REFRACTIVE OUTCOMES OF THREE-PORT LENS-SPARING VITRECTOMY FOR RETINOPATHY OF PREMATURITY (AN AOS THESIS)

BY Eric R. Holz MD

ABSTRACT

Purpose: To study the refractive outcomes of 3-port lens-sparing vitrectomy (LSV) for subtotal retinal detachments due to retinopathy of prematurity (ROP). Lens-sparing vitrectomy may provide superior refractive outcomes by limiting induced myopia of prematurity.

Methods: This is a retrospective, consecutive, nonrandomized, comparative (paired eye) study. Entrance criteria were previous complete ablative laser for threshold ROP in both eyes, followed by LSV in one eye for stage 4A traction retinal detachment. Both eyes then maintained complete retinal attachment. Main outcome variables were cycloplegic refraction, keratometry, and biometric values for axial length, lens thickness, and anterior chamber depth.

Results: Nine patients met inclusion criteria. Lens-sparing vitrectomy eyes were significantly less myopic than control eyes (-6.78 D vs -10.33 D, $P < .005$). The reduction in myopia in LSV eyes was predominantly due to increased anterior chamber depth (3.81 mm ± 0.217 vs 2.96 mm ± 0.232, $P < .005$). There was a minor contribution from reduced corneal power in LSV eyes (43.89 D ± 0.253 vs 44.20 D ± 0.265, $P < .005$). There was a minor negative impact from increased lens thickness in LSV eyes (3.85 ± 0.32 mm vs 3.74 ± 0.31, $P < .005$). There was no significant difference in axial length or lens power between the LSV and control groups.

Conclusions: The data demonstrate that infant eyes undergoing 3-port LSV for stage 4A ROP develop less myopia than fellow eyes treated with laser alone. The difference is due to posterior displacement of the lens-iris diaphragm with a smaller contribution from reduced corneal power. The reduction in myopia may improve functional outcomes following 3-port LSV for stage 4A ROP.

Trans Am Ophthalmol Soc 2009;107:300-310

INTRODUCTION

The management of tractional retinal detachments due to retinopathy of prematurity (ROP) continues to evolve. Indeed, ROP-related retinal detachments were initially repaired by use of scleral buckle procedures; subsequently, vitrectomy with lensectomy (early on, open-sky, and then through the pars plicata) was used, and most recently, repair has been accomplished with lens-sparing vitrectomy (LSV). This thesis will highlight how surgical advances have improved structural and functional outcomes, with special emphasis on the advantages of the 3-port LSV procedure, and will address the novel question of whether LSV limits myopia of ROP.

SCLERAL BUCKLING

The first case series of scleral buckling for the treatment of selected ROP-related retinal detachments was published by McPherson and Hittner in 1979.[1] In that and subsequent case series, macular reattachment success rates have ranged from 31% to 75%[1-11] (Table 1). The wide range of anatomic success is readily explicable by variable inclusion criteria, with some studies including stage 5 ROP, as well as variable degrees of vascular activity preoperatively, with some of the early studies having been performed before the current screening and treatment criteria for peripheral retinal ablation had been established. Additionally, there is disparity in the techniques used for buckling (segmental or encircling element), in whether draining of subretinal fluid was carried out, and in whether additional cryoablation was performed intraoperatively.

Although it is clear that scleral buckling can achieve anatomic success, the procedure has 4 inherent disadvantages:

- First, a second procedure is required to divide or remove the buckle in order to allow normal ocular growth.[2]
- Second, scleral buckling is associated with strabismus when applied to premature eyes, in one series in as many as 12 of 13 treated infants (92%).[7]
- Third, it induces high levels of myopia.[2,7,12] Indeed, in one series,[7] myopia (-5 D to -15 D) was found in all 13 eyes despite buckle removal 6 to 10 months following buckle placement; in another series,[12] the mean induced myopia was -11 D (induced anisometropia of -9.5 D) following unilateral scleral buckle placement, which decreased to -5.7 D following division of the scleral buckle.
- Finally, and most important, functional success commonly does not mirror successful macular reattachment.

While undoubtedly retinal damage due to the detachment contributes to poor functional outcomes of stage 4B and stage 5 detachments, poor functional outcomes may also be related, to a certain extent, to the induced strabismus and high myopia/anisometropia results in strabismic and anisometropic amblyopia, respectively. Indeed, in stage 4A retinal detachments treated with scleral buckling alone, 6 of 10 eyes had measurable Teller visual acuity with 3 of 6 having normal Teller visual acuity at 9 months follow-up in a multicenter study.[11] For vascularly active stage 4A ROP, visual acuity was at least fix-and-follow in 5 of 7 eyes and light perception only in 2 of 7.[8] For stage 4B, visual acuity reported results are much poorer: Noorily and associates[5] achieved fix-and-follow vision in only 3 of 15 cases (20%), with 11 of 15 (73%) having light perception only vision. Greven and Tasman[4] reported visual outcomes of 20/200, 20/300, and fix-and-follow in the 3 eyes with stage 4B ROP in their series. In addition, following scleral buckle for stage 5 ROP, Greven and Tasman[4] reported 3 of 19 eyes (16%) with at least fix-and-follow vision, 5 of 19 (26%) with light perception, and 9 of 19 (47%) with no light perception.

Early, aggressive sectioning/removal of the buckle, correction of induced refractive errors, and patching may significantly improve functional outcomes following a scleral buckle procedure; however, there is still a subgroup of patients with unsatisfactory results following scleral buckling.

From the Baylor Eye Clinic, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas.

TABLE 1. ANATOMIC SUCCESS RATES OF SCLERAL BUCKLING SURGERY FOR RETINOPATHY OF PREMATURITY–RELATED RETINAL DETACHMENT

STUDY	STAGES*	ANATOMIC RESULTS
McPherson[1] (1979)	4A, 5	6/14 (43%)
McPherson[2] (1982)	4A, 4B, 5	24/32 (75%)
Topilow[3] (1985)	4A, 4B	5/7 (71%)
Greven[4] (1990)	4B, 5	13/22 (59%)
Noorily[5] (1992)	4B	10/15 (67%)
Trese[6] (1994)	4A, 4B, 5	45/70 (64%)
Ricci[7] (1996)	4A, 4B	13/28 (46%)
Hinz[8] (1998)	4A	6/8 (75%)
Chuang[9] (2000)	4A, 4B	15/23 (65%)
Hartnett[10] (2004)	4A, 4B	5/16 (31%)
Repka (ETROP)[11] (2006)	4A, 4B, 5	6/10 (60%)

ETROP, Early Treatment for Retinopathy of Prematurity.
*Stage 4A, subtotal, macula-sparing retinal detachment; stage 4B, subtotal, macula-involving retinal detachment; stage 5, complete/total traction retinal detachment.

PARS PLICATA VITRECTOMY WITH LENSECTOMY

Initially, vitrectomy techniques for ROP-related traction retinal detachments included lens removal, as it was thought that the relatively large infant lens precluded access to the anterior vitreous membranes so commonly found in ROP. Although this technique may achieve anatomic success, visual results are disappointing. In a large series of mixed stage 4 and stage 5, Zilis and coworkers[13] found attachment rates of 64% (9 of 14) for stage 4 and 9% (11 of 121) for stage 5. Visual acuity of fix-and-follow occurred in only 43% of eyes (6 of 14) with stage 4 and 11% of eyes (13 of 121) with stage 5.[13] Visual results from the Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) clinical trial were similarly disappointing utilizing both open-sky and closed vitrectomy techniques for stage 5 ROP, resulting in 2 of 71 eyes (2.8%) with pattern vision at the lowest measurable threshold.[14,15] Because of the difficulties of managing aphakia during infancy and the high risk of anisometropic amblyopia in monocular cases, the pars plicata vitrectomy with lensectomy technique is now reserved for cases with severe traction and lens-retina apposition or when the lens is compromised during planned LSV.

LENS-SPARING VITRECTOMY

Maguire and Trese[16] reported the first use of LSV in infants in 1992. By modifying location and incision technique, and with a 2-port approach (infusing light pipe), the investigators were able to retain the crystalline lens during vitrectomy for a mixed infant population of ROP, familial exudative vitreoretinopathy, and vitreous hemorrhage due to shaken baby syndrome. Capone and Trese[17] reported the first series of ROP eyes treated with LSV in 2001, achieving an overall anatomic success rate of 90% (36 of 40) for treated stage 4A eyes. Additional investigators[18-23] have subsequently reported anatomic success rates of 69% to 94% (Table 2).

Ferrone and coworkers[24] were the first to address the issue of lens clarity following the LSV procedure. Studying a mixed population of ROP, familial exudative vitreoretinopathy, and vitreous hemorrhage, they found that 19% of eyes (13 of 70) undergoing LSV only developed cataracts over a follow-up ranging from 10 to 55 months. Hubbard and associates[19] reported no cataract development following LSV for a mixed population of stage 4A and 4B ROP with a median follow-up of 13 months (range, 6 to 27 months).

Reported visual outcomes following LSV for stage 4A and stage 4B are excellent and compare favorably to the outcomes for scleral buckling procedures outlined above. Capone and Trese[17] reported fixation behavior (central steady maintained) in 36 of 40 eyes (90%) at a mean of 12 months following LSV for stage 4A. Comparing visual results for stage 4A to stage 4B, Hubbard and coworkers[19] found vision of fix-and-follow in 19 of 25 eyes (76%) with stage 4A and 10 of 12 eyes (83%) with stage 4B. Formalized vision testing in former premature infants is difficult because of the frequent comorbidities encountered, particularly severe developmental delay due to prior intraventricular hemorrhage and the long follow-up required for maturation. Studying a cohort of 23 eyes of 20 children that could be tested, Prenner and coworkers[25] found an average logMAR visual acuity of 20/58. The eyes had all undergone previous successful LSV for stage 4A ROP, and the children were an average age of 3½ years at the time of vision testing.

The 2-port technique may prove problematic when switching hands and during sclerotomy closure, and as a result, some surgeons use the more familiar 3-port technique for LSV. Lakhanpal and coworkers[20,26-28] have reported the anatomic success rate, lens clarity outcomes, and visual outcomes following LSV.

TABLE 2. ANATOMIC SUCCESS RATES OF LENS-SPARING VITRECTOMY FOR RETINOPATHY OF PREMATURITY–RELATED RETINAL DETACHMENT

STUDY	STAGES*	ANATOMIC RESULTS
Capone[17] (2001)	4A	36/40 (90%)
Moshfeghi[18] (2004)	4A	30/32 (94%)
Hubbard[19] (2004)	4A, 4B	32/37 (86%)
Lakhanpal[20] (2005)	4A, 4B	92/108 (85%)
Yu[21] (2006)	4A, 4B	9/13 (69%)
Sears[22] (2007)	4A, 4B	8/9 (89%)
Rayes[23] (2008)	4B	18/24 (75%)

*Stage 4A, subtotal, macula-sparing retinal detachment; stage 4B, subtotal, macula-involving retinal detachment.

Anatomic Outcomes With 3-Port LSV

Lakhanpal and coworkers[20] reported the anatomic success rates of 108 consecutive eyes with stage 4 ROP (76 with stage 4B, 32 with stage 4A) that underwent 3-port LSV. The mean gestational age was 25.5 weeks and mean weight 815 grams. Ninety-two of 108 eyes (85%) achieved complete retinal reattachment with a single surgical procedure. Ninety-four percent were attached with additional surgical procedures of either a second LSV or vitrectomy with lensectomy.

Lens Clarity With 3-Port LSV

In addition, Lakhanpal and associates[27] examined whether 3-port LSV maintained lens clarity over the first few years of visual development. In a review of the same cohort of patients, 94% of lenses remained clear at an average follow-up of 32 months. The most frequent associations with cataract formation were found to be the use of postoperative tamponade agents, extensive anterior dissection for lens-retina apposition, and instrument-lens touch.

Visual Outcomes With 3-Port LSV

The single most important outcome of ROP surgery is functional success. Lakhanpal and associates[28] addressed visual outcomes in patients with anatomic success and intact neurologic pathways. Thirty eyes of 26 patients were tested, 14 with stage 4A and 16 with stage 4B. For stage 4A, the mean visual acuity was 0.51 ± 0.09 (Snellen approximate 20/62) and for stage 4B, 1.03 ± 0.19 (Snellen approximate 20/200). These results are consistent with those previously reported by Prenner and colleagues,[25] who found an average visual acuity of 20/58 following successful 2-port LSV for stage 4A ROP.

This study is an effort to better characterize the factors contributing to functional success following 3-port LSV besides anatomy and lens clarity.

MYOPIA OF PREMATURITY AND RETINOPATHY OF PREMATURITY

The refractive power of the eye is determined by corneal curvature, anterior chamber depth, lens thickness, lens power, and axial length. Prematurity, in itself, is a risk factor for the development of myopia.[29,30] Eyes of premature infants[29,30] are found to have shallower anterior chambers, steeper (more powerful) corneas, and shorter axial lengths compared to term infants. The anterior chamber shallowing and corneal steepening more than offset the expected hypermetropia caused by shorter axial lengths, resulting in significantly myopic refractive errors.

Retinopathy of prematurity confers additional risk for the development of myopia. The CRYO-ROP study reported refractive outcomes, noting an increasing incidence of myopia with increasing severity of ROP: at 5 years of age, eyes without ROP had a 10% prevalence of myopia compared to 35% prevalence with moderate-acute ROP and an 82% prevalence with ROP residua (ie, straightened temporal vessels or macular heterotopia).[31] Clearly, the prevalence and severity of myopia increase with increasing levels of ROP severity and cicatrization. Hints in establishing the cause of this propensity to myopia have been gleaned from a study by Garcia-Valenzuela and Kaufman,[32] who compared a cohort of highly myopic eyes with a history of ROP to a group of similarly myopic eyes in full-term infants. The myopia in full-term infants was due to increasing axial length, whereas the premature infants had myopia predominantly due to increased lens power and thickness. Anterior chamber depth was the same in both cohorts.

The role of cryoablation and laser photocoagulation in the development of myopia is controversial. Although it is commonly understood that treated eyes are more myopic, the data do not support this conclusion. Comparing eyes treated with cryoablation to untreated, spontaneously regressed fellow eyes, the CRYO-ROP group found no difference in the distribution of refractive errors.[33] When controlling for the severity of ROP, there is no difference in the prevalence of myopia between cryoablation-treated and untreated eyes. Choi and coworkers[30] found an increasing incidence of myopia in proportion to the severity of ROP, but no difference in the degree of myopia related to the use of cryotherapy. Similarly, Nissenkorn and associates[34] reported a positive correlation between degree of myopia and the severity of cicatrical ROP, but no difference in the frequency and degree of myopia between cryoablated and spontaneously cicatrized eyes. In a small cohort of patients treated with cryoablation in only one eye, there was no influence on refractive error.[35] When comparing threshold laser-treated eyes to subthreshold untreated ROP, McLoone and associates[36] found more myopia in the treated cohort. It is likely, however, that eyes achieving threshold, a more advanced stage of

ROP, were more likely to become myopic than the subthreshold control group. It is clear that the prevalence and severity of myopia increase with the severity of ROP, but the influence of ablative treatment has no proven additive effect.

Confounding the issue are the findings of multiple studies that compare the refractive outcomes of cryoablation-treated eyes to those of laser ablation. Multiple investigators[37-41] have reported an increased prevalence and severity of myopia in eyes treated with cryoablation. Connolly and coworkers[41] found that the excess myopia was due to differences in anterior chamber depth and lens power/lens thickness rather than increased axial length. However, not all investigators agree with this difference. Paysse and coworkers[42] found no difference in refractive error between eyes treated with laser and cryoablation. Considering the evidence above, it seems likely that laser-treated eyes develop less myopia than might be expected when controlling for ROP disease severity. The data from Connolly and associates[41] hints at more complete emmetropization in laser-treated eyes.

In summary, myopia is a common problem in ROP eyes. The level of myopia increases with prematurity and the severity of ROP. Perhaps surprisingly, the myopia is not due to axial lengthening but to increased lens power/lens thickness and shallower anterior chamber depths. The impact of laser photoablation and cryotherapy is controversial, but the literature implies no additional risk of myopia with treatment if controlled for severity of ROP.

Although a great deal has been published regarding myopia due to prematurity and ROP, very little is understood to explain the pathoanatomy responsible for the observed differences in biometric values.

The Refractive Impact of Surgery for Retinopathy of Prematurity

Scleral buckling procedures are associated with high levels of myopia. Choi and Yu[43] reported myopia ranging from -20.0 D to -27.5 D (average, -22.4 D) in treated eyes, which decreased to -14.5 D to -20.0 D (average, -17.1 D) after buckle removal 2 years later. Buckle removal decreased myopia by +5.3 D on average. This number is strikingly similar to the +5.5 D reduction in myopia reported by Chow and associates[11] following sectioning of scleral buckles. Although the high levels of myopia found in eyes treated for ROP-related retinal detachments surely correlate with the severity and cicatrization of the disease, there is clearly an excess of myopia due to the scleral buckling procedure. Little is known about the refractive outcomes of LSV for ROP.

HYPOTHESIS

The present study examines the refractive outcomes of LSV for subtotal ROP-related retinal detachments. Lens-sparing vitrectomy may induce less myopia and lead to better refractive outcomes.

METHODS AND MATERIALS

Institutional Review Board approval was obtained for this study. This is a retrospective, nonrandomized, comparative (paired eye) study. The records were reviewed of 102 patients who underwent LSV for ROP-related retinal detachments from February 1998 through January 2004.

Entrance criteria consisted of previous complete ablative laser at threshold ROP in both eyes, followed by LSV in one eye only for a stage 4A traction retinal detachment, with both eyes having subsequently maintained complete retinal attachment. Main outcome variables were cycloplegic refraction, keratometry, and A-scan values for axial length, lens thickness, anterior chamber depth, and calculated lens power.

All infants received adequate laser photocoagulation in both eyes and were vascularly quiescent prior to treatment with LSV. Eyes with subtotal, macula-sparing detachments (stage 4A) were identified by indirect funduscopy preoperatively by the author. Contralateral eyes were also examined to exclude retinal detachments. A primary, standard 3-port LSV in eyes with stage 4A retinal detachments was performed in all cases by the author.

The surgical technique involves standard conjunctival opening for a 3-port vitrectomy followed by a single sclerotomy placed 1 mm posterior to the limbus in the inferotemporal quadrant. The incision path of the microvitreoretinal blade is oriented parallel to the visual axis and is advanced only until the widest portion of the blade cuts the pars plicata epithelium to avoid damaging the retina immediately behind the sclerotomy. After incision, a 7-0 Vicryl suture is placed across the sclerotomy. Then a 2.5-mm, 20-gauge infusion cannula is inserted into the eye and tied in place. Supporting the sclera during cannula insertion with toothed forceps ensures that the short tip penetrates the pars plicata epithelium fully. The infusion cannula tip position is confirmed with the endoilluminator prior to turning on the infusion line. Additional sclerotomies are made in the superonasal and superotemporal quadrants 1 mm posterior to the limbus. A standard 20-gauge endoilluminator and Accurus Innovit probe (Alcon Surgical, Fort Worth, Texas) are used for vitrectomy. Vitreous and membranes are removed with machine settings of 1200 to 1800 cuts per minute and 150 to 200 mm Hg suction. Gas-forced infusion settings for intraocular pressures are 20 mm Hg, as higher pressures frequently close the central retinal artery or blanche the optic nerve head in these infants.[20]

Surgical planes of vitreous are addressed in the following order: (1) ridge/retina to lens/anterior hyaloid face, (2) ridge to ridge, (3) ridge to nerve, (4) ridge to vitreous base, and (5) circumferential along the ridge. Most dissection is carried out with the vitrectomy probe, but intraocular scissors are occasionally used, particularly to begin dissection of the anterior trough. Layers of sheet-like vitreous membranes are dissected sequentially approaching the retina. The posterior hyaloid face is often nondissectible and cannot be removed. The ridge may have peripheral vitreous attachments that require careful segmentation so as to not cause iatrogenic retinal tears. This is done to ensure that no attachment to the ridge remains. A thorough peripheral retinal examination with scleral depression is then performed. No LSV had a retinal break, so no tamponade agents were used in any patient in this series.[20] No surgical, laser, or cryotherapy treatment was performed on either eye following the primary LSV.

Minimum postoperative follow-up included at least one clinic visit per month for 6 months, then every 3 to 6 months thereafter.

All eyes were examined by the author at each postoperative visit. Ocular biometric data were obtained prior to dilation on both eyes of all infants using a Zeiss A-scan. Cycloplegic refraction was obtained using streak retinoscopy 30 minutes following administration of cyclopentolate 1% ophthalmic solution.

This was a retrospective study with no prior data available for sample size estimation. For statistical analysis, the mean and standard deviations were obtained, and the Wilcoxon rank test was used to compare results for statistical significance. A probability value less than .05 was considered statistically significant. The nonparametric test was chosen because with the small sample size, the normalcy of data could not be confirmed. Using the thin lens vergence formula, predicted refraction was calculated using the obtained biometric data, where P (lens power), AL (axial length), ACD (anterior chamber depth), K (corneal power/keratometry), CR (cycloplegic refraction), and V (vertex distance) are used as follows:

$$P = \frac{1336}{AL-ACD} - \frac{1336}{\dfrac{1336}{\dfrac{1000}{\dfrac{1000}{CR}-V}-K}-ACD}$$

Varying the different parameters of paired eyes and back-calculating for differing refractive errors, the estimated impact of biometric differences was calculated.

RESULTS

Nine patients (5 male, 4 female) met the inclusion criteria. All eyes maintained complete retinal reattachment/attachment during the study period. No retinal breaks were identified intraoperatively in the LSV eyes, and as a result, no eye required gas or oil tamponade. Cataractous lens changes were observed during the study period.

The average age at biometric testing was 3.9 years (range, 2.25 to 4.25 years). The interval from LSV surgery to biometric testing was 3.6 years. The right eye had been the operative eye in 5 of 9 patients. The cycloplegic retinoscopy data are presented in Table 3. In all patients, the eye that had undergone LSV was less myopic than the control eye (Figure 1). The average spherical equivalent was -6.78 D for LSV eyes compared to -10.3 D for control eyes, yielding an average of 4.5 D less myopia in LSV eyes (*P* < .005). Two of 9 patients had ≥5 D of anisometropia.

TABLE 3. REFRACTIVE DATA FOR LASER/LENS-SPARING VITRECTOMY PAIRED EYES

PATIENT	AGE (yr)	EYE	TREATMENT	CR (diopters)
1	2.25	OD	LSV	-7.25
		OS	Laser	-11.00
2	2.67	OD	Laser	-9.25
		OS	LSV	-6.75
3	3	OD	LSV	-6.50
		OS	Laser	-9.00
4	3.25	OD	LSV	-7.25
		OS	Laser	-10.50
5	3.5	OD	Laser	-11.50
		OS	LSV	-6.25
6	3.67	OD	Laser	-10.25
		OS	LSV	-7.25
7	4.08	OD	Laser	-9.50
		OS	LSV	-6.50
8	4.17	OD	LSV	-7.50
		OS	Laser	-12.50
9	4.25	OD	LSV	-5.75
		OS	Laser	-9.50

CR, cycloplegic retinoscopy; LSV, lens-sparing vitrectomy; OD, right eye; OS, left eye.

Raw biometric data are presented in Table 4 and mean biometric data in Table 5. Keratometry data showed significantly steeper corneas in control eyes, with LSV values of 43.89 D ± 0.253 compared to 44.20 D ± 0.265 for controls (*P* < .005). Interestingly, there was no difference in axial lengths between the groups, with measurements of 24.26 mm ± 0.79 and 24.17 mm ± 0.599 for LSV and controls, respectively. There was a significant difference in lens thickness between the two groups, with increased lens thickness in the LSV group (3.85 ± 0.32 vs 3.74 ± 0.31, *P* < .005). There was a highly significant difference in anterior chamber depth between the two groups, with measurements for LSV of 3.81 mm ± 0.217 compared to 2.96 mm ± 0.232 (*P* < .005) (Figure 2).

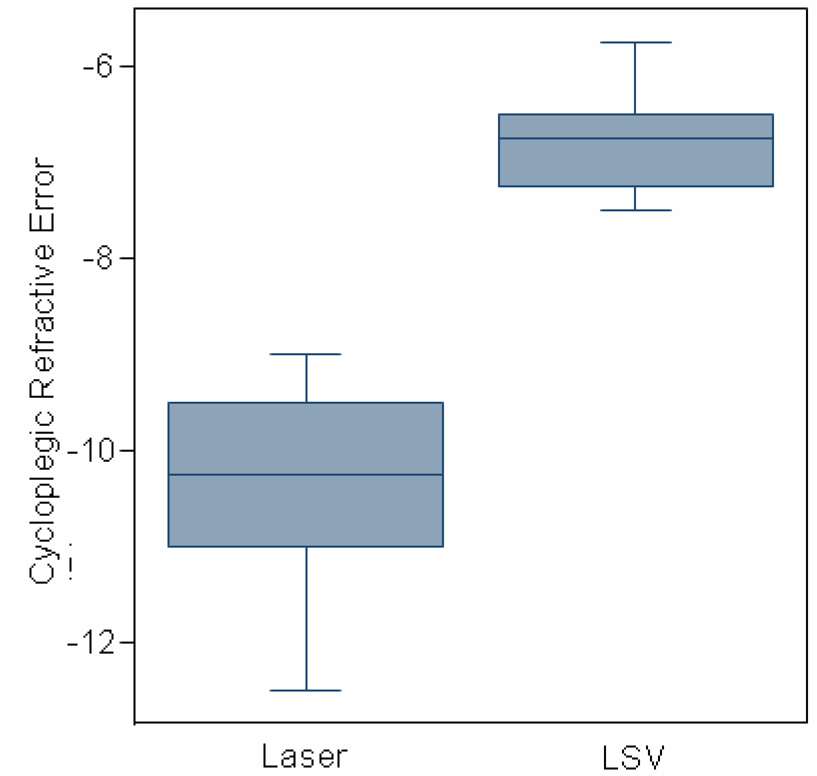

FIGURE 1

Cycloplegic refraction in laser and lens-sparing vitrectomy groups.

TABLE 4. RAW BIOMETRIC DATA FOR LASER/LENS-SPARING VITRECTOMY PAIRED EYES

PATIENT	EYE	TREATMENT	KERATOMETRY (D)	AXIAL LENGTH (mm)	LENS THICKNESS (mm)	LENS POWER (D)	ANTERIOR CHAMBER DEPTH (mm)
1	OD	LSV	44.25	23.55	3.74	23.33	3.45
	OS	Laser	44.50	23.67	3.62	22.78	2.98
2	OD	Laser	44.15	24.12	3.61	24.12	2.88
	OS	LSV	43.80	23.88	3.67	23.78	3.66
3	OD	LSV	44.10	23.45	3.32	23.56	3.76
	OS	Laser	44.55	23.65	3.21	23.32	2.76
4	OD	LSV	43.71	24.12	3.57	22.67	3.72
	OS	Laser	44.33	24.43	3.45	22.14	3.02
5	OD	Laser	44.25	23.78	3.78	22.34	2.57
	OS	LSV	44.20	24.13	3.83	22.71	3.77
6	OD	Laser	43.66	23.47	3.77	22.34	2.85
	OS	LSV	43.56	23.55	3.92	22.55	3.85
7	OD	Laser	44.22	24.36	3.98	22.03	2.98
	OS	LSV	44.05	24.78	4.13	22.33	3.82
8	OD	LSV	43.67	25.22	4.22	22.45	4.02
	OS	Laser	44.00	24.88	4.10	22.16	3.23
9	OD	LSV	43.75	25.67	4.33	21.45	4.22
	OS	Laser	44.20	25.22	4.18	21.05	3.34

D, diopter; LSV, lens-sparing vitrectomy; OD, right eye; OS, left eye.

TABLE 5. MEAN BIOMETRIC DATA FOR LASER/LENS-SPARING VITRECTOMY GROUPS

TREATMENT GROUP	LENS-SPARING VITRECTOMY	LASER	*P* VALUE*
Cycloplegic refraction (D)	-6.78 ± 0.57	-10.33 ± 1.17	<.005
Keratometry (D)	43.89 ± 0.25	44.20 ± 0.26	<.005
Axial length (mm)	24.26 ± 0.79	24.17 ± 0.59	NS
Lens thickness (mm)	3.85 ± 0.32	3.74 ± 0.31	<.005
Lens power (D)	22.76 ± 0.71	22.48 ± 0.86	.025
Anterior chamber depth (mm)	3.81 ± 0.21	2.96 ± 0.23	<.005

D, diopters; NS, not significant.
*Wilcoxon rank test.

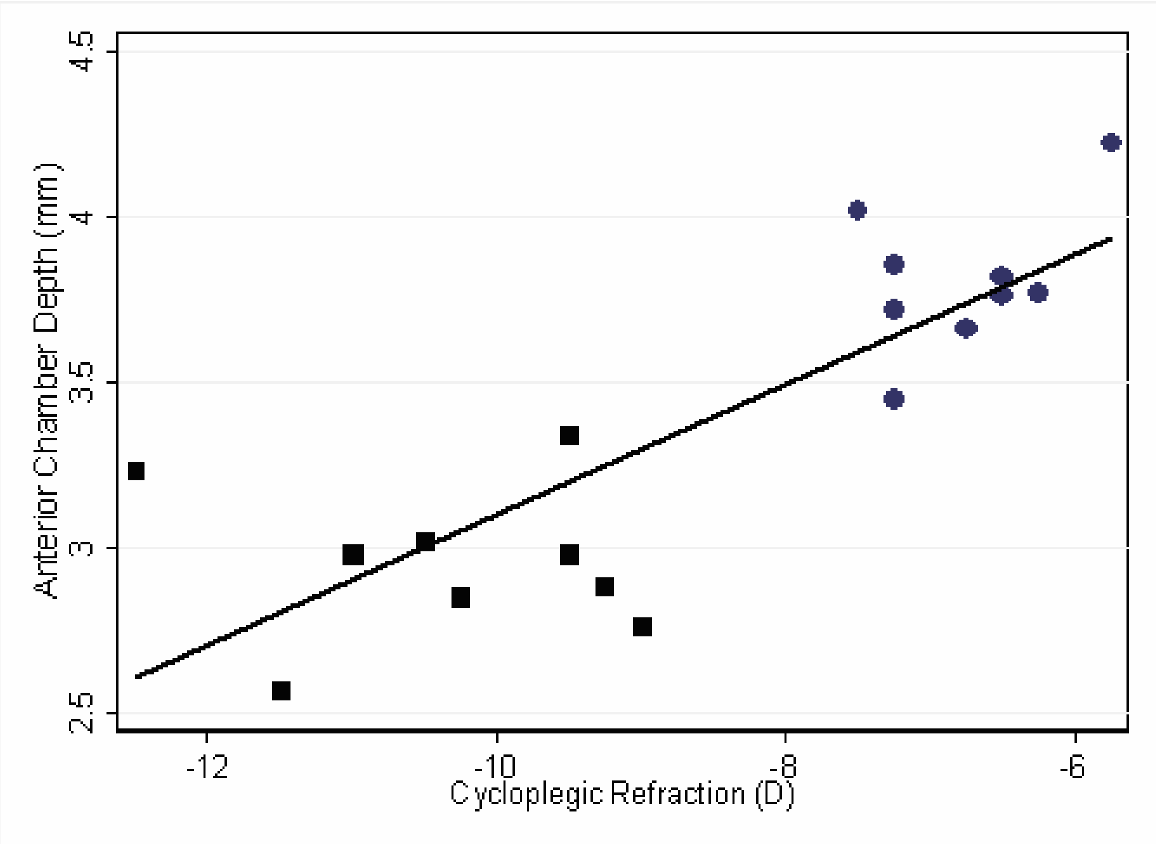

FIGURE 2

Refraction vs anterior chamber depth in laser (squares) and lens-sparing vitrectomy (circles) groups.

DISCUSSION

This thesis represents a logical continuation of the study of 3-port LSV for ROP-related retinal detachments. Having established an 85% anatomic success rate for the procedure for a mixed population of 4A and 4B traction retinal detachments,[20] further investigation established that the overwhelming majority (94%) of lenses stay clear during the early amblyopia risk period following 3-port LSV.[27] Functional results yielded a mean visual acuity of 20/62 for stage 4A and 20/200 for stage 4B for a subgroup of patients in whom visual acuity could be determined.[28] This report addresses the hypothesis that 3-port LSV may limit induced myopia of prematurity and ROP.

The refractive power of the eye is determined by corneal curvature (power), anterior chamber depth, lens thickness/lens power, and axial length. It remains unclear which among these variables are the major determinants of myopia in ROP. Most investigators agree that reduced anterior chamber depth with concomitant increased lens thickness and power is the major causative factor rather than increased corneal power or longer axial lengths.[32,36,41] In comparison to data of Garcia-Valenzuela and Kaufman,[32] this study's treatment and control groups both had slightly longer axial lengths than the previously reported ROP group (24.3 mm and 24.2 mm vs 23.4 mm), but both were significantly shorter than the 27.0 mm found in full-term myopic controls. The anterior chamber depth comparison between their ROP group and the control (laser) group of this study was strikingly similar with values of 2.80 mm and 2.95 mm, respectively. Eyes treated by LSV have significantly deep anterior chamber measurements of 3.80 mm compared with their full-term control value of 3.54 mm. It then follows that although LSV does not significantly alter the axial length, it significantly deepens the anterior chamber to values similar to those seen in full-term myopic infants. The question then arises as to whether the difference in anterior chamber depth in the LSV cohort is due to a difference in lens thickness or lens location. The data indicate that LSV eyes had thicker lenses than control eyes, so it follows then that the difference in lens position had a greater impact on final refractive power than the difference in lens power. The lens position was significantly more posterior in LSV-treated eyes. Via lens effectivity, a crystalline lens that is moved farther toward the retina will have less effective power and, therefore, reduce myopia or increase hyperopia.

It is difficult to compare long-term refractive outcomes of scleral buckling surgery to the current data set for LSV eyes. Although the average refractive error following buckling and buckle sectioning was -5.7 D in one study[12] (-6.78 D for LSV in the current study), the heterogeneity of induced myopia varies greatly in this population based on ROP severity. It may be that eyes that had undergone scleral buckling in this series had less severe cicatrization, membrane formation, and retinal detachment causing a selection bias. As such, one cannot draw any comparative conclusion from previous reports and the current study.

By employing the biometric data and using the vergence formula, the amount of refractive difference between LSV and control eyes could be established for each biometric parameter (Table 6). The major difference maker was the anterior chamber depth, which accounted for 32% to 87% (average 56%) of the refractive difference in these patients. There was a minor impact from reduced corneal power of 1% to 22% (average 12%).

TABLE 6. REFRACTION CHANGE BY BIOMETRIC PARAMETER

PATIENT	REFRACTION (D)			AMOUNT OF REFRACTION (D) EXPLAINED BY DIFFERENCE IN	
	LASER	LSV	DIFFERENCE	ACD	K
1	-11.00	-7.25	3.75	1.20 (32%)	0.33 (8%)
2	-9.25	-6.75	2.50	1.68 (67%)	0.44 (17%)
3	-9.00	-6.50	2.50	2.18 (87%)	0.56 (22%)
4	-10.50	-7.25	3.25	1.21 (37%)	0.80 (24%)
5	-11.50	-6.25	5.25	2.97 (56%)	0.07 (1%)
6	-10.25	-7.25	3.00	2.55 (85%)	0.13 (4%)
7	-9.50	-6.50	3.00	1.79 (59%)	0.22 (7%)
8	-12.50	-7.50	5.00	1.89 (38%)	0.45 (9%)
9	-9.50	-5.75	3.75	1.68 (45%)	0.57 (15%)

ACD, anterior chamber depth; D, diopters; K, corneal power; LSV, lens-sparing vitrectomy.

There is one report of a patient similar to this cohort in the literature. Moshfeghi and associates[44] reported a case of ROP treated with diode laser in both eyes at threshold ROP. One eye subsequently detached and was treated with 2-port LSV. Refraction was -6.50 + 0.50 × 045 in the LSV-treated eye and -10.25 + 0.75 × 125 in the laser-only eye. Both eyes achieved a final visual acuity of 20/40 using Allen figures. The fact that LSV was less myopic than the fellow laser-only eye is consistent with the current data. Unfortunately, the investigators did not include further biometric data in their report.

Several theories have been suggested to explain the biometric changes observed in myopia of prematurity. One such theory was that arrested development of the anterior segment by ROP interrupts the normal emmetropization process. Prior to birth, the lens is very thick, the anterior chamber shallow, and the cornea steep. Following birth, emmetropization involves thinning of the lens, deepening of the anterior chamber, and flattening of the cornea. If this process fails to unfold naturally, it might serve to explain the thicker lenses and shallower anterior chambers found in ROP eyes.[45] Exactly how ROP might cause this arrest is unknown, but speculation involves unknown “trophic factors” and tractional elements.[46] How, then, in this context, are we to interpret the data? There are several possible avenues for exploration. It is intriguing to consider whether LSV unblocks arrested anterior segment development, thereby allowing some parts of emmetropization to occur. Lens-sparing vitrectomy eyes in this study did have much deeper anterior segments, similar to those of full-term controls, without any change in lens thickness. Also, the cornea was less steep in LSV eyes. If interrupted emmetropization is due to trophic factor, up-regulation, or down-regulation, then LSV might serve to increase diffusion of oxygen, or other factors to the anterior segment, or the surgery may serve to wash out a reservoir of signaling factors from the vitreous.[46]

Differences in traction[46] seem less likely to explain the differences observed as the control group did not have traction retinal detachments. As stated above, myopia of ROP correlates well with disease severity; and as a result, LSV eyes with retinal detachments would be expected to be more myopic than less diseased controls. The data proved the opposite.

Another explanation of these results may be that the biometric data obtained are due to a direct mechanical result of LSV. The infant vitreous is a highly organized, thickly gelatinous extracellular matrix. Removal of the core vitreous may allow the lens to fall posteriorly, moving the lens-iris diaphragm away from the cornea and deepening the anterior chamber. It seems unlikely that the corneal flattening observed is due to scleral sutures. Comparing the current cohort to a new set of eyes following sutureless small-gauge LSV will answer the question regarding corneal curvature in the future.

While the underlying mechanism behind the biometric differences is unclear, it is felt that they are clinically significant. Achieving good anatomic outcomes in these patients is only half the battle. Ultimately, the goal is to improve functional/visual outcomes. The reduction in myopia following LSV may partly explain the encouraging visual outcome data presented here. By avoiding anisometropia, so common with unilateral scleral buckling and vitrectomy with lensectomy procedures, it is believed that LSV may significantly reduce the impact of anisometropic amblyopia. One concern is that the more emmetropic LSV eye may be preferred over the laser/control eye, resulting in amblyopia in the eye without prior retinal detachment. Further investigation to answer this question is ongoing, since accurate visual outcomes are better assessed as these patients mature.

There are limitations to this study. A larger cohort of patients would further strengthen the data and perhaps provide more insight into any keratometric differences between the groups. The data were derived from a single time point in development. Indeed, the interval from surgery to testing ranged from 2.0 to 4.0 years (average, 3.6 years), although the difference in refractive error does not seem to increase or decrease with increasing postoperative intervals. Additional time points and different ages would provide evidence as to whether the differences observed will be maintained or change as children age and grow. Most of the ocular growth is complete by age 3, and average age at last follow-up was 32 months in this study; but in the setting of ROP, biometrics may continue to change.

In conclusion, the data suggest that infant eyes undergoing LSV for stage 4A ROP develop less myopia than fellow eyes treated with laser alone. This difference in refraction is due to posterior displacement of the lens-iris diaphragm and increased anterior chamber depth in the LSV group. Future study will add both patients and new time points to the data in an effort to better understand the effects of 3-port LSV in the hopes of improving visual outcomes in the future.

ACKNOWLEDGMENTS

Funding Support: None.

Financial Disclosures: None.

Conformity With Author Information: The study was approved by the Institutional Review Board of Baylor College of Medicine, Houston, Texas.

Other Acknowledgements: The author wishes to thank Rohit R. Lakhanpal, MD, Jed Poll, MD, and Mitchell P. Weikert, MD, of Baylor College of Medicine, Houston, Texas, for their assistance with data collection and statistics. I also sincerely thank Petros E. Carvounis, MD, Dan B. Jones, MD, and Kirk R. Wilhelmus, MD, of Baylor College of Medicine, for reviewing this thesis and providing helpful suggestions.

REFERENCES

1. McPherson A, Hittner HM. Scleral buckling in 2½- to 11-month-old premature infants with retinal detachment associated with acute retrolental fibroplasia. *Ophthalmology* 1979;86:819-836.
2. McPherson AR, Hittner HM, Lemos R. Retinal detachment in young premature infants with acute retrolental fibroplasia. Thirty-two new cases. *Ophthalmology* 1982;89:1160-1169.
3. Topilow HW, Ackerman AL, Wang FM. The treatment of advanced retinopathy of prematurity by cryotherapy and scleral buckling surgery. *Ophthalmology* 1985;92:379-387.
4. Greven C, Tasman W. Scleral buckling in stages 4B and 5 retinopathy of prematurity. *Ophthalmology* 1990;97:817-820.
5. Noorily SW, Small K, de Juan E Jr, Machemer R. Scleral buckling surgery for stage 4B retinopathy of prematurity. *Ophthalmology* 1992;99:263-268.
6. Trese MT. Scleral buckling for retinopathy of prematurity. *Ophthalmology* 1994;101:23-26.
7. Ricci B, Santo A, Ricci F, Minicucci G, Molle F. Scleral buckling surgery in stage 4 retinopathy of prematurity. *Graefes Arch Clin Exp Ophthalmol* 1996;234:S38-S41.
8. Hinz BJ, de Juan E Jr, Repka MX. Scleral buckling surgery for active stage 4A retinopathy of prematurity. *Ophthalmology* 1998;105:1827-1830.
9. Chuang YC, Yang CM. Scleral buckling for stage 4 retinopathy of prematurity. *Ophthalmic Surg Lasers* 2000;31:374-379.
10. Hartnett ME, Maculuri S, Thompson HW, McColm JR. Comparison of retinal outcomes after scleral buckle or lens-sparing vitrectomy for stage 4 retinopathy of prematurity. *Retina* 2004;24:753-757.
11. Repka MX, Tung B, Good WV, et al. Outcome of eyes developing retinal detachment during the early treatment for retinopathy of prematurity study (ETROP). *Arch Ophthalmol* 2006;124:24-30.
12. Chow DR, Ferrone PJ, Trese MT. Refractive changes associated with scleral buckling and division in retinopathy of prematurity. *Arch Ophthalmol* 1998;116:1446-1448.
13. Zilis JD, de Juan E, Machemer R. Advanced retinopathy of prematurity. The anatomic and visual results of vitreous surgery. *Ophthalmology* 1990;97:821-826.
14. Quinn GE, Dobson V, Barr CC, et al. Visual acuity in infants after vitrectomy for severe retinopathy of prematurity. *Ophthalmology* 1991;98:5-13.

15. Quinn GE, Dobson V, Barr CC, et al. Visual acuity of eyes after vitrectomy for retinopathy of prematurity. Follow-up at 5-1/2 years. *Ophthalmology* 1996;103:595-600.
16. Maguire AM, Trese MT. Lens-sparing vitreoretinal surgery in infants. *Arch Ophthalmol* 1992;110:284-286.
17. Capone A Jr, Trese MT. Lens-sparing vitreous surgery for tractional stage 4A retinopathy of prematurity retinal detachments. *Ophthalmology* 2001;108:2068-2070.
18. Moshfeghi AA, Banach MJ, Salam GA, Ferrone PJ. Lens-sparing vitrectomy for progressive tractional retinal detachments associated with stage 4A retinopathy of prematurity. *Arch Ophthalmol* 2004;122:1816-1818.
19. Hubbard GB III, Cherwick DH, Burian G. Lens-sparing vitrectomy for stage 4 retinopathy of prematurity. *Ophthalmology* 2004;111:2274-2277.
20. Lakhanpal RR, Sun RL, Albini TA, Holz ER. Anatomic success rate after 3-port lens-sparing vitrectomy in stage 4A or 4B retinopathy of prematurity. *Ophthalmology* 2005;112:1569-1573.
21. Yu YS, Kim SJ, Kim SY, Choung HK, Park GH, Heo JW. Lens-sparing vitrectomy for stage 4 and stage 5 retinopathy of prematurity. *Korean J Ophthalmol* 2006;20:113-117.
22. Sears JE, Sonnie C. Anatomic success of lens-sparing vitrectomy with and without scleral buckle for stage 4 retinopathy of prematurity. *Am J Ophthalmol* 2007;143:810-813.
23. Rayes EN, Vinekar A, Capone A Jr. Three-year anatomic and visual outcomes alter vitrectomy for stage 4B retinopathy of prematurity. *Retina* 2008;28:568-572.
24. Ferrone PJ, Harrison C, Trese MT. Lens clarity after lens-sparing vitrectomy in a pediatric population. *Ophthalmology* 1997;104:273-278.
25. Prenner JL, Capone A Jr, Trese MT. Visual outcomes after lens-sparing vitrectomy for stage 4A retinopathy of prematurity. *Ophthalmology* 2004;111:2271-2273.
26. Lakhanpal RR, Sun RL, Albini TA, Holz ER. Anatomical success rate after primary three-port lens-sparing vitrectomy in stage 5 retinopathy of prematurity. *Retina* 2006;26:724-728.
27. Lakhanpal RR, Davis GH, Sun RL, Albini TA, Holz ER. Lens clarity after 3-port lens-sparing vitrectomy in stage 4A and 4B retinal detachments secondary to retinopathy of prematurity. *Arch Ophthalmol* 2006;124:20-23.
28. Lakhanpal RR, Sun RL, Albini TA, Coffee R, Coats DK, Holz ER. Visual outcomes after 3-port lens-sparing vitrectomy in stage 4 retinopathy of prematurity. *Arch Ophthalmol* 2006;124:675-679.
29. Cook A, White S, Batterbury M, Clark D. Ocular growth and refractive error development in premature infants without retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2003;44:953-960.
30. Choi MY, Park IK, Yu YS. Long term refractive outcome in eyes of preterm infants with and without retinopathy of prematurity: comparison of keratometric value, axial length, anterior chamber depth, and lens thickness. *Br J Ophthalmol* 2000;84:138-143.
31. Quinn GE, Dobson V, Kivlin J, et al, for the Cryotherapy for Retinopathy of Prematurity Cooperative Group. Prevalence of myopia between 3 months and 5-1/2 years in preterm infants with and without retinopathy of prematurity. *Ophthalmology* 1998;105:1292-1300.
32. Garcia-Valenzuela E, Kaufman LM. High myopía associated with retinopathy of prematurity is primarily lenticular. *J AAPOS* 2005;9:121-128.
33. Quinn GE, Dobson V, Siatkowski M, et al, for the Cryotherapy for Retinopathy of Prematurity Cooperative Group. Does cryotherapy affect refractive error? Results from treated versus control eyes in The Cryotherapy for Retinopathy of Prematurity Trial. *Ophthalmology* 2001;108:343-347.
34. Nissenkorn I, Yassur Y, Mashkowski D, Sherf I, Ben-Sira I. Myopia in premature babies with and without retinopathy of prematurity. *Br J Ophthalmol* 1983;67:170-173.
35. Seiberth V, Knorz MC, Trinkmann R. Refractive errors after cryotherapy in retinopathy of prematurity. *Ophthalmologica* 1990;201:5-8.
36. McLoone EM, O'Keefe M, McLoone SF, Lanigan BM. Long-term refractive and biometric outcomes following diode laser therapy for retinopathy of prematurity. *J AAPOS* 2006;10:454-459.
37. Algawi K, Goggin M, O'Keefe M. Refractive outcome following diode laser versus cryotherapy for eyes with retinopathy of prematurity. *Br J Ophthalmol* 1994;78:612-614.
38. Knight-Nanan DM, O'Keefe M. Refractive outcome in eyes with retinopathy of prematurity treated with cryotherapy or diode laser: 3 year follow up. *Br J Ophthalmol* 1996;80:998-1001.
39. Laws F, Laws D, Clark D. Cryotherapy and laser treatment for acute retinopathy of prematurity: refractive outcomes and longitudinal study. *Br J Ophthalmol* 1997;81:12-15.
40. 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;34:83-87.
41. Connolly BP, Ng EY, McNamara JA, Regillo CD, Vander JF, Tasman W. A comparison of laser photocoagulation with cryotherapy for threshold retinopathy at prematurity at 10 years. Part 2. Refractive outcome. *Ophthalmology* 2002;109:936-941.
42. Paysse EA, Lindsey JL, Coats DK, Contant CF Jr, Steinkuller PG. Therapeutic outcomes of cryotherapy versus transpupillary diode laser photocoagulation for threshold retinopathy of prematurity. *J AAPOS* 1999;4:234-240.
43. Choi MY, Yu YS. Efficacy of removal of buckle after scleral buckling surgery for retinopathy of prematurity. *J AAPOS* 2000;4:362-365.

44. Moshfeghi AA, Awner S, Salam GA, Ferrone PJ. Excellent visual outcome and reversal of dragging after lens sparing vitrectomy for progressive tractional stage 4A retinopathy of prematurity retinal detachment. *Retina* 2004;24:615-616.
45. Cook A, White S, Batterbury M, Clark D. Ocular growth and refractive error development in premature infants with or without retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2008;49:5199-5207.
46. Fielder AR, Quinn GE. Myopia of prematurity: nature, nurture, or disease? *Br J Ophthalmol* 1997;81:2-3.