

# Binocular Summation With Quantitative Contrast Sensitivity Function: A Novel Parameter to Evaluate Binocular Function in Intermittent Exotropia

Xiaolan Chen,<sup>1</sup> Jing Liu,<sup>1</sup> Zixuan Xu,<sup>1</sup> Yijing Zhuang,<sup>1</sup> Yusong Zhou,<sup>1</sup> Yunsu He,<sup>1</sup> Ying Yao,<sup>1</sup> Junpeng Yuan,<sup>1</sup> Lei Feng,<sup>1</sup> Qingqing Ye,<sup>1</sup> Yun Wen,<sup>1</sup> Yu Jia,<sup>1</sup> Zhong-Lin Lu,<sup>2-4</sup> Xiaoming Lin,<sup>1</sup> and Jinrong Li<sup>1</sup>

<sup>1</sup>State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangdong Provincial Key Laboratory of Ophthalmology and Visual Science, Guangzhou, China

<sup>2</sup>Division of Arts and Sciences, NYU Shanghai, Shanghai, China

<sup>3</sup>Center for Neural Science and Department of Psychology, New York University, New York, New York, United States

<sup>4</sup>NYU-ECNU Institute of Brain and Cognitive Neuroscience, Shanghai, China

Correspondence: Jinrong Li, State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, 54 Xianlie South Road, Guangzhou 510060, China; [lijingr3@mail.sysu.edu.cn](mailto:lijingr3@mail.sysu.edu.cn).

Xiaoming Lin, State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, 54 Xianlie South Road, Guangzhou 510060, China; [linxiaom139@139.com](mailto:linxiaom139@139.com).

XC and JL contributed equally to this work as co-first authors.

**Received:** June 30, 2023

**Accepted:** December 4, 2023

**Published:** January 2, 2024

Citation: Chen X, Liu J, Xu Z, et al. Binocular summation with quantitative contrast sensitivity function: A novel parameter to evaluate binocular function in intermittent exotropia. *Invest Ophthalmol Vis Sci*. 2024;65(1):3. <https://doi.org/10.1167/iov.65.1.3>

**PURPOSE.** Intermittent exotropia (IXT) is the most common form of strabismus. Surgery can potentially improve binocular function in patients with IXT. We aimed to evaluate binocular function using a novel parameter—binocular summation ratio (BSR), measured using quantitative contrast sensitivity function (CSF) in patients with IXT before and after surgery.

**METHODS.** Prospective study of 63 patients with IXT and 41 healthy controls were consecutively enrolled and underwent quantitative CSF testing binocularly and monocularly. BSR was calculated by dividing the CSF of the binocular value by the better monocular value. Forty-eight patients with IXT underwent strabismus surgery. BSR, stereoacuity, fusion ability, and strabismus questionnaires were assessed pre-operatively and 2 months postoperatively.

**RESULTS.** Sixty-three patients with IXT (median age = 9 years) compared with 41 healthy controls showed a worse mean BSR based on all CSF metrics at baseline (the area under the log CSF [AULCSF], spatial frequency [SF] cutoff, and contrast sensitivity at 1.0–18.0 cpd SF). All 48 patients with IXT showed successful alignment after surgery, and there were significant improvements in BSR based on the AULCSF, SF cutoff, and contrast sensitivity at 6.0, 12.0, and 18.0 cpd SF, respectively. The distance stereoacuity and fusion ability also improved after surgery, and a better BSR was associated with better stereoacuity and fusion. For strabismus questionnaires, the psychosocial subscale scores improved postoperatively, whereas the functional subscale scores did not change.

**CONCLUSIONS.** BSR based on quantitative CSF can characterize binocular function across a range of spatial frequencies and can be used as a supplemental measurement for monitoring binocularity in patients with IXT in clinical settings.

**Keywords:** binocular summation, contrast sensitivity function (CSF), intermittent exotropia (IXT), strabismus surgery

Intermittent exotropia (IXT) is the most common form of strabismus, with a prevalence varying from 1.0 to 3.9% across geographic regions.<sup>1-3</sup> Surgery is the primary treatment for patients with IXT to align eye deviation<sup>4-6</sup> and restore binocular functions.<sup>7,8</sup> However, the current battery of clinical binocular function assessments before and after strabismus surgery, such as stereoacuity and fusion tests, is based on dichoptic methods.<sup>9</sup> These measurements have certain limitations, some of which may introduce artifacts due to glasses<sup>10</sup>; some measurements may only classify binocular vision into discrete values and require patients to have some level of binocular function.<sup>11</sup> Therefore, it is necessary to develop a more sensitive method for assess-

ing binocular function among patients with IXT in clinical practice.

Binocular summation is an index of superior visual performance on visual threshold tasks of binocular over monocular vision.<sup>12</sup> In normal individuals, visual function for binocular viewing is usually better than monocular viewing.<sup>13-15</sup> In contrast, patients with strabismus may have worse visual function for binocular viewing over monocular viewing due to eye deviation.<sup>16</sup> Even after successful alignment, their binocular vision may still be inferior to that of normal individuals.<sup>17</sup> However, some patients with strabismus exhibit some amount of summation even with no binocular function. Therefore, assessing binocular summation

can provide valuable insights into subtle binocular visual changes in patients with strabismus. Binocular summation can be calculated based on different psychophysical vision tasks to characterize binocular function. Previous studies have demonstrated that binocular summation is diminished in patients with strabismic.<sup>16,18</sup> However, there is heterogeneity in the subtype of strabismus and in the methods for measuring binocular summation, leading to different manifestations of binocular summation in strabismus. In a previous study of patients with IXT, binocular summation was measured at low and high contrasts, and the results showed that patients with IXT had abnormal binocular summation at low contrast.<sup>19</sup> Pineles et al. studied the effect of surgical intervention on binocular summation in patients with strabismus and compared the binocular summation before and after surgery by low- and high-contrast visual acuity tests. They found that the binocular summation was worse at low-contrast visual acuity, and the impaired binocular summation can be improved after successful alignment.<sup>20</sup> However, the patients they analyzed contained different types of strabismus with only a small sample size of patients with IXT. The relationship among binocular summation, other binocular vision measurements in clinical settings (such as stereopsis and fusion ability), and quality of life have not been analyzed.

To date, binocular summation has been measured using chart visual function tests, which have single-scale measurements, such as fixed-letter acuity testing<sup>18</sup> or limited-range contrast sensitivity testing.<sup>21</sup> Although some computerized tests based on contrast sensitivity function (CSF) provide more comprehensive visual assessments, their clinical application is limited due to imprecision and time-consuming procedures.<sup>22,23</sup> The quantitative contrast sensitivity function provides a solution.<sup>24</sup> This method utilizes a Bayesian adaptive algorithm and incorporates 10 alternative forced-choice (10AFC) identification tasks, thus enabling the measurement of the complete contrast sensitivity function within a clinically feasible testing duration. Therefore, quantitative contrast sensitivity function can provide more reliable and sensitive measures of contrast sensitivity for detecting small visual changes under various visual conditions.<sup>25–27</sup>

This study aimed to investigate a novel parameter for assessing binocular function in patients with IXT, that is, the binocular summation ratio (BSR), which is measured using the quantitative contrast sensitivity function. We compared the BSR between patients with IXT and healthy controls. Additionally, we compared the changes in the BSR before and after strabismus surgery in patients with IXT. Traditional binocular function measurements, such as stereoacuity and fusion ability, as well as the quality-of-life scores before and after surgery in patients with IXT were also analyzed.

## METHODS

### Participants

This study was approved by the Institutional Ethics Committee of Zhongshan Ophthalmic Center (ZOC) of Sun Yat-Sen University, a tertiary ophthalmic center in Guangzhou, China. Eligible patients were individuals who were 5 to 45 years old with a diagnosis of basic IXT<sup>28</sup> from July 1, 2021, to May 31, 2022. Informed consent was obtained from all participants or parents. The exclusion criteria were as follows: (1) amblyopia; (2) constant exotropia, vertical deviation > 5 prism degrees (PDs), and paralytic or restrictive exotropia; (3) pathologic nystagmus; (4) known global

developmental or neurological impairments; (5) myopia  $\geq$  6.00 diopters (D); (6) anisometropia  $\geq$  1.50 D; and (7) previous eye surgery or trauma. The inclusion criteria for the control group were as follows: (1) best corrected visual acuity (BCVA)  $\geq$  20/20; (2) anisometropia  $\leq$  1.50 D; (3) myopia < 6.00 D; (4) orthotropia or exophoria < 8 PDs; and (4) no history of eye diseases other than refractive error.

All participants underwent a comprehensive assessment, including BCVA (Early Treatment Diabetic Retinopathy Study [ETDRS] tumbling E Chart; WEHEN Vision, Guangzhou, Guangdong, China), subjective refraction, slit-lamp biomicroscopy, fundus examination, near stereoacuity (Random Dot Stereo Acuity Test; Vision Assessment Corporation, Elk Grove Village, IL, USA), distance stereoacuity (Random dot Stereoacuity Test; Stereo Optical, Inc., Chicago, IL, USA), distance and near binocular fusion (Worth-4-dot test), the magnitude of the deviation (at 33 cm and 6 m using the prism-and-cover test), monocular and binocular contrast sensitivity function using quantitative CSF (Manifold Contrast Vision Meter; Adaptive Sensory Technology, Inc., San Diego, CA, USA) and strabismus questionnaires (for the details of questionnaires see the Supplementary Methods). All tests were performed by trained technicians for participants 1 month before and 2 months after surgery. All procedures were performed in ZOC by an experienced surgeon. Surgical success was defined as orthotropia, X(T)  $\leq$  10 prism diopters (PD) and E(T)  $\leq$  5 PD in the primary position at distance and near fixations, and without diplopia.<sup>8</sup>

### Contrast Sensitivity Function Measurement and Binocular Summation Calculation

The quantitative CSF displayed the optimal test stimulus, which was selected from a total of 2432 possible stimuli in each trial, to maximize the information gained about the subject's individual CSF. Unlike other CSF assessments that use sine-wave gratings, quantitative CSF utilizes a 10AFC digit identification task. This approach not only captures the narrowband frequency information characteristic of gratings but also reduces the guessing rate and improves test efficiency.<sup>29</sup> Moreover, it is user-friendly for both young and old non-Latin alphabet-using observers.<sup>30</sup>

The CSF measurement was implemented in a dark room at a test distance of 3 m with a GAMMA-corrected LCD monitor (40-inch, NEC LCD Monitor MultiSync P404), which had a resolution of 1920  $\times$  1080, an average luminance of 150 cd/m<sup>2</sup>, and a vertical refresh rate of 24 to 85 Hz. The stimuli for the tests were a set of three Sloan digits. These digits had varying spatial frequencies and contrasts, with contrast decreasing from left to right (for an example of stimuli, see Supplementary Fig. S1). Each trial began with a brief beep, and then a white bounding box appears for 500 ms to cue the size and location of the upcoming stimulus. Then, participants were asked to verbally report the three digits presented on the screen to the examiner, who operated the test with a hand-held tablet and recorded the responses. The stimulus disappeared after all responses were entered. A new trial began 500 ms later. No feedback was provided during the test. Subjects took 25 trials with their right eye, their left eye, and with both eyes together, with approximately 3 to 5 minutes per test, whereas the nontested eye was occluded. To avoid learning effects, each participant was thoroughly briefed and provided with multiple practice pretests. Additionally, there was a short break for every test to minimize visual fatigue.

The binocular summation value was indicated by the BSR, which is calculated by dividing the CSF of the binocular value by the better monocular value:

$$BSR = \frac{CSF_{binocular}}{CSF_{better\ eye}}$$

The CSF metrics include contrast sensitivity at six spatial frequencies (1.0, 1.5, 3.0, 6.0, 12.0, and 18.0 cpd), the area under the log CSF (AULCSF), and the spatial frequency (SF) cutoff, which were chosen to calculate the BSR separately. The AULCSF indicated a broad measure of spatial vision, which was calculated based on the CSF curve from 1.5 to 18.0 cpd as a summary metric. The SF cutoff was defined as the spatial frequency at which contrast sensitivity = 1.0 and was used to characterize the resolution of the visual system.

### Statistical Analysis

The categorical variables were expressed as frequencies and proportions, and the continuous variables were

expressed as the mean and SD or median and interquartile range (IQR). The normality of the data was assessed with the Shapiro-Wilks test. For continuous variables, the IXT and control groups were compared using a *t* test or Mann-Whitney *U* test. Pre- and postoperative BSRs and questionnaire scores were compared using paired *t* tests or Wilcoxon signed-rank tests. For categorical variables,  $\chi^2$  and McNemar tests were used. The correlation between the BSR and clinical characteristics was calculated using Pearson's or Spearman's correlation analysis. The *P* values less than 0.05 were considered statistically significant.

### RESULTS

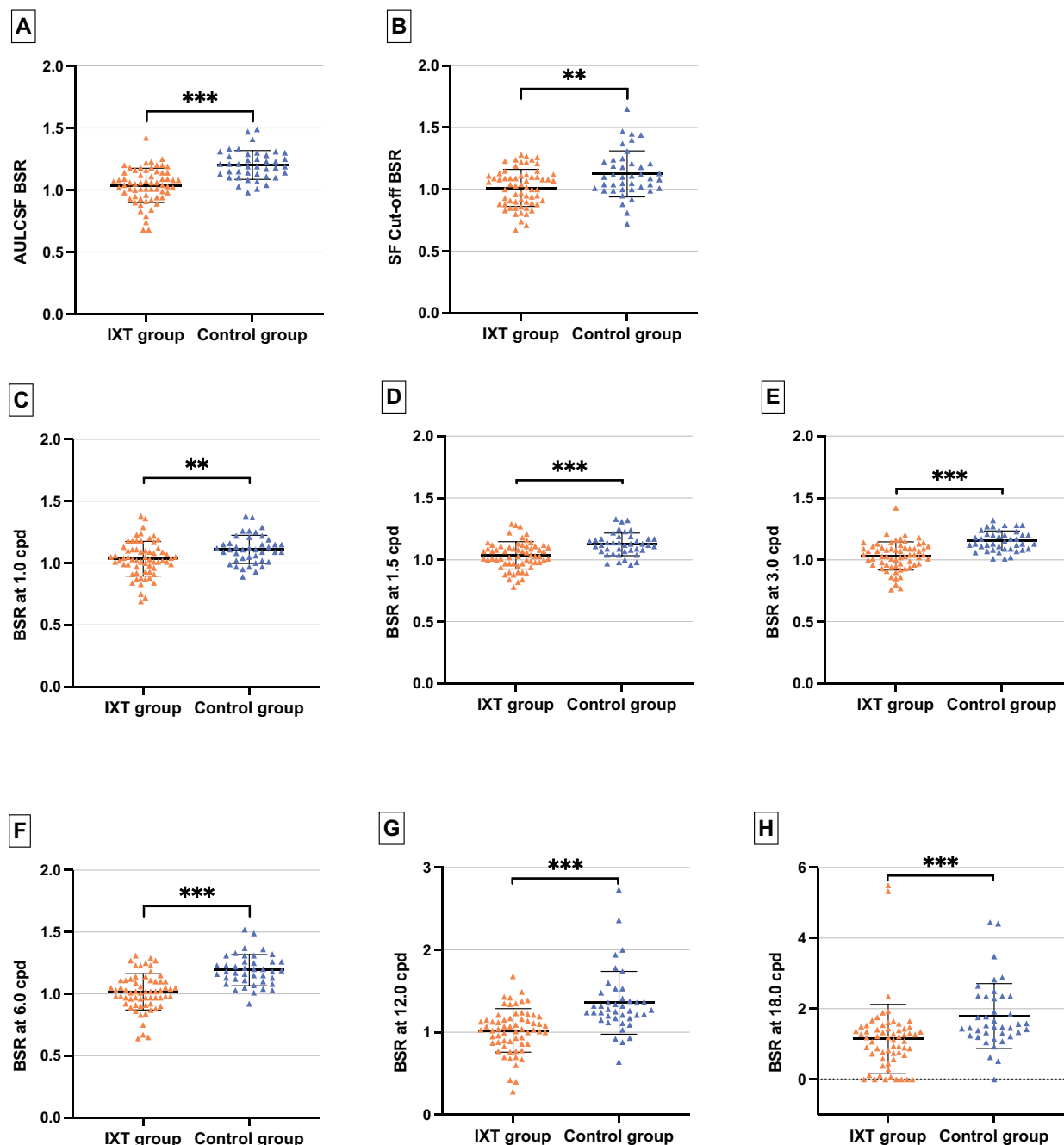
Sixty-three patients with IXT with a median age of 9 years (IQR = 7–21) and 41 healthy controls with a median age of 10 years (IQR = 7–24) were enrolled in the study. A summary of the demographic information of the two groups is provided in Table 1.

TABLE 1. Detailed Information of the IXT Group and Control Group

Characteristics	IXT Group <i>N</i> = 63	Control Group <i>N</i> = 41	<i>P</i> Value
Gender, females, <i>n</i> (%)	33 (52.4)	19 (46.3)	0.55
Age, median (IQR), years	9 (7–21)	10 (7–24)	0.52
BCVA, LogMAR			
Right eye	−0.01 ± 0.05	−0.00 ± 0.06	0.46
Left eye	−0.01 ± 0.05	−0.00 ± 0.06	0.34
SER, diopter			
Right eye	−0.34 ± 1.54	−0.65 ± 1.89	0.27
Left eye	−0.36 ± 1.42	−0.52 ± 1.93	0.66
BCVA-IOD, LogMAR	0.01 ± 0.03	0.02 ± 0.03	0.52
Stereoacuity <sup>a</sup> , log arcsec			
Near random dot	2.68 ± 0.96	1.82 ± 0.10	<b>&lt;0.001</b>
Distance random dot	3.28 ± 0.89	1.84 ± 0.20	<b>&lt;0.001</b>
Angle of deviation, PD			
Near	37 ± 13	1 ± 2	<b>&lt;0.001</b>
Distance	33 ± 12	1 ± 2	<b>&lt;0.001</b>
Ability to fuse, <i>n</i> (%)			
Near	38 (60.3)	40 (97.6)	<b>&lt;0.001</b>
Distance	9 (14.3)	40 (97.6)	<b>&lt;0.001</b>
Monocular CSF metrics—average of 2 eyes			
AULCSF, log unit	1.14 ± 0.19	1.11 ± 0.20	0.38
SF cutoff, cpd	1.33 ± 0.09	1.34 ± 0.11	0.73
1.0 cpd, log CS	1.30 ± 0.19	1.29 ± 0.14	0.58
1.5 cpd, log CS	1.35 ± 0.17	1.33 ± 0.14	0.42
3.0 cpd, log CS	1.35 ± 0.17	1.31 ± 0.16	0.23
6.0 cpd, log CS	1.13 ± 0.20	1.09 ± 0.22	0.37
12.0 cpd, log CS	0.64 ± 0.23	0.62 ± 0.26	0.69
18.0 cpd, log CS	0.24 ± 0.20	0.26 ± 0.22	0.72
BSR of CSF metrics			
AULCSF	1.04 ± 0.14	1.20 ± 0.12	<b>&lt;0.001</b>
SF cutoff	1.01 ± 0.15	1.12 ± 0.19	<b>0.001</b>
1.0 cpd	1.04 ± 0.14	1.11 ± 0.11	<b>0.005</b>
1.5 cpd	1.04 ± 0.11	1.13 ± 0.09	<b>&lt;0.001</b>
3.0 cpd	1.03 ± 0.11	1.15 ± 0.08	<b>&lt;0.001</b>
6.0 cpd	1.02 ± 0.15	1.19 ± 0.13	<b>&lt;0.001</b>
12.0 cpd	1.02 ± 0.26	1.36 ± 0.38	<b>&lt;0.001</b>
18.0 cpd	1.15 ± 0.97	1.79 ± 0.92	<b>&lt;0.001</b>

AULCSF, the area under the log contrast function; BCVA, best corrected visual acuity; BSR, binocular summation ratio; CS, contrast sensitivity; CSF, contrast sensitivity function; IOD, interocular difference, calculated by subtracting the BCVA of the right eye from the left eye; LogMAR, the logarithmic minimum angle of resolution; PDs, prism degrees; SER, spherical equivalent refraction; SF, spatial frequency. Values are shown in mean ± SD, unless otherwise indicated. Statistically significant *P* values are shown in bold. CS represents 1/contrast threshold.

<sup>a</sup> Nil stereoacuity was assigned a value of 4.0 log arcsec.



**FIGURE 1.** Comparison of baseline mean BSR based on CSF metrics between patients with IXT and healthy controls. (A) AULCSF BSR. (B) SF cutoff BSR. (C) BSR at 1.0 cpd. (D) BSR at 1.5 cpd. (E) BSR at 3.0 cpd. (F) BSR at 6.0 cpd. (G) BSR at 12.0 cpd. (H) BSR at 18.0 cpd. \*\*\* $P < 0.001$ , \*\* $P < 0.01$ . AULCSF, the area under the log contrast function; BSR, binocular summation ratio; SF, spatial frequency.

### The Baseline Binocular Summation and Monocular Function of Patients With IXT Compared With Healthy Controls

We compared baseline BSR from patients with IXT before surgery with that from healthy subjects. BSR was significantly decreased in all CSF metrics in the IXT group compared with the controls, including AULCSF, SF cutoff, 1.0 cpd, 1.5 cpd, 3.0 cpd, 6.0 cpd, 12.0 cpd, and 18.0 cpd (all  $P < 0.01$ ; Fig. 1). We divided the subjects into two subgroups

based on age: the pediatric group (5–17 years old) and the adult group (18–45 years old). Among children, except for the BSR at 1.0 cpd, the BSRs were consistently lower in patients with IXT than in healthy controls. Among adults, except for the BSR based on the SF cutoff, the BSRs were still lower in patients with IXT than in healthy controls (see Supplementary Table S1).

However, there was no significant difference in any monocular CSF metrics, monocular visual acuity, refractive error, or interocular visual acuity difference between the

**TABLE 2.** Clinical Metrics of Patients With IXT After Successful Corrective Surgery

Characteristics	Pre-Operative <i>n</i> = 48	Postoperative <i>n</i> = 48	<i>P</i> Value
Angle of deviation, PDs <sup>a</sup>			
Near	37 ± 12	−1 ± 5	<b>&lt;0.001</b>
Distance	33 ± 12	−1 ± 6	<b>&lt;0.001</b>
BCVA-surgical eyes, LogMAR	−0.01 ± 0.05	−0.02 ± 0.05	0.07
Stereoacuity, log arcsec			
Near random dot	2.63 ± 0.99	2.35 ± 0.78	0.13
Distance random dot	3.22 ± 0.89	2.90 ± 0.93	<b>0.048</b>
Ability to fuse, <i>n</i> (%)			
Near	30 (62.5)	38 (79.2)	0.12
Distance	8 (16.7)	33 (68.8)	<b>&lt;0.001</b>
Monocular CSF metrics – surgical eyes			
AULCSF, log unit	1.15 ± 0.21	1.15 ± 0.24	0.96
SF cutoff, cpd	21.22 ± 4.19	20.77 ± 6.87	0.99
1.0 cpd, log CS	1.36 ± 0.19	1.34 ± 0.20	0.54
1.5 cpd, log CS	1.40 ± 0.18	1.43 ± 0.22	0.26
3.0 cpd, log CS	1.37 ± 0.19	1.39 ± 0.22	0.66
6.0 cpd, log CS	1.13 ± 0.23	1.12 ± 0.28	0.82
12.0 cpd, log CS	0.61 ± 0.23	0.59 ± 0.30	0.98
18.0 cpd, log CS	0.22 ± 0.17	0.24 ± 0.22	0.47
BSR of CSF metrics			
AULCSF	1.04 ± 0.15	1.15 ± 0.27	<b>0.016</b>
SF cutoff	1.00 ± 0.15	1.14 ± 0.27	<b>0.008</b>
1.0 cpd	1.02 ± 0.14	1.04 ± 0.16	0.613
1.5 cpd	1.03 ± 0.11	1.07 ± 0.15	0.166
3.0 cpd	1.03 ± 0.12	1.10 ± 0.19	0.099
6.0 cpd	1.03 ± 0.16	1.17 ± 0.49	<b>0.023</b>
12.0 cpd	1.03 ± 0.28	1.29 ± 0.44	<b>0.002</b>
18.0 cpd	1.20 ± 1.07	1.66 ± 0.72	<b>0.003</b>

AULCSF, the area under the log contrast sensitivity function; BCVA, best corrected visual acuity; BSR, binocular summation ratio; CS, contrast sensitivity; CSF, contrast sensitivity function; LogMAR, logarithmic minimum angle of resolution; PDs, prism degrees; SF, spatial frequency.

Values are shown in mean ± SD, unless otherwise indicated. Statistically significant *P* values are shown in bold. CS represents 1/contrast threshold.

<sup>a</sup> Negative value indicates esotropia.

two groups. The interocular visual acuity difference in the two groups was compared to exclude the effect on BSR results.<sup>31,32</sup> The pre-operative stereoacuity and fusion ability in patients with IXT was significantly worse than that in healthy controls (all *P* < 0.001; see Table 1). Overall, patients with IXT had significantly diminished binocular visual function, including the BSR at all CSF metrics, stereoacuity, and fusion ability, compared to healthy controls. Monocular visual function was not significantly different from that of healthy controls.

### Binocular Function of Patients With IXT Before and After Surgery

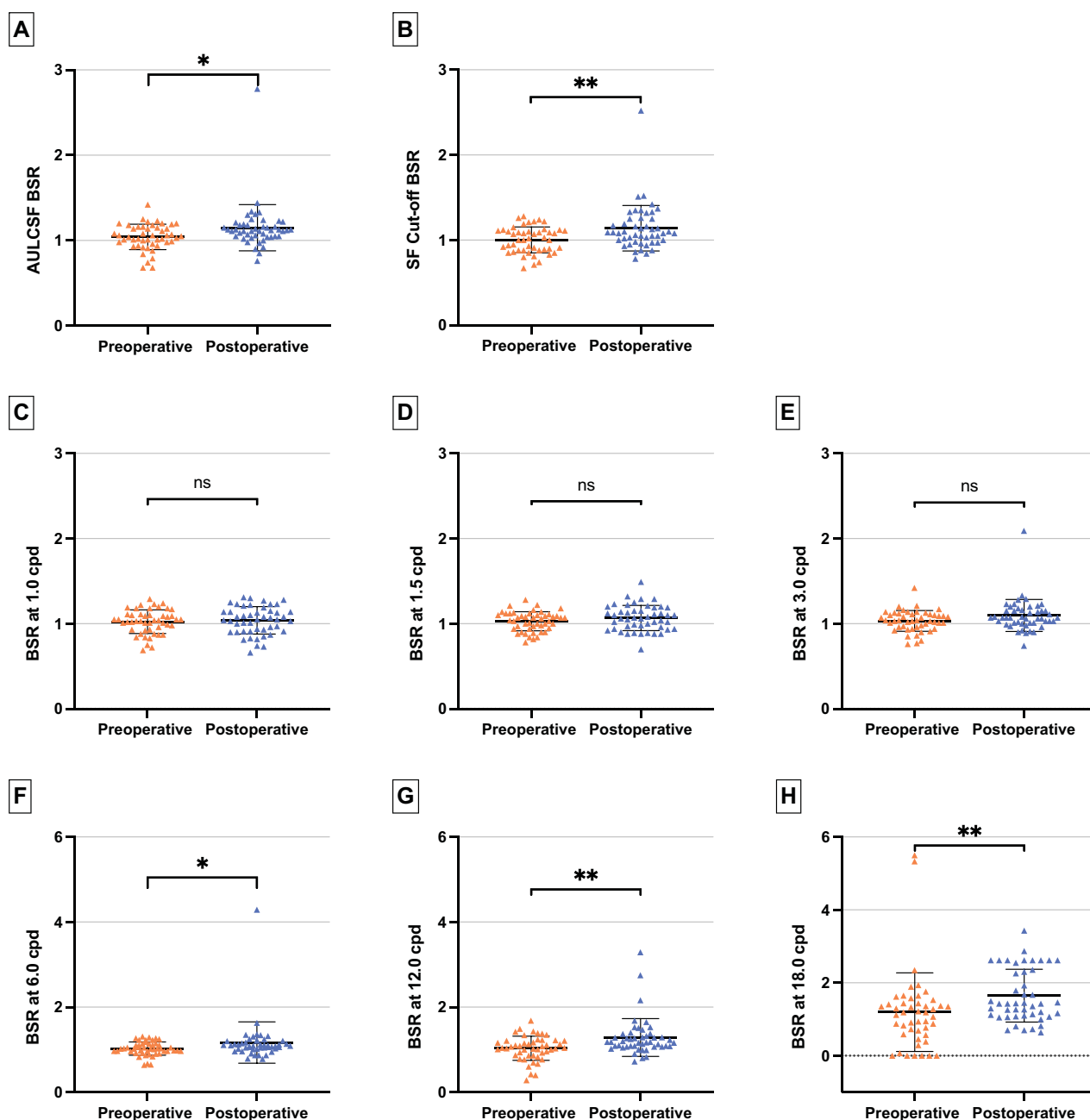
Forty-eight patients with IXT underwent unilateral strabismus surgery. The median age (IQR) was 11 years (IQR = 7–20 years), and 25 patients (52.1%) were female patients. All patients met the criteria for surgical success. Measurements before and after surgery are summarized in Table 2. After surgery, more than 62.5% of patients with IXT showed an increase in the BSR at different spatial frequencies. The BSR based on AULCSF, SF cutoff, 6.0 cpd, 12.0 cpd, and 18.0 cpd improved significantly (all *P* < 0.05; Fig. 2). However, there was no significant improvement in the BSR at 1.0 cpd, 1.5 cpd, and 3.0 cpd (all *P* > 0.05). We also conducted age subgroup analysis on the postoperative changes in the BSR. The pattern of results in the pedi-

atric group (aged 5–17 years) was consistent with the original analysis. However, in the adult group (aged 18–45 years), there was no significant improvement in the post-operative BSR across all spatial frequencies (see Supplementary Table S2). In addition, there was no significant difference in any monocular CSF metrics before and after surgery (all *P* > 0.05). To further evaluate BSR recovery, we compared the patients' BSR after surgery with normal controls. We found that the patients' BSR based on SF cutoff and the BSR at 12.0 and 18.0 cpd after surgery was similar to that of normal controls (*P* = 0.815, *P* = 0.061, and *P* = 0.466, respectively), whereas the BSR based on AULCSF, 1.0, 1.5, 3.0, and 6.0 cpd were still worse than that of normal controls.

In terms of stereoacuity, there was a significant difference in distance stereoacuity before and after surgery, whereas there was no statistically significant difference in near stereoacuity (see Table 2). Nineteen patients (39.60%) had improved distance stereoacuity after the procedure. There was also a significant difference between patients with measurable distance fusion ability before and after surgery (8 [16.7%] vs. 33 [68.8%], *P* < 0.001), although there were no changes in measurable distance fusion ability and near fusion ability.

We further analyzed the relationship among the BSR, stereoacuity, and fusion ability. The improvement in the BSR at 1.0 cpd correlated with the improvement in distance stereoacuity. In addition, both the pre-operative AULCSF BSR



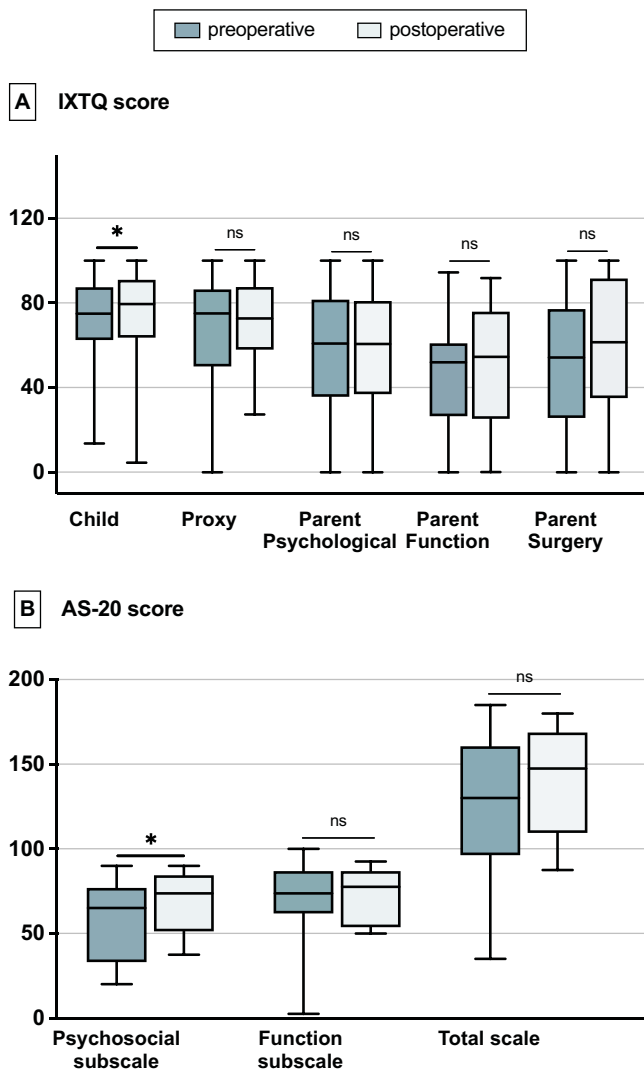


**FIGURE 2.** Summary of improvement in the mean BSR based on CSF metrics in patients with IXT after surgery. (A) AULCSF BSR. (B) SF cutoff BSR. (C) BSR at 1.0 cpd. (D) BSR at 1.5 cpd. (E) BSR at 3.0 cpd. (F) BSR at 6.0 cpd. (G) BSR at 12.0 cpd. (H) BSR at 18.0 cpd. ns, not significant, \*\* $P < 0.01$ , \* $P < 0.05$ . AULCSF, the area under the log contrast function; BSR, binocular summation ratio; SF, spatial frequency.

and BSR at 6.0 and 18.0 cpd were correlated with preoperative near stereoacuity, whereas the postoperative BSR at 1.0 cpd, 1.5 cpd, and 3.0 cpd were also correlated with postoperative distance stereoacuity (see Supplementary Fig. S2). For fusion ability, the postoperative AULCSF BSR and BSR at 1.0 cpd, 1.5 cpd, 3.0 cpd, and 6.0 cpd were correlated with near fusion ability (all  $P < 0.05$ ), whereas the postoperative AULCSF BSR and BSR at 1.0 cpd, 1.5 cpd, and 3.0 cpd were correlated with distance fusion ability (all  $P < 0.05$ ). Overall, a better BSR indicates better stereoacuity and fusion ability.

### Health-Related Quality of Life and Functional Binocular Vision According to Strabismus Questionnaires

Thirty-six children with IXT and adolescents completed the Intermittent Exotropia Questionnaire (IXTQ) before and 2 months after surgery; the mean age of respondents was 9 years (range = 5–15 years), and 50% of them were girls, with one of their parents also completing the questionnaire. Twelve adult patients with IXT completed the Adult Strabismus Questionnaire (AS-20); the mean age of respon-



**FIGURE 3.** Box plots of preoperative and postoperative IXTQ and AS-20 scores in all patients with IXT after surgery. Notes: ns, not significant,  $*P < 0.05$ . Changes in the IXTQ and AS-20 scores were evaluated as the difference between the pre-operative and postoperative scores. IXTQ, intermittent exotropia questionnaire; AS, adult strabismus.

dents was 29 years (range = 21–45 years), and 58.4% of them were women. In the IXTQ, there was a significant difference in child subscale scores before and after surgery (72.7 [59.1–86.3] vs. 77.3 [63.6–90.9],  $P = 0.03$ ; Fig. 3A). However, there was no significant difference in the proxy, psychological, function, and surgery subscales before and after surgery (see Supplementary Table S3). Adults who completed the AS-20 showed significant differences in the psychosocial subscale scores (65.0 [33.1–76.9] vs. 73.8 [51.3–84.4],  $P = 0.04$ ; Fig. 3B) after surgery, whereas there was no significant improvement in the function and total scale scores (see Supplementary Table S3). Both the child subscale of the IXTQ and the psychosocial subscale of the AS-20 are psychosocial-related scales. The questions for the child subscale of the IXTQ and the psychosocial subscale of the AS-20 are shown in Supplementary Tables S4 and S5, respectively.

## DISCUSSION

In this study, we utilized the BSR based on a quantitative contrast sensitivity function to evaluate binocular function in patients with IXT. We found widespread decreased BSRs in patients with IXT compared with healthy controls at all spatial frequencies but improved BSRs at mid and high spatial frequencies after successful alignment, although not at normal individual levels. The BSR based on quantitative contrast sensitivity function was correlated with traditional clinical binocular visual function tests, and a better BSR was associated with better distance stereoacuity and fusion ability.

Binocular summation is an index of functional binocular vision that has been well studied in the laboratory setting in healthy individuals.<sup>33</sup> The results of traditional stereoacuity tests vary greatly without measurable stereoacuity, and the absence of measurable stereoacuity is common in patients with strabismus who have impaired binocular function.<sup>34</sup> Unlike stereoacuity, binocular summation is not affected by dichoptic viewing and therefore is increasingly used in some clinical studies as a measure of functional binocular vision.<sup>35,36</sup> A recent study found that a chart-based contrast sensitivity measure decreased binocular contrast sensitivity at all spatial frequencies in patients with IXT compared to healthy subjects.<sup>37</sup> Although binocular metrics were used instead of the BSR, this is consistent with the decreased BSR we observed for all spatial frequencies of patients with IXT. Furthermore, subgroup analysis based on age revealed a similar decrease for both adult and pediatric patients.

A decrease in binocular summation in patients with strabismus has been reported to be restored by surgery.<sup>20,38</sup> Pineles et al. demonstrated that a diminished binocular summation in several different subtypes of strabismus based on the chart visual acuity test can be improved after successful alignment, most frequently improved at low-contrast acuity.<sup>20</sup> A study on BSR changes after strabismus surgery in patients with IXT found that when the BSR was measured using LEA number acuity tests, improvements were observed at both high contrasts (100%) and low contrasts (10, 5, and 2.5%) postoperatively.<sup>19</sup> These studies about binocular summation were based on chart vision function tests with limited contrast levels. In our study, binocular summation was measured with different contrast levels across different spatial frequencies. We also found that BSR improvements following successful surgery were most evident at mid and high spatial frequencies in the patients with IXT. However, we observed no significant recovery in the BSR for low spatial frequency. This difference could be attributed to two factors. First, it may be due to the different measurement methods of different studies. Second, it is possible that the recovery time courses vary for different spatial frequencies.<sup>39</sup> After surgery, BSR recovery first occurs at mid and high spatial frequencies, whereas recovery was not observed at a low spatial frequency during our follow-up time. The recovery trend in the child subgroup aligned with the overall trend, although no significant improvement was observed in the adult subgroup, possibly due to the limited sample size.

Stereoacuity and fusion at distance also improved after surgery. There was a positive correlation between the improvement in the BSR at low spatial frequencies and distance stereoacuity improvement. Better BSRs at low spatial frequencies are associated with better distance stereoacuity and distance fusion ability. This finding is consistent with Kattan's study comparing the relationship

between binocular summation using chart visual acuity tests and stereoacuity within the same follow-up interval.<sup>40</sup> Patients had a more significant effect on distance stereoacuity and fusion ability after surgery in our study because binocular vision impairment in IXT usually starts with a decrease in distance binocular visual function first. More parameters make the BSR more measurable and sensitive to changes in interventions. More than 62.5% of patients with IXT showed an increase in the BSR at different spatial frequencies after surgery, whereas only approximately 39.6% of patients with IXT demonstrated improvement in stereoacuity.

We also investigated the quality of life and functional vision questionnaire improvements as a subjective assessment of the benefits of surgery. Several studies have discussed the psychosocial and functional benefits of surgery in both pediatric and adult patients with IXTs.<sup>41,42</sup> In our study, we also observed a significant improvement in the child subscale of the IXTQ for children and the psychosocial subscale of the AS-20 questionnaire adults. However, scores on the functional subscales did not change after the surgery. First, this may be because previous studies showed significant improvements that were generally performed more than 6 months after surgery, and our follow-up period was only 2 months. Second, although none of our patients complained of symptoms of postoperative diplopia, there were also some other non-strabismus-related factors, such as depression symptoms and type D personality, that were associated with the failure of the scales to evaluate improvement after strabismus surgery.<sup>43</sup> Therefore, a longer time is necessary to follow the improvement of the function subscale and enables exploration of the relationship between functional scales and BSR.

There are some limitations in this work. First, the follow-up time of our study was only 2 months. Therefore, some metrics of binocular function with late recovery or functional scales may not be observed. Second, the sample of adults who completed the scale was still small. Furthermore, we did not find significant improvements in functional subscales during the observation period or recovery after surgery, which may be related to additional clinical demographic and psychological factors in addition to strabismus. Last, the subjects who underwent surgery had their contrast testing twice, whereas the control subjects only underwent a single test session. Therefore, future studies are recommended to investigate the long-term improvement of BSR in larger populations and consider the practice effect on the results by conducting multiple test sessions. Additionally, health-related quality of life (HRQOL) should also add other related clinical and psychological assessments.

In conclusion, this study represents the largest cohort of patients with IXT in a real-world clinical setting using a novel BSR parameter calculated by the quantitative contrast sensitivity function, which represents a highly discriminating measure of binocularity to assess surgical intervention. This study is also the most comprehensive analysis, including traditional clinical binocular function tests, stereoacuity and fusion at a distance and near, and strabismus scales. We found the impairment characteristics of functional binocular vision of BSR in patients with IXT across a wide range of spatial frequencies and how surgery restores patients' with IXT binocularity in mid- and high-spatial frequencies. These findings help advance our understanding of real-life vision activities of binocular function in patients with IXT. Furthermore, the efficiency of the algorithm-derived quanti-

tative contrast sensitivity function measurement also offers the opportunity for large-scale clinical trials for patients with IXT in the future in clinical management or research work.

### Acknowledgments

The authors thank the Adaptive Sensory Technology (AST) group for providing the contrast sensitivity test.

Supported by the National Key Research & Development Project, 2020YF2003905.

Disclosure: **X. Chen**, None; **J. Liu**, None; **Z. Xu**, None; **Y. Zhuang**, None; **Y. Zhou**, None; **Y. He**, None; **Y. Yao**, None; **J. Yuan**, None; **L. Feng**, None; **Q. Ye**, None; **Y. Wen**, None; **Y. Jia**, None; **Z.-L. Lu**, Intellectual property interests in methods for measuring contrast sensitivity function and equity interests in Adaptive Sensory Technology, Inc. (San Diego, CA, USA) and Jiangsu Juehua Medical Technology, Ltd. (Jiangsu, China); **X. Lin**, None; **J. Li**, None

### References

- Govindan M, Mohny BG, Diehl NN, Burke JP. Incidence and types of childhood exotropia: a population-based study. *Ophthalmology*. 2005;112(1):104–108.
- Chia A, Roy L, Seenyen L. Comitant horizontal strabismus: an Asian perspective. *Br J Ophthalmol*. 2007;91(10):1337–1340.
- Pan CW, Zhu H, Yu JJ, et al. Epidemiology of intermittent exotropia in preschool children in China. *Optom Vis Sci*. 2016;93(1):57–62.
- Lavrich JB. Intermittent exotropia: continued controversies and current management. *Curr Opin Ophthalmol*. 2015;26(5):375–381.
- Lee HJ, Kim SJ. Long-term outcomes following resection-recession versus plication-recession in children with intermittent exotropia. *Br J Ophthalmol*. 2020;104(3):350–356.
- Jeon H, Jung J, Choi H. Long-term surgical outcomes of early surgery for intermittent exotropia in children less than 4 years of age. *Curr Eye Res*. 2017;42(11):1435–1439.
- Singh A, Sharma P, Singh D, Saxena R, Sharma A, Menon V. Evaluation of FD2 (Frisby Davis distance) stereotest in surgical management of intermittent exotropia. *Br J Ophthalmol*. 2013;97(10):1318–1321.
- Peng T, Xu M, Zheng F, et al. Longitudinal rehabilitation of binocular function in adolescent intermittent exotropia after successful corrective surgery. *Front Neurosci*. 2021;15:685376.
- McCaslin AG, Vancleef K, Hubert L, Read JCA, Port N. Stereotest comparison: efficacy, reliability, and variability of a new glasses-free stereotest. *Transl Vis Sci Technol*. 2020;9(9):29.
- Simons K, Elhatton K. Artifacts in fusion and stereopsis testing based on red/green dichoptic image separation. *J Pediatr Ophthalmol Strabismus*. 1994;31(5):290–297.
- O'Connor AR, Tidbury LP. Stereopsis: are we assessing it in enough depth? *Clin Exp Optom*. 2018;101(4):485–494.
- Campbell FW, Green DG. Monocular versus binocular visual acuity. *Nature*. 1965;208(5006):191–192.
- Meese TS, Georgeson MA, Baker DH. Binocular contrast vision at and above threshold. *J Vis*. 2006;6(11):1224–1243.
- Meese TS, Hess RF. Low spatial frequencies are suppressively masked across spatial scale, orientation, field position, and eye of origin. *J Vis*. 2004;4(10):843–859.
- Baker DH, Meese TS. Interocular transfer of spatial adaptation is weak at low spatial frequencies. *Vision Res*. 2012;63:81–87.



16. Dorr M, Kwon M, Lesmes LA, et al. Binocular summation and suppression of contrast sensitivity in strabismus, fusion and amblyopia. *Front Hum Neurosci*. 2019;13:234.
17. Baker DH, Meese TS, Mansouri B, Hess RF. Binocular summation of contrast remains intact in strabismic amblyopia. *Invest Ophthalmol Vis Sci*. 2007;48(11):5332–5338.
18. Pineles SL, Velez FG, Isenberg SJ, et al. Functional burden of strabismus: decreased binocular summation and binocular inhibition. *JAMA Ophthalmol*. 2013;131(11):1413–1419.
19. Li Y, Ding J, Zhang W. Improvement of binocular summation in intermittent exotropia following successful postoperative alignment. *Sci Rep*. 2021;11(1):15584.
20. Pineles SL, Demer JL, Isenberg SJ, Birch EE, Velez FG. Improvement in binocular summation after strabismus surgery. *JAMA Ophthalmol*. 2015;133(3):326–332.
21. Pineles SL, Velez FG, Yu F, Demer JL, Birch E. Normative reference ranges for binocular summation as a function of age for low contrast letter charts. *Strabismus*. 2014;22(4):167–175.
22. Castro JJ, Soler M, Ortiz C, Jiménez JR, Anera RG. Binocular summation and visual function with induced anisocoria and monovision. *Biomed Opt Express*. 2016;7(10):4250–4262.
23. Maehara G, Hess RF, Georgeson MA. Direction discrimination thresholds in binocular, monocular, and dichoptic viewing: motion opponency and contrast gain control. *J Vis*. 2017;17(1):7.
24. Lesmes LA, Lu ZL, Baek J, Albright TD. Bayesian adaptive estimation of the contrast sensitivity function: the quick CSF method. *J Vis*. 2010;10(3):17.11–21.
25. Chen Z, Zhuang Y, Xu Z, et al. Sensitivity and stability of functional vision tests in detecting subtle changes under multiple simulated conditions. *Transl Vis Sci Technol*. 2021;10(7):7.
26. Stalin A, Dalton K. Relationship of contrast sensitivity measured using quick contrast sensitivity function with other visual functions in a low vision population. *Invest Ophthalmol Vis Sci*. 2020;61(6):21.
27. Wai KM, Vingopoulos F, Garg I, et al. Contrast sensitivity function in patients with macular disease and good visual acuity. *Br J Ophthalmol*. 2022;106(6):839–844.
28. Meng Q, Wang L, Zhao M, Wu X, Guo L. Comparing myopic error in patients with basic and convergence insufficiency intermittent exotropia in China. *BMC Ophthalmol*. 2023;23(1):290.
29. Hou F, Lesmes L, Bex P, Dorr M, Lu ZL. Using 10AFC to further improve the efficiency of the quick CSF method. *J Vis*. 2015;15(9):2.
30. Zheng H, Wang C, Cui R, et al. Measuring the contrast sensitivity function using the qCSF method with 10 digits. *Transl Vis Sci Technol*. 2018;7(6):9.
31. Cuesta JR, Anera RG, Jiménez R, Salas C. Impact of interocular differences in corneal asphericity on binocular summation. *Am J Ophthalmol*. 2003;135(3):279–284.
32. Jiménez JR, Ponce A, Anera RG. Induced aniseikonia diminishes binocular contrast sensitivity and binocular summation. *Optom Vis Sci*. 2004;81(7):559–562.
33. Baker DH, Lygo FA, Meese TS, Georgeson MA. Binocular summation revisited: beyond  $\sqrt{2}$ . *Psychol Bull*. 2018;144(11):1186–1199.
34. Read JC. Stereo vision and strabismus. *Eye (Lond)*. 2015;29(2):214–224.
35. Leguire LE, Rogers GL, Bremer DL. Visual-evoked response binocular summation in normal and strabismic infants. Defining the critical period. *Invest Ophthalmol Vis Sci*. 1991;32(1):126–133.
36. Leguire LE, Rogers GL, Bremer DL. Flash visual evoked response binocular summation in normal subjects and in patients with early-onset esotropia before and after surgery. *Doc Ophthalmol*. 1995;89(3):277–286.
37. Moradi F, Mirzajani A, Akbari MR, Khorrami-Nejad M, Abolghasemi J, Masoomian B. Binocular contrast sensitivity in patients with intermittent exotropia in relation to angle of strabismus and level of compensation. *Strabismus*. 2023;31(1):1–8.
38. Bae YH, Choi DG. Changes in contrast sensitivity after surgery for intermittent exotropia. *Sci Rep*. 2022;12(1):6542.
39. Jeantet C, Laprevote V, Schwan R, et al. Time course of spatial frequency integration in face perception: an ERP study. *Int J Psychophysiol*. 2019;143:105–115.
40. Kattan JM, Velez FG, Demer JL, Pineles SL. Relationship between binocular summation and stereoacuity after strabismus surgery. *Am J Ophthalmol*. 2016;165:29–32.
41. Holmes JM, Hercinovic A, Melia BM, et al. Improvement in health-related quality of life following strabismus surgery for children with intermittent exotropia. *J AAPOS*. 2021;25(2):82.e1–82.e7.
42. Hatt SR, Leske DA, Liebermann L, Holmes JM. Incorporating health-related quality of life into the assessment of outcome following strabismus surgery. *Am J Ophthalmol*. 2016;164:1–5.
43. Hatt SR, Leske DA, Philbrick KL, Holmes JM. Factors associated with failure of adult strabismus-20 questionnaire scores to improve following strabismus surgery. *JAMA Ophthalmol*. 2018;136(1):46–52.