• Clinical Research •

# Femtosecond laser corneal refractive surgery for the correction of high myopic anisometropic amblyopia in juveniles

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## Abstract

**● AIM: To evaluate the effects of femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) and small-incision lenticule extraction (SMILE) to correct high myopic anisometropic amblyopia in juvenile patients.**

**● METHODS: From November 2013 to January 2015, 33 amblyopic patients with high myopic anisometropic amblyopia were studied. FS-LASIK (30 eyes) or SMILE (3 eyes) was performed in the amblyopic eyes. Visual acuity, refraction, contrast sensitivity, stereoacuity and complications were evaluated. Patients completed follow-up examinations at 3d, 1mo, 3mo and the last follow-up time (mean 8.17±3.23mo) after surgery.**

**● RESULTS: The mean age at surgery was 9.04±3.04y (range 6-16y). The mean spherical equivalent in the amblyopic eyes was significantly decreased from -10.00±2.39 D preoperatively to -0.06±1.06 D at 1mo, -0.19±1.33 D at 3mo and -0.60±1.43 D at approximately 8mo postoperatively (*P*<0.05 for all). The mean myopic anisometropia was significantly decreased from -9.45±2.33 D preoperatively to +0.37±1.48 D at 1mo, -0.46±1.47 D at 3mo and -0.09±1.83 D at approximately 8mo (*P*<0.05 for all). The logarithm of the minimum angle of resolution (logMAR) for uncorrected and corrected distance visual acuity (UDVA and CDVA, respectively) of the amblyopic eye improved from 1.74±0.35 and 0.98±0.63 preoperatively to 0.45±0.31 and 0.41±0.33 at approximately 8mo after surgery, respectively. The logMAR CDVA at 3d, 1, 3 and 8mo postoperatively improved by means of 1.42, 2.22, 2.96, and 4.39 lines, and a gain of more than two lines accounted for 45%, 50%, 74% and 86% of all patients, respectively. The contrast sensitivity of both amblyopic eyes and dominant eyes at 0.5, 2, 8 cycles per degree was significantly improved postoperatively (*P*<0.05 for all). Of the 33 pediatric patients, no patients had near stereopsis preoperatively and seven patients (21.2%) recovered near stereopsis (400″ to 60″) at approximately 8mo after surgery. No intraoperative or postoperative complications occurred in any patient.**

**● CONCLUSION: FS-LASIK or SMILE can be promising alternative methods to correct high myopic anisometropic amblyopia in juvenile patients who have failed with traditional approaches.**

**● KEYWORDS:** refractive surgery; myopic anisometropic; amblyopia; pediatric patients; small-incision lenticule extraction; femtosecond laser-assisted *in situ* keratomileusis

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## INTRODUCTION

Amblyopia is typically manifested by a decrease in visual acuity, contrast sensitivity and damaged of binocular stereopsis. Anisometropia is one of the main causes of amblyopia. The deeper anisometropia is also associated with poorer monocular and binocular visual functions. Spectacles and contact lenses (CLs) are the traditional treatment options for refractive correction for anisometropic amblyopia. However, with spectacles, most patients will have different perceived retinal image sizes with over 3.00 diopters (D) antimetropia. Meanwhile, severe aniseikonia might produce some clinical symptoms that include dizziness, nausea, and an inability to walk steadily. Thus, patients with severe myopic anisometropia are commonly intolerant to aniseikonia and diplopia caused by the full correction of the spectacle lens[1-3]. Although CLs have the advantages of relieving aniseikonia and improving visual quality, these are still difficult to use in most of pediatric and adolescent patients due to the foreign body sensation and the potential risks of corneal infections[4-5]. Cornea refractive surgeries, including photorefractive keratectomy (PRK), laser *in situ* keratomileusis (LASIK), and laser-assisted subepithelial keratectomy (LASEK) have been

reported as being efficacious and offer safety alternatives in children with anisometropic amblyopia who have failed with conventional approaches[6-17]. Nonetheless, limiting factors of these surgeries have still been observed in previous studies[18-21]. PRK is especially not suitable for high refractive error corrections. With PRK there can be complications including severe corneal irritative symptoms and higher risks of corneal haze formation. Corticosteroid glaucoma may also occur due to the removal of the corneal epithelium and Bowman's layers following long-term corticosteroid use. LASIK avoids the disadvantages of PRK, however, serious side effects like flap-related complications and iatrogenic keratectasia still occur. LASEK, having the advantages of both PRK and LASIK, can be performed in patients with high refractive errors and thin corneas, but complications are also associated with the flap.

With advances in femtosecond laser technology, it cannot only be used to make corneal flaps instead of a microkeratome but it can also independently complete refractive corrections[20]. Previous studies have reported the effectiveness, safety, predictability of femtosecond laser surgeries in adults[21-24]. Nevertheless, the use of femtosecond laser techniques in children is relatively new. Therefore, the purpose of this prospective study was to evaluate the efficacy and safety of femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) and small-incision lenticule extraction (SMILE) in juvenile patients with myopic anisometropic amblyopia.

## SUBJECTS AND METHODS

Thirty-three patients (16 males and 17 females) diagnosed with unilateral high myopic amblyopia in the Zhongshan Ophthalmic Center of Sun Yat-sen University were included in our study. FS-LASIK (33 eyes) or SMILE (3 eyes) was performed in the more myopic eye. Inclusion criteria were as follows: 1) age between 5 to 17y; 2) refractive error difference between the two eyes was ≥5.00 D; 3) corrected distance visual acuity (CDVA) was below 20/25 (Snellen) in amblyopia eye and above 20/25 in the fellow eye or the binocular visual acuity difference was two or more lines, or without near stereopsis; 4) patients could not tolerate or comply with wearing spectacles and/or CLs for correcting refractive error combinations with standard occlusion therapy. Exclusion criteria were 1) patients with an active ocular inflammation, suspected or confirmed keratoconus, glaucoma or other ocular organic diseases; 2) a history of intraocular surgery or severe ocular trauma; 3) a residual stromal bed thickness <280 μm; 4) a severe systemic disease. One child with a myelinated nerve fiber sheath but normal posterior pole in our study was included.

A detailed explanation of the surgical procedures and potential limitations were clearly stated before surgery. All parents or guardians were signed the informed consent from the U.S. Food and Drug Administration (FDA) off-label use of the laser corneal refractive surgery. All the study procedures were conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Zhongshan Ophthalmic Center. The demographic characteristics as well as the baseline refractive and visual data are shown in Table 1.

**Preoperative Management** Complete preoperative ophthalmologic examinations were done and included tests for uncorrected distance visual acuity (UDVA) and CDVA using the Early Treatment of Diabetic Retinopathy Study (EDTRS) converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analyses. Examinations also included tests for cycloplegic refraction, ocular alignment by the Hirschberg method and alternate cover test, an anterior segment evaluation by slit-lamp microscopy, a fundus examination through a dilated pupil with a 90 D lens, and an intraocular pressure (IOP) evaluation by noncontact tonometry. Furthermore, we performed corneal topography with the Orbscan IIz and the WaveLight Oculyzer anterior segment analysis system (Alcon, Fort Worth, Texas, USA), a central corneal thickness with an A-ultrasound corneal pachymetry, and near stereopsis with the Randot preschool stereoacuity test. Contrast sensitivity was measured with Psykinematix psychophysics software (KyberVision, Quebec, Canada) using previously described methods[25-26]. Briefly, the sinusoidal gratings stimuli, generated by a MacBook Pro (Apple Inc., California, USA), was presented on an EIZO 21-inch cathode ray tube (CRT) monitor (EIZO Corporation, Ishikawa, Japan, resolutione: 1280′1024 pixels, refresh ratee: 85 Hz). During the 200ms presentation time, patients had to judge the orientation of the grating following a two-alternative, forced-choice method, with a 120 cm viewing distance in a dark room. The test was measured using a 3-down 1-up interleaved staircase procedure with six reversals converging on 79.4% accuracy. Contrast sensitivity was assessed at 0.5, 2 and 8 cycles per degree (cpd), with the nonviewing eye covered by an opaque eyepatch.

**Surgical Methods** Femtosecond laser corneal refractive surgery was performed by the same surgeon (Yu KM ). Five children (15.6%) required general anesthesia with intubation, and the other patients were successfully treated under topical anesthesia with proxymetacaine hydrochloride eyedrops (Alcaine, Alcon, Inc., USA). For FS-LASIK surgery, a corneal flap with a superior hinge was created using femtosecond laser by the VisuMax femtosecond laser system (Carl Zeiss Meditec AG, Jena, Germany). The flap diameter was 8.0 mm, and the flap thickness was 90 to 110 μm. After lifting the flap, the stromal bed with a 6.0-6.5 mm optical zone was ablated using excimer laser by the WaveLight® Allegretto Eye-Q 400 Hz excimer laser system (Alcon Laboratories Inc, Fort Worth, TX, USA). The residual stromal bed was washed with a balanced salt solution, and the flap was repositioned.

**Table 1 Clinic details for the patients with high anisometropic amblyopia preoperatively**

| Pts/sex | Age (a) | Eye | Refraction (D) | Ocular alignment | LogMAR (Snellen) | |
|---|---|---|---|---|---|---|
| | | | | | UDVA | CDVA |
| 1/M | 11.3 | OD | -10.75DS/-4.00DC×30 | Ortho | 1.4 (20/500) | 0.9 (20/167) |
| | | OS | -1.5DS/-0.75DC×170 | | 0.7 (20/100) | 0.0 (20/20) |
| 2/M | 9.1 | OD | -0.25DS/-0.75DC×170 | Ortho | 0.2 (20/32) | 0.0 (20/20) |
| | | OS | -7.50DS/-1.00DC×65 | | 2.4 (20/2500) | 0.6 (20/80) |
| 3/F | 16.6 | OD | -7.50DS/-0.75DC×129 | Ortho | 2.0 (20/2000) | 0.2 (20/32) |
| | | OS | -1.00DS | | 0.3 (20/40) | 0.0 (20/20) |
| 4/F | 10.3 | OD | -1.50DS | Ortho | 0.5 (20/63) | -0.1 (20/16) |
| | | OS | -13.50DS/-1.50DC×5 | | 1.4 (20/500) | 0.4 (20/50) |
| 5/M | 9.5 | OD | -12.00DS/-4.00DC×30 | Ortho | 1.22 (20/333) | 0.9 (20/167) |
| | | OS | + 0.00DS/ + 0.50DC×85 | | 0.0 (20/20) | 0.0 (20/20) |
| 6/M | 6.6 | OD | -15.00DS/-1.50DC×30 | Ortho | 2.0 (20/2000) | 1.7 (20/1000) |
| | | OS | -6.75DS/-0.75DC×15 | | 1.0 (20/200) | 0.1 (20/25) |
| 7/F | 6.0 | OD | -6.50DS/-2.00DC×12 | Ortho | 1.7 (20/1000) | 1.0 (20/200) |
| | | OS | + 2.25DS/ + 0.5DC×90 | | 0.2 (20/32) | 0.1 (20/25) |
| 8/F | 6.5 | OD | -8.50DS/-5.00DC×175 | Ortho | 2.0 (20/2000) | 1.3 (20/400) |
| | | OS | + 0.25DS/-2.00DC×175 | | 0.2 (20/32) | 0.2 (20/32) |
| 9/F | 6.4 | OD | -10.00DS/-3.50DC×180 | Ortho | 2.4 (20/2500) | 2.4 (20/2500) |
| | | OS | + 0.75DS/ + 1.25DC×80 | | 0.1 (20/25) | 0.1 (20/25) |
| 10/M | 8.3 | OD | -5.25DS/-3.75DC×17 | Exo | 1.3 (20/400) | 0.5 (20/67) |
| | | OS | + 0.00DS/-1.00DC×70 | | 0.2 (20/32) | 0.2 (20/32) |
| 11/F | 6.7 | OD | -9.25DS/-2.75DC×20 | Ortho | 2.0 (20/2000) | 0.5 (20/67) |
| | | OS | -0.25DS/-1.25DC×175 | | 0.15 (20/28) | 0.0 (20/20) |
| 12/M | 6.7 | OD | -0.25DS/-4.75DC×170 | Ortho | 0.4 (20/50) | 0.1 (20/25) |
| | | OS | -6.00DS/-5.5DC×180 | | 1.3 (20/400) | 0.7 (20/100) |
| 13/M | 6.0 | OD | + 0.25DS/-0.75DC×10 | Ortho | 0.1 (20/25) | 0.1 (20/25) |
| | | OS | -9.50DS/-2.5DC×180 | | 2.4 (20/2500) | 1.7 (20/1000) |
| 14/M | 8.0 | OD | -10.00DS/-2.75DC×180 | Ortho | 2.4 (20/2500) | 1.3 (20/400) |
| | | OS | +1.00DS/-1.25DC×5 | | 0.0 (20/20) | 0.0 (20/20) |
| 15/M | 16.0 | OD | -1.00DS/-0.75DC×180 | Ortho | 0.2 (20/32) | 0.0 (20/20) |
| | | OS | -11.25DS/-1.25DC×25 | | 1.3 (20/400) | 0.5 (20/67) |
| 16/F | 10.3 | OD | -6.25DS/-2.00DC×170 | Ortho | 1.3 (20/400) | 0.6 (20/80) |
| | | OS | -1.25DS | | 0.2 (20/32) | 0.0 (20/20) |
| 17/M | 13.7 | OD | +0.50DS | Ortho | 0.0 (20/20) | 0.0 (20/20) |
| | | OS | -9.50DS/-1.00DC×60 | | 2.0 (20/2000) | 1.3 (20/400) |
| 18/M | 6.5 | OD | -6.75DS/-1.00DC×125 | Exo | 1.3 (20/400) | 0.8 (20/133) |
| | | OS | +0.5DS/+0.5DC×95 | | 0.0 (20/20) | 0.0 (20/20) |
| 19/F | 7.0 | OD | -9.00DS/-2.25DC×175 | Ortho | 2.0 (20/2000) | 0.5 (20/67) |
| | | OS | +1.00DS/-1.25DC×5 | | 0.7 (20/100) | 0.1 (20/25) |
| 20/M | 13.8 | OD | -12.00DS/-1.25DC×10 | Ortho | 2.0 (20/2000) | 1.4 (20/500) |
| | | OS | -1.75DS | | 0.2 (20/32) | 0.0 (20/20) |
| 21/F | 9.2 | OD | -5.25DS/-1.5DC×165 | Ortho | 1.3 (20/400) | 0.2 (20/32) |
| | | OS | +0.5DS/+0.5DC×100 | | -0.1 (20/16) | -0.1 (20/16) |
| 22/F | 10.0 | OD | -3.75DS/-2.00DC×5 | Exo | 0.7 (20/100) | 0.0 (20/20) |
| | | OS | -10.00DS/-2.75DC×170 | | 1.7 (20/1000) | 0.4 (20/50) |
| 23/F | 6.0 | OD | -9.00DS/-4.5DC×180 | Ortho | 2.0 (20/2000) | 0.7 (20/100) |
| | | OS | +1.25DS/-1.75DC×180 | | 0.1 (20/25) | 0.0 (20/20) |
| 24/F | 7.2 | OD | -5.00DS/-3.00DC×170 | Ortho | 2.0 (20/2000) | 0.2 (20/32) |
| | | OS | +0.25DC×90 | | -0.1 (20/16) | -0.1 (20/16) |
| 25/M | 10.6 | OD | -11.00DS/-1.5DC×175 | Ortho | 2.0 (20/2000) | 1.0 (20/200) |
| | | OS | +0.25DS/+0.75DC×90 | | -0.1(20/16) | -0.1 (20/16) |
| 26/F | 6.1 | OD | -7.00DS | Ortho | 2.0 (20/2000) | 1.0 (20/200) |
| | | OS | PL | | 0.0 (20/20) | 0.0 (20/20) |
| 27/F | 8.0 | OD | -8.00DS/-4.5DC×5 | Ortho | 1.7 (20/1000) | 0.9 (20/167) |
| | | OS | +1.75DS/-2.25DC×180 | | 0.1 (20/25) | 0.0 (20/20) |
| 28/F | 8.3 | OD | -7.75DS/-1.00DC×20 | Ortho | 1.7 (20/1000) | 0.1 (20/25) |
| | | OS | -1.75DS/-0.5DC×10 | | 0.7 (20/100) | 0.0 (20/20) |
| 29/F | 8.5 | OD | +0.75DS | Ortho | 0.0 (20/20) | 0.0 (20/20) |
| | | OS | -10.00DS/-0.5DC×155 | | 1.7 (20/1000) | 0.6 (20/80) |
| 30/F | 10.8 | OD | -9.00DS/-1.5DC×5 | Ortho | 2.4 (20/2500) | 2.4 (20/2500) |
| | | OS | -2.25DS | | 0.8 (20/133) | -0.1 (20/16) |
| 31/M | 6.7 | OD | -8.5DS/-1.00DC×115 | Ortho | 2.4 (20/2500) | 2.4 (20/2500) |
| | | OS | PL | | 0.0 (20/20) | 0.0 (20/20) |
| 32/M | 14.5 | OD | -0.25DS | Ortho | 0.1 (20/25) | 0.0 (20/20) |
| | | OS | -8.5DS/-2.00DC×160 | | 1.7 (20/1000) | 0.7 (20/100) |
| 33/M | 6.0 | OD | +0.5DS/+0.75DC×80 | Ortho | 0.2 (20/32) | 0.2 (20/32) |
| | | OS | -6.75DS/-3.5DC×180 | | 2.0 (20/2000) | 0.9 (20/167) |

Pts: The number of patients; PL: Plain lens; Ortho: Orthophoria; Exo: Exotropia.

For SMILE surgeries, the same femtosecond laser system was used. First, the eye was well centered and achieved the appropriate suction. Then, the femtosecond laser created the posterior surface of the refractive lenticule and the lenticule border. The cap thickness was set at 120 μm. Finally, the anterior surface of the refractive lenticule was formed and a rim cut was created at 10-12 o'clock position. The edge of the refractive lenticule was separated and then grasped from a single small incision. The optical zone diameter of the lenticule was approximately 6.0-6.5 mm.

**Postoperative Treatment and Assessment** Postoperatively, tobramycin (0.3%)-dexamethasone (0.1%) eyedrops (Tobradex) were administered locally four times daily for 1wk, and carboxymethylcellulose sodium eye drops were given four times daily for 1mo. The postoperative follow-ups included visits at 1, 3d, 1wk, 1, 3, 6mo, and 1y, then 6mo thereafter. Except 1d and 1wk visits, complete eye examinations were performed at each follow-up visits. These examinations included UDVA, CDVA, refraction, contrast sensitivity, stereoacuity, and repeat anterior segment, fundus evaluations and binocular vision testing when possible. All patients continued postoperative amblyopia therapy 1mo after surgery with occlusion of the dominant eye for 4-6h daily. The residual error was corrected by glasses (if needed), and physical training included, among others, Haidinger's brush and the red filter method.

**Statistical Analysis** The data is presented as the mean± standard deviation (SD). Paired *t*-tests or Wilcoxon-signed rank tests compared preoperative values versus quantitative results from 3d, 1, 3mo, and the last postoperative follow-up time using IBM SPSS Statistics 19 (SPSS Inc., Chicago, IL, USA). The Pearson correlation coefficient was used as a measure of correlation. For multiple comparisons of postoperative quantitative results, a repeated measures analysis of variance was applied to the normal distribution, homogeneity of variance parameters data, while nonparametric data was analyzed using the related-samples Friedman test. All tests were two tailed, and *P* values less than 0.05 were considered statistically significant.

## RESULTS

The mean age of the patients was 9.04±3.04y (range 6-16y). Patients completed follow-ups examinations at 3d, 1, 3mo, and the last follow-up time [mean: 8.17±3.23 (range 6-16mo)] after surgery and were attended by 100% (*n*=33), 97% (*n*=32), 70% (*n*=23), and 70% (*n*=23) of all patients, respectively.

**Refraction** The achieved spherical equivalent (SE) at 1 postoperative month was within ±0.50 D of the attempted power in 21 eyes (70%), within ±1.00 D in 26 eyes (87%), within ±1.50 D in 28 eyes (93%) (Figure 1). Figure 2 shows the SE refraction changes over time after FS-LASIK or SMILE surgery in children with high myopic anisometropia. There was a significant reduction for both the mean SE

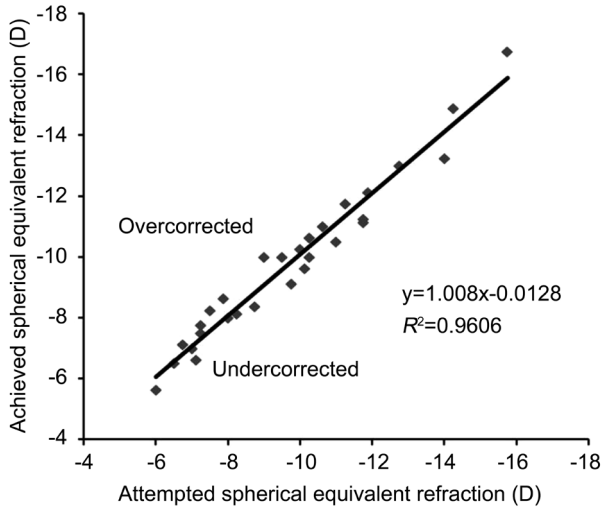


**Figure 1 Attempted *vs* achieved SE refraction in amblyopia eyes for FS-LASIK or SMILE surgery (*n*=30).**

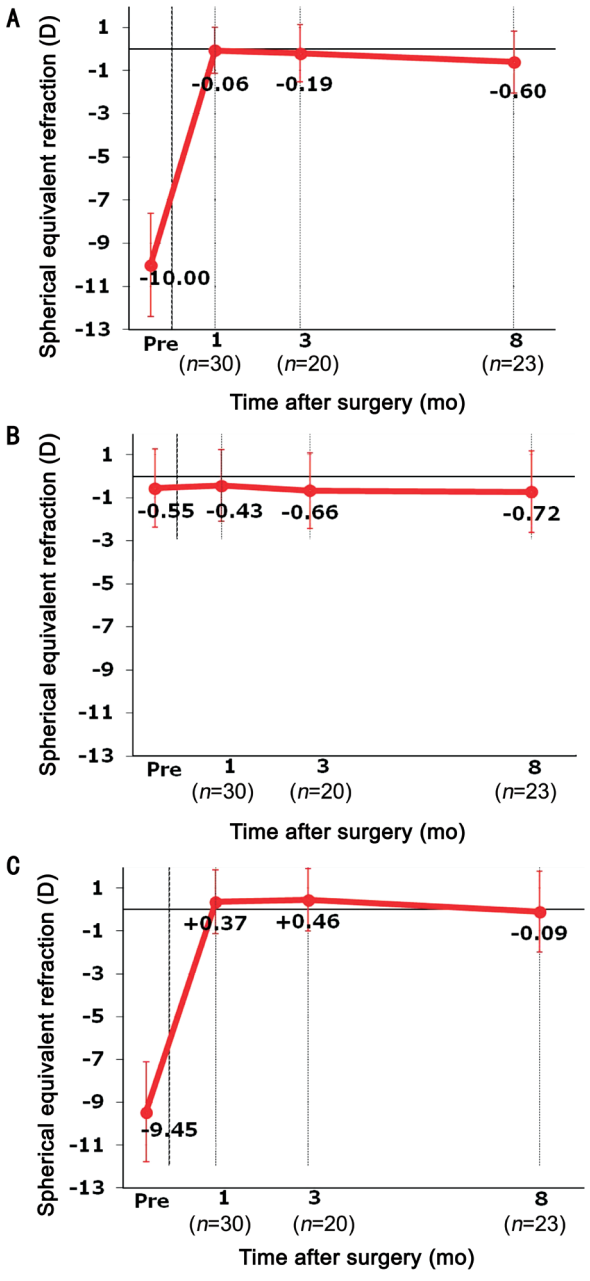


**Figure 2 Stability of SE refraction after FS-LASIK or SMILE surgery in children with high myopic anisometropia** A: SE of amblyopic eyes; B: SE of fellow eyes; C: Anisometropia.

**Table 2 Refraction changes over time in patients with high anisometropic amblyopia after femtoseond laser corneal refractive surgery**

| Time (*n*) | Spherical equivalent (D) | | Anisometropia (D) |
|---|---|---|---|
| | Operated eye | Un-operated eye | |
| Preop. (33) | -10.00±2.39 (-6.00, -15.75) | -0.55±1.81 (+2.50, -7.13) | -9.45±2.33 (-6.00, -14.25) |
| Postop. 1mo (30) | -0.06±1.06[a] (+1.75, -4.25) | -0.43±1.66 (+2.38, -6.25) | +0.37±1.48[a] (+2.88, -3.00) |
| Postop. 3mo (20) | -0.19±1.33[a] (+1.75, -4.38) | -0.66±1.76 (+1.25, -6.50) | +0.46±1.47[a] (+2.75, -3.25) |
| Postop. 8mo (23) | -0.60±1.43[a] (+1.38, -4.63) | -0.72±1.89 (+2.00, -5.88) | -0.09±1.83[a] (+2.75, -4.25) |
| [1]*P* | 0.307 | 0.549 | 0.336 |

*n*: Sample size; Preop.: Preoperation; Postop.: Postoperation; D: Diopters. [a]Compared with preop., *P*<0.05 significantly difference; [1]Difference among postop. follow up time.

**Table 3 Changes of logMAR visual acuity over time for amblyopic eyes after FS-LASIK or SMILE surgery**

| Time (*n*) | UDVA | CDVA |
|---|---|---|
| Preop. (33) | 1.74±0.35 (1.22, 2.40) | 0.98±0.63 (0.10, 2.40) |
| Postop. 3d (33) | 0.77±0.54 (0.00, 2.00)[a] | 0.75±0.56 (0.00, 2.00)[a] |
| Postop. 1mo (32) | 0.66±0.49 (0.00, 1.70)[a] | 0.60±0.44 (0.00, 1.70)[a] |
| Postop. 3mo (23) | 0.51±0.39 (-0.10, 1.30)[a] | 0.48±0.39 (-0.10, 1.30)[a] |
| Postop. 8mo (23) | 0.45±0.31 (0.10, 1.00)[a] | 0.41±0.33 (0.00, 1.00)[a] |
| [1]*P* | 0.000 | 0.000 |

*n*: Sample size; Preop.: Preoperation; Postop.: Postoperation; [a]Compared with preop. *P*<0.05 significantly difference; [1]Difference among postop. follow up time.

**Table 4 Changes in contrast sensitivity over time in patients after FS-LASIK or SMILE surgery**

| Groups | Time | Space frequency | | |
|---|---|---|---|---|
| | | 0.5 cpd (*n*) | 2 cpd (*n*) | 8 cpd (*n*) |
| Un-operated eye | Preop. | 100.03±35.38 (30) | 128.08±53.47 (30) | 50.73±43.45 (22) |
| | Postop. 3d | 111.51±31.29[a] (28) | 177.43±82.07[a] (28) | 62.37±35.07 (20) |
| | Postop. 1mo | 118.40±35.99[a] (28) | 190.11±78.40[a] (28) | 68.02±46.83 (21) |
| | Postop. 3mo | 112.59±52.20 (20) | 199.14±96.93[a] (20) | 66.29±39.60[a] (16) |
| | Postop. 8mo | 130.37±36.76[a] (21) | 220.36±78.88[a] (21) | 48.49±31.87 (16) |
| *P* | | 0.002 | 0.077 | 0.312 |
| Operated eye | Preop. | 44.57±24.05 (28) | 29.15±34.56 (31) | 5.90±5.08 (16) |
| | Postop. 3d | 52.98±25.34[a] (28) | 41.35±36.73[a] (29) | 9.32±11.76 (14) |
| | Postop. 1mo | 57.80±25.14[a] (28) | 44.76±35.75[a] (29) | 9.90±10.66[a] (15) |
| | Postop. 3mo | 75.88±46.93[a] (21) | 56.78±40.73[a] (21) | 12.05±10.44[a] (11) |
| | Postop. 8mo | 72.87±30.59[a] (21) | 61.91±49.66[a] (22) | 12.24±12.41[a] (11) |
| *P* | | 0.052 | 0.005 | 0.012 |

*n*: Sample size, Preop.: Preoperation; Postop.: Postoperation. [a]Represent compared with preoperative, *P*<0.05 significantly difference.

and SE anisometropia at 1, 3mo, and approximately 8mo postoperatively (*P*=0.000). However, the SE refraction of amblyopic eye, the SE refraction of the fellow eye, and the SE anisometropia during approximately 8mo were not significantly changed (*P*=0.307, *P*=0.549, *P*=0.336, respectively; Table 2).

**Visual Acuity** Table 3 and Figure 3A show that both UDVA and CDVA of amblyopic eyes at 3d, 1mo, and 3 and approximately 8mo after surgery were significantly improved compared to preoperative levels (*P*=0.000 for all).There was also a significant increase of both UDVA and CDVA in amblyopic eyes during approximately 8mo follow-up time postoperatively (*P*=0.000 for all). Figure 3B shows the cumulative logMAR CDVA in amblyopic eyes, postoperatively. Figure 3C shows that the logMAR CDVA of amblyopic eyes at 3d, 1mo, and 3 and approximately 8mo after surgery improved 1.42±1.44 (0, 5) lines, 2.22±2.01 (0, 7) lines, 2.96±2.27 (0, 8) lines, and 4.39±2.79 (0, 9) lines, and gains of more than 2 lines accounted for 45% (15 eyes), 50% (16 eyes), 74% (17 eyes) and 86% (19 eyes), respectively. No patients lost any lines of visual acuity after surgery.

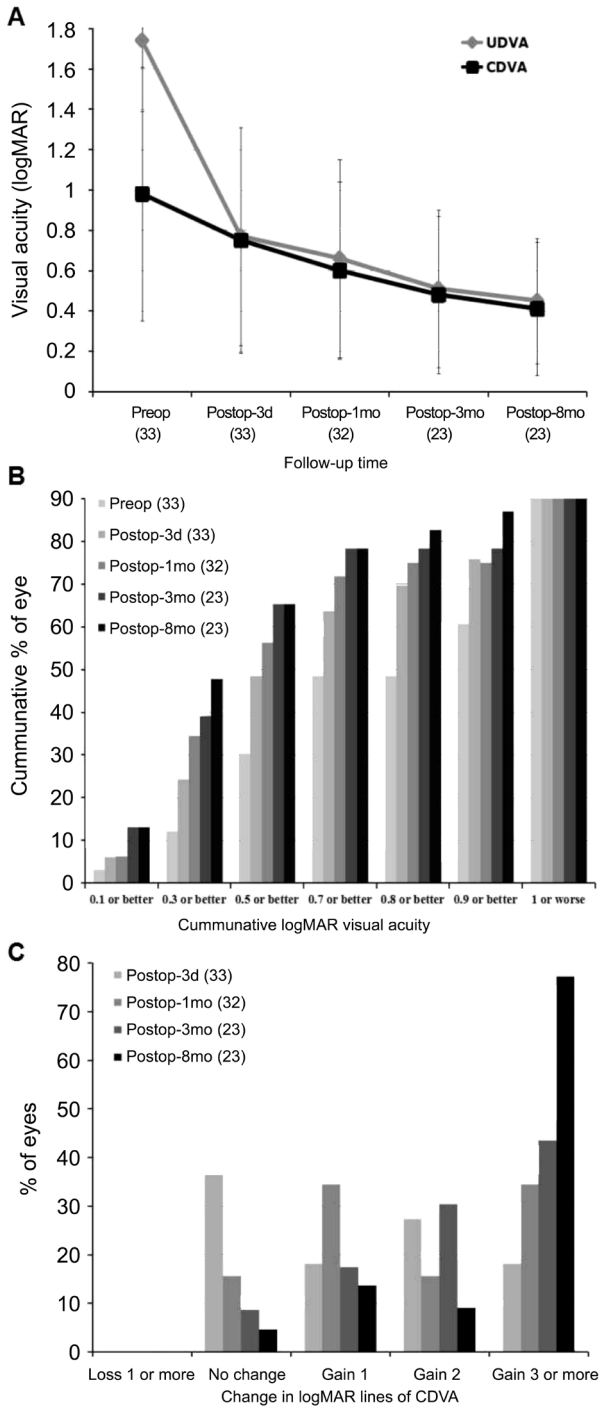


**Figure 3 LogMAR visual acuity changes in the amblyopic eyes after FS-LASIK or SMILE surgery** A: The changes of UDVA and CDVA; B: The cummunative of logMAR CDVA; C: The changes in lines of logMAR CDVA.

**Contrast Sensitivity** Two patients were too young to finish the contrast sensitivity test, and the visual acuities of several patients were so poor that only 16 amblyopic eyes and 22 fellow eyes completed at 8 cpd (Table 4). The contrast sensitivity of amblyopic eyes was significantly improved at 0.5 and 2 cpd for postoperative day 3, and significantly improved at 0.5, 2, and 8 cpd at 1, 3mo, and approximately 8mo postoperatively ($P$<0.05 for all). The contrast sensitivities of the dominant eyes were significantly increased to 0.5 cpd and 2 cpd at 3d, 1mo and approximately 8mo postoperatively, and significantly increased to 2 cpd and 8 cpd at 3mo after surgery ($P$<0.05 for all). The contrast sensitivity of amblyopic eyes at 2 and 8 cpd and the contrast sensitivity of dominant eyes at 0.5 cpd were significantly increased during the follow up time (all $P$<0.05), but not significantly changed in other spatial frequencies ($P$>0.05 for all ).

**Stereopsis** Of the 33 pediatric patients, no patients had near stereopsis preoperatively and 7 patients (21.2%) recovered near stereopsis (400″ to 60″) at approximately 8mo after surgery.

**Complications** Surgical procedures were successfully carried out for all patients and no anesthesia complications, intraoperative or postoperative complications occurred either the procedures or follow-up time.

## DISCUSSION

The etiological treatment for children with unilateral high myopic amblyopia is to correct refractive errors and eliminate or reduce anisometropia. Mild to moderate myopic anisometropia can always successfully be treated with spectacles. However, a refractive error between the two eyes greater than -3 D is usually difficult to fully correct with spectacles due to intolerable aniseikonia, and it is also not feasible to correct with CLs in many children and adolescents due to potential infection risks. Several previous studies[6-17] have reported the effectiveness and safety of corneal refractive surgeries for the correction of high anisometropia in pediatric patients who were unable to tolerate or failed with conventional refractive correction methods.

In recent years, femtosecond laser corneal refractive surgeries have gradually popularized in adults, and studies have shown that they were much safer than conventional LASIK surgery[21-23,27]. However, the application of femtosecond laser corneal refractive surgeries in children or adolescents for correction of high anisometropia has rarely been reported. In our study, most of pediatric patients with unilateral high myopic amblyopia (all SE anisometropia greater than 6 D) had already been corrected with glasses for a period of time but the effect was poor. FS-LASIK or SMILE was selected to correct refraction in amblyopic eyes to relieve anisometropia. The amblyopic eyes showed a significant reduction in the mean SE (-10.00 D) and SE anisometropia (-9.45 D) preoperatively to -0.06 D and +0.37 D at 1mo after FS-LASIK or SMILE, respectively. There were 70% of the eyes within ±0.50 D and 87% of the eyes within ±1.00 D of the achieved SE at 1mo postoperatively. Our results were comparable with those of Ghanem *et al*[16] studied 18 children with myopic anisometropic amblyopia and reported 77.8% of eyes and 55.6% of eyes were within ±1.00 D of the achieved SE at 6mo and at 2y after LASIK, respectively. Myopic shifts in children after corneal refractive surgery has also been reported in previous studies. Ghanem *et al*[16] observed a -2.25 D myopic

shift at 2y postoperatively. Lin *et al*[11] reported a -2.74 D mean myopic regression in 12 children with myopic anisometropia after a mean of 33.3±14.2mo after LASIK. Although the refraction changes over time after FS-LASIK or SMILE were not statistically significantly, a -0.35 D myopic shift in amblyopic eyes and a -0.20 D refractive error were deepened in the fellow eyes at approximately 8mo compared to 1mo postoperatively were observed in our study. Continued axial growth that accompanies emmetropia, vigorous healing, and an inflammatory reaction following corneal surgery may be attributed to unstable refractions seen in children. However, myopic regression was not considered a contraindication to corneal refractive surgery for children who were failed with non-operative methods for high anisometropia amblyopia.

Ghanem *et al*[16] reported 18 children with myopic anisometropic amblyopia had an improvement in logMAR CDVA from 0.72±0.13 preoperatively to 0.47±0.17 after 2y following LASIK. Astle *et al*[28] reported a mean of 1.6 lines (range 0 to 7 lines) of visual acuity improvement in 28 eyes at a mean of 5.15y follow-up, and patients with measurable stereopsis were improved from 18% preoperatively to 49% after PRK or LASEK. Astle *et al*[15] also reported that 63.6% of 33 measurable children had an improvements in CDVA after LASEK, and patients with positive stereopsis improved from 39.4% preoperatively to 87.9% at 1y postoperatively. Our results showed that logMAR CDVA of amblyopic eyes was improved from 0.98±0.63 preoperatively to 0.41±0.33 after a mean of 8mo after FS-LASIK or SMILE with or without maintenance subsequent to amblyopia therapy in the selected pediatric patients. Of the 23 patients who completed the last follow up examination, 86% had gains of more than two lines in logMAR CDVA, and 21.2% recovered different levels of near stereopsis. The effectiveness of visual acuity improvements and binocular vision achievement for patients with unilateral high myopic anisometropia after FS-LASIK or SMILE was in accordance with previous studies.

A decrease in contrast sensitivity is one of the clinical characteristics of amblyopia. Previous studies have shown that contrast sensitivity was significantly reduced during the early stages after PRK or LASIK in adults, and needed about 3mo for LASIK and 6 to 12mo for PRK to recover[29-30]. The decrease in contrast sensitivity after PRK was considered to be related to the absence of Bowman's membrane, an irregular healing of the corneal epithelium, the formation of haze and an irregular astigmatism postoperatively. Reasons behind the deceased contrast sensitivity after LASIK may be due to corneal edema, corneal flap and stromal layer not completely attached residual tissue debris, corneal wound healing reactions, and an increase in high order aberrations might be the reasons for the decrease of contrast sensitivity after LASIK. Psychophysical contrast sensitivity measurement software can be used to detect contrast sensitivity in different contrast and spatial frequencies. Our results showed that contrast sensitivities of amblyopic eyes in the low and mild spatial frequencies (0.5, 2 and 8 cpd) were significantly improved after SMILE or FS-LASIK, and the contrast sensitivities of amblyopic eyes at 2 and 8 cpd and dominant eyes at 0.5 cpd were significantly increased during a mean 8-month follow-up time. The improvement in contrast sensitivity in our study might be attributed to refractive correction and/or the elimination of anisometropia and aniseikonia, and further benefits from postoperative amblyopia therapy. A transfer effect of amblyopic eyes and a learning effect might be the reasons for the improvement in contrast sensitivity in the untreated fellow eyes[25]. However, due to the poor visual acuity of the amblyopic eyes, only the low and mild spatial frequency contrast sensitivities were measured, and longer-term changes in contrast sensitivity should be observed further.

There were no intraoperative or postoperative complications happened during follow-ups after FS-LASIK and SMILE in our study. Specific complications of femtosecond laser refractive surgeries in adults have been reported previously. These complications have included a negative pressure ring depigmentation, the formation of opaque small bubbles, a corneal flap that is difficult to lift or a lenticule that is difficult to separate[31]. These complications were related to among others, the experience of the surgeons, patient cooperation and surgical equipments. SMLIE procedures can avoid corneal flap-associated complications, while also being minimally invasive and offering a rapid recovery. In our study, only three patients underwent SMILE procedures, and more patients and longer follow-ups were needed for further observations. In all, we observed that there were several advantages of FS-LASIK and SMILE over traditional refractive surgeries in minor patients. First, for it was not necessary to flatten the cornea but just parallel to the surface of the cornea in FS-LASIK and SMILE, the negative pressure produced by femtosecond laser was smaller than that of mechanical microkeratome done. The smaller the negative pressure, the lower the discomfort symptoms, and the smaller the potential damage to the intraocular tissues. Second, the smaller diameter of the femtosecond laser negative pressure ring was much more suitable for younger patients with a smaller eyelid width that needed for traditional LASIK. Third, the surgeon can use their hands to help fix the head of the child when the flap is made by the femtosecond laser. Therefore, compared with the traditional LASIK, less cooperation requirements of the femtosecond laser corneal refractive surgery were needed.

Our results agreed with previous studies that the femtosecond laser corneal refractive surgery procedure was a promising alternative to high myopic anisometropic amblyopia, particularly for those patients who were failed with spectacles and/or CLs,

and more patients and longer term follow-ups are still needed to further study.

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