• Clinical Research •

Comparison of visual outcomes between bilateral EDOF IOL implantation and combined EDOF and bifocal IOL implantation

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Abstract

● **AIM:** To compare the visual outcomes between bilateral implantation of Tecnis ZXR00 extended depth-of-focus (EDOF) intraocular lenses (IOLs) and mixed implantation of Tecnis ZXR00 (EDOF) with Tecnis ZMB00 (bifocal) IOLs.

● **METHODS:** This postoperative cross-sectional study enrolled patients who underwent phacoemulsification combined with IOL implantation. Patients were divided into two groups: the bilateral ZXR00 group (ZXR00-only group) and the mixed IOL group (ZXR00+ZMB00 group). Primary outcome measures included uncorrected and corrected distance visual acuity (UDVA, CDVA), uncorrected and distance-corrected near visual acuity (UNVA, DCNVA), uncorrected and distance-corrected intermediate visual acuity (UIVA, DCIVA), and defocus curves. Secondary outcome measures were visual quality, spectacle independence, patient satisfaction, photic phenomena, and stereopsis.

● **RESULTS:** A total of 47 patients (94 eyes) were included, with 26 patients (11 males, 15 females) in the ZXR00-only group (mean age: 62.73±7.24y) and 21 patients (7 males, 14 females) in the mixed group (mean age: 65.71±9.16y). There was no statistically significant difference in age between the two groups (*P*=0.218). The mixed group showed significantly better binocular DCNVA compared to the ZXR00-only group (*P*=0.002). Defocus curve analysis revealed that the mixed group exhibited superior performance at −2.5 to −4.0 D but inferior performance at −0.5 and −1.5 D. Near stereoacuity was significantly poorer in the mixed group (Randot: 5.589±0.744 *vs* 6.240±0.394 ln arcsec; Contour: 4.966±0.973 *vs* 5.740±0.833 ln arcsec; both *P*<0.01). Both groups achieved high levels of spectacle independence and patient satisfaction, with no significant differences in photic phenomena or questionnaire scores.

● **CONCLUSION:** Mixed implantation of EDOF and bifocal IOLs improve near visual acuity but may compromise near stereopsis. This approach provides a viable option for patients prioritizing near vision; however, caution is recommended for individuals requiring fine stereoscopic vision for daily or professional tasks.

● **KEYWORDS:** extended depth-of-focus intraocular lens; bifocal intraocular lens; mixed intraocular lens implantation; near visual acuity; stereopsis; visual quality

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INTRODUCTION

Presbyopia-correcting extended depth-of-focus intraocular lens (EDOF IOL) bridge the gap between monofocal and multifocal intraocular lenses (IOLs) by providing continuous and high-quality visual acuity[1]. EDOF IOLs work by elongating a single focal point, in contrast to the multifocal lenses, which focus incoming waves in several points[2]. In this way, EDOF IOLs could cause less severe visual disturbances[3]. Various technologies are currently used to elongate the continuous range of focus, including negative spherical aberration optics[4], small-aperture design[3], diffractive optics[5], and bioanalogic design[6].

The Tecnis Symfony ZXR00 (Abbott Medical Optics, USA), the only EDOF IOLs approved in China[7], provides excellent distance and intermediate vision with minimal visual disturbances[8-11]. However, most studies have reported poor near vision after ZXR00 IOLs implantation. Farvardin *et al*[12] and Liu *et al*[13] found that the near visual acuity after ZXR00 implantation was much worse than that after multifocal IOLs implantation.

To balance the wide range of vision and visual quality, mix-and-match implantation of multifocal IOLs and EDOF IOLs was put forward. This method combines the advantages of two types of IOLs, which can provide better postoperative vision and high visual quality. Multiple studies have shown that a mixed method can significantly improve near visual acuity after EDOF IOLs implantation[14-16]. However, the effect of mixed-and-match implantation on the postoperative visual quality remains unknown. Therefore, our study evaluates whether mixed implantation of ZXR00 (EDOF) and ZMB00 (bifocal) IOLs improves near vision in cataract patients without compromising visual quality and provide an optional personalized design scheme for EDOF IOLs implantation.

PARTICIPANTS AND METHODS

Ethical Approval This study was performed at the Eye Hospital of Wenzhou Medical University between September 2021 and July 2022. This study was approved by the Institutional Review Board of the Eye Hospital of Wenzhou Medical University and adhered to the tenets of the Declaration of Helsinki (H2022-029-K-29). It was registered at www.clinicaltrials.gov (NCT05594537). Informed consent was obtained from all participants.

Participants Patients with bilateral cataracts who underwent implantation of ZXR00 or ZMB00 IOL were enrolled. The inclusion criteria were 1) the predicted corneal astigmatism <1.0 D postoperatively, 2) macular morphology and function were normal, 3) the preoperative kappa and alpha were ≤0.50, 4) postoperative corrected distance visual acuity (CDVA) ≤0.096 logMAR. Exclusion criteria were systemic or ocular medication that could affect vision, any chronic or acute systemic or eye disorders that could alter the result, previous ocular surgery, capsular or zonular abnormalities with the potential to induce IOL decentration or tilting, and intraoperative or postoperative complications.

Patients were divided into two groups: the ZXR00-only group, which underwent bilateral implantation of ZXR00 IOLs, and the mixed ZMB00 group, which received a combination of ZXR00 (dominant eye) and ZMB00 IOLs (non-dominant eye). The dominant eye was determined using the hole-in-the-card method. The last preoperative patient visit and surgery were retrospectively documented, and the postoperative visit was performed more than 3mo after surgery.

Preoperative Examinations A comprehensive preoperative ophthalmological examination was performed in all cases, including measurement of uncorrected distance visual acuity (UDVA) and CDVA, respectively, manifest refraction, noncontact tonometry, slit-lamp anterior segment examination, optical biometry, keratometry, and fundus examination under pupil dilation. IOL power was calculated using the Barrett Universal II formula, targeting 0 to -0.5 D for ZXR00 and 0±0.25 D for ZMB00.

Surgical Technique All surgeries were performed by a single surgeon (Zhao YE). A 2.0 mm clear corneal incision was made, followed by a 1.0 mm side-port incision. The viscoelastic was injected into the anterior chamber. A 5.0 to 5.5 mm continuous curvilinear capsulorhexis was created. Phacoemulsification was performed using a Centurion machine with a 45-degree aspiration bypass system intrepid balanced tip. After aspiration of the lens cortex, implantation of ZXR00 or ZMB00 IOLs, and removal of the viscoelastic, the procedure was completed with incision hydration.

Postoperative Examination Follow-up examinations were performed >3mo postoperatively. The following parameters were evaluated: UDVA and CDVA, uncorrected near visual acuity (UNVA) and distant corrected near visual acuity (DCNVA) measured at 40 cm, uncorrected intermediate visual acuity (UIVA) and distant corrected intermediate visual acuity (DCIVA) measured at 66 cm. All visual parameters were evaluated monocularly and binocularly. Binocular corrected defocus curve was created at intervals of 0.5 D from +2.00 to −4.00 D.

Stereoscopic vision was assessed using an OCULUS Binoptometer 4P. The Binoptometer automatically adjusted the distance to measure the stereoacuity at distance, intermediate, and near, including the Randot and contour tests.

Finally, subjective outcomes for patient satisfaction and spectacle independence were assessed using subjective questionnaires. The Chinese-translated Visual Function-14 (VF-14)[17] Questionnaire was used to assess postoperative visual performance. The Quality of Vision Questionnaire (QoV)[18] was designed with 10 symptoms rated on each of three scales (frequency, severity, and bothersome), scoring each item (0, 1, 2, and 3), with higher scores indicating worse frequency, severity, and bothersome. In addition, we used the Glare&Halo simulator[19] to simulate the size and intensity of the halo, glare, and starburst that patients see in real life. This simulator replicates three types of photic phenomenon perceived by patients: glare (diffuse glare), halo (distinct halo ring) and starbursts. Likewise, the simulator uses a scale for intensity and size of both halos and glare from 0 (none) to 100 (extremely disturbing).

Table 1 Demographic characteristics of patients

Parameters	Total	ZXR00-only group	Mixed group	*P*
Gender (M/F)	18/29	11/15	7/14	0.529
Age (y)	64.06±8.20	62.73±7.24	65.71±9.16	0.218
AL (mm)	23.44 (1.40)	23.46 (0.78)	23.17 (1.71)	0.828
Implanted IOL (D)	22.2 (3.88)	22.50 (3.00)	22.00 (6.13)	0.320
Corneal keratometry (D)	44.03±1.33	44.01±1.40	44.06±1.26	0.863
UDVA (logMAR)	0.301 (0.301)	0.350 (0.301)	0.301 (0.301)	0.575
CDVA (logMAR)	0.222 (0.301)	0.097 (0.301)	0.222 (0.301)	0.417
Follow up time (mo)	7.23±5.04	7.12±5.22	7.38±4.94	0.860

M/F: Male/female; AL: Axial length; IOL: Intraocular lens; D : Diopters; UDVA: Uncorrected distance visual acuity; CDVA: Corrected distance visual acuity.

Table 2 Visual acuity (logMAR) of the ZXR00-only and mixed groups

Parameters	Binocular			Dominant eye			Non-dominant eye		
	ZXR00-only group	Mixed group	*P*	ZXR00-only group	Mixed group	*P*	ZXR00-only group	Mixed group	*P*
UDVA	0.019±0.042	0.016±0.035	0.805	0.061±0.079	0.050±0.078	0.625	0.057±0.076	0.070±0.103	0.638
UIVA	0.017±0.042	0.042±0.097	0.279	0.050±0.103	0.047±0.103	0.942	0.053±0.063	0.195±0.146	0.000
UNVA	0.116±0.093	0.090±0.113	0.381	0.190±0.144	0.214±0.097	0.525	0.198±0.150	0.108±0.133	0.038
CDVA	0.000±0.000	0.005±0.021	0.329	0.004±0.019	0.014±0.031	0.210	0.023±0.045	0.016±0.032	0.557
DCIVA	0.035±0.062	0.061±0.086	0.225	0.087±0.130	0.081±0.098	0.842	0.099±0.123	0.223±0.176	0.010
DCNVA	0.198±0.114	0.083±0.138	0.002	0.319±0.135	0.262±0.120	0.137	0.304±0.141	0.122±0.144	0.000

logMAR: Logarithm of minimum angle of resolution; UDVA: Uncorrected distance visual acuity; UIVA: Uncorrected intermediate visual acuity; UNVA: Uncorrected near visual acuity; CDVA: Corrected distance visual acuity; DCIVA: Distant corrected intermediate visual acuity; DCNVA: Distant corrected near visual acuity. The ZXR00-only group: Patients who underwent bilateral implantation of ZXR00 intraocular lenses (IOLs); The mixed group: Patients who received ZXR00 IOLs in the dominant eye and ZMB00 IOLs in the non-dominant eye.

Statistical Analysis Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 26 software. The Student's *t*-test was performed to compare the parametric data. The Mann-Whitney *U* test was used to analyze the differences between independent groups for nonparametric analysis. The Chi-square test was used to compare categorical variables, and a *P*-value of <0.05 was considered statistically significant. Stereoacuity values, originally recorded in arcseconds, showed a non-normal distribution and were therefore logarithmically transformed using the natural logarithm (ln arcsec) before analysis. G-Power was used to analyze the required sample size in the study, with the bilateral DCNVA as the primary efficacy analysis. The medium effect size f=0.25, 1-β=0.8, and significance level α=0.05 were prespecified. The sample size was ≥7 cases.

Intraocular Lens The ZXR00 is a single-piece hydrophobic acrylic EDOF IOL with a wavefront-designed anterior aspheric surface which provided a negative spherical aberration of 0.27 μm, while the posterior surface composed of nine concentric diffraction rings combines two diffractive designs[1]. One is the echelette diffraction technique which aims to extend the range of vision. The second is the achromatic diffraction technique, which aims to improve the visual quality[5,20-21].

Tecnis ZMB00 is a single-piece, hydrophobic acrylic multifocal IOLs with an aspheric anterior surface and a posterior surface composed of 22 concentric diffraction rings with a near addition of +4.00 D[13]. The IOL combines diffractive and aspheric optics with a 1:1 distribution between the two foci[22].

RESULTS

Study Patients This study comprised 94 eyes of 47 patients, 26 patients in the ZXR00-only group and 21 patients in the mixed group. The mean age was 62.73±7.24y in the ZXR00-only group and 65.71±9.16y in the mixed group (*P*=0.218). The demographic characteristics were summarized in Table 1.

Visual Outcomes The median postoperative manifest spherical equivalent was -0.50 (0.47, range from -1.13 to +0.50) D in the ZXR00-only group and -0.25 (0.63, range from -1.63 to +1.13) D in the mixed group (*P*=0.037). The mean postoperative visual acuity values are shown in Table 2. The binocular DCNVA was better in the mixed group. UNVA and DCNVA of the non-dominant eye were better in the mixed group, whereas the UIVA and DCIVA of the non-dominant eye were better in the ZXR00-only group.

Defocus Curve Outcomes The two groups exhibited different defocus curves (Figure 1). The ZXR00-only group achieved continuous visual acuity above 0.2 logMAR in the range of +1.0 to -2.0 D, while the mixed group showed obvious bimodal shape, peaking at 0.0 and -3.0 D. The best-corrected binocular visual acuity of the mixed group was significantly

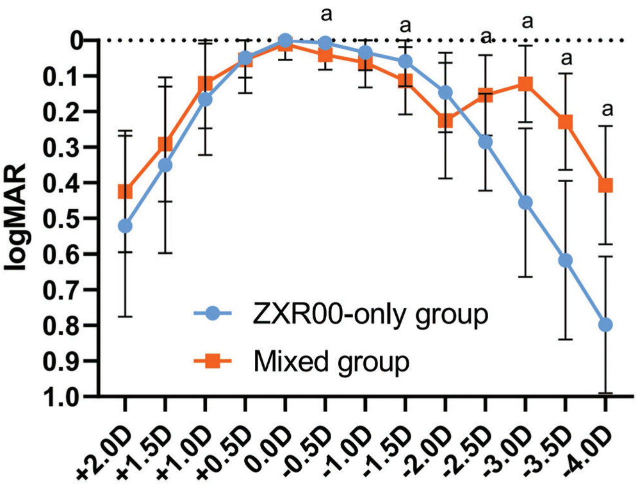

Figure 1 Binocular corrected defocus curve of the ZXR00-only group and the mixed group [a]Significantly different between the two groups (P<0.05).

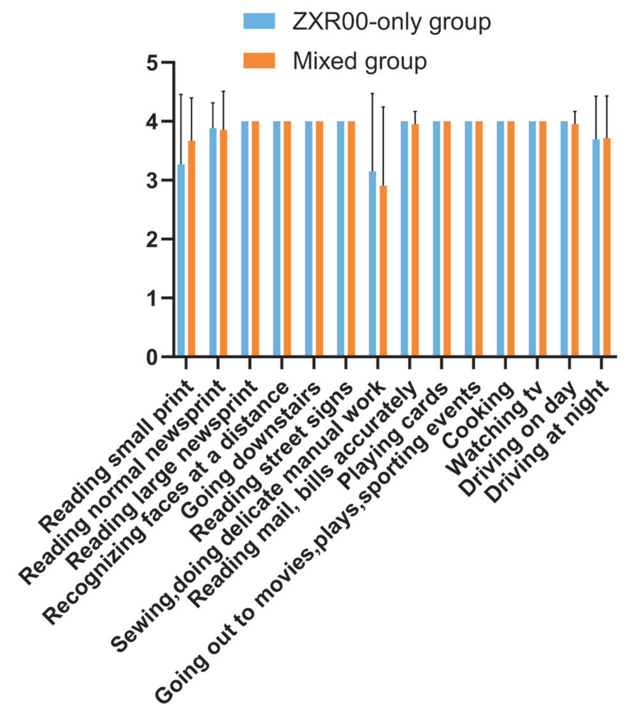

Figure 2 VF-14 outcomes of the ZXR00-only group and the mixed group.

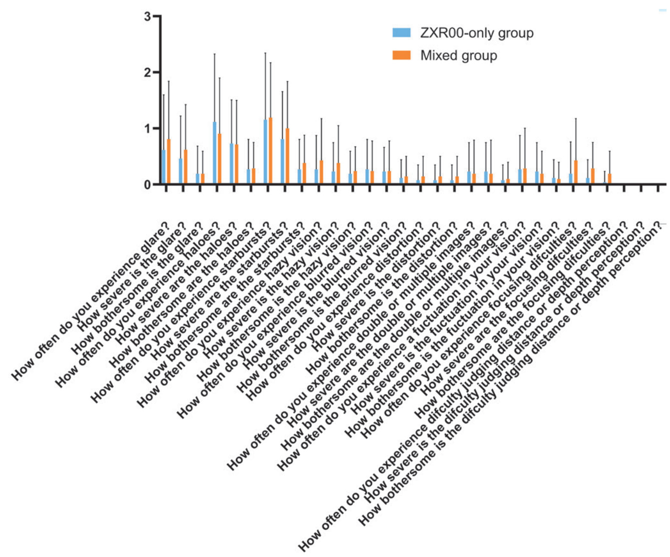

Figure 3 QoV outcomes of the ZXR00-only group and the mixed group.

better than that of the ZXR00-only group from a defocus of -2.5 to -4.0 D (P=0.001, <0.001, <0.001, <0.001), while at -0.5 D and -1.5 D it was significantly better in the ZXR00-only group (P=0.002, P=0.027).

Photic Phenomenon Outcomes The incidence of photic phenomena is shown as follow. Glare, halo, and starburst were reported by 34.62%, 53.85%, and 46.15% in the ZXR00-only group and by 42.86%, 47.62%, and 66.67%, respectively, in the mixed group (P=0.563, 0.671, and 0.160, respectively). The incidence of glare and starburst was higher in the mixed group, while that of halo was higher in the ZXR00-only group but not statistically significant. In addition, we analyzed the size and intensity of glare and halo using Halo&Glare Simulators (Table 3). Although there were no significant differences between the two groups, the size and intensity of glare were larger in the mixed group, and that of halo were larger in the ZXR00-only group, inversely.

Patient-Reported Outcomes The reported rates of postoperative spectacle independence at far and intermediate distances were 100% in both groups. At the near distance, the rate was 65.38% in the ZXR00-only group and 85.71% in the mixed group (P=0.112), showing no difference between the two groups. The mean patient satisfaction score (from 0 to 10) in the ZXR00-only group was 8.73±1.00, and that in the mixed group was 8.43±1.16 (P=0.344); the difference was not statistically significant. The results of the VF-14 questionnaire are shown in Figure 2. The total score in the ZXR00-only group was 54.00±2.91, while in the mixed group was 54.05±2.78. Both groups had high visual performance scores for the questioned activity, with no significant differences (all P>0.05). The results of the QoV questionnaire are shown in Figure 3 (all P>0.05). The total score in the ZXR00-only group was 8.65±6.96, while in the mixed group was 10.14±8.33. Both groups had a low frequency, severity, and level of bother of visual symptoms, with no significant differences (all P>0.05).

Table 3 Size and intensity of glare and halo

Parameters	ZXR00-only group	Mixed group	P
Glare size	15.54±24.36	20.71±25.69	0.483
Glare intensity	20.04±30.42	23.10±31.71	0.738
Halo size	27.69±31.96	26.76±31.23	0.921
Halo intensity	26.62±29.52	28.76±32.51	0.814

Stereopsis The stereopsis results for the two groups are presented in Table 4. For the ZXR00-only group, the mean stereopsis at near distance in Randot was 5.589±0.744 ln arcsecs, and for the mixed group, it was 6.240±0.394

Table 4 Stereopsis outcomes

Parameters	ZXR00-only group	Mixed group	*P*
Randot			
Distance (ln arcsecs)	5.935±0.744	5.858±0.782	0.732
Intermediate (ln arcsecs)	5.263±1.029	5.813±0.848	0.068
Near (ln arcsecs)	5.589±0.744	6.240±0.394	0.000
Contour			
Distance (ln arcsecs)	5.090±1.171	5.495±1.143	0.240
Intermediate (ln arcsecs)	5.216±0.886	5.507±1.166	0.336
Near (ln arcsecs)	4.966±0.973	5.740±0.833	0.006

(P<0.001). The near stereoacuity was 4.966±0.973 in the ZXR00-only group, and in the mixed group was 5.740±0.833 (P=0.006). No significant differences were observed between the two groups in terms of far or intermediate stereopsis.

DISCUSSION

The recent advancement of presbyopia-correcting IOLs has facilitated the emergence of EDOF IOLs, which generate an elongated focal point, thereby improving the depth of focus. EDOF IOLs provide excellent distance and intermediate visual acuity with high-level visual qualities. However, near vision after EDOF IOLs implantation is still unsatisfactory[23]. Multifocal IOLs can provide good near vision, but due to their spectral phenomenon, they lead to a decline in postoperative contrast sensitivity and an increase in light interference[24]. Mixed implantation leverages the strengths of EDOF (intermediate/distance) and multifocal (near) IOLs, addressing the near-vision limitations of EDOF-only approaches. In our study, we compared the visual function and quality after bilateral implantation of EDOF IOLs and mixed implantation of EDOF IOLs with bifocal IOLs. We found that mixed implantation of ZXR00 and ZMB00 significantly improved postoperative near vision. However, the disparity in focal points between ZXR00 and ZMB00 may disrupt binocular summation, explaining the reduced near stereopsis.

Tarib *et al*[25] compared the vision outcomes between bilateral implantation of the EDOF IOL (AT LARA 829, Carl Zeiss Meditec, Jena, Germany) and mixed implantation of the EDOF IOL and trifocal IOL (AT LISA tri 839MP, Carl Zeiss Meditec, Jena, Germany). They found that binocular DCNVA in the mixed implantation group was significantly better than that in the EDOF-only group (P=0.03), which is similar to the results of our study. Near vision significantly improved in the mixed implantation group. Our study found that although the UIVA and DCIVA of non-dominant eye (implanted ZMB00) in the mixed group was inferior to that in the ZXR00-only group (implanted ZXR00), there was no significant difference in binocular intermediate distance vision outcomes between the two groups, indicating that compared with binocular implantation of ZXR00, the mixed implantation of ZXR00 and ZMB00 could significantly improve the postoperative near vision without compromising the intermediate distance vision. This result was also consistent with the diffraction design principle of these two types of IOLs.

The defocus curve is an effective way to understand how IOLs can improve postoperative visual acuity, and it is widely used in evaluating postoperative clinical effects of multifocal IOLs and EDOF IOLs[26]. Our study found the binocular corrected defocus curve showed a continuous excellent visual acuity of 0.2 logMAR or better in the range of +1.0 to -2.0 D in the ZXR00-only group, while the mixed group showed obvious bimodal shape, peaked at 0 and -3.0 D, similar to a previous study[13]. Wang *et al*[27] compared the corrected monocular defocus curve between the ZMB00 and ZXR00 groups, they observed two peaks in the ZMB00 group (at 0 and -3.0 D, respectively), with a trough forming between -1.0 and -2.0 D. Compared to the ZXR00 group, the defocus curve of the ZMB00 group exhibited a lag from 0 to -2.0 D. In our study, the binocular corrected defocus curve of the mixed implantation group showed the typical shape similar to the multifocal IOLs, with the lowest point occurring exclusively at -2.0 D. At the -2.0 D point, no significant difference was observed between the two groups. This finding suggests that the intermediate-distance vision deficiency associated with multifocal IOL implantation may be mitigated through the mixed implantation. In contrast to the ZXR00-only group, the mixed group advanced in defocus curve from -2.5 to -4.0 D, but lagged at -0.5 and -1.5 D. The mixed group was further proven to significantly improve patients' near vision.

The main cause of dissatisfaction after multifocal IOL implantation is photic phenomena, such as halo, glare, and starbursts. Two Meta-analyses[23,28] showed that compared with the ZXR00 implantation group, the incidence of the photic phenomena was significantly higher in the trifocal IOL implantation group. In addition, a multifocal IOL with a higher near addition is more likely to produce photic phenomena. The EDOF IOL reduces the incidence of photic phenomena and the size of the generated halo by reducing the near addition, diffraction achromatic, and diffraction ring[29]. Savini *et al*[19] found that the halo size after implantation of the EDOF IOL was significantly smaller than that after implantation of the multifocal IOL, whereas the glare size was not significantly different. Our study found that the ZXR00-only group appeared to be more prone to producing halo with larger size and higher density, although the difference was not significant. This differs from previous studies and may be related to the implantation of the ZXR00 eye target for minimal residual myopia and the ZMB00 eye target for emmetropia. According to Zhao *et al*[30] and Rementería-Capelo *et al*[31], postoperative myopia resulted in an increased incidence of the halo phenomenon and the greater the power of myopia, the larger the size of the halo. The mixed group was more prone to glare and starburst;

however, in our study, there was no statistical difference in the incidence, size, or intensity photic phenomena between the two groups. Therefore, the mixed group did not show a significant increase in photic phenomena.

Our results showed that patients in both groups reported high postoperative satisfaction, with no significant differences. At far and intermediate distances, the rate of spectacle independence was 100% in both groups. At near distance, the rate of spectacle independence at near distances was higher in the mixed group, although there were no significant differences between the two groups. The VF-14 questionnaire score showed that both groups had difficulties reading small prints, doing fine work, and driving at night. The QoV questionnaire results showed no significant differences between the two groups regarding frequency, severity, and level of visual symptoms. These results show that both groups had high visual quality.

In addition to evaluating the visual quality after IOLs implantation, stereopsis is an important evaluation index. It is one of the most important characteristics of the visual system, which affects the quality of life and has an important impact on work[32]. In the mixed group, different IOLs types were implanted in each eye, which may affect postoperative stereopsis. Ke *et al*[16] found that the mixed implantation group performed best in both far and near stereopsis. Since stereopsis is affected by visual acuity, this result may be related to the fact that the mixed group had the best far and intermediate distance visual acuities in the study. Zhu *et al*[33] found that the average near stereopsis of the trifocal only group was significantly better than that of the mixed group. The difference between the two groups was statistically significant. This suggests that mixing different types of IOLs may affect postoperative stereopsis. In our study, the near stereopsis in the mixed group was significantly worse, indicating that the implantation of different types of IOLs may have destroyed postoperative stereopsis. This may be related to the different near points of the two IOLs. Our defocus curve shows that the near point of ZXR00 was 50 cm, whereas it was 30 to 40 cm of ZMB00. The specific reasons for this need to be further analyzed and explored.

Furthermore, we found that although the mixed group had significantly better near vision, the score for doing fine work was lower. This may be because doing fine work is not only related to near visual acuity but also to near stereopsis. Stereopsis provides detailed and precise information on its objectives. The defects of stereopsis will affect accurate motion, grip, and sense of distance, which leads to difficulties in performing fine work[34]. Our study showed that although the mixed group had better near visual acuity compared with the ZXR00-only group, near stereopsis was worse. Decreased near stereopsis may have contributed to the low score of fine work in the mixed group. Therefore, patients who engage in fine work should be cautious when choosing a mixed implantation of ZXR00 and ZMB00.

Our study had some limitations. First, stereopsis test is a psychophysical examination that reflects the subjective and real feelings of patients. However, it can also be influenced by many factors, such as visual fatigue, learning and memory effect, and it is difficult to control the specificity of patients. Second, neurological adaptation existed after EDOF IOLs or multifocal IOLs implantation, and different follow-up times of the patients in the study might introduce bias. However, the follow-up time of the two groups was generally close, which effectively made up for the deficiency. Third, no pure ZMB00 control group in this study. Previous research[12-13] has shown that bilateral implantation of multifocal IOLs (ZMB00) enhances near vision but increases visual disturbances. Conversely, bilateral implantation of EDOF IOLs (ZXR00) reduces visual disturbances but compromises near vision. Our initial study design aimed to optimize the near vision performance of the ZXR00-only group by comparing it with the ZXR00+ZMB00 mixed group.

In conclusion, mixed implantation of ZXR00 and ZMB00 IOLs enhances near vision while preserving visual quality but may impair near stereopsis. Thus, when considering the implantation of ZXR00, Surgeons should weigh these trade-offs, particularly for patients reliant on precise depth perception.

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Data Availability: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest: Fang JY, None; **Jin J,** None; **Jiang YL,** None; **Yang FM,** None; **Chang PJ,** None; **Zhao YY,** None; **Zhao YE,** None.

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