Refractive Surgery in Children: Is It Ready for Prime Time?

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ABSTRACT

Introduction: Potential indications for excimer laser procedures in children include accommodative esotropia, bilateral high ametropia, and severe anisometropia. Treatment of these conditions has traditionally included spectacle or contact lens use. This treatment, however, is often ineffective in children with severe anisometropia or bilateral ametropia, especially those with neuropsychological disorders. Refractive surgery may be a viable treatment option for these conditions.

Methods: The visual and refractive results from our studies on photorefractive keratectomy for pediatric anisometropic amblyopia are discussed. Also, I will present a review of the world literature on excimer laser procedures for accommodative esotropia, pediatric high anisometropia, and pediatric bilateral high ametropia.

Results: In our study, at 36 months follow-up, 7 of 9 patients who were able to perform psychophysical acuity testing preoperatively had improvement of two or more lines of uncorrected visual acuity and 6 of 9 had improvement of two or more lines of best corrected visual acuity. Fifty percent of the myopic patients and 100% of the hyperopic patients were within 2 D of refractive target at the 36-month follow-up visit. Refractive error stability has been good and corneal haze has been minimal.

Conclusions: Refractive surgery in children to reduce amblyopiogenic levels of refractive error is proving to be relatively stable. Best corrected and uncorrected visual acuity has also been shown to improve following the excimer laser procedures. Refractive surgery also appears to be effective for pure accommodative esotropia. Randomized clinical trials are needed to fully establish safety and efficacy. Other refractive procedures, such as clear lens extraction and phakic intraocular lenses, may also prove to be valid treatment options for these conditions in the future.

INTRODUCTION

Twenty years from now we may be saying, “Certain types of amblyopia are surgical diseases.” In the future, as alien as it may currently sound, refractive surgery may be the best treatment for severe anisometropia and severe bilateral ametropia. We are standing on a frontier where a rev-
olutionary new treatment strategy for amblyopia has the real potential to come to fruition. We may be on the verge of a paradigm shift.

Treatments for refractive error have been around for a very long time. Spectacle correction has been in use since the thirteenth century, but most other refractive treatments have come along in the last 150 years. Contact lenses were introduced in 1888. Modern surgical treatment for refractive error began with radial keratotomy in the 1970s, followed by epikeratophakia in the 1980s. Both of these procedures have been supplanted by newer and better procedures.

Since the early 1990s, excimer laser refractive procedures, including photorefractive keratectomy (PRK) laser in situ keratomileusis (LASIK), and, most recently, laser assisted subepithelial keratectomy (LASEK), have been used extensively in adults to correct refractive error. Conductive keratoplasty is being used to correct hyperopia and presbyopia with mixed results. Ophthalmologists outside of the United States and Canada have been performing clear lens extraction for extremely high refractive errors for the last twenty or more years, but in the United States, lensectomy for this purpose has only recently been used. Phakic intraocular lenses for high refractive error are currently being investigated in adults. Refractive correction, as we all know, greatly improves the quality of life of the affected person. Now that we have effective, predictable, and enduring good results from excimer laser procedures, there is a burgeoning popular interest in using these more permanent solutions for correcting refractive error rather than removable contact lenses or spectacles.

Does refractive surgery have a role in the treatment of refractive error in children? When attempting to answer this question, one must consider many issues. One must remember that the pediatric eye is growing and therefore may need more than one refractive procedure. We know that excimer refractive surgery in adults can cause corneal haze and keratectasia. What we still do not know in children is if the long-term corneal response to refractive surgery is different from that of the adult. Could multiple procedures that may be required in children cause more of the complications that have been reported in adults, like corneal haze and keratectasia? The good news from medium-term (3–4 years) results in children who have undergone PRK, LASIK, or LASEK is that corneal haze has been minimal and the refractive correction following these procedures has been relatively stable. We do not know, however, what will happen ten, twenty, or fifty years from now.

Regarding growth of the eye, a remarkable amount of refractive power change occurs in the first two years of life where roughly 90% of the growth of the eye occurs. The eye at birth has a mean corneal power of approximately 50 D, a mean lens power of 34 D, and a mean axial length of 17 mm. By two years of age, the eye loses approximately 20 D of its dioptric power through lens growth and corneal flattening, and it loses more from axial elongation. Approximately 90% of the growth of the eye has occurred by 2 years of age. Therefore, if one were to consider refractive surgical intervention as an option for certain conditions in childhood, two years of age would probably be the earliest reasonable age at which to consider it.

There are several potential areas for consideration of refractive surgery in children, which include accommodative esotropia, bilateral high refractive error (bilateral ametropia), and anisometropia with or without amblyopia. Possible refractive procedures to consider include: PRK, LASIK, LASEK, clear lens extraction, phakic intraocular lenses, and intrastromal corneal rings. Very little research has yet been published on clear lens extraction,
phakic intraocular lenses, and intrastromal corneal rings in children, so most of my discussion will focus on excimer laser procedures and my own personal experience with PRK for severe anisometropia in children.

REFRACTIVE SURGERY FOR ACCOMMODATIVE ESOTROPIA

A strong theoretical basis exists for considering refractive surgery as a potential treatment for accommodative esotropia. Accommodative esotropia is esotropia with a refractive etiology. As accommodation occurs in a patient with hyperopia and accommodative esotropia, there is an overabundant convergence response that results in esotropia. If the hyperopia could be reduced through a refractive procedure, then there should be a corresponding decrease in accommodation and a secondary decrease in accommodative convergence. In theory, it should work perfectly. Accommodative esotropia, however, occurs in many forms (pure refractive accommodative esotropia, partially accommodative esotropia, high accommodative convergence/accommodation ratio esotropia), which understandably appears to affect the outcome following refractive surgery.

There have been a handful of studies published thus far that deal with excimer refractive surgery for accommodative esotropia. All of these studies have only included adults and teenagers. Patients with lower levels of hyperopia (i.e., 5 D or less) and pure refractive accommodative esotropia experienced much better results with regards to ocular alignment following an excimer laser procedure (Table 1).

The potential issues/limitations of refractive surgery for accommodative esotropia include the following:

1. Hyperopia decreases with age. Therefore, the age at time of intervention might have to be in the late teens for maximum success.
2. Excimer refractive surgery at this point is not reliable for hyperopia of more than 5 D.
3. There is more postoperative corneal haze with high hyperopic refractive treatments than myopic refractive treatments, which could lead to a decrease in best-corrected visual acuity.
4. Normalizing the refractive error in this patient population could lessen the magnitude of the esotropia to a microtropia and create monofixation syndrome. Because the child looks aligned to his parents, the parents could stop following up, and then the child could develop secondary amblyopia and lose stereopsis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Procedure</th>
<th>Age</th>
<th>Number of patients</th>
<th>Mean Preop SE (D)</th>
<th>% Success</th>
<th>F/u (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoyos</td>
<td>LASIK</td>
<td>Adults</td>
<td>9</td>
<td>+5.00</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>Nemet</td>
<td>LASIK</td>
<td>Adults</td>
<td>6</td>
<td>+3.00</td>
<td>100</td>
<td>36</td>
</tr>
<tr>
<td>Nucci</td>
<td>PRK</td>
<td>Adults</td>
<td>8</td>
<td>+3.70</td>
<td>100</td>
<td>12</td>
</tr>
<tr>
<td>Stidham</td>
<td>LASIK</td>
<td>Adults</td>
<td>27</td>
<td>+7.50</td>
<td>58</td>
<td>6</td>
</tr>
<tr>
<td>Sabetti</td>
<td>LASIK</td>
<td>Adults</td>
<td>18</td>
<td>—</td>
<td>94</td>
<td>24</td>
</tr>
<tr>
<td>Hittner</td>
<td>LASIK</td>
<td>Adolescents</td>
<td>15</td>
<td>+5.35</td>
<td>53% with 1 procedure</td>
<td>16</td>
</tr>
</tbody>
</table>

Adoles = adolescents, F/u = follow up, LASIK = laser in situ keratomileusis, PRK = photorefractive keratectomy
Many questions still remain regarding the possibility of treating accommodative esotropia with excimer refractive surgery:

1. How long should the refractive error be stable prior to undergoing a refractive procedure?
2. What is the maximum amount of hyperopia one should treat?
3. Is the preoperative sensory status important to success?
4. What is the youngest age at which these procedures should be considered for this problem?

The ideal patient with accommodative esotropia to consider for refractive surgery would be 13 years of age or older, have less than 5 D of hyperopia and good stereopsis, and have a stable refractive error. This ideal patient, however, is usually well controlled with glasses or contact lenses. Should we then intervene in this situation with a procedure that has the potential of causing corneal haze and a decrease in best-corrected visual acuity when the child is well treated with conventional therapy?

REFRACTIVE SURGERY FOR BILATERAL AMETROPIA

Another potential disorder that could be considered for treatment with refractive surgery is bilateral high ametropia. There have been several excimer laser pediatric refractive surgery studies that included children with high bilateral ametropia and developmental delay, cerebral palsy, or mental retardation who refused to wear refractive correction. These studies demonstrated a stable reduction in refractive error and no serious complications. In these studies, the authors also mentioned that there was an observable “improvement in quality of life” in these patients; however, this improvement was not formally evaluated. At our institution, we have performed refractive surgery on several such patients, who also had an excellent reduction in the refractive error and improvement in activities of daily living and social interaction.

The condition of high bilateral refractive error in developmentally challenged patients is an area in which refractive surgery could hold great potential promise. These children are frequently tactilely averse and subsequently often refuse to wear their glasses (and contact lenses are impractical). Additionally, because of their behavioral and/or cognitive deficits, they are very difficult to manage and follow. Bilateral high ametropia is becoming a relatively common problem as more and more former extremely premature infants with a history of severe retinopathy of prematurity are surviving with the sequelae of extreme myopia and developmental delay or cerebral palsy/mental retardation. This area deserves further investigation.

REFRACTIVE SURGERY FOR ANISOMETROPIC AMBLYOPIA

The conventional treatment for anisometropic amblyopia includes refractive correction with spectacles or contact lenses and forced use of the amblyopic eye using either occlusion therapy or pharmacologic and/or optical penalization. The success rate for this seemingly simple strategy overall ranges between 25–90% depending on the level of anisometropia and the definition of success, with most falling around 60%. It is also known that the success rate of standard therapy decreases with increasing anisometropia and that the severity of the amblyopia increases with increasing anisometropia.

There are several significant problems with conventional therapy for anisometropic amblyopia. Spectacles can cause aniseikonia or diplopia and are often cosmetically unacceptable. Contact lenses are difficult to insert, loss can be frequent, cost can be an issue, and there is an increased...
risk theoretically of microbial keratitis in children who can be less hygienic than adults. With occlusion therapy and optical penalization, compliance is the most important difficulty, and atropine side effects including photophobia and other anticholinergic side effects can be problematic when using pharmacologic penalization. One must also not forget about the known long-term negative psychosocial effects of all of these interventions.\textsuperscript{14–16}

Most of the published research to date on refractive surgery in children has dealt with anisometropia. Thus far, the results of excimer refractive surgery in approximately 220 children have been published in the literature. All children have shown good refractive error response, mild to excellent visual acuity improvement, and minimal or no complications.\textsuperscript{17–31}

How much anisometropia should a child have before considering refractive surgical intervention? This is an important question. We know that amblyogenic levels of anisometropia are 2 D anisomyopia, 1 D anisohyperopia, and 1.5 D anisocylindermia;\textsuperscript{31} however, most patients with this entry level of anisometropia do well with spectacles alone. From Kivlin’s data, anisometropia of 3 D or less was associated with good visual outcome with standard therapy.\textsuperscript{13} Success rates plummeted with more anisometropia to 25% with 6 D or more of anisometropia. There is no consensus yet with regards to how much anisometropia is acceptable before considering refractive surgery, but probably 4 D of anisometropia would be reasonable, based on data from Kivlin\textsuperscript{13} and the Amblyopia Treatment Studies.\textsuperscript{9, 10, 12}

To summarize briefly the results of all published studies to date on this subject, approximately 220 children have undergone excimer refractive surgical procedures for anisometropic amblyopia. The follow-up has ranged between 12 and 48 months. The age of the patients at time of treatment ranged between 2 and 19 years. All studies have shown a reliable refractive response to the laser procedure, mild to excellent improvement in visual acuity ranging between 2 and 7 lines of acuity improvement, and minimal complications (Table 2) (Figure 1).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>SUMMARY OF ALL PUBLISHED STUDIES ON EXCIMER LASER PROCEDURES FOR ANISOMETROPIC MYOPIA</th>
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</thead>
<tbody>
<tr>
<td>Procedure</td>
<td>Age (years)</td>
</tr>
<tr>
<td>Payse PRK</td>
<td>2–11</td>
</tr>
<tr>
<td>Astle PRK</td>
<td>6.3</td>
</tr>
<tr>
<td>Alio PRK</td>
<td>5–7</td>
</tr>
<tr>
<td>Singh PRK</td>
<td>10–15</td>
</tr>
<tr>
<td>Nucci Both</td>
<td>9–14</td>
</tr>
<tr>
<td>Nano PRK</td>
<td>11–14</td>
</tr>
<tr>
<td>Agarwal LASIK</td>
<td>5–11</td>
</tr>
<tr>
<td>Rashad LASIK</td>
<td>7–12</td>
</tr>
<tr>
<td>Tychsen PRK/L</td>
<td>4–16</td>
</tr>
<tr>
<td>O’Keefe LASIK</td>
<td>2–12</td>
</tr>
<tr>
<td>Nassaralla LASIK</td>
<td>8–15</td>
</tr>
<tr>
<td>Autrata PRK/L</td>
<td>4–7</td>
</tr>
<tr>
<td>Rybintseva LASIK</td>
<td>9–15</td>
</tr>
<tr>
<td>Hittner LASIK</td>
<td>8–19</td>
</tr>
</tbody>
</table>

BCVA = best corrected visual acuity, F/U = follow-up, LASIK = laser in situ keratomileusis, Post = postoperative, PRK = photorefractive keratectomy, Pre = preoperative, SE = spherical equivalent
At Baylor College of Medicine we have approached the idea of treating children with photorefractive keratectomy for anisometropic amblyopia very conservatively. Above all we wanted to not do harm. Therefore, we decided to conduct some preliminary studies. We first performed a retrospective study to determine risk factors in patients with anisometropic amblyopia that could predict failure with conventional therapy. We also performed a prospective study of corneal thickness in normal children to determine if the pediatric cornea was thick enough to undergo excimer refractive procedures, as there were no previously published normative data for children except for in infants. Then, we enrolled 11 patients in a prospective long-term interventional case series. These children had severe anisometropia with amblyopia and were noncompliant with conventional therapy. We followed them for corneal status, visual acuity, refractive error correction, treatment stability, and stereopsis. We now have follow-up for over four years on this group. The results from the three-year follow-up have been published and will be discussed here. The results have not changed at the four-year follow-up.

From the preliminary studies, we found that the significant risk factors for failure with conventional therapy for anisometropic amblyopia included anisastigmatism of ≥ 1.5 D, age > 6 years at the initiation of amblyopia therapy, poor compliance with amblyopia therapy, and initial visual acuity of less than 20/200. Regarding pediatric corneal thickness, pachymetry measurements reached adult levels by 2–4 years of age, and at no age was the cornea too thin to perform any excimer laser procedure currently in use.

In our prospective interventional case series, all myopic patients had an anisometropia of at least 6 D and all hyperopic patients had at least 4 D of anisohyperopia. They also had at least three lines of best-corrected visual acuity difference between the two eyes, and no significant abnormality of the macula, optic nerve, lens or cornea. The mean age at time of treatment was 6.1 years (2–11 years), the maximum refractive treatment for myopia was 11.5 D and for hyperopia was 5.25 D, even though some of the myopic children had preoperative refractive errors that were much higher (mean spherical equivalent in the myopic group of −13.57 and in the hyperopic group of +4.75 D). Nine children required general anesthesia because of cooperation issues. The protocol for general anesthesia has been published previously.

Corneal haze three years after the laser procedure was negligible with a mean corneal haze measurement of 0.3+ on a scale of 0 to 4+ where 0 meant the corneal was crystal clear and 4+ meant the cornea was totally opaque with no view of the iris detail. Refractive error response was good. Fifty percent of the myopic patients and 100% of the hyperopic patients were within 2 D of target. The reason the percentile was
lower for the myopic group was that the extremely high myopic children had a larger response than expected from the treatment dose. This larger than expected treatment response was actually beneficial as these patients’ eyes had −17 D and −22 D of spherical equivalent refractive error preoperatively (Figure 2).

Refractive error stability has also been quite good over the three-year follow-up period. In the myopic group, there was a mean regression of 2.50 D over the first 12 months, but thereafter it was stable up to the 36-month follow-up. The hyperopic group demonstrated regression over a longer period of time with a 1.10 D regression in the first 12 months and then 0.60 D more over the next two years.

Visual acuity improved in almost all patients. At the 36-month follow-up examination, 7 of the 9 patients who were able to perform psychophysical acuity testing preoperatively had an improvement of two or more lines in uncorrected visual acuity, and 6 of 9 had improvement of two or more lines of best corrected visual acuity (Figure 3). Our youngest participant was 2 years of age at treatment and had the most remarkable response. Preoperatively, he had anisomyopia of 13.75 D and a preoperative

vision in the affected eye of fix and follow. He was never compliant with spectacle wear or occlusion therapy before or after the PRK, and at his three-year postoperative follow-up, his refractive error was −0.75 D in the treated eye, his uncorrected visual acuity was 20/40 and his best corrected visual acuity was 20/30.

When compared to a noncompliant control group with similar levels of anisometropia, our PRK group demonstrated statistically significant best-corrected visual acuity improvement at a level of $P = 0.003$. Fifty-six percent of the orthotropic
group experienced a marked improvement in stereopsis as well. We are continuing to follow this group and beginning to treat others that qualify.

OTHER POTENTIAL REFRACTIVE TREATMENTS FOR CHILDREN

There are several other refractive surgical procedures that may become useful in children in the future. These include clear lens extraction, phakic intraocular lenses, and intrastromal corneal rings. Intrastromal corneal rings are not presently practical for children because they do not correct enough refractive error. Clear lens extraction has been used for years in Latin America for adults with extremely high refractive error with good results.38–42 Ali et al. recently reported excellent refractive and visual outcomes in children with high anisometropic myopia following refractive lensectomy.43 An important potential risk of clear lens extraction in children with high axial myopia is the increased risk of retinal detachment. Highly myopic patients often have axial myopia and are at increased risk of retinal detachment already. The lensectomy just increases this risk. Phakic intraocular lenses (IOLs) have been successfully used in adults with high refractive error,44–46 and there have been a few case reports of good visual results using phakic IOLs in children.47–50 The potential serious risk(s) with phakic IOLs are corneal endothelial cell loss with subsequent corneal decompensation and cataract development.51 These potential complications, though they have not been reported in children, could be devastating. If these procedures are found to be effective in children, we must carefully weigh the risks and benefits of these procedures against the definite result of permanent visual impairment from amblyopia in the noncompliant child with high uncorrected refractive error.

CONCLUSION

So, getting back to the title question of my lecture, “Is refractive surgery in children ready for prime time?”, I would have to say that at this point the answer is “No.” Even though the results have been good, all studies to date have had small sample sizes, and only two studies have included a control group.26, 29 Excimer laser procedures appear to be safe and effective at the medium-term follow-up; however, longer follow-up is needed to ensure that there are no serious late complications, such as keratectasia that have been reported with LASIK in adults. Surgical intervention at a younger age when there is more plasticity in the visual cortex may also yield better visual outcomes. Randomized clinical trials with larger patient numbers are needed where children are randomized to conventional therapy or an excimer laser refractive procedure with continuing attempt at occlusion or penalization therapy. This would determine with statistical proof whether these new treatments truly improve final visual outcome more than traditional therapy. Research in this exciting area of ophthalmology is ongoing, and other procedures may also become viable and possibly even better options in the future.

REFERENCES


**Key words:** refractive surgery, excimer laser procedures, accommodative esotropia, anisometropia, ametropia