

## Update on Paediatric Refractive Surgery

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### Abstract

**Purpose:** To provide a summary of the most recent evidence-based data on the paediatric refractive surgery. **Methods:** A review of the published studies from 1990 to 2015 was undertaken with emphasis on recent articles from 2010 to 2015. **Results:** Searching Scopus and PubMed, using the keywords of refractive surgery, phakic, paediatric, IOL, children and amblyopia alone or in various combinations yielded a total of about 48 articles on this topic from 1990 to 2015. Excluding review articles, fewer than 35 articles were included. Original research articles were only in the form of case reports/series on corneal laser surgery and phakic intraocular lens implantation or clear lens extraction. A total of fewer than 800 patients and 700 eyes had undergone a form of refractive surgery listed above. No randomised clinical trial (RCT) study was available on the topic. Age varied from 7 months to 17 years for non-corneal cross-linking studies. Most commonly performed operations were corneal laser ablative procedures (photorefractive keratectomy [PRK], laser-assisted sub-epithelial keratectomy [LASEK], laser-assisted *in situ* keratomileusis [LASIK]), phakic intraocular lens implantations (p-IOL, anterior or posterior chamber) and clear lens extraction. The indications for surgical intervention were for refractive – high amplitude iso-ametropic or anisometropic – amblyopia in the setting of the previously failed medical interventions and spectacle intolerance or non-compliance (physical or neurobehavioral in nature) and high accommodative esotropia with/without amblyopia. The main objective of the studies was to assess for visual acuity gained or lost following surgery and for correction of strabismus, i.e. achieving orthophoria. Further search on the keywords ‘cross-linking, cornea, rings and children’ from the same databases resulted in 130 articles. No RCT study was available on the topic. Age varied from 7 months to 17 years for non-corneal cross-linking studies. The focus of the most recent refractive surgery articles has been on the treatment and stabilisation of irregular myopic astigmatism from kerato-ectatic conditions by means of corneal cross-linking and intrastromal ring/in-lay implantation. **Discussion:** Refractive surgery remains a controversial topic in paediatric age population. However, the evidence clearly supports refractive surgery for treatment of children with refractive amblyopia and for treatment of accommodative esotropia in children unable or unwilling to wear spectacles or contact lenses. **Conclusion:** Consensus exists among published authors that refractive surgery may be considered in children with refractive amblyopia after exhausting various therapeutic medical options for amblyopia. Published authors have universally endorsed undertaking prospective multi-centred RCTs to conclusively establish the long-term safety and efficacy of various types of refractive surgery in the paediatric patients of different age groups.

### Keywords

Children, myopia, refractive surgery, laser, intraocular lens, anisometropia, cross-linking, amblyopia, strabismus, paediatric, ametropia, phakic, keratoconus

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Subsequent to the first published feasibility study of photorefractive keratectomy (PRK) on treatment of highly anisometropic, myopic and hyperopic, amblyopia in children by Singh et al. in 1994, a slew of articles on corneal laser refractive and lens-based intraocular surgery for treatment of paediatric refractive amblyopia in select clinical settings have followed.<sup>1</sup> Whereas modern refractive surgery in adults has taken monumental and giant leaps at times in the past 2 decades driven by ever-incessant demand for achieving better outcomes, faster recovery and fewer potential operative complications, paediatric ophthalmology community and institutions have been struggling with the quintessential factors of safety of refractive surgery in children,<sup>2</sup> general anaesthesia, added costs of having laser platforms in or near the operating room

theatre and the legal liability stemming from performing refractive surgery in children when such procedures are not US Food and Drug Administration (FDA)-sanctioned. As a result, the focus of the main body of published work has been on establishing the efficacy and safety of refractive surgery in a very select group of visually impaired children. The principal method of proving efficacy has been on showing a gain in the best-corrected visual acuity (BCVA) in an amblyopic eye when conventional treatments have been tried and failed. Lack of visually compromising events following surgery has been used as an index of safety. Recent data also add to the support of refractive surgery for treatment of accommodative esotropia and for early interventional treatment of keratoectatic diseases in children.

**Table 1: Representative Studies of Corneal Laser Refractive Surgery in Bilateral High Myopic Amblyopia**

Series	Year	Procedure	Patients (Age)	Pre/SE	Post/SE	Follow-up	Complication
Astle <sup>16</sup>	2002	PRK	10 (1–6 years)	–10.7	–1.4	12 months	40 % mild haze, 3 reduced vision
Astle <sup>17</sup>	2004	LASEK	11 (1–17 years)	–8.0	–1.2	12 months	22 % mild haze, ~2–3 % worse VA
Astle <sup>23</sup>	2006	LASEK	1 (7 years)	–7.5	–3.3	12 months	None
Tychsen <sup>110</sup>	2006	LASEK	9 (3–16 years)	–7.1	NR	6–36 months	35 % mild haze, regression –0.81 D/year
<b>Summary: 31 patients (1–17 years) Pre-op SE: –7.1 → –11.5 Post-op SE: –1.4 → –3.3</b>							

*D = diopter; LASEK = laser-assisted sub-epithelial keratectomy; NR = not reported; PRK = photorefractive keratectomy; SE = spherical equivalent in D; VA = visual acuity.*

**Table 2: Representative Studies of Corneal Laser Refractive Surgery for High Myopic Anisometropia and Amblyopia**

Series	Year	Procedure	Patients (Age)	Mean Pre/SE	Mean Post/SE	Follow-up	Complication
Singh <sup>1</sup>	1995	PRK	6 (10–15 years)	–12.1	–2.9	10 months	1 severe haze
Nano <sup>8</sup>	1997	PRK	5 (10–14 years)	–8.0	–1.6	12 months	20 % mild haze
Alio <sup>10</sup>	1998	PRK	6 (5–7 years)	–9.6	–2.0	24 months	1 severe haze
Rashad <sup>9</sup>	1999	LASIK	14 (7–12 years)	–7.9	–0.6	12 months	None
Agarwal <sup>11</sup>	2000	LASIK	16 (5–11 years)	–14.9	–1.4	36 months	2 flap, 2 lost one line of VA
Rybinsteva <sup>111</sup>	2001	LASIK	38 (9–15 years)	–6.0	NR	NR	None
Nucci <sup>12</sup>	2001	PRK/LASIK	14 (9–14 years)	–8.0	–0.7	20 months	None
Nassaralla <sup>13</sup>	2001	LASIK	9 (8–15 years)	–7.2	–0.2	12 months	None
Astle <sup>16</sup>	2002	PRK	13 (1–6 years)	–10.7	–1.4	12 months	Mild haze
Autrata <sup>18</sup>	2004	PRK/LASEK	27 (4–7 years)	–8.3	–1.6	24 months	Mild haze
Astle <sup>17</sup>	2004	LASEK	13 (1–17 years)	–8.0	–1.2	12 months	Mild haze, ~2 % worse VA
O'Keefe <sup>15</sup>	2004	LASIK	6 (2–12 years)	–10.2	–3.0	24 months	None
Tychsen <sup>21</sup>	2005	PRK/LASEK	35 (4–16 years)	–11.5	–3.0	29 months	8 % 3–4 grade haze
Paysse <sup>22</sup>	2006	PRK	11 (2–11 years)	–13.8	–3.6	31 months	Minimal haze
Astle <sup>23</sup>	2006	LASEK	5 (1–7 years)	–4.65	–0.25	12 months	Regression one case
Yin <sup>25</sup>	2007	LASIK	32 (6–14 years)	–10.1	–2.2	36 months	Minimal haze
Astle <sup>24</sup>	2007	LASEK	31 (10 months–15 years)	–9.5	–2.4	12 months	NR
<b>Summary: 281 patients (0.8–19 years) Pre-op SE: –6.0 → –14.9 Post-op SE: –0.9 → –3.3</b>							

*LASEK = laser-assisted sub-epithelial keratectomy; LASIK = laser-assisted in situ keratomileusis; NR = not reported; PRK = photorefractive keratectomy; SE = spherical equivalent in diopters (D).*

The negative effect of untreated high refractive errors on intellectual and social development is quite considerable. Studies have shown an improvement of VA in highly ametropic children increases the developmental quotient and social skills of children.<sup>3</sup> Previous high-impact studies have shown that a mere refractive correction of moderate to high refractive errors in anisometropic or high ametropic amblyopic children would result in a gradual resolution of amblyopia and strabismus in 30–74 % of patients (without occlusion therapy) as well as a gain in binocular VA following 52 weeks of just spectacle therapy alone in children under age of nine.<sup>4–7</sup> This is a critically important concept worth appreciating and understanding in paediatric refractive surgery and in considering to perform refractive surgery in children with moderate to high refractive amblyopia who have been non-compliant to traditional medical therapy of contact lens/spectacle wear and/or occlusion treatment. Refractive surgery by collapsing high refractive errors in ametropic amblyopic children follows a similar path of improving vision over time by creating a refractive equilibrium

or near emmetropia state and by collapsing the previously existing anisometropic aniseikonia.

We will provide a summary of the recently published articles on paediatric refractive surgery for treatment of highly ametropia or anisometropic amblyopia and for accommodative esotropia, will briefly review the novel role of refractive surgery in the management of paediatric keratoectatic diseases and will discuss the preventive approaches of myopic progression in children.

## Methods

We used the keywords of 'refractive surgery', 'children', 'laser', 'IOL' [intraocular lens], 'myopia', 'hyperopia', 'anisometropia', 'amblyopia', 'pediatric', 'strabismus', 'intraocular lens implantation', 'keratoconus' and 'cross-linking' in various combinations on PubMed and Scopus from 1990 to 2015 in generating a list of published peer-reviewed articles on the topic of 'pediatric refractive surgery'. Review articles

**Table 3: Representative Studies of Corneal Laser Refractive Surgery for Hyperopic Anisometropia and Amblyopia**

Series	Year	Procedure	Patients (Age)	Pre/SE	Post/SE	Follow-up	Complication
Singh <sup>1</sup>	1995	PRK	3 (10–15 years)	+7.6	+0.4	8.3 months	Mild haze
Phillips <sup>20</sup>	2004	LASIK	30 (mean 13.9 years)	+5.35	+0.9	15.7 months	47 % enhancement
Dvali <sup>51</sup>	2005	PRK	63 (8–16 years)	+1–6	NR	NR	None
Paysee <sup>22</sup>	2006	PRK	3 (8–11 years)	+4.8	+1.4	36 months	None
Yin <sup>25</sup>	2007	LASIK	42 (6–14 years)	+6.1	+0.6	36 months	Minimal haze
Astle <sup>24</sup>	2007	LASEK	3 (0.8–5.5 years)	+5.5	+2.3	12 months	NR
Utine <sup>28</sup>	2008	LASIK	32 (4–15 years)	+5.17	+1.37	20 months	Flap (one line loss)
<b>Summary: 176 patients (0.8–16 years) Pre-op SE: +1.0 → +7.6 Post-op SE: –0.9 → –2.3</b>							

LASEK = laser-assisted sub-epithelial keratectomy; LASIK = laser-assisted in situ keratomileusis; NR = not reported; PRK = photorefractive keratectomy; SE = spherical equivalent in diopters (D).

were excluded from our analysis. The majority of other articles, which were either case reports or case series, were included in our final analysis as listed in the reference section. There were 33 articles on corneal laser refractive surgery, 21 articles on myopic ametropia or anisometropia, 11 articles on hyperopic anisometropia and 12 articles on phakic (anterior chamber [AC] or posterior chamber [PC]) intraocular lens implantation. There were more than 20 articles on laser refractive surgery for accommodative esotropia of which four were on children. We searched for articles on corneal rings, kerataconus and children, but only one was in a child. There were 11 recent articles (out of 130) on corneal cross-linking in children. Age, pre- and post-operative spherical equivalent (SE) and post-operative complications are summarised on the most relevant topics.<sup>8–44</sup> SPSS software was used to carry out the statistical analysis (SPSS Statistics, IBM, Chicago, IL, US).

## Results

### Laser Corneal Procedures and [AC-PC] Phakic-Intraocular Lens Implantation

For all types of corneal laser surgery studies, which were included in our analysis, mean age at the time of the procedures was 8.22±3.11 (in years). For phakic IOL-implantation surgery studies, mean age at the time of surgery was 7.98±3.34 (in years). The mean SE in paediatric corneal laser-ablative group for the treatment of high bilateral myopia (see Table 1) and high myopic anisometropia (see Table 2) was –10.13±2.73 D and for hyperopic anisometropia (see Table 3) was +5.58±1.28 D. The mean SE in paediatric phakic-IOL implantation for myopic anisometropia (see Table 4) was –14.01±1.93 D.<sup>8–44</sup>

The corrected distance VA (CDVA) improved from 0.68±0.15LogMAR to 0.37±0.12LogMAR for corneal laser studies. In (AC-PC) p-IOL studies, the CDVA improved to 0.43±0.11LogMAR from 0.98±0.08LogMAR. Stereo-acuity improvement of 50 % was reported in a small number of phakic-IOL articles. In corneal laser refractive group, only 12 articles had information on binocular fusion. Stereopsis had improved from 11.1 % (pre-operatively) to 71.4 % of patients at the last post-operative visit.<sup>8–44</sup> Authors performing corneal laser ablative procedures, LASIK/PRK/LASEK, frequently employed a personalised driven nomogram, primarily driven by the ‘individual age’ and the ‘pre-operative spherical equivalent’ of children, in laser ablative treatments to best achieve a goal of bilateral emmetropia or near emmetropia in targeting the post-operative refractive errors, particularly in

those children younger than 5–7 years of age in order to optimise their surgical outcome and maintain a state of near emmetropia for the first 7–8 years of children’s lives.

As for complication rate, an overall incidence of post-operative subepithelial haze for PRK/LASEK was reported to be at 8–27 % and interface haze at 5–12 % for LASIK.<sup>9–30</sup> Loss of two lines of BCVA was 2–7.5 % for all groups.<sup>9–30</sup> Only one study had shown severe haze at the rate of 2.5 % with one patient who had lost six lines of VA.<sup>16</sup> Endothelial cell loss increased from 1.4 % at 6 months to 3.6 % at 12 months.<sup>13</sup> Recently, a case of an acute hydrops with secondary bacterial keratitis as a sequela of paediatric refractive surgery was reported in a young adult with a history of trabeculectomy and PRK and RK around 5–6 years of age.<sup>45</sup> An already accepted awareness as well as a profound concern exists among refractive surgeons over the long-term safety of such procedures on the mechanical stability of cornea following LASIK (and less so on the other surface tissue ablative procedures, such as PRK or LASEK) in the correction of high (≥6 D) myopic refractive errors in young children and infants as a potential source of iatrogenic corneal ectasia decades after these procedures are performed.

Instability of refraction after laser refractive surgery either as regression or physiological myopic progression have been the expected events involved with corneal laser surgery in children. Overall the SE refraction has been shown to be at 45–55 % within 1 D of targeted treatment at 6 months and 67 % within 1 D at 9 months with an overall anticipated regression of 0.8–1.7 D at 6 months.<sup>17,22–24,30</sup> Younger patients have shown more axial length growth and more epithelial hyperplasia following corneal laser ablative procedures. In one of latest articles on LASIK for treatment of highly myopic anisometropic amblyopia, the post-operative mean SE was –0.97±1.16 D at 2 years in children with mean age of 6.5±1.6 years.<sup>46</sup>

In a 3-year anterior chamber phakic IOL-implantation study, endothelial cell loss was at 7–15 % and myopic regression was at –1.0 D.<sup>40</sup> In a 5-year phakic IOL-implantation study, the CDVA had improved to 0.36±0.38LogMAR from 0.84±0.52 in patients with mean pre-operative SE refraction of –10.14±6.96 D and endothelial cell density was greater than 2,000 c/mm<sup>2</sup> in 80 % of patients.<sup>42</sup> In one of the first studies of foldable iris-fixated intraocular lens in children with bilateral and unilateral myopia, CDVA had improved from mean 0.84±0.4LogMAR to post-operative 0.67±0.34 LogMAR at 15 months in patients who

**Table 4: Representative Studies of Phakic-Intraocular Lens Implantation and Amblyopia**

Series	Year	Procedure	Patients (Age)	Pre/SE	Post/SE	Follow-up	Complication
Lesueur <sup>32</sup>	1999	ICL™	5 (3–16 years)	–12.8	+0.5	11.8 months	None
BenEzra <sup>31</sup>	2000	ICL™	3 (9–18 years)	–12.5	–1.0	9 months	Pigment dispersion
Chipont <sup>33</sup>	2001	Artisan™	1 (6 years)	–15.5	–4.0	18 months	None
Saxena <sup>35</sup>	2003	Artisan™	1 (4 years)	–12.5	–2.5	36 months	ECC loss
Tychsen <sup>112</sup>	2006	Lensectomy/RLE	26 (1–18 years)	–14.3	81 % 2 D	56 months	RD
Alj <sup>113</sup>	2007	Lensectomy/RLE	7 (4–20 years)	–16.7	86 % 3.0 D	44 months	3 hyphema
Pirouzian <sup>36</sup>	2007	Verisyse™	6 (5–11 years)	–14.2	–1.1	12 months	None
Tychsen <sup>38</sup>	2008	Verisyse™	11 (4–17 years)	–10/–22	–1.0 ≥2.0	12 months	IOL-exchange (trauma)
Tychsen <sup>38</sup>	2008	Verisyse™	2 (9 years)	+10.25	+0.10	9 months	None
Pirouzian <sup>40</sup>	2010	Verisyse™	7 (5–11 years)	–12.5/–17	–2.0/+1.25	34 months	ECC loss
Ryan <sup>43</sup>	2012	Fold–Verisyse™	6 (8–15 years)	–14.6	–2.4	15 months	ECC loss
Alio <sup>42</sup>	2011	Verisyse™	11 (2–15 years)	–10.14	–1.2	60 months	ECC loss

Summary: 84 patients (1–18 years) Pre-op SE: –10 → –22 Post-op SE: +0.50 → –4.0

ECC = endothelial cell count; ICL = Implantable Collamer Lens; IOL = intraocular lens; SE = spherical equivalent in diopters (D); Post = post-operative, Pre = pre-operative; RD = retinal detachment; RLE = refractive lens exchange.

had mean pre-operative SE of  $-14.6D \pm 4.2$  SD.<sup>43</sup> In a meta-analysis article covering most of the laser refractive surgery studies (PRK, LASEK and LASIK) for treatment of anisometropia, Alio et al. concluded that corneal laser surgery is an effective option for improving VA in children with anisometropic amblyopia and age at the time of surgery and pre-operative CDVA ( $r=0.34$ ) had a statistically significant positive correlation to the change in CDVA after surgery ( $r=-0.38$ ).<sup>44</sup>

### Laser Refractive Surgery for Accommodative Esotropia

The safety and efficacy of LASIK in facilitating strabismus management in non-compliant children and adults with fully and stable accommodative esotropia has been investigated by a number of authors for the past 15 to 20 years.<sup>47–56</sup> Efficacy of LASIK for treatment of accommodative esotropia was shown in 20 eyes of 10 children (5–9 years) who were non-compliant to spectacles and had hyperopia of +3.5 to +6.75 and fully stable accommodative esotropia.<sup>55</sup> Efficacy of hyperopic LASIK (VISX S2, AMO [VISX Star S2 Laser Platform Model, AMO, Abbott Medical Optics, Santa Clara, CA, USA]) in treating partially and fully accommodative esotropia was also shown in patients with mean age of  $25 \pm 12.6$  years and mean hyperopia of  $3.67 \pm 1.28$  D (before surgery) and  $0.21 \pm 0.59$  D (after surgery).<sup>56</sup> The mean angle of deviation without correction was 21.0 prism diopters ( $\Delta$ ) before surgery and 3.7 $\Delta$  after surgery. Progressive astigmatism following LASIK in a 7-year-old child with partially accommodative esotropia and consecutive exotropia in a 22-year-old patient after LASIK with accommodative esotropia from lack of fusion have also been reported.<sup>57,58</sup> Therefore, in considering refractive surgery for treatment of accommodative esotropia, clinicians should do their best to carry out detailed and comprehensive preoperative screenings, investigate for ocular motor and sensory functions, analyse for corneal bio-mechanical properties and assess for stability of angle deviation over an extended time in an attempt to continually improve the safety index of these procedures in younger patients. By providing a thorough counselling on the potential and the unknown long-term risks of these procedures, short/long term benefits and alternative surgical procedures, patients/parents are then allowed to most appropriately make their informed choices and reasonably consider whether they should have the

procedure at all and if so which type of refractive procedure is best suited to their individual needs.

### Intrastromal Ring Implantation for Keratoconus

In a single case report, feasibility and positive outcome of intrastromal ring implantation in an 11-year-old keratoconus patient using simultaneous bilateral implantation of ICRS (Intra-Corneal Ring Segments, INTACTS SK, Addition Technology) of 0.40 segments resulted in improvement of uncorrected distance visual acuity (UDVA) to 0.48LogMAR through pinhole using the manual technique. At the 6-week visit, the UDVA had improved to 0.17LogMAR with pinhole. At 6 months, UDVA had improved to 0.18LogMAR in the right eye and 0.2LogMAR in the left. The study reported no complication.<sup>59</sup>

### Corneal Cross-linking for Keratoconus

Of the 27 published reports on this new indication of refractive surgery for progressive keratoconus, 11 had information and data on children and corneal cross-linking.<sup>60–72</sup>

The latest study by O'Keefe et al. assessed VA, refractive and tomographic outcomes of corneal collagen cross-linking (CXL-epithelium off) in paediatric patients (13–18 years) with keratoconus. The study concluded CXL effectively stabilised uncorrected VA, refractive indices and keratometry values at 1 year, while improving BCVA.<sup>61</sup> Evaluating for the effectiveness and safety of accelerated corneal collagen cross-linking (ACXL with UV-A irradiation of 9 mW/cm<sup>2</sup> for 10 minutes) in children below 14 years of age with progressive keratoconus, 30 eyes of 18 patients showed stable refraction following the procedure at 2 years. SE decreased from  $-4.70 D \pm 3.86$  to  $-3.75 D \pm 3.49$ . However, three eyes of two patients with vernal keratoconjunctivitis (VKC) showed progression.<sup>66</sup> In a study by Buzzonetti et al., transepithelial CXL, although it was shown to be safe and improved CDVA at 18 months after treatment, could not effectively halt KC progression compared with standard CXL.<sup>68</sup> In a study of transepithelial corneal collagen crosslinking using riboflavin 0.1 %, dextran 15.0 %, trometamol (Tris) and ethylenediaminetetraacetic acid for progressive keratoconus in patients of 11 to 26 years, Caporossi et al., showed that after relative improvement in the first 3 to 6 months, the

**Table 5: Indications of Paediatric Refractive Surgery**

**Reported indications for corneal laser surgery in children without corneal disease**

1. Children with high-magnitude isoametropia who are spectacle non-compliant or intolerant and have neurobehavioral abnormalities
2. Children with severe anisometropia who are non-compliant or intolerant of spectacle and contact lens wear
3. Children with high ametropia, either anisometropia or isoametropia, who have other special medical, ocular and physical conditions unable to wear spectacles

**Reported indications for phakic intraocular implantation surgery in children**

1. Children with >10 D of myopia and >6 D of hyperopia without suspected corneal pathology and documented corneal ectatic conditions and are unable or unwilling to wear contact lenses
2. Children with >10 D of myopia and >6 D of hyperopia who do not wish to undergo refractive lens exchange or clear lens extraction and are unable or unwilling to wear contact lenses

**Reported indications for corneal laser surgery in children for accommodative strabismus**

1. Children who are orthophoric with spectacle or contact lens wear and are unable to wear them
2. Children with developmental and neurobehavioral and social conditions unable or unwilling to wear glasses or contact lenses

**Reported indications for corneal in-lays or rings and corneal cross-linking in children with corneal ectatic disease, keratoconus**

1. Documented visual acuity decline and proven corneal topography of advancing disease → corneal cross-linking
2. Children who do not tolerate contact lens wear or do not wish or unable to undergo corneal transplantation → corneal in-lays or rings

*D = diopter.*

UDVA and CDVA gradually returned to baseline pre-operative values at 12 months and the simulated maximum K value worsened at 24 months. The study concluded functional regression in patients between 19 years and 26 years old after 24 months of follow-up.<sup>71</sup>

## Discussion

Original research and review articles on corneal laser ablative procedures, PRK/LASEK/LASIK, as well as phakic IOLs have established the safety and efficacy of these procedures for treatment of high anisometric or ametropic amblyopia in children. Although post-operative complications of corneal haze, lamellar keratitis and off-centred laser treatment have been and do remain a concern in children following corneal laser procedures, the fifth and sixth generation of laser platforms with innovative technology comprising faster and higher spot scanning laser pulse energy, reduced eye-tracking latency time, mechanisms to compensate for pupillary cyclotorsion and pupillary centroid shifts and wavefront-guided technology for customised ablation will result in significantly reducing the incidence of complications in children.<sup>73</sup>

Concerns over endothelial cell loss following AC-pIOL implantation and cataract formation after the PC-pIOL implantation can be credibly reduced through meticulous pre-operative screening measures.<sup>74-76</sup> Ferreira et al. concluded that minimum endothelium-IOL (E-IOL) distance should be no less than 1.7 mm from the centre of the IOL to minimise the risk of endothelial cell loss. The authors also showed a statistically significant reduction of the E-IOL distance over the 3-year follow-up period with the mean annual reduction being 24.70 µm.<sup>74</sup> Fallah Tafti et al., in evaluation of 16 patients (26 eyes), showed that by using pre-operative pIOL simulation template for iris-fixated pIOL implantation through placement of the anterior segment optic coherence tomography (AS-OCT) in the middle of the iris rather than posterior pigment epithelium of the iris, patient selection criteria for anterior segment pIOL implantation and the predictability in the post-operative pIOL position can be improved.<sup>75</sup> Kojima and authors presented a novel regression equation superior to previously described formulas (*optimal ICL size (mm)* = 3.75 + 0.46x(STS) + 0.95x ACD) + 1.25 x (STSL), ACD = anterior chamber depth; STS = sulcus-to-sulcus diameter; STSL

= STS to anterior lens surface distance) in selecting the most proper ICL size in the pre-operative stage and to achieve the optimal appropriate vault size after ICL implantation surgery. The authors concluded that in order to achieve an optimal vault, ICL lengths with 0.25 mm increments would be preferable to those with 0.5 mm increments.<sup>76</sup>

Refractive laser and IOL procedures are reserved for non-compliant contact-lens wearing children who have a significant anisometric myopia or hyperopia and spectacle correction cannot be safely considered as a therapeutic option for them due to induction of aniseikonia and secondary loss of sensory binocular fusion.<sup>77,78</sup> Wearing extended soft contact lenses in children for years is not without risks. Studies have shown wearing certain daily soft contact lenses to have the same or higher risk as of undergoing LASIK, particularly when frequent hand-eye rubbing may also be of additional and a particular concern in select group of children.<sup>79-82</sup> In a comparative risk study analysis of daily wear soft contact lens wear and LASIK, risk of long-term contact lens wear was higher than LASIK surgery for low to moderate myopia.<sup>79,80</sup>

One of the main concerns with laser refractive surgery in younger children is requirement for general anaesthesia. This will impair self-fixation of the pupil into the laser target beam, thus possibly allowing for ablative treatment zone not to be aligned with visual axis. The new and upcoming variable and flying spot scanning EXCIMER laser technology sixth- and seventh-generation laser will capture the foveal fixation and pupillary margin in relation to visual axis and iris registration pre-operatively while the child is partly awake. As such, the centre of the ablation zone will match the centre of the visual axis and pupillary centre/margin under general anaesthesia, thus negating the need for self-fixation and averting a possible off-centred laser ablation in conjunction with wavefront treatment profile (wavefront guided or optimised).<sup>73</sup>

Recent literature has also provided the required evidence in expanded applicability of corneal laser surgery for treatment of paediatric accommodative esotropia in children who are unable or unwilling to comply with spectacle correction and when strabismus is stable. Paediatric refractive surgery has also been laying the foundation for

numerous treatment options such as corneal rings/inlays/cross-linking in arresting the progression of corneal ectatic diseases in their earliest stages, thus forestalling and averting the need for corneal transplantation surgery entirely.

## Prevention

As recently as 2 years ago, articles were reporting that there is no true treatment option for prevention and progression of myopia.<sup>83</sup> A number of recent clinical trials, however, has given us the hope in arresting and even reversing myopic progression. Efficacy of various doses of topical atropine, multifocal contact lenses, progressive added lenses and orthokeratology therapy, alone or in combination, have been shown to effectively control myopic progression and reduce the incidence of high ametropia and anisometropia to a great extent.<sup>84–106</sup> Although the complex mechanisms of arresting the progression of myopia are not yet completely and well understood, reducing and/or reversing progressive myopia or hyperopia will certainly lead to new pathways in significantly decreasing the need for laser refractive surgery or IOL implantation in children.

Conventional theories of refractive defocus and mechanical tension on myopic progression are being challenged with novel theories of corneal multi-focality and coma aberrations measured from total higher order aberrations in the orthokeratology clinical trials as a result of which new therapies will arise.<sup>89,104,105</sup> Optical strategies that induce myopic defocus at the retina such as peripheral defocus reducing lenses, simultaneous defocus lenses, bifocals, and orthokeratology as well as environmental influences such as increased outdoor activity show promise and provide a substantially risk-free environment in which to control eye growth.<sup>107</sup> The ultimate goal of any myopia-control therapy would be to slow myopic progression during the years that the eye has the greatest potential for growth and axial-length elongations so that the eventual level of myopia would be lower than if the eye was allowed to grow naturally (i.e., to reduce the incidence of high myopia).<sup>89</sup> As such, relentless efforts are also underway in discovering and mapping the genes that may also contribute to the onset of pathological myopia.<sup>93,94</sup>

To date, the consensus among experts is to consider refractive surgery in children with high refractive errors or for accommodative esotropia in those who are unable and unwilling to adhere with conventional medical treatment and have clearly demonstrated failure to medical therapy. Paediatric ophthalmologists are encouraged to assess for both the subjective and objective quantity and optical quality of vision through the currently available diagnostic devices on the market. A few examples include: 1. HD Analyzer System (Visual Performance Diagnostics, Visiometrics, Terassa, Spain), which provides the following variables of point-spread function, objective scattering index and modulation transfer function and amplitude of accommodation; 2. Adaptive Optics Technology System (Adaptive Optics Vision Analyzer; Voptica S.L, Murcia, Spain); 3. Various numbers of Wavefront Aberrometry Optical Systems for evaluation of corneal and total ocular higher order aberrations. Data on contrast sensitivity, levels of stereo-acuity, status of motor/sensory fusion and quality of life questionnaires should also be included whenever feasible.<sup>108</sup>

## Conclusion

Paediatric refractive surgery, either in the form of corneal laser or phakic-IOL, is a safe and efficacious therapeutic option in highly anisometropic and ametropia amblyopic children who have failed traditional medical therapy at the present time. Long-term safety, efficacy and risks of each of the specific procedures will likely be independently validated in future randomised clinical trials in which the quality and quantity of VA under the investigation will be assessed for variables including motor alignment, sensory fusion, contrast sensitivity, stereo-acuity and corneal profile analysis (such as endothelial cell numbers, central corneal thickness, corneal topography, corneal wavefront aberrometry, corneal hysteresis and corneal-resistant factor) in a format and a design similar to the previously conducted paediatric eye disease investigative group (PEDIG) multi-centred clinical trials.<sup>109</sup> In the near future, preventive measures in reducing and reversing the rate of myopic and hyperopic progression will take the centre stage of therapeutic intervention for the children at risk of developing high refractive errors, thus significantly lowering the overall incidence of high anisometropia or ametropia and the potential consideration for surgical correction of it altogether. ■

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