

# Refractive outcome following diode laser versus cryotherapy for eyes with retinopathy of prematurity

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## Abstract

**The refractive error in 15 eyes with threshold retinopathy of prematurity treated with diode laser photocoagulation was compared with 25 eyes with the same disease severity treated by cryotherapy. Myopia was present in 40% (six eyes) of the first group ranging from -1.50 to -3.50 dioptres, while 92% (23 eyes) showed myopia which ranged from -0.50 to -8.00 dioptres in the cryotherapy group. Sixty per cent (nine eyes) were hypermetropic at less than +3.0 dioptres in the laser group, while only 8% (two eyes) of the cryotherapy group showed hypermetropia. There was no significant difference in astigmatism between the two groups. Eyes with threshold disease treated with diode laser photocoagulation developed significantly less myopia than those treated with cryotherapy ( $p=0.0006$ , two tailed value). (Br J Ophthalmol 1994; 78: 612-614)**

Retinopathy of prematurity (ROP) is the cause of blindness in 11% of blind children in the Republic of Ireland.<sup>1</sup> The high survival rate of premature infants means an increasing number of cases of ROP every year. Management of this problem, whether in the form of prophylaxis or as an active treatment of established disease, is a matter of great concern to ophthalmologists.

Xenon arc photocoagulation for ROP was reported in 1970<sup>2</sup> and cryopexy in 1972 by Yamashita.<sup>3</sup> The reports of the CRYO-ROP Cooperative Group have contributed significantly towards the management of ROP. Their study has demonstrated the effectiveness of cryotherapy for 'threshold' disease.<sup>4</sup>

Laser photocoagulation for ROP has emerged as an effective alternative to cryopexy. Landers *et al* reported that eyes treated for ROP stage 3 threshold by argon laser photocoagulation (treating the avascular retina) showed favourable outcome in 73%.<sup>5</sup> These favourable results were confirmed by Preslan.<sup>6</sup> Diode laser has been shown to achieve similar results.<sup>7</sup> Prematurity and low birth weight have long been known to be associated with myopia.<sup>8,9</sup> Retinopathy of prematurity increases the incidence of myopia.<sup>9,10</sup>

This study examines the refractive outcome in patients treated with diode laser and compares it with those treated with cryotherapy.

## Materials and methods

Thirty two premature infants (15 females and 17 males) with threshold ROP (stage 3+ disease of 5 or more contiguous clock hours [30° sectors] or 8 cumulative clock hours) or more, received treat-

ment by diode laser or cryopexy. (In view of the known asymmetrical nature of the disease, eyes instead of patients are studied.)

The laser group consisted of 21 eyes of 12 infants who received diode laser retinal photocoagulation in the period between February and November 1992 using the Iris OcuLight SL diode laser system. Postnatal age, when refraction was done, ranged from 8 to 15 months (mean 13 months). Gestational ages of this group ranged from 24 to 32 weeks. The birth weight range was 700 to 1200 g.

The cryotherapy group consisted of 32 eyes of 20 infants who were treated by cryopexy of the avascular retina in the period between January 1989 and February 1992. Gestational age ranged from 25 to 30 weeks with a birthweight range of 620 to 1500 g.

The indications and methods of treatment of both groups are described elsewhere.<sup>7,11</sup> Visual functions were assessed by either fixation pattern or preferential looking technique. Manual refraction was performed after the installation of cyclopentolate 0.5% and phenylephrine 2.5% eye drops in all patients. The refraction at 1 year of postnatal age of the cryotherapy group was used for comparison. Statistical analysis was performed by using the EPI INFO program and comparison of proportions was done by using the Fisher exact method. A figure of <0.05 is regarded as statistically significant.

## Results

Fifty three eyes were treated; 21 received laser and 32 cryotherapy. Three eyes in the laser group were at or beyond stage 4, one eye progressed to total retinal detachment with difficult refraction, and two eyes of one patient who died before full post treatment assessment were excluded from this group, leaving 15 eyes for analysis. Five eyes in the cryotherapy group were at or beyond stage 4 and two other eyes had progressed to total retinal detachment, making refraction impossible; these seven eyes were excluded, leaving 25 eyes in this group.

In the laser group six eyes (40%) showed myopia with a spherical equivalent of less than or equal to -3.50 dioptres; nine eyes were hypermetropic with a spherical equivalent less than or equal to +2.50 dioptres; five eyes showed significant astigmatism of less than or equal to 0.75 dioptre; and none had more than 3.0 dioptres of astigmatism (Table 1).

In the cryotherapy group 23 eyes (92%) showed myopia, 12 of which were less than or equal to -3.0 dioptres; seven were between -3.25 and -6.0 dioptres; and five eyes had

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**Table 1** The extent of retinopathy of prematurity when first treated, refraction (in spherical equivalent), and retinal outcome in the laser group (all treated eyes had stage 3 + plus disease)

No	Extent (clock hours)	Refraction (spherical equivalent)	Retinal outcome
11	6	-0.625	flat, scars
12	6	-0.625	flat, scars
13	5	+2.50	flat, scars, pale disc
14	12	+1.00	flat, scars, pale disc
17	6	+1.75	flat, scars
21	8	-1.625	flat, scars
24	12	+2.00	flat, scars
25	12	+2.00	flat, scars
44	8	+1.75	flat, scars
45	9	-3.50	flat, scars
48	5	+1.50	flat, scars
49	5	+1.50	flat, scars
50	12	-3.50	flat, scars, dragged disc
52	8	-1.50	flat, scars, localised detachment
53	5	+2.25	flat, scars

greater than or equal to -6.25 dioptres (spherical equivalent). Only two eyes (8%) showed hypermetropia and five eyes had significant astigmatism (Table 2).

Myopia was encountered significantly less in the laser group than the cryotherapy group ( $p=0.0006$ , two tailed value). Conversely hypermetropia was noticed more in the laser group ( $p=0.0006$ , two tailed value).

Astigmatic refractive errors did not show any significant difference between the two groups ( $p=0.4$ ). Two eyes of one patient had lensectomies for infantile cataract; vitreoretinal surgery was carried out in the left eye with the final outcome of partial retinal detachment and perception of light only, while the right eye developed total retinal detachment with no light perception. Details of diode laser retinal photocoagulation and retinal cryotherapy for the treatment of these ROP patients are discussed elsewhere.<sup>7 11</sup>

## Discussion

The incidence of myopia in premature infants

**Table 2** The extent of retinopathy of prematurity when first treated, refraction (in spherical equivalent), and retinal outcome in the cryotherapy group (all treated eyes had stage 3 + plus disease)

No	Extent (clock hours)	Refraction (spherical equivalent)	Retinal outcome
1	6	-6.00	flat, scars
2	8	-6.75	flat, scars
3	12	-4.00	flat, scars
4	12	-4.00	flat, scars
5	12	-2.00	flat, scars
6	5	+2.00	flat, scars
7	12	-1.375	flat, scars
10	6	+2.00	flat, scars
16	9	-8.00	flat, scars, ONH
18	8	-2.50	flat, scars
19	12	-2.00	flat, scars
20	12	-0.50	flat, scars
28	12	-1.25	flat, scars
29	12	-1.25	flat, scars
30	12	-3.00	flat, scars
31	12	-3.00	flat, scars, pale disc
33	12	-5.00	flat, scars, ONH
34	12	-6.00	flat, scars, ONH
35	12	-4.00	flat, scars
36	8	-2.75	flat, scars
37	9	-8.00	flat, scars
38	9	-8.00	flat, scars
42	6	-3.00	subtotal retinal detachment
43	9	-3.00	total retinal detachment
51	8	-6.25	flat, dragged disc

ONH=optic nerve hypoplasia.

and its severity correlated positively with the severity of ROP and cicatrization.<sup>9</sup> Zaharias *et al* demonstrated that eyes affected with ROP were most often myopic; they also correlated myopia and its degree with the severity of the early retinal changes during the active phase of ROP, as well as with the cicatrization phase.<sup>12</sup>

No significant statistical difference in degree of myopia was found between ROP eyes treated with cryopexy and those without.<sup>13</sup> This was confirmed by Seiberth *et al*.<sup>14</sup> Argon and diode laser treatment for ROP has resulted in a favourable outcome.<sup>5 7</sup> The advantages of laser treatment for ROP when compared with cryotherapy include the fact that laser treatment of delicate fibrovascular tissues might lessen the haemorrhagic complications often associated with cryotherapy. Despite the fact that intense diode laser burns cause full thickness choroidal involvement and even thermal injury to the inner scleras of rabbit's eyes,<sup>15</sup> it seems that these injuries are less extensive than those produced by cryotherapy. The creation of large areas of scarring by cryopexy may lead to the development of rhegmatogenous retinal detachment years after treatment.<sup>16</sup>

Indirect ophthalmoscope laser applications to the retina cause minimal conjunctival chemosis and subconjunctival haemorrhage.<sup>7</sup> Diode laser in particular may have the following added advantages: its 'near' infrared emission wavelength of 810 nm has theoretically superior transmission properties through haemorrhage compared with argon laser; high energy conversion efficiency, which means lower power supply needed for its operation (standard household current or batteries) making it light and portable<sup>17 18</sup> and allowing treatment in the neonatal intensive care unit.

Diode laser hardware is less expensive than argon laser hardware.<sup>17 18</sup> On the other hand the drawbacks of laser treatment are the requirement of clear optical media for proper treatment, and haemorrhage, small pupils, and prominent tunica vasculosa lentis can limit the treatment. There are reports of accidental corneal and iris burns by indirect laser delivery system,<sup>19</sup> though corneal burns were not experimentally reproducible.<sup>15</sup>

The high percentage of eyes with myopia by comparison with other reports in the cryotherapy group may be explained by the fact that all the eyes studied had stage 3+ disease, whereas other reports of myopia and ROP did not specifically study eyes with advanced stages of ROP.<sup>8-10</sup> Myopia occurs more frequently with prematurity, low birth weight, ROP, and visual deprivation.<sup>8 9 20 21</sup> Gordon and Donzis analysed the components of refractive errors in 10 eyes with myopia and ROP. These eyes showed lenticular and axial myopia, though only the high lens powers were found to be statistically significant compared with a control group.<sup>22</sup> Christensen and Wallman looked at the scleras of visually deprived chicks and their findings suggested increase in the size and weight of the scleras by cell proliferation and increased synthesis of extracellular matrix.<sup>21</sup> Fielder *et al* suggested that myopia of prematurity may be due to failure of flattening the usually steep intra-

uterine cornea,<sup>23</sup> while Majima and Hibino *et al* suggested that myopia is due to combination of increased axial length and lenticular thickness.<sup>24,25</sup> Fledelius has highlighted myopia of prematurity as a change which usually disappears with time and cautioned against confusing it with that associated with ROP.<sup>26</sup> We find it quite difficult to differentiate between the two types of myopia at this stage.

Stone *et al* observed reduced concentrations of dopamine and its metabolites in myopic eyes compared with controls.<sup>27</sup> These studies may give some insight into the association of myopia and ROP, but cannot explain the reason behind the reduced incidence of myopia in the laser group in our series. It is unlikely that cryopexy alone is the cause as Seiberth *et al*<sup>14</sup> and Teller *et al*<sup>13</sup> found no significant difference in myopia between cryotreated and untreated eyes. This makes our findings all the more interesting.

We speculate that ablating the avascular retina with diode laser destroys the source of the possible 'chemical mediators of myopic changes' with minimal scleral damage that can influence the size of the eye that subsequently develops myopia.

It must be stated that our results are based on only a 1 year follow up for children who had laser therapy and our numbers are small. We feel that this early finding should be highlighted, but the longer follow up will be more interesting. In conclusion, myopia is a major complication in children with ROP<sup>9,12,28</sup> and any treatment that significantly reduces this complication will have major longer term benefit.

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