormalities in cicatricial retinopathy of prematurity. Ophthalmology 1979;86:803–16.
15. Kelly SP, Fielder AR. Microcornea associated with retinopathy of prematurity. Br J Ophthalmol 1987;71:201–3.
16. Fledelius HC. Pre-term delivery and subsequent ocular development. A 7–10 year follow-up of children screened 1982–84 for ROP. 4. Oculometric and other metric considerations. Acta Ophthalmol Scand 1996;74:301–5.
17. O'Brien C, Clark D. Ocular biometry in preterm infants without retinopathy of prematurity. Eye 1994;8:662–5.
18. Committee for the Classification of Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: preliminary results. Arch Ophthalmol 1984;102:1130–3.
19. Twelker JD, Kirschbaum S, Zadnik K, Mutti DO. Comparison of corneal versus through-the-lid A-scan ultrasound biometry. Optom Vis Sci 1997;74:852–8.
20. Laws F, Laws D, Wood ICJ, Clark D. Assessment of a new through-the-eyelid technique for 'A' scan ultrasound ocular axial length measurement. Ophthalmic Physiol Opt 1998;5:408–14.
21. Lavery JR, Gibson JM, Shaw DE, Rosenthal AR. Refraction and refractive errors in an elderly population. Ophthalmic Physiol Opt 1988;8:394–6.
22. White JE, Repka MX. Randomized comparison of diode laser photocoagulation versus cryotherapy for threshold retinopathy of prematurity: 3-year outcome. J Pediatr Ophthalmol Strabismus 1997;34:83–7.
23. Schaffer DB, Quinn GE, Johnson L. Sequelae of arrested mild retinopathy of prematurity. Arch Ophthalmol 1984;102:373–6.
24. Kushner BJ. Strabismus and amblyopia associated with regressed retinopathy of prematurity. Arch Ophthalmol 1982;100:256–61.

25. Teller J, Nissenkorn I, Ben-Sira I, Abraham FA. Ocular dimensions following cryotherapy for active stage of retinopathy of prematurity. Metabolic Pediatr Systemic Ophthalmol 1988;11:81–2.
26. Gordon RA, Donzis PB. Refractive development of the human eye. Arch Ophthalmol 1985;103:785–9.
27. Fielder AR, Quinn GE. Myopia of prematurity: nature, nurture, or disease? Br J Ophthalmol 1997;81:12–5.
28. Benner JD, Huang M, Morse LS, Hjelmeland LM, Landers MB. Comparison of photocoagulation with the argon, krypton, and diode laser indirect ophthalmoscopes in rabbit eyes. Ophthalmology 1992;99:1554–63.
29. Nissenkorn I, Kremer I, Ben-Sira I, Cohen S, Garner A. A clinicopathological case of retinopathy of prematurity (ROP) treated by peripheral cryopexy. Br J Ophthalmol 1984;68:36–41.